BIOLOGICAL DEFINITIONS, CAUSALITY, AND REDUCTIONISM IN PSYCHIATRY

by

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ABSTRACT

The main focus of this thesis is the project of *biological psychiatry* to classify psychiatric conditions, such as schizophrenia and depression, on the basis of biological features—as opposed to psychological and behavioural features, which constitute the basis for their current classification. Written as a collection of independent papers, this thesis mainly deals with three issues related to said project.

The first issue is the following: classifying medical conditions on the basis of biology requires individual conditions to be *defined* in terms of a biological factor—asthma is, for instance, defined in terms of inflammation of the airways. The standard view is that individual psychiatric conditions are to be defined in terms of their (hypothesised) "single, clear" biological causes. However, critics of biological psychiatry rely on current evidence to point out these conditions are caused, instead, by a *variety* of biological, psychological, and social factors. This causal heterogeneity is thought by critics to preclude the development of psychiatric definitions based on biology. I argue (roughly speaking) that biological definitions could be achieved for those conditions notwithstanding causal heterogeneity.

The second issue is the following: biological psychiatry's search for biological definitions has been deemed to be biologically *reductionist*. Biological reductionism, however, is nowadays standardly refused. Hence, if the search for psychiatric biological definitions is committed to reductionism, it could be construed as a search for a *prima facie* defective understanding of psychiatric illness, namely, a biologically reductionist understanding which is nowadays standardly rejected. Also, if the search in question is committed to reductionism, then this search is subject to criticisms that have been advanced against reductionism. Nevertheless, I will argue that the quest for psychiatric biological

definitions does *not* involve a commitment to reductionism, and thus it does not prompt a biologically reductionist understanding in psychiatry. Consequently, complaints against reductionism do not apply to said quest.

Finally, the third issue is the following: critics remark that the above quest allows the possibility that psychiatric conditions are given *purely biological* definitions. These are definitions according to which a patient has the relevant condition if and only they have certain biological features—regardless of whether they have symptoms or not. Hence, purely biological definitions allow the existence of *a*symptomatic cases of the condition in question, and of symptomatic patients who do *not* to have the condition. Critics believe that if psychiatric conditions were given purely biological definitions, those definitions would *not* pick out the very same conditions that are currently defined in terms of symptoms. I argue, to the contrary, that those definitions would, in fact, pick out the conditions that are currently defined in terms of symptoms.

Two complementary issues will also be addressed. One of them concerns how to best understand current medical classification; the other concerns what exactly distinguishes biological from non-biological approaches to psychiatric illness. If my arguments are correct, the quest of biological psychiatry for biological definitions overcomes the three difficulties mentioned above.

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INTRODUCTION

Psychiatric conditions, such as schizophrenia or depression, are nowadays characterised as *syndromes*, that is, as mere clusters of psychological and behavioural symptoms without specified biological causes. Nevertheless, many psychiatrists seek to characterise psychiatric conditions, instead, based on the biological causes of those symptoms. The quest for this change is the major focus of this thesis. The thesis is a collection of papers, and it addresses three issues related to the quest in question—as well as two other, complementary issues. In what follows, I will elaborate on this quest; I will describe the three aforementioned issues; and I will provide summaries of all chapters.

1. The Quest

Psychiatric conditions such as schizophrenia or depression are currently classified as *syndromes*, that is, as mere clusters of psychological and behavioural symptoms without specified biological causes. As Will Davies & Rebecca Roache note, however,

> [a]s a branch of medicine, psychiatry is under pressure to conform to a biomedical model, on which genuine mental disorders are classified as *diseases*, to be characterised primarily in *biological terms* (2017, p. 3; my emphasis).

Thus, psychiatry is expected to adhere to a *biomedical* classification of psychiatric conditions. On a biomedical classification, a psychiatric condition is conceived of as a disease—i.e., "a constellation of signs and symptoms for which *there is* a known physical

cause" (Peterson & Keeley, 2015, p. 1; my emphasis)—and defined in terms of biological features. Relatedly, James Phillips claims that "[t]he 'official' way of classifying in psychiatry is biomedical, [and] [p]sychiatric disorders and diagnoses are expected to follow the [biomedical] model of the rest of medicine" (2015, p. 179). Thus, according to Phillips, too, psychiatry is under pressure to endorse a biomedical classification of psychiatric conditions.

The project of construing a biological classification of psychiatric conditions is generally understood as the project of classifying these conditions on the basis of their biological causes. Psychiatry's shift towards this biomedical classification, however, has been hindered by the longstanding and persistent lack of reliable evidence of specific biological causes for psychiatric conditions. This is a widely acknowledged problem in current psychiatry, and it is usually referred to as the "lack of biological validation" of diagnostic categories of mental illness. Thomas Insel (2014), Jeffrey Poland (2015), The British Psychological Society (2018, ch. 5), and many others have elaborated on this issue. In summary, it is generally accepted that

> [t]he entire history of the field […] is driven by a frustratingly persistent fact: no one has ever found a dependable biological marker for a mental disorder. Nor has it discovered the etiology [i.e., causes] of mental disorders (Whooley & Horwitz, 2013, p. 80-81).

In the absence of known, specific biological causes for psychiatric conditions, psychiatrists have not been able to classify them on the basis of biological features, nor, therefore, as diseases—i.e., as clusters of symptoms *with specified biological causes*. Despite this lack of evidence, however, the search for a biomedical classification remains alive. Now, those who

advocate for a shift towards a biomedical classification are *biological psychiatrists*. Michael R. Trimble and Mark S. George (2010), for instance, claim that "it is now the time […] to move [psychiatric] classification away from […] the phenomenological to the anatomical" (p. 332). According to these authors, then, it is time to move from a classification based on the psychological states experienced by patients (p. 85)—i.e., their symptoms—, to one based on biological features.

Another defender of the shift towards a biomedical classification is Steven E. Hyman (2010). Hyman claims that current classification in psychiatry is based "of necessity, on phenomenology" (p. 161), given that there are no known, specific biological causes of psychiatric conditions. He claims, additionally, that a "major change" he supports "is [the] reclustering of current [psychiatric] disorders according to the best current hypotheses about underlying neural circuitry or compelling genetic data" (p. 172). That is, Hyman proposes that psychiatric classification, currently based "of necessity" on phenomenology, should be revised, so that the best hypotheses concerning biological features are incorporated into it.

A more recent example of the quest for a shift in psychiatric classification is the *Biological Classification of Mental Disorders* (BeCOME) (Brükl *et al*, 2020), an ambitious research project which is intended, in the long term, to "contribute to a novel taxonomy of mental disorders that integrates the underlying pathomechanisms into diagnoses" (p. 2), and is aimed at "identify[ing] biology-based classes of mental disorders" (p. 1).

All these are just some examples of the generalised aspirations of biological psychiatrists to shift towards (what they call) a biomedical classification in psychiatry. For the most part, this thesis concerns the quest for said shift. I will address three main issues in connection with it, and two other, complementary issues.

2. Issues addressed

The first issue which I will address is the following: classifying medical conditions on the basis of biological features customarily requires individual conditions to be *defined* on the basis of a biological factor: asthma, for instance, is defined in terms of inflammation of the airways. The standard view amongst biological psychiatrists with regard to psychiatric conditions is that these conditions are to be defined specifically in terms of their (hypothesised) "single, clear" biological causes. However, critics of biological psychiatry rely on current evidence to point out that these conditions are caused, instead, by a *variety* of biological, psychological, and social factors. This causal heterogeneity is thought by critics to preclude, *tout court*, the development of psychiatric definitions based on biological causes—i.e., "biological definitions" in my terminology. I argue, roughly speaking, that biological definitions could be achieved for those conditions notwithstanding causal heterogeneity.

The second issue is the following: the search of biological psychiatry to implement a biomedical classification can be understood as an attempt to develop biological definitions of psychiatric conditions. Nevertheless, said search has been deemed to be biologically *reductionist* (see summary of Chapter IV below for a definition of reductionism). Biological reductionism, however, is nowadays standardly rejected. Hence, if the search for psychiatric biological definitions is committed to reductionism, it can be construed as a search for a *prima facie* objectionable, and nowadays standardly rejected, understanding of psychiatric illness. Additionally, if the search in question is committed to reductionism, then this search is subject to the criticisms that have been advanced against reductionism. Nevertheless, I will

argue that the quest for psychiatric biological definitions does *not* involve a commitment to reductionism.

Finally, the third issue is the following: critics believe that the quest for a psychiatric classification based on biology allows the possibility that psychiatric conditions are given *purely biological* definitions. These are definitions according to which a patient has the relevant condition if and only if they have certain biological features which are considered to cause the symptoms associated with that condition—and regardless of whether the patient has those symptoms or not. Purely biological definitions allow the existence of *a*symptomatic cases of the condition in question, and symptomatic patients who do *not* have the condition. Critics believe that, if psychiatric conditions were given purely biological definitions, those definitions would *not* pick out the very same conditions that are currently defined in terms of symptoms. I argue, to the contrary, that those definitions would, in fact, pick out the conditions that are currently defined in terms of symptoms.

I also address two complementary issues in this thesis. First: as I mentioned earlier, the standard view amongst biological psychiatrists is that psychiatric conditions are to be defined in terms of single, clear biological causes. This view sticks to the *aetiological model* of disease classification, which has dominated medicine. Roughly, this model defines diseases in terms of their (hypothesised) single, biological causes. Nevertheless, the model in question has been proven to be highly defective, and it has been observed that many diseases are currently classified under the alternative *constitutive model*. As I reconstruct it, the constitutive model states that medical conditions are defined in terms of features which are necessary and sufficient for them, but are neither their causes nor their effects. In my thesis, I argue that medical classification in general is best understood to be constitutive, thus

attributing to the constitutive model a wider generality than has been previously attributed to it.

Then I argue also that the quest of biological psychiatry for a psychiatric biological classification is best understood as a quest for a biological, constitutive classification—rather than an aetiological one. Along the way, I consider—and reject—a third understanding of diseases, viz., the realisation view, according to which diseases are *realised* in certain biological processes.

The second complementary issue is the following: The quest for psychiatric biological definitions has been considered characteristic of *biological psychiatry*. Biological psychiatry is standardly understood as a stance which conflicts with non-biological stances. However, it is not immediately obvious what the exact conflict between biological and non-biological stances is, for, currently, both of them admit that psychiatric illness results from a variety of heterogeneous causes. I dedicate some space to elucidate that conflict. In doing so, I note that both stances commit to a classificatory, a causal, and a definitional commitment, and that the commitments of each one of them are incompatible with the commitments of the other. Thus, I conclude that the exact point of conflict between them lies in the incompatible commitments they endorse.

It is important to note that the main issues described above are not more central to the thesis than the complementary ones. I called these issues "main issues" simply because they occupy most of the total length of my thesis. The complementary issues, on the other hand, I called "complementary" because they occupy a smaller portion of my thesis, and because these are not linked between them, nor directly to the main issues.

3. Summaries of chapters

I address the issues described above throughout six chapters. All of these chapters were originally written as independent papers. The two issues qualified as complementary above are key to understanding the preliminaries of the main issues of the thesis; and, accordingly, the complementary issues are the first to be addressed.

Thus, *Chapter I* concerns the issue of medical classification. As I explained earlier, most of the thesis is devoted to the quest for the aim that psychiatry adheres to the model of classification which is currently employed in the rest of medicine. In light of this, it is imperative to figure out exactly which model this is. In Chapter I, I consider three candidate analyses of this model—viz. the *aetiological* analysis, the *realisation* analysis and the *constitutive* analysis, and conclude that the latter is the correct one.

Chapter II concerns the conflict between the biological and the non-biological stances in psychiatry. More specifically, this chapter is focused on elucidating what exactly the point of conflict between them is. As I mentioned earlier, in order to elucidate this point of conflict, I will attribute, to each of the two parts of this conflict, a classificatory, a causal, and a definitional commitment. Then I will show that the two classificatory commitments are incompatible with one another, as well as the causal and definitional ones. Then, the exact point of conflict between these approaches thus lies in the incompatible commitments they endorse.

The first of the main issues described above is addressed in *Chapter III*. As I explained earlier, biological psychiatry seeks to develop a biological classification for psychiatric conditions. In this chapter, I will deal with a particular objection against said search—an objection, in particular, that states that current scientific evidence suggests that the project of

developing a biological classification of psychiatric conditions is unrealistic. My aim in this chapter is to counter said objection.

The second of the main issues described above is addressed in *Chapter IV*. A common presumption among the critics of biological psychiatry is that, in searching for biological definitions, biological psychiatrists commit to *explanatory reductionism*—i.e., the view that explanations of the psychological manifestations of psychiatric conditions can be *adequately* stated exclusively in terms of biological factors, such as brain or genetic abnormalities. Since reductionism is standardly rejected, the presumption in question is detrimental for biological psychiatry. I argue, however, that biological psychiatry is not committed to reductionism.

Chapters V and IV both concern the third of the main issues listed above. Both, then, concern the following line of thought: psychiatric conditions are currently defined in terms of symptoms and, according to critics, any purely biological definition of any one of these conditions would, in fact, pick out not that very condition but a different one. In Chapter V, I counter Roache's (2019) version of this argument; in Chapter VI, I counter Hanna Pickard's (2009), Walter Sinnott-Armstrong's & Jesse S. Summers' (2020), and Roache's (2020) versions.

4. One remark

If sound, my arguments in this thesis contribute to correcting the common perceptions, still widely spread among critics, that the search of biological psychiatry for biological definitions is "unrealistic"; that it constitutes a reductionist—and, hence, objectionable—project; and that it entails unacceptable conceptual consequences—e.g. us not being able anymore to pick

out the very conditions that we nowadays pick out with our current, symptom-based definitions.

My arguments may be characterised as mainly negative insofar as they attack a number of objections against biological psychiatry. Nevertheless, these arguments may be construed positively as well: these arguments, I contend, develop a novel understanding of the quest of biological psychiatry for biological definitions. If my arguments are sound, then, in conjunction, they constitute a novel understanding of this quest as a project that is *feasible and worthwhile* even in the light of the existing evidence that psychiatric conditions are caused by heterogeneous factors. Notwithstanding causal heterogeneity, I submit, psychiatric conditions *could* be defined biologically, and those definitions, under certain circumstances, *could* pick out the very conditions that are currently picked out and studied by psychiatrists.

Since this understanding of the quest for biological definitions is novel, I believe, my overall contention may be rightly thought of as a positive. Since the quest for biological definitions is currently subject to a number of substantial objections, promoting the thesis that this quest constitutes a feasible and worthwhile project persuasively requires us to address the objections in question. That is the reason why considerable amounts of space are occupied in my thesis by rebuttals of those objections. Nevertheless, the resulting defence of the quest for psychiatric biological definitions involves a novel understanding of it and, consequently, I believe that the arguments that I advance in what follows are not to be considered plainly negative.

5. Final remarks

I include two papers as appendixes at the end of this thesis. One of them is a paper I co-authored with Lisa Bortolotti (Ambríz González & Bortolotti, 2023), and is published in *Interdisciplinary Science Reviews*. The other is a paper I published in Spanish (Ambríz González, 2023) in *Aporia: International Journal for Philosophical Investigations*.

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CHAPTER I

The Constitutive Approach to Medical Classification

I explained in the Introduction to this thesis that psychiatric conditions such as schizophrenia or depression are classified by current medicine as *syndromes*, that is, as mere clusters of symptoms with unspecified biological causes, and that such a classification is widely recognised to result from a lack of sufficient knowledge concerning the specific biological causes of specific psychiatric conditions[1]. Further, I also pointed out that biological psychiatrists aim at developing a biomedical classification, which would classify psychiatric conditions as *diseases*, that is, as medical conditions involving symptoms with a known biological cause, and that such a classification would presumably result from acquiring sufficient knowledge concerning specific biological causes of specific psychiatric conditions. Then, a change from a "symptomatic" classification—as I call it—to a biomedical classification is sought in psychiatry. As I elaborated in the Introduction as well, the biomedical classification has been thought to be applied in "the rest of medicine", in which, according to this line of thought, the biomedical classification is the norm.

However, as I will point out later, it is far from obvious what exact pattern medicine employs to classify *diseases*, the sort of medical conditions claimed to fall under a biomedical classification. Since most of this thesis concerns the quest for a change in psychiatric classification, and since such a change would allegedly align psychiatry with the rest of medicine, it is imperative to provide an analysis that accounts for the best way of understanding disease classification, in order to make explicit the exact sort of classification sought to be implemented in psychiatry. Then, in this chapter, I will survey three analyses on

[1] An issue on which I will extensively elaborate in Chapter II as well.

the matter, i.e., the aetiological analysis, the realisation analysis, and the constitutive analysis, and will conclude that only the latter is satisfactory. The upshot will be that—as I approach the constitutive analysis—diseases are best understood to be defined, for classificatory purposes, in terms of certain features which are necessary and sufficient for them, but which are neither their causes nor their effects.

An important issue is that, as I will elaborate in due course, according to the constitutive analysis as I propose it, medical conditions which are not diseases such as syndromes and other medical ailments—e.g., acne and comma—are best understood to be classified constitutively as well. If this is correct, then, medicine can be viewed as applying a general model of classification—i.e., the constitutive—to diseases, syndromes, and other medical ailments, which are classified based on features necessary and sufficient for them, but which are neither their causes nor their effects.

As I mentioned, the idea of a change in psychiatric classification, from a symptomatic one to a biomedical one, is a main focus of this thesis. Such an idea, however, seems to imply that there are, at least, two different ways of classifying in current medicine—the symptomatic and the biomedical. So, one might wonder how to understand said idea in light of the constitutive analysis, according to which medicine employs just one general model of classification. As I will argue, the aim of classifying psychiatric conditions biomedically can simply be understood in light of the constitutive analysis *not* as an aim to change their classification, but to change the way that at least some of them are characterised—from syndromes to diseases. As I will explain in detail, if such a change came to happen, then, at least some psychiatric conditions would come to be defined constitutively in terms of a biological factor *or* in terms of a biological factor and symptoms—as opposed to the present,

constitutive classification, which is made solely in terms of psychological and behavioural symptoms.

The plan for this chapter is as follows. In §1, I will show that it is unclear which exact pattern current medicine employs to classify diseases. Then, in §2, I will address the *aetiological analysis*, according to which single biological causes of diseases are employed to classify them. I will later elaborate, in §2.1, on three problems posed by the aetiological model demonstrating that it fails to be an adequate model of disease classification.

In §3, I will address the *realisation analysis*—as I call it—, which is a reconstruction of Dominic Murphy's ideas concerning disease classification and explanation developed in several works (2006, 2009, 2011, 2013). This analysis states that, for classificatory purposes, current medicine conceives of specific diseases as involving an aetiology—that is, a compound of distinct causes that can come from different levels of explanation—which leads to a single biological (or cognitive) pathology—that is, a certain destructive process—which, in turn, leads to characteristic symptoms. This understanding of disease classification is accompanied in the realisation analysis by the claim that diseases are *realised* in biological (or cognitive) destructive processes (Murphy, 2009, 2011). But, as I will elaborate, although current medicine does conceive of diseases as having aetiology, pathology, and symptoms, I will explore in §3.1 and §3.2 two ways in which "being realised" can be understood, and will conclude that an explanation of diseases as being realised in destructive processes in either of those ways is *not* general.

Later, I will draw on Jonathan Fuller's (2017) account of disease classification to present, in §4, the *constitutive analysis*. I will introduce some changes to Fuller's version, and, based on them, I will argue that current disease classification is best understood

constitutively, that is, as defining specific diseases for classificatory purposes in terms of certain features which are neither their causes nor their effects, which are necessary and sufficient for the disease. Further, I will point out in §5 that the constitutive analysis can not only be understood to be applied to *diseases*, but also to other medical conditions, being a general classification model. In §5.1, I will elaborate on how to understand the quest for a change in psychiatric classification in light of the constitutive analysis.

I will finally present some brief, concluding remarks in §6, noting that the three analyses of disease classification addressed are fundamentally based on the description of disease classification, but they involve other elements as well—e.g., the constitutive analysis *proposes* that medical conditions are best understood to be classified constitutively, including those conditions which, superficially, do not appear to be so classified.

1. Disease classification

I noted in the introductions to this thesis and to the present chapter that current psychiatry classifies psychiatric conditions as *syndromes*, that is, as mere clusters of (psychological and behavioural) symptoms with unspecified biological causes, and that biological psychiatrists seek to follow what they call a biomedical model, which would classify psychiatric conditions as *diseases*. To clarify, a disease is usually understood to be "a constellation of signs and symptoms for which *there is* a known physical cause" (Peterson & Keeley, 2015, p. 1; my emphasis). So, for instance, diabetes, involving symptoms like intense thirst and tiredness which are known to be caused by abnormally elevated blood sugar levels—a "physical cause"—is understood as a disease.

An important issue is that it is far from obvious how exactly current medicine classifies diseases, which are the sort of medical conditions alleged to fall under a biomedical classification. As I am about to elaborate, current disease classification appears at first glance to be made on the basis of heterogeneous aspects of diseases. For instance, infectious diseases are normally understood by reference to a specific pathogen—e.g., a virus or a bacterium—that *causes* them. Thus, e.g., tuberculosis is claimed to be "a human disease caused by Mycobacterium tuberculosis" (Adigun & Singh, 2023; my emphasis). As it appears, then, infectious diseases seem to be classified based on single factors that cause them, and an infectious disease appears to be distinct from another if it has a distinct cause. But non-infectious diseases such as diabetes seem to be understood in terms of what "characterises" them. As the World Health Organization states, "[d]iabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose" (World Health Organization [WHO], 2024). So, these diseases appear to be classified based on features that characterise them—whatever this might mean—, and not based on their causes. A non-infectious disease thus seems to be distinct from another if the features that characterise it are distinct.

One might think that there is a pattern: infectious diseases are classified based on causes, and non-infectious diseases on characterising features. However, some *infectious* diseases appear not to be understood by reference to their causes. As an example, the MSD Manuals, a prestigious medical source, state that "[m]alaria is infection with *Plasmodium* species" (Marie & Petri, 2022). Here, malaria is not understood to be the disease *caused* by an infection with *Plasmodium*, but as *the* infection itself. Further, some *non*-infectious diseases appear to be understood in terms of causes. For instance, the National Health Service (NHS) states that "Cushing's syndrome is a condition caused by having too much of a

hormone called cortisol in your body" (2024a). So, Cushing's syndrome appears to be classified based on its cause—abnormally high cortisol. On the other hand, other diseases are straightforwardly defined in terms of some, non-infectious, biological process—rather than based a cause or on features that *characterise* them. For instance, the MSD Manuals state that "[g]astritis is inflammation of the gastric mucosa" (Vakil, 2023). So, whether there is a general pattern for disease classification in current medicine is not obvious.

Since most of this thesis concerns the psychiatric quest for a biomedical classification—which is supposedly employed in "the rest" of medicine—, it is imperative to provide an analysis that satisfactorily accounts for the way diseases are currently classified, to make explicit the exact sort of classification sought to be implemented in psychiatry. In what follows, I will survey three analyses on the matter, i.e., the aetiological analysis, the realisation analysis, and the constitutive analysis, and will conclude that only the latter is satisfactory. As it will become clear, a significant part of the dispute is whether any specific disease in current classification is best understood as "the disease *caused* by" a certain biological state or process, or as "being *realised* by a biological, pathological process". Based on the constitutive analysis, I will favour the alternative view that the features based on which any disease is classified are necessary and sufficient for it, and formulations such as "disease D is biological factor(s) B—*or* biological factor(s) B and symptoms" will be preferred.

2. The aetiological analysis

I will address the aetiological analysis in this section. It focuses on the *aetiological model*, which is based on what I call the "monocausal tenet", i.e., that diseases are classified based on *single*, biological causes which are specific to individual diseases. As I will elaborate,

there has been debate about how to best understand the monocausal tenet, and most of this subsection will focus on this issue. Drawing on the mentioned debate, I will propose a way to better understand said tenet but, later, in §2.1, I will address three problems of the aetiological model which demonstrate that it fails to be an adequate model of disease classification.

To begin with, a brief historical note is in place. It is worth noting that disease classification was based on symptoms, anatomical lesions, or a combination of both before the 19th century (Carter, 2003; Fuller, 2017). As an example, Jonathan Fuller (2017) notes that, before the finding, in the 19th century, that *Mycobacterium tuberculosis* (*M. tuberculosis*) causes tuberculosis, the disease "was understood symptomatically and pathologically in terms of 'tubers' in the lungs" (p. 10-11). However, disease classification changed by the end of the century, and it began to be based on biological causes, a sort of classification that I call "aetiological classification". In fact, with the discovery of *M. tuberculosis* by Robert Koch, tuberculosis came to be classified as "a parasitic disease *caused* by the invasion of the bacilli and primarily influenced by the growth and proliferation of the latter" (Koch, 1876; quoted in Broadbent, 2009, p. 303; my emphasis). Later, the aetiological classification came to be applied to various other infectious diseases such as syphilis or anthrax.

A notable feature of the aetiological classification is that it is based on the idea that specific diseases are caused by *single* biological factors—something which has been widely noted (e.g., by Broadbent, 2009, 2013; Fuller, 2017; Murphy, 2009, 2011; and Radden, 2018). As an illustration of this, Alex Broadbent (2009) considers Koch's claim that "each disease is caused by one particular microbe—and by one alone. Only an anthrax microbe

causes anthrax; only a typhoid microbe can cause typhoid fever" (1876; quoted in Broadbent, 2009 p. 303). This idea that specific diseases are caused by single biological factors is reflected in what I call "the monocausal tenet" of the aetiological classification, namely, that diseases are classified based on their specific, single biological cause.

As I will now elaborate, there has been debate about how to best understand the monocausal tenet. Later, I will propose a characterisation of such a tenet drawing on some aspects of the debate. So, first, I will address Codell Carter's (2003) analysis of the aetiological classification, which he calls the "aetiological standpoint". More precisely, the latter is characterised by the author as

> the belief that diseases are best controlled and understood by means of causes and, in particular, by causes that are *natural* (that is, they depend on forces of nature as opposed to the wilful transgression of moral or social norms), *universal* (that is, the same cause is common to every instance of a given disease), and *necessary* (that is, a disease does not occur in the absence of its cause) (2003, p. 1; emphasis in the original).

According to Carter's analysis, then, late 19th-century medicine began to "understand and control" specific diseases by seeking natural causes which were common to every instance of them—that is, that were universal—, and without which the diseases would not occur—that is, that were necessary. The standard example is tuberculosis. As understood in Carter's view, an infection with *M. tuberculosis* is a natural cause of the disease, and the infection causes all instances of it; further, the disease does not occur in the absence of the infection. So, tuberculosis has an *M. tuberculosis* infection as a natural, universal, and necessary cause and, consequently, tuberculosis can be understood as the disease *caused* by *M. Tuberculosis*.

Carter's analysis thus accounts for the monocausal tenet in terms of single causes of diseases being natural, universal, and necessary, so that, thus understood, the classification of diseases in the aetiological model is made on the basis of the *one* cause that is natural, universal, and necessary for a particular disease.

However, Broadbent (2009, 2013) points out a problem with Carter's analysis. Broadbent argues that specific diseases "may have lots of different causes" (2009, p. 303), posing the example that having an infection with the *Vibrio cholerae* bacterium can be thought of as a cause of cholera but, in his view, the presence of oxygen would also count as a cause of the disease. Along these lines, Broadbent claims that Carter's analysis

> is vulnerable to an irritating but persistent objection. The presence of oxygen is a universal, necessary cause of cholera; it is present in every case, and without it there would be no cholera, as the virus relies on its host being alive. Can we therefore classify cholera as oxygen-disease? (2009, p. 303).

The answer to that question is, of course, that medicine has never classified cholera as an oxygen disease. So, Broadbent rejects Carter's analysis for not being "entirely precise" (2009, p. 303). Although it is not easy to see how the *mere* presence of oxygen causes cholera, we can better understand Broadbent's criticism by thinking of *breathing* oxygen as a cause for cholera. Breathing oxygen can be thought of as triggering, say, relevant pathophysiological processes that sustain the proliferation of *Vibrio cholerae*, thus causing cholera. Further, it is clear that, thus understood, breathing oxygen is a universal and necessary cause of cholera, for all cases of the disease are (partly) caused by breathing oxygen, and patients cannot have cholera without it.

Based on that, we can summarise the criticism as follows: in Carter's analysis, (what I call) the monocausal tenet is explained by the fact that classification of diseases in the aetiological model is based on the *one* cause that is natural, universal, and necessary for a particular disease; but, as illustrated by cholera and breathing oxygen, diseases have *more* than one natural, necessary and universal cause. Then, Carter's analysis does not restrict the number of causes based on which diseases can be classified to *one*, as the monocausal tenet requires. Broadbent then proposes that (what I call) the monocausal tenet of the aetiological classification is best explained in terms of necessary and circumstantially sufficient causes of diseases (2009, p. 304). To understand this, let us first briefly elaborate on Broadbent's view.

By "circumstantially sufficient causes", the author means causes which are sufficient for a disease only given a compound of background circumstances. Among these circumstances, Broadbent claims, are that "the patient would have to be well supplied with oxygen; the Earth would need to continue a peaceful orbit" (2009, p. 304), and so on. Based on this, Broadbent summarises his analysis in two conditions, (i) and (ii), as follows: "[t]he first condition states that *C* [the cause of a disease] is causally necessary for *D* [the disease]. The second states that, in certain circumstances, *C* is sufficient" (2009, p. 303). In Broadbent's view, the circumstances under which *C* is sufficient for *D* would have to be specified by an aetiological classification.

What is of interest here is that, in Broadbent's account, the monocausal tenet is explained by the fact that, according to him, "*at most* one [cause] will satisfy" (i) and (ii) as above (Broadbent, 2009, p. 303; emphasis in the original)[2]. So, in other words, in Broadbent's

[2] Broadbent claims: "[t]o see this, suppose that two kinds of cause, C_1 and C_2, are proposed with respect to disease D. If there is any case where C_1 is present and C_2 is absent, then either (i) or (ii) will be violated with respect to C_1, depending on whether D is present or absent in that case. (And vice versa for C_2.) And if C_1 and C_2 are universally present or absent together, then the chances are that this is no mere coincidence, and that

analysis, the monocausal tenet is explained by the fact that a specific disease is classified based on the *one* biological cause that is necessary and circumstantially sufficient for it[3].

But Broadbent's analysis is not without problems. As Jonathan Fuller (2017) notes, "[o]ne of Broadbent's motivations for including a circumstantial sufficiency requirement is to limit the number of causes that could satisfy the monocausal model to one" (p. 10). Fuller casts doubt, however, that such a requirement in fact accomplishes that purpose. He claims that

> [o]ne factor likely to be found in the 'given circumstances' listed in a circumstantial sufficiency requirement is 'lack of a sufficient immune response'. Then we would define a disease like tuberculosis as 'the disease caused by tubercle bacillus given lack of a sufficient immune response against the tubercle bacillus', plus other circumstances. But now tuberculosis is defined in terms of at least two causes: the tubercle bacillus, and lack of a sufficient immune response against the bacillus. (Fuller, 2017, p. 10).

Fuller's view is that Broadbent's analysis cannot respond to the question "[w]hy should we regard the 'tubercle bacillus' [as opposed to the lack of sufficient immunity to the pathogen] as the defining cause?" (2017, p. 10). To see the problem another way, consider that,

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they are related either as cause to effect or as effects of a common cause. If the former, we have grounds to consider them parts of the same cause; and if the latter, it will in principle be possible to bring about cases where C1 occurs without C2, or vice versa. Then, again, either (i) or (ii) will be violated, depending on whether D is present or absent" (2009, p. 303).

[3] One important thing here is that the monocausal model of disease is taken by Broadbent to be a *normative* model. As he claims, "[i]nterpreted as a descriptive claim […] the monocausal model would have been simply false when it was initially proposed: the number of recognised diseases satisfying it would have been close to zero […] The monocausal model ought to be interpreted as a normative model. It tells us that we ought to identify diseases so that they satisfy the model" (Broadbent, 2009, p. 304). In other words, the monocausal model tells physicians the way they ought to classify diseases: based on single, biological causes which are necessary and circumstantially sufficient for them.

according to Broadbent, among the causes of a disease, only *one* is necessary and circumstantially sufficient for it. Nevertheless, Fuller's example illustrates that *both* an *M. tuberculosis* infection and a lack of sufficient immunity to it are causally necessary and circumstantially sufficient for tuberculosis.

As a matter of fact, as understood in the late 19th century, no case of the disease could occur in the absence of an *M. tuberculosis* infection—so, it is necessary for tuberculosis—and, further, the infection is sufficient for the disease *in the circumstances* among which lack of sufficient immunity to it is present. Conversely, there are no cases of tuberculosis in the absence of lack of immunity to the pathogen—so the latter is necessary for the disease—, and lack of sufficient immunity to the pathogen is sufficient for the disease *in the circumstances* among which *M. tuberculosis* is present. So, there are two necessary and circumstantially sufficient causes for tuberculosis, and Broadbent's analysis does not successfully restrict the number of cases based on which diseases can be classified to *one*.

At this point, it should be remarked that the monocausal tenet can be understood as conferring certain causes a special status as compared with others: in the aetiological model, diseases are classified based on only *one* cause which is picked out from among their varied causes, so that one cause has some special status as compared with the others, which are not employed in classification. According to Broadbent, "[t]he special status that the monocausal model offers to certain causes is not an empirical status, but a conceptual one. Certain causes define the disease in question" (2013, p. 156).

In fact, as I previously mentioned, before the discovery of *M. tuberculosis*, tuberculosis "was understood symptomatically and pathologically in terms of 'tubers' in the lungs" (Fuller, 2017, pp. 10-11; Carter, 2003). Bur, as Fuller notes, "[s]o defined,

'tuberculosis' had several infectious causes, and could occur in the absence of Koch's tubercle bacillus" (2017, p. 11). Then, before tuberculosis was defined as the disease caused by *M. tuberculosis*, the latter was *not* a necessary cause for the disease, for patients could have it in the absence of an infection with that pathogen. But defining tuberculosis as the disease caused by *M. tuberculosis* made the latter necessary for the disease for, so defined, no patient can have tuberculosis in the absence of *M. tuberculosis*.

What is of interest here is that, at the same time, the above definition of tuberculosis ensures that the disease is classified based on just one of its causes: it is classified based on the single cause that is stipulated to *define* it. So, the monocausal tenet of the aetiological classification turns out to be best explained as a result of *defining* diseases in terms of a single cause—and not as a result of merely identifying natural, universal, necessary causes, nor by establishing necessity and circumstantial sufficiency requirements.

A final note is in place before I propose a way to characterise the monocausal tenet. I mentioned that, by defining diseases in terms of their causes, the latter become necessary for the former. Notably, as Fuller points out, "if a certain cause is necessary for the disease, then that cause will always occur whenever the disease occurs" (2017, p. 9), so this means that, by being necessary for a disease, a cause is also universal to it, for it is among the causes of *all* cases of the disease. Then, a single, natural cause that is stipulated to define a disease becomes necessary and, also, universal to it. Therefore, natural, universal, and necessary causes do somehow relate to the monocausal tenet of the aetiological classification after all.

But, as I explained, Carter's analysis fails to capture the monocausal tenet of the aetiological classification, for it does not limit the number of causes based on which diseases can be classified to one. So, if a more accurate characterisation of the aetiological model is

sought, natural, universal, and necessary causes are to be understood in a slightly different manner than in Carter's analysis. Drawing on Fuller's remarks and on some aspects of Broadbent's and Carter's views, I propose to characterise the aetiological model simply as one that *defines* diseases for classificatory purposes in terms of single, natural causes which then become necessary and, consequently, universal for the diseases[4]. So, more precisely, it is not just that *any* natural, universal, and necessary cause that matters for classificatory purposes in an aetiological approach, but *only* the single, natural, universal, and necessary causes in terms of which diseases are defined.

Two brief, final issues should be addressed. First, the fact that some causes become necessary for some diseases only until after the latter are defined in terms of the former does *not* imply that the aetiological classification is based only on the stipulation that a certain pathogen defines a certain disease. Stipulation is, in fact, involved, but discovery is as well. All three Carter, Broadbent, and Fuller correctly remark that Koch did, in fact, discover that *M. tuberculosis* causes (some cases of) tuberculosis *as it was defined* before the discovery. The insight of their analyses, though, is that, had Koch not defined tuberculosis as a disease caused by that pathogen, *M. tuberculosis* would not have become a necessary cause for it.

Second, I have only described that, in an aetiological classification, certain causes are selected by researchers as the defining causes of some diseases, but I have not provided an account of the reasons based on which researchers select specifically those causes—and not others—as the defining ones. The problem, however, lies in the aetiological approach itself.

[4] All this is not to say that Carter is unaware of the role stipulation plays for the aetiological classification. In fact, Carter argues that "[c]auses are made universal and necessary by adopting suitable disease characterizations" (2003, p. 110). The correction here is that Carter's analysis suffers from some imprecision. By describing the aetiological classification as just understanding and controlling diseases based on natural, universal, and necessary causes, Carter leaves the possibility open that a disease has more than one natural, universal, and necessary cause relevant for classificatory purposes—e.g., breathing oxygen.

The latter just tells us that diseases have single biological causes—recall, e.g., Koch's claims concerning anthrax and syphilis—, and that diseases are classified based on these. But this approach does not instruct us as to what we should do in case diseases had more than just one cause—which is, in fact, the case.

The aetiological model entails further problems which demonstrate that it fails to be a satisfactory model of disease classification, and those problems will be the focus of the following subsection.

2.1 Problems with the aetiological classification

I will address three problems posed by the aetiological model which have been previously pointed out in the literature. It will become clear throughout that that the aetiological model fails to be an adequate model of disease classification.

The first problem is that the notion of disease causation has changed and, rather than conceiving of diseases as caused by single causes, current medicine conceives of them as caused by a variety of factors which can come from different levels of explanation. An aetiological approach to classification simply does not conform to this new understanding of disease causation (Murphy, 2011; Broadbent, 2009, 2013). Broadbent notes, in fact, that "[m]any modern epidemiologists feel that it is unhelpful to presume that they are seeking causes of disease that are in any sense necessary or sufficient" (p. 305). Further, he claims that

> [i]t is hard to see how insistence that, for example, bowel cancer must be defined by reference to a single causal factor could further our understanding of that condition, when so many factors seem to be relevant (2009, p. 305).

Broadbent's claim is in fact plausible in light of the present understanding of disease causation. The latter, as Dominic Murphy (2011) claims, "is not really the same as the early nineteenth century" (p. 435). Murphy points out that the difference lies in that "modern thinking has incorporated statistical methods to give much greater empirical content to the claim that different risk factors cause the same disease" (2011, p. 435). At present, much focus is placed on the probabilistic relationships held between the different causes and the diseases—e.g., how likely is it that high consumption of carbohydrates and a sedentary lifestyle lead to the development of type 2 diabetes—, and on the way different, non-necessary factors interact and cause diseases.

Then, in the context of this understanding of disease causation, widely based on statistical methods and probabilistic relationships, it is hard to see how an aetiological approach to classification, requiring single, necessary defining causes, plays any role in classifying many diseases considered to be caused by a variety of non-necessary factors. Furthermore, it will become clear in §4.2 that even those diseases which currently have an (apparently) aetiological definition are currently best understood to be classified on a non-aetiological basis.

The second problem with the aetiological classification is that paradigmatic examples of aetiologically classified diseases resist an aetiological classification as they are currently understood. As Fuller notes, "[w]e now recognize [tuberculosis] as a disease caused by the "Mycobacterium tuberculosis complex (MTBC)" (2017, p. 12). MTBC is formed by *M. tuberculosis*, *M. bovis, M. africanum*, *M. microti*, "and other less common mycobacteria" (Nardell, 2022). What this implies is that, as currently understood, tuberculosis "occasionally

results" from those mycobacteria in the complex which are not *M. tuberculosis* (Nardell, 2022).

In fact, the most recent version of the *International Classification of Diseases* (ICD) defines tuberculosis as "[a] disease caused by an infection with bacteria of the Mycobacterium tuberculosis complex" (WHO, 2022a). So, as tuberculosis is currently defined, *M. tuberculosis* is no longer necessary for the disease—patients can have tuberculosis caused by, say, *M. africanum*. Further, given the current definition, no specific bacteria from the MTBC is individually necessary for tuberculosis either. And, consequently, no single bacteria from the complex is a universal cause of tuberculosis. So, tuberculosis is currently defined by the ICD in terms of at least *four* different, individually non-necessary and, therefore, non-universal pathogens. Therefore, tuberculosis is not classified monocausally anymore, even though, as Fuller remarks, "[t]uberculosis is supposed to be our paradigm monocausal disease" (2017, p. 12).

Other infectious diseases are now understood to be caused by a variety of pathogens as well. For instance, "[t]he common cold is caused by over 100 different viruses, and pneumonia is caused by several different types of microbe" (Fuller, 2017, p. 12). These diseases are, then, not classified monocausally either.

A third problem with the aetiological model is that allows misclassifying diseases. For instance, Fuller (2017, p. 12) poses the case of opportunistic infections, which are those occurring when the immune system is compromised. As an example, patients with acquired immunodeficiency syndrome (AIDS)—which, if we followed an aetiological approach, could be defined as the disease caused by a Human Immunodeficiency Virus (HIV) infection—are especially prone to developing opportunistic infections, for their immune

system is attacked by the HIV. In fact, an opportunistic infection common in ADIS patients is tuberculosis, which most commonly attacks the lungs.

Fuller points out that a monocausal approach to classification allows *tuberculosis* to be (mis)classified as *the disease caused by an HIV infection* (2017, p. 12). To see why, consider that the aetiological approach does not tell us which one cause to employ in the definition of a disease when it has more than one cause. And, further, HIV is a cause of lack of sufficient immunity to *M. tuberculosis*, which, in turn, altogether with the pathogen, is a cause of tuberculosis. So, Fuller's example illustrates that, in the absence of a constraint on which cause to employ in a monocausal definition, the aetiological model allows an HIV infection, being a distal cause of tuberculosis, to be employed to define tuberculosis. In other words, the aetiological model allows respiratory diseases such as tuberculosis to be classified as being caused by an infection attacking the immune system (an HIV infection), and not as being caused by an infection attacking the respiratory system. So, the aetiological model allows misclassification of diseases.

The lesson we can draw from Fuller's example is that, if the purpose of a model of disease classification is to classify diseases satisfactorily, the aetiological model, with its monocausal tenet, fails in accomplishing its purpose, and, thus, it fails to be an adequate model of disease classification.

To summarise, the aetiological model does not conform to the current understanding of disease causation; paradigmatic examples of aetiologically classified diseases are no longer thus classified; and the aetiological model allows misclassification of diseases. So, the aetiological model fails as a model of disease classification. I will now elaborate on the realisation analysis.

3. The realisation analysis

An alternative analysis of disease classification is the "realisation analysis", which I call that way because, as I will elaborate later, it states that diseases are *realised* in destructive (pathological) processes. What I call the "realisation analysis" is a reconstruction of Dominic Murphy's ideas concerning disease classification and explanation developed in several works (2006, 2009, 2011, 2013). As it will become clear in this section, the realisation analysis' way of conceiving of disease classification does better in accounting for the current conception of disease causation than the aetiological approach, even though the motivation for developing it is not merely to respond to the latter. However, in surveying two possible senses of "realisation", I will argue that the realisation analysis does not adequately account for several diseases, thus not being a general analysis. In further sections, I will show that both the diseases accommodated and not accommodated by the realisation analysis are adequately explained by the constitutive analysis.

My presentation of the realisation analysis is in two parts. In this subsection, I will mainly focus on the idea that medicine sees diseases as involving an aetiology, pathology and symptoms—which are notions that I will define in due course—, and, in §3.1 and §3.2, I will address the "realisation" part of this analysis, i.e., that diseases are realised in destructive, pathological processes.

So, to begin with, we should note that the realisation analysis focuses on psychiatry, and on the way psychiatric conditions are to be understood by those who seek a change in psychiatric classification. Its starting point is the idea that medical conditions are currently understood by two distinct interpretations of the medical model, i.e., the *minimal* and the *strong*. Regarding the former, Murphy claims that "[a] minimal interpretation thinks of

diseases as collections of symptoms that occur together and unfold in characteristic ways, but it makes no commitments about the underlying causes" (2009, p. 103). Psychiatric conditions in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) and the ICD fit the minimal interpretation: current medicine does not commit to, say, (the syndrome of) depression having a specific underlying biological (or cognitive) cause, but it is still incorporated into medical taxonomy.

But Murphy claims that the *strong* interpretation

> says that what psychiatrists describe as "mental illnesses" are diseases that are causally explained by their underlying pathophysiology. It is committed to specific causal hypotheses in terms of abnormalities in underlying neurobiological systems, which are responsible for the observed patterns of signs and symptoms (2013, p. 967).

In other words, in contrast with the minimal medical model, an understanding of psychiatric conditions according to the strong medical model is committed to the idea that these conditions, understood merely as clusters of symptoms at present, are caused by specific abnormalities in neurobiological systems[5]—yet mostly unknown. So, (at least some) psychiatric conditions are thought to involve a specific—though yet unknown—abnormality

[5] We should note that, according to Murphy (2011), "[t]he strong interpretation argues that mental illnesses are caused by distinctive pathophysiological processes in the brain. However […] there is nothing in the strong interpretation that requires this destructive process to be understood at only one level of explanation" (p. 449). So, according to Murphy, the strong medical model is not *in*compatible with the possibility that non-biological abnormalities caused the symptoms of psychiatric conditions in some cases. In particular, Murphy believes that, besides biological abnormalities, the model could admit *cognitive* abnormalities to be causes of psychiatric syndromes. This means that, in Murphy's view, the strong medical model allows a conception of (psychiatric) diseases as involving cognitive abnormalities leading to symptoms, in addition to a conception of them as involving (neuro)biological abnormalities leading to symptoms. Other authors have argued along the same lines (e.g., Phillips, 2015) as well. However, I will only focus on *biological* characterisations of diseases in this thesis, so I will only address the strong medical model as long as it concerns *biological* characterisations of psychiatric conditions, without addressing cognitive characterisations of them.

causing characteristic symptoms and, then, according to the realisation analysis, (at least some of) those conditions fit the notion of "disease" (as opposed to that of "syndrome"). Because of that, in the realisation analysis, "the simplest way to get a handle on classifying mental illnesses is by analogy with physical disease" (Murphy, 2006, p. 350), that is, by analogy with (non-psychiatric) diseases. Here, the question is, then, how (non-psychiatric) diseases are classified exactly. The realisation analysis takes it that "the simplest way to understand the taxa of medicine is as conjunctions of etiology and pathology" (Murphy, 2006, p. 350), so, to understand its take on disease classification, I will briefly address the notions of aetiology and pathology. Later, I will provide examples to illustrate the conception of disease classification in the realisation analysis.

"Aetiology" is employed to designate the cause or causes of a medical condition—whether a disease or a syndrome, and a medical condition can have *more* than one cause. As Murphy notes, moreover, the notion of aetiology

> covers phenomena at a number of levels of explanation. As well as interactions between genes and biological agents like germs, for example, we may want to recognize a wide variety of factors, including disruptions to the normal functioning of cognitive systems, psychodynamic factors, or even marital difficulties (2006, p. 351).

Furthermore, in most cases, all these factors are *not* individually necessary nor sufficient for the relevant disease.

On the other hand, "pathology" can be understood as an abnormal or destructive process which, in Murphy's view, could be at the cognitive or at the biological level—although I will only deal with *biological* pathology (see footnote 5).

In the realisation analysis, aetiology and pathology are related because "[t]he picture [of disease classification] is one in which an etiology causes a pathology that causes the clinical syndrome" (2006, p. 350). That is, the realisation analysis takes it that disease classification is currently understood as implying that certain factors—the *aetiology* as described above—jointly cause a biological *pathology* which, in turn, causes characteristic symptoms. Further, the realisation analysis points out that, in current disease classification, symptoms are understood to be "manifestations of the pathology" (Murphy, 2006, p. 350). Thus considered, symptoms are not employed as the basis for *disease* classification, and the latter is rather based on aetiology and pathology.

A final issue concerning the picture of disease classification is as follows. It is clear now that specific diseases can be caused by more than one aetiological factor. However, according to the realisation analysis, the interaction of all the aetiological factors of a given condition

> produce the pathology that is common to all cases of a condition. On this view, all the people who share a diagnosis do so in virtue of having a common destructive process (Murphy, 2011, p. 435).

So, according to the realisation analysis, a specific disease can be caused by multiple aetiological factors, and it has only *one* pathological, destructive process that is common to all of its cases in a way that all and only patients who develop the pathology have the disease. In sum, the "picture" of classification in the realisation analysis is that diseases have an aetiology—which can involve multiple causes at different levels of explanation—which causes a (single) pathology which, in turn, causes symptoms.

To better understand the "picture" of disease classification just described, I will now present two examples illustrating it, originally addressed by Murphy (2006, pp. 352-354), i.e., Sydenham's Chorea and Paediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcus (PANDAS). These conditions are related to obsessive-compulsive disorder, for symptoms of the latter can be present in both cases. Further, both conditions are complications derived from poorly treated infections with Group A beta-hemolytic Streptococcus (GAS) bacteria.

As Murphy notes, "Sydenham's Chorea and PANDAS differ with respect to some key aspects of the pathology" (2006, p. 353). In fact, Sydenham's chorea is thought to be associated with disruptions to the basal ganglia-thalamo-cortical (CBGTC) circuits (Vreeland *et al*, 2023, p. 362) and, although it is still a matter of debate what the exact pathological process associated with PANDAS is (see La Bella *et al*, 2023, p.1), a growingly accepted hypothesis is that it has to do with a "breach" to the blood-brain barrier—a membrane lying between the blood and certain nanostructures of the brain—, leading to an attack to non-neuronal and neuronal cells and neurotransmitter receptors (Vreeland *et al*, 2023, p. 365).

The pathology of Sydenham's chorea thus relates to disruptions to CBGTC circuits, and the pathology of PANDAS to disruptions to the blood-brain barrier. This example illustrates the picture of disease classification proposed by the realisation analysis: we have an *aetiology*—a streptococcus infection for both diseases—which causes a *pathology*—disruptions to CBGTC circuits in one case and disruptions to the blood-brain barrier in the other—, which causes characteristic symptoms.

With this picture of classification in the background, I can now address the "realisation" part of this analysis. In fact, it is claimed that"[t]he medical model privileges explanations that cite underlying processes as the *realization* of a disease entity" (Murphy, 2009, p. 114; my emphasis), that "the core insights of the strong medical model […] are that diseases are destructive processes *realized* in bodily systems" (Murphy, 2011, p. 449; my emphasis), and that "we are better off thinking of diseases as being *realized* in biological systems rather than caused by them [as they would be understood by an aetiological classification]" (2009, p. 109; my emphasis). Based on these and other relevant claims, I will address the idea that diseases are realised in biological systems in the following subsection.

As I will elaborate, the notion of "realisation" has a standard sense in philosophy which I will address in §3.2, but it will become clear in §3.1 that realisation can also be understood in the realisation analysis as *identity*, so it is worth exploring such an analysis by considering this, non-standard sense first.

3.1 Realisation as identity

The purpose of this and the following subsection is to elucidate the sense in which "realisation" should be understood in the realisation analysis and to evaluate whether diseases can be adequately explained to be realised in pathological, destructive processes. Since the idea that diseases are so realised is illustrated with the examples of atherogenesis and depression (Murphy, 2011, p. 436), I will take a moment to briefly elaborate on these conditions.

First, atherogenesis is "the process of forming [fat] plaques in the intima layer of arteries" (Lambros, Dimitrios & Lampros, 2017, p. 9), and it is involved by atherosclerosis,

a "disease in which there is a build up of plaques inside arteries" (Pahwa & Jialal, 2023). Further, atherosclerosis—and, consequently, atherogenesis—is known to be caused by a variety of factors such as consuming fast food and smoking.

Regarding depression, a brief, superficially unrelated remark is in place first. We should note that a corollary of understanding psychiatric conditions in light of the strong medical model is that (at least some of them) should be presumed to be diseases[6] fitting the picture of classification described previously. So, if we commit to the strong medical model, we should think of depression in the following way: given that "[a] huge number of variables have been shown to influence depression" (Murphy, 2006, p. 351), we can understand that "huge number of variables" as the aetiology of the condition, which causes a yet undiscovered (*neuro*)*pathology* common to all patients with it, which, in turn, causes the characteristic syndrome we currently call "depression".

Then, if we commit to the strong medical model, we might think that certain neuropathology so far undiscovered *causes* depression. But the realisation analysis has another take on this, i.e., that the neuropathology *realises* depression, not that it causes it. In fact, addressing both atherogenesis and depression, Murphy claims that

> [w]e might prefer to say that the neuropathology realizes the disease [depression], rather than causes it. On this view, atherogenesis *just is* a biochemical process of plaque formation and its sequelae, and it can be caused in many ways. For instance, it can happen in blood vessels whose narrowing is of no physiological consequence, and hence not a disease process. Similarly, one might think that major depression *just is* some, as yet unknown, cognitive and/or neurological process (or, perhaps, a family of specific

[6] Though they are not currently so characterised because of a lack of causal, biological knowledge about psychiatric syndromes, as I mentioned.

> processes) that can be triggered in diverse ways depending on one's genetic inheritance, acquired psychology and contingent biography (2011, p. 435; emphasis in the original).

So, the realisation analysis takes it that, if we commit to the strong medical model, depression is to be viewed as *realised* by a (so far unknown) neuropathology, and not as *caused* by it. What does this mean, though? Murphy does not provide an explicit definition of "realisation" but, based on the above quotation, I take it that, to explain what it is to *realise*, he provides the example of atherogenesis: saying that the latter just *is* a biochemical process of plaque formation is to say that such a process *realises* atherogenesis. Then, to realise something can be understood in the realisation analysis as *just being* that something—i.e., as being identical to it. In fact, in addressing the very same issue in an earlier work, Murphy claims that "[o]n that view, atherogenesis is simply *identical* to a biochemical process of plaque formation and its sequelae, which can be caused in many ways" (Murphy, 2009, p. 113; my emphasis). This suggests, then, that, in the realisation analysis, *realising* something is to be *identical* to that something.

This interpretation of realisation is further supported by considering the second part of Murphy's claim, quoted above, that we can think that depression *just is* an undiscovered neuropathology—or family of neuropathologies. In an earlier work and, addressing the very same issue, Murphy claims that "one might think that major depression is *the same thing as* a specific, as yet unknown, cognitive and/or neurological process (or, perhaps, a family of specific processes)" (Murphy, 2009, p. 113; my emphasis). So, it seems as if saying that a neuropathology realises depression is to say that the neuropathology is the same thing as depression, or, conversely, that depression is the same thing as the neuropathology.

So, one way we can understand realisation in this analysis is as identity[7]. Now, the claims on realisation are illustrated by depression and atherogenesis, but passages quoted earlier make *general* claims concerning diseases. Just to recall, for instance, Murphy claims that "we are better off thinking of diseases as being realized in biological systems rather than caused by them" (2009, p. 109). So, I take it that, according to the realisation analysis, diseases (psychiatric and non-psychiatric) are best understood as realised in pathological, destructive biological processes. In this subsection, I will evaluate this idea by considering realisation as identity and, in §3.2, by considering realisation in a different—but standard—sense. Later, it will become clear that a better way to understand diseases from a classificatory point of view is in light of the constitutive analysis—as *defined* in terms of certain features which are necessary and sufficient for them, and which are neither their causes nor their effects[8].

A remark is important here. It is important to note that an understanding of disease classification as the one proposed by the realisation analysis does much better than the aetiological approach in incorporating the current conception of disease causation. As Murphy claims, thinking of diseases as being realised in destructive processes "permits strong medical thinking to acknowledge that a realization which is shared across patients might have a variety of specific, peculiar causes" (2009, p. 112), something which is not allowed by a classification based on a single, universal, necessary causes as in the aetiological

[7] Given this understanding, then, depression should be understood by the strong medical model as *identical* to certain neuropathology (or family of neuropathologies)—so far undiscovered—, with the relevant symptoms being understood just as *manifestations* of the (undiscovered) neuropathology, and *not* as identical to depression.

[8] Further, in connection with footnote 7, I will elaborate in §5.1 that this implies that, if psychiatric conditions came to be characterised as diseases, they will be best understood by the constitutive analysis as defined by biological factors *or* by biological factors plus symptoms, rather than as realised in pathological, destructive processes.

classification. The realisation analysis, however, implies the problem that it is not a general analysis, as I will now elaborate.

It should be noted that, if we understand realisation as *identity*, then the realisation analysis seems to be right in some non-psychiatric cases. For example, the MSD Manual states that

> [g]astritis is inflammation of the gastric mucosa caused by any of several conditions, including infection (*Helicobacter pylori*), drugs (nonsteroidal anti-inflammatory drugs, alcohol), stress, and autoimmune phenomena (atrophic gastritis). Many cases are asymptomatic, but dyspepsia and gastrointestinal bleeding sometimes occur (Vakil, 2023).

Assuming that inflammation is a destructive process, we can see inflammation of the gastric mucosa as the destructive, pathological process of gastritis. Since, according to the MSD description, gastritis *is* inflammation of the gastric mucosa, then it seems that gastritis is thought to be identical to it—so, inflammation of the gastric mucosa, a destructive, pathological process, *realises* gastritis (in the identity sense). Further, the pathology sometimes causes characteristic symptoms such as dyspepsia—a sensation of discomfort in the upper abdomen—and it is *caused* by "several conditions" which include, e.g., infections, drugs, and stress. That is, the aetiology of gastritis encompasses a variety of factors at different levels of explanation—biological and psychological.

Gastritis, then, is a non-psychiatric example which illustrates the way diseases are classified according to the realisation analysis: characteristic symptoms are caused by a pathological, destructive process, the latter is caused by an aetiology which can involve

several factors at different levels of explanation, and the destructive process realises the disease.

However, there are other cases of non-psychiatric conditions fitting the picture of having an aetiology, pathology and symptoms in which it is not clear that the relevant pathological process realises the disease. One such case is Sydenham's chorea, previously addressed. The United States' National Organization for Rare Disorders (NORD) states that

> [s]ydenham chorea is a rare neurological disorder characterized by sudden onset chorea, usually in childhood […] Symptoms in arms and legs are often worse on one side of the body. Additional symptoms of Sydenham chorea may include slurring of speech and difficulty maintaining steady hand grip. Anxiety, sadness, inattention, and obsessive compulsive thoughts and behaviors may also occur. […] Sydenham chorea usually develops within weeks to months following group A beta-hemolytic streptococcal infection (NORD, 2020).

This passage does not mention Sydenham's chorea's pathology but, as I pointed out earlier, the latter relates to disruptions to CBGTC circuits. Notably, symptoms and aetiology are mentioned, but the disease is *not* claimed to be something like a disruption to CBGTC circuits, so it is not clear that the disease is identical to its specific destructive process.

One might think that the disease is not so described because "[t]he exact underlying mechanisms that cause Sydenham chorea are poorly understood" (NORD, 2020). So, perhaps, once the underlying mechanisms are adequately explained, the disease could be described to be identical to its specific destructive process. However, Sydenham's chorea is a form of *chorea*, which is "random, flowing, nonsuppressible involuntary movements" (Rajput & Noyes, 2024a)—that is, a set of symptoms—so, as long as it continues to be so

conceived, it is hard to envision the disease as being identical to an underlying pathological, destructive process regardless of whether the latter causes chorea.

On the other hand, there are other diseases fitting the picture of having an aetiology, a pathology, and symptoms which have more well-established research, and which are nevertheless *not* described by current medicine to be identical to their pathology. For instance, it is claimed from Parkinson's disease that it is

> a slowly progressive, degenerative disorder characterized by resting tremor, stiffness (rigidity), slow and decreased movement (bradykinesia), and eventually gait and/or postural instability […] (Rajput & Noyes, 2024b).

Though only the symptoms of Parkinson's disease are mentioned in this passage (tremor, stiffness, and so on), we have to note that "the key pathology [of Parkinson's disease] is the loss of dopaminergic neurons that lead to the symptoms" (Zafar & Yaddanapudi, 2023), and that among its aetiology we can find "the use of pesticides, herbicides and proximity to industrial plants", genetics, and others (Zafar & Yaddanapudi 2023). However, Parkinson's disease is not described as a loss of dopaminergic neurons, so it is not clear that current medicine conceives of it as identical to its pathological, destructive process.

A last example is Cushing's syndrome. The MSD Manuals state that

> [c]ushing syndrome is a constellation of clinical abnormalities caused by chronic high blood levels of cortisol or related corticosteroids […] Typical symptoms and signs include moon face and truncal obesity, easy bruising, and thin arms and legs (Grossman, 2024).

Chronic, high blood levels of cortisol or related corticosteroids (hypercortisolism) can be understood as the destructive, pathological process specific to the disease, and its aetiology includes "prolonged use of glucocorticoids" or "excessive production of cortisol by adrenal glands" (Chaudhry & Singh, 2023). Despite having a well-identified pathology, i.e., hypercortisolism, Cushing's syndrome is not described as *being* just hypercortisolism. In fact, a distinction has been recently made between asymptomatic hypercortisolism—also called "subclinical hypercortisolism"—and Cushing's syndrome. It has been claimed that [s]ubclinical hypercortisolism (SH) is defined as excessive cortisol secretion without the classic manifestations of clinically overt Cushing syndrome. (Pizzorno & Pizzorno, 2022, p. 8).

So, Cushing's syndrome is the symptomatic version of hypercortisolism. But if Cushing's syndrome was identical to its specific, pathological destructive process, then the condition would be the same as hypercortisolism even in the absence of symptoms—such as gastritis is inflammation of the gastric mucosa regardless of whether it causes symptoms. In this case, the very name of the disease, "Cushing's syndrome", suggests that the condition is a syndrome, and not just an underlying destructive process. However, the point here is that the condition has well-identified aetiology, pathology, and symptoms and it is, nonetheless, far from clear that the condition is realised—in the identity sense—by its underlying pathological process.

So, diseases such as gastritis seem to be adequately explained by the realisation analysis as being realised by their specific destructive process in the identity sense of realisation. But it is far from clear that Sydenham's chorea, Parkinson's disease and

Cushing's syndrome can be adequately explained as being realised in destructive, pathological processes.

Moreover, Sydenham's chorea, Parkinson's disease, and Cushing's syndrome are neither accounted for by what Murphy calls the *minimal* interpretation of the medical model. It was mentioned that the minimal medical model "thinks of diseases as collections of symptoms […] but it makes no commitments about the underlying causes" (2009, p. 103). Nevertheless, current medicine does not conceive of those diseases as being just collections of symptoms, and it makes in fact commitments about the causes of the relevant symptoms: those of Sydenham's chorea are (hypothesised to be) caused by disruption to CBGTC circuits, those of Parkinson's disease by the loss of dopaminergic neurons, and those of Cushing's syndrome by hypercortisolism. These diseases are, then, not accommodated by the minimal interpretation at all.

So, under the identity sense of realisation, the realisation analysis is *not* a general account of disease classification. Later, in §4.3, I will show that the constitutive analysis can successfully accommodate the cases covered by the realisation analysis but also Sydenham's chorea, Parkinson's disease, and Cushing's syndrome, thus being a more general analysis.

3.2 Realisation in the standard sense

I mentioned earlier, however, that "realisation" is employed in a standard sense in philosophy, different from identity. In this subsection, I will explore the realisation analysis based on such a standard sense in order to answer the question of whether diseases can be adequately explained to be realised—in that sense—in destructive, pathological processes.

To begin with, the term "realisation" denotes a dependence relation that holds between certain higher-level properties or states and certain lower-level properties or states, and it is said that the latter are the *realisers* of the former—and that the former are *realised* by the latter. Here, a preliminary remark is needed. It is worth noting that, specifically regarding *properties*, expressions such as "property P1 realises property P2" are common. However, as Sidney Shoemaker (2007) notes,

> [s]trictly speaking, the realizer in a case of property-realization is the instantiation of a property, i.e. a property *instance*, and what is realized is likewise a property *instance*—to speak of one property as realizing another is shorthand for saying that instances of the one are among the possible realizers of instances of the other (p. 3; my emphasis).

So, in other words, saying, e.g., that property P1 realises property P2 is shorthand for saying that *instances* of property P1 realise *instances* of property P2. I will stick to this use in what follows.

A few examples will help illustrate the nature of realisation, on which I will elaborate in a moment. Perhaps the most common cases in which a realisation relation is claimed to hold are those concerning (higher-level) mental properties and (lower-level) brain properties: it is generally claimed that the latter *realise* the former and, consequently, that the former are *realised* by the latter. A classic example is that of pain: the brain property of *having C-fibre stimulation* is thought to realise the mental property of *being in pain*. Another famous example is that of scarlet, a specific shade of red which is said to realise such a colour (Yablo, 1992; Shoemaker, 2001; Wilson, 2009). Finally, a third group of examples concerns macro-

physical properties such as size, shape, colour, mass, and electrical charge (Shoemaker, 2007, see, e.g., p. 4), each of which is thought to be realised by *some* micro-physical property.

To explain now what characterises realisation relations exactly we should first note that there is abundant discussion concerning several aspects of realisation, and various, slightly distinct formulations have been proposed to fit specific theoretical purposes (see Baysan, 2015). In elaborating on the nature of realisation, however, I will avoid engaging in discussions concerning aspects of it that have elicited controversy, and will only focus on providing a *minimal formulation* of realisation. Since my purpose is not to discuss the notion of realisation itself, but to explore whether or not diseases can be described as being realised by specific destructive, pathological processes, a minimal formulation will do.

So, to begin with, consider Shoemaker's (2007) claim that, "[i]n general, X realizes Y just in case the existence of X is constitutively sufficient for the existence of Y" (p. 4). So, on the one hand, for a genuine realisation relation to be obtained, X and Y must have a constitutive relation—that is, a relation akin to that a statute and the piece of clay it is made of have—and, in addition, on the other hand, X must be sufficient for Y. Now, the relation between the realiser and the realised property or state is also usually described as a *necessitation* relation, so that realisers are said to *necessitate* the realised properties or states, and, conversely, the latter are understood to be *necessitated* by the realiser[9]. This is just a way of expressing the following entailment, which is usually accepted to describe realisation relations:

[9] See e.g., Baysan (2015), who claims that, in realisation relations, "the instantiation of a higher-level property or a state depends on, and is necessitated by, the instantiation of its lower-level realizer (or realizers)" (p. 2).

(Entailment) If P realizes Q, then, as a matter of metaphysical necessity, if something has P, then it has Q (Baysan, 2015, p. 5).

Put in terms of possible words, we can say, then, that realisation relations are such that, in every possible world where individual *i* has *P*, *i* has also *Q*.

A further feature commonly attributed to realisation relations is that they are *explanatory* (e.g., LePore and Loewer, 1989; Baysan, 2015): the existence of the realiser *explains* the existence of the realised property or state. So, e.g., assuming that *C-fibre stimulation* realises *having pain*, then, the former explains the presence of *having pain*—i.e., that an instantiation of pain occurs.

As a summary, a minimal formulation of realisation in the standard sense is as follows:

P realises Q if and only if P is constitutively sufficient for Q and P explains Q.

Returning to the examples above, then, *C-fibre stimulation* realises *having pain* in the standard sense if and only if *C-fibre stimulation* is constitutively sufficient for *having pain*, and in case the presence of the former *explains* the presence of the latter. A similar reasoning applies to the cases of scarlet and red, and the other examples of realisation above.

Now, we should recall that the sense of "realisation" explored in the previous section was that of *identity*, so that, according to it, a realiser is identical to the thing it realises. However, the standard notion of realisation "is incompatible with identity. What is realized is not identical to its realizer or realizers" (Polger & Shapiro, 2016, p. 21). To see why, recall

that scarlet has been claimed to realise red. But there is, indeed, nothing special with scarlet, so other shades such as, say, carmine, might also be considered to be realisers of red. So, the realis*ed* property, i.e., being red, has more than one realis*er* property—e.g., being scarlet and being carmine. Assuming all this is correct, then, being red is *multiply realised*. So, provided that the realisers are distinct from each other, being red is not identical to any of its realisers. Notably, the idea that the realised properties or states have more than one realis*er* is widely shared among those who debate about realisation, and so it is the derived idea that the realised properties or states are *not* identical to their realisers.

Put in terms of necessary and sufficient conditions, we can say that, in the identity sense of realisation, the realiser is necessary and sufficient for the thing it realises. But in the standard sense of realisation, as Robert Wilson and Carl Craver (2006) point out, having the realis*er* property or state is sufficient "but not necessary" for having the realis*ed* property or state (see p. 93). As they note, "[t]o accommodate the possibility of multiple realization, both the metaphysician and scientist will want to allow that O's having [the realiser property or state] is unnecessary for its having [the realised property or state]" (2006, p. 93)[10]. So, in genuine realisation relations according to the standard sense, the realis*er* is (constitutively) sufficient (and explanatory) but not necessary for the realis*ed* property or state.

Now, the question to be addressed in this subsection is whether diseases can be satisfactorily explained as being realised—in the standard sense—by specific destructive, pathological processes. To respond, I will consider first a paradigmatic example of a disease,

[10] In fact, focusing on the philosophy of mind, Robert Wilson (2001) explains that, as the idea that mental states are multiply realised in physical states "rather than strictly identical to those states, the claim that physical states were metaphysically necessary and sufficient for particular mental states, appropriate when considering an identity theory, was weakened to one of sufficiency only" (p. 4).

i.e., ischemic heart disease (also called "coronary heart disease" or "coronary artery disease"). The *Harrison's Principles of Internal Medicine,* a prestigious medical textbook, states that

> *ischemic heart disease* (IHD) is a condition in which there is an inadequate supply of blood and oxygen to a portion of the myocardium […] The most common cause of myocardial ischemia is atherosclerotic disease (Antman & Loscalzo, 2022; emphasis in the original).

Based on this passage, we can note that the specific pathological, destructive process associated with the disease is an inadequate supply of blood and oxygen to a portion of the myocardium—a muscular layer of the heart. Further, since, as the quotation states, one of the most common causes of ischemic heart disease is atherosclerosis—which, just to recall, is the accumulation of fat plaques in the arteries—, then atherosclerosis and ischemic heart disease partially share aetiology. Among the causes of atherosclerosis are smoking, high blood pressure, high cholesterol, and others (NHS, 2024b). On the other hand, characteristic symptoms of the disease include chest pain, shortness of breath, and others.

The question here is whether such an inadequate supply—being the relevant destructive process—realises ischemic heart disease in the standard sense. For this to be the case, the inadequate supply of blood and oxygen to the myocardium should be constitutively sufficient, but *not* necessary, for ischemic heart disease, and the former should explain the latter. To examine whether this is the case, it is important to remark first that "[*i*]*schemia* is defined as inadequate blood supply (circulation) to a local area due to blockage of the blood vessels supplying the area" (Institute of Medicine, 2010; my emphasis). So, ischemic heart

disease is, thus, ischemia occurring in a portion of the myocardium. In light of the definition of *ischemia* and the description of ischemic heart disease above, then, ischemic heart disease can, in fact, be understood as *an inadequate supply of blood and oxygen to a portion of the myocardium*.

According to this understanding, then, if patients have ischemic heart disease, they have an inadequate supply of blood and oxygen to the myocardium. And, as the disease is currently understood, it follows that patients who do *not* have such an inadequate supply do not have ischemic heart disease. Then, the relevant, inadequate supply is necessary for the disease. So, the purported realiser, i.e., an inadequate supply of blood and oxygen to the myocardium, is necessary for the purported realis*ed* state, i.e., ischemic heart disease. However, as I mentioned, in genuine realisation relations, the realiser is (constitutively) sufficient (and explanatory) but *not* necessary for the thing it realises, and, then, the relation between an inadequate supply of blood and oxygen to the myocardium and ischemic heart disease is *not* a genuine realisation relation. Thus, ischemic heart disease, a disease having aetiology, pathology, and symptoms, is not realised by its specific pathological, destructive process—in the standard sense.

It is important to note that, since ischemic heart disease is defined in terms of its pathological process, then such a process is necessary for the disease for, thus defined, no patient can have the latter without having an inadequate supply of blood and oxygen to the myocardium. Notably, current medical sources define many diseases in terms of the relevant destructive processes and, in these cases, then, such destructive processes are necessary for the diseases they define. In all these cases, the (purported) realiser, i.e., the relevant destructive process (pathology), is necessary for the (purported) realised state, i.e., the

disease. But, in genuine realisation relations, the realiser is (constitutively) sufficient (and explanatory) for the thing it realises, but not necessary, so, in all these cases, the relation between the relevant pathology and the diseases simply does not fit a realisation relation in the standard sense.

Just to mention some examples of this sort that have been addressed in this chapter, we have gastritis, diabetes, malaria, and atherosclerosis. Since "[g]astritis is inflammation of the gastric mucosa" (Vakil, 2024), then patients *without* inflammation of the gastric mucosa do not have gastritis, so the latter is necessary for the disease. A similar reasoning applies to chronic, elevated blood glucose levels caused by insulin defects and diabetes; with infection with *Plasmodium* and malaria; and with the building of plaques inside arteries and atherosclerosis. Since, in these cases, the diseases are defined in terms of the respective destructive processes, then the latter are necessary for the diseases. So, diabetes, malaria, and atherosclerosis, in addition to gastritis, do not have a genuine realisation relation with their related destructive processes and, thus, they are not realised—in the standard sense—by them.

Consequently, an analysis according to which diseases are realised—in the standard sense—in biological destructive processes does not provide a general account of disease classification. In fact, in the cases of ischemic heart disease, gastritis, diabetes, malaria, atherosclerosis, and also in all other cases of diseases defined in terms of the relevant pathological, destructive processes, the relevant pathological processes do *not* realise the diseases. All these diseases are, then, not adequately explained if they are accounted for as being thus realised.

Further, as I elaborated in the previous section, an understanding of realisation as identity does not provide a general account of disease classification either, for although certain diseases such as gastritis can be understood to be identical to their respective pathology, it is not clear that other diseases such as Sydenham's chorea, Parkinson's disease, and Cushing's syndrome, which have a well-identified aetiology, pathology, and symptoms, are understood by current medicine to be identical to the relevant destructive process. As I also pointed out, these diseases are not accounted for by the minimal interpretation of the medical model either. Therefore, the realisation analysis, in either the identity or the standard sense of realisation, is not a general account of disease classification.

In the following section, I will survey the final analysis on disease classification, which, as it will become clear, accommodates all cases of diseases so far discussed.

4. The constitutive analysis

A further alternative to the aetiological analysis is the "constitutive analysis", proposed originally by Jonathan Fuller (2017). Drawing on Fuller's account, I will argue in this section that the constitutive analysis is an accurate account of current disease classification, and that the constitutive model resists the problems entailed by the aetiological approach. I will also argue that the constitutive analysis provides a more general explanation than the realisation analysis. So, current disease classification is best explained by the constitutive analysis. Because of that, I will address in the following section the issue of how to understand the aspiration for a change in psychiatric classification—from a symptomatic one to a biomedical one—in light of this analysis.

To begin with, the constitutive analysis is based on Fuller's observation that a "typical contemporary pattern" in disease classification is that "chronic and noncommunicable conditions are primarily classified according to what the condition is […] and not based on a specific etiologic agent" (2017, p. 11). In this passage, Fuller attempts to point out a difference between the way the *aetiological model* classifies diseases and the way *current medicine* classifies chronic and non-communicable diseases (CNCDs) such as diabetes, gastritis and cancers. After presenting some examples provided by Fuller to illustrate his claim and addressing some aspects of his view, I will argue that his formulation of the difference between the aetiological classification and the CNCDs classification is defective. However, there is, in fact, one such difference, as I will show, and it is crucial in understanding the constitutive analysis. Later, I will elaborate that the constitutive analysis accurately describes the current CNCDs classification, and that other sorts of diseases such as infectious diseases are best understood to be classified in the same way—i.e., the constitutive.

So, let us look now at the examples provided by Fuller to illustrate his claim. The author notes that,

> [f]or instance, chronic obstructive pulmonary disease (COPD) is often defined as "a disease state characterized by airflow limitation that is not fully reversible" […] Osteoporosis is defined as "a bone density that falls 2.5 standard deviations (SD) below the mean for young healthy adults of the same sex" […] Meanwhile heart failure is defined […] as "a complex clinical syndrome" consisting characteristically of dyspnea, fatigue, edema and rales […] Turning to the realm of cancers, "The World Health Organization (WHO) defines lung cancer as tumors arising from the respiratory

> epithelium (bronchi, bronchioles, and alveoli)" […] myocardial infarction is defined as "myocardial necrosis in a clinical setting consistent with acute myocardial ischemia" […] Finally, "[a] stroke, or cerebrovascular accident, is defined as an abrupt onset of a neurologic deficit that is attributable to a focal vascular cause" […] (Fuller, 2017, p. 11).

In all these cases, Fuller claims, "diseases are classified according to their constitution - what the disease is" (2017, p. 11), and not based on their causes. Fuller calls this pattern the "constitutive disease model", and he claims that, "[w]e can […] represent the constitutive model as follows: *a* is a case of disease *D* if and only if *a* is a *C*" (2017, p. 11). To illustrate this, Fuller considers osteoporosis and claims that "a bodily state (*a*) is a case of osteoporosis (*D*) if and only if *a* is a bone density that falls 2.5 standard deviations below the demographic mean (*C*)" (2017, p. 11). The author further claims that, in the constitutive model, "*C* need not refer to a specific entity (it might, for instance, refer to a disjunction of factors), but – whatever *C* includes – *D* only ever occurs when *C* occurs" (Fuller, 2017, p. 11).

I will expand on all these claims shortly, but let us first evaluate Fuller's formulation of the difference between the aetiological classification and the current CNCDs classification. According to Fuller, a disease is classified in the *aetiological model* in terms of its aetiological agent, and a CNCD is classified by *current medicine* according to what the disease *is*. This formulation of the difference is, however, defective. To see this, consider that, if we classify tuberculosis *aetiologically*, we can still say what the disease *is*: tuberculosis *is* the disease caused by an *M. Tuberculosis* infection. So, if the difference between the aetiological classification and the current CNCDs classification is thus

formulated, there is no sharp distinction: *both* of them actually classify based on what the diseases *are*.

Another way Fuller distinguishes the two ways of classifying is by stating that the current CNCDs classification is based on the *constitution* of diseases, as opposed to the aetiological model, which classifies based on causes. As I quoted above, Fuller claims that "[chronic and noncommunicable] diseases are classified according to their constitution - what the disease is" (2017, p. 11). But the notion of the *constitution of a disease* is explained by Fuller as *what the disease is*, as it can be seen in the passage just quoted. Then, the problem with Fuller's formulation of the difference between the two ways of classifying—i.e., that, as he formulates it, there is actually no difference—remains.

However, the list of examples provided by Fuller—quoted above—illustrates that there is, in fact, a crucial difference between the aetiological classification and the current CNCDs classification: that the latter does *not* cite causes of diseases in the definitions. So, the difference can initially be thus understood: the aetiological model classifies diseases based on their causes—and, thus, in this model, specific diseases are defined just as *effects* of their causes—, whereas current CNCDs classification does *not* classify based on causes—and CNCDs are not defined as effects of whatever causes they have. In sum, CNCDs are not classified based on causes at present.

Before further elaborating on the constitutive analysis, it is important to note that the specific way CNCDs are classified should be further qualified. To see why, it should be emphasised that the distinctive feature of CNCDs classification as opposed to the aetiological classification is that the former *gets rid of causes* for classificatory purposes. But, as I am about to elaborate, this should not only include the causes of diseases. For the CNCDs

classification to be understood as satisfactory, it should avoid classifying diseases based on what *they cause* as well—that is, it should avoid classifying diseases based on their effects. To see why, let us suppose that we took it, simply, that CNCDs classification does not classify based on causes. Thus understood, then, the specific way of classifying which is currently applied to CNCDs could, as a matter of possibility, be employed to classify diseases not based on their causes, but based on their (alleged) effects.

For instance, diabetes *could* be defined for classificatory purposes as, say, the disease that *causes* intense thirst, constant need to urinate and tiredness (its characteristic symptoms). In this definition, the disease is understood as a *cause* of certain effects—rather than as the effect of certain causes. The problem is that this allows misclassification: diabetes insipidus, a disease involving a kidney abnormality which is unrelated to diabetes, causes intense thirst, constant need to urinate and tiredness. So, cases of diabetes insipidus would count as diabetes if the latter is defined as the disease that causes those symptoms. Moreover, the problem does not only concern diabetes. Such a problem is a threat in all cases in which a set of symptoms is caused by different, underlying biological factors. If a disease D1 is defined as the disease that causes set of symptoms S, but D2 also causes S, then cases of D2 would be misclassified as cases of D1.

So, for the current way CNCDs are classified to be understood as satisfactory—avoiding the misclassification problem just pointed out—it should be understood as getting rid of causes at all, so that it does not classify based on the causes of diseases, but neither based on what the diseases *cause*. Then, more precisely, CNCDs are currently classified based on features which are neither the causes nor the effects of diseases.

Here, we should return to Fuller's claim concerning the constitutive analysis. As it was noted, the author represents the constitutive model as "*a* is a case of disease *D* if and only if *a* is a *C*" (2017, p. 11). Then, as conceived of by Fuller, the constitutive model, based on the way CNCDs are currently classified, states that diseases are classified based on features which are necessary and sufficient[11] (*C*) for a bodily state (*a*) to be a case of the disease (*D*). Then, in connection with my previous considerations regarding the specific ways CNCDs are currently classified, I characterise the constitutive model as follows:

> CONSTITUTIVE MODEL: defines diseases for classificatory purposes in terms of features which are neither their causes nor their effects, which are necessary and sufficient for a bodily state to be an instance of the disease.

And, as it was also mentioned, in the constitutive model, those necessary and sufficient conditions are not required to be just one single factor, but they can be a disjunction of several factors—or a conjunction of them, as I will illustrate with an example shortly.

I believe that the constitutive analysis as I characterise it accurately describes the current classification of CNCDs, and I will provide examples to illustrate this in a moment. As will elaborate later, moreover, infectious diseases—and not only CNCDs—can be accommodated by the constitutive analysis as well.

Regarding CNCDs, consider, e.g., rheumatoid arthritis. The most recent version of the ICD states that

[11] Note that this necessary and sufficient conditions requirement is represented by the biconditional in Fuller's characterisation of the constitutive analysis.

> [r]heumatoid arthritis (RA) is persistent and/or erosive disease that is defined as the confirmed presence of synovitis in at least 1 joint, absence of an alternative diagnosis that better explains the synovitis, and achievement of a total score of 6 or greater (of a possible 10) from the individual scores in 4 domains: number and site of involved joints, serologic abnormality, elevated acute-phase response, and symptom duration (WHO, 2022b).

As we can note, only factors which are not causes nor effects of RA and which make a bodily state a case of RA are cited in this passage. Specifically, the features mentioned are (i) confirmed presence of synovitis—i.e., inflammation of the membrane which lines some of the joints—in at least 1 joint; (ii) absence of an alternative diagnosis which better explains the synovitis; *and* (iii) individual scores of 6 or greater in four evaluated domains. Given that, as the ICD states, RA "is defined" by these three features, we can understand them as necessary and jointly sufficient for the disease: as defined by the ICD, no patient can have RA without having all the three features and, by having the three of them, patients do have RA. Then, the ICD defines RA in terms of factors (i), (ii) and (iii), which are, jointly, necessary and sufficient for the disease. RA is, thus, classified *constitutively*: it is defined for classificatory purposes in terms of certain features which are neither its causes nor its effects, which are necessary and sufficient for it.

However, the features that define a specific disease can also be single factors in a constitutive classification. For instance, as mentioned earlier, gastritis is defined as "inflammation of the gastric mucosa" (Vakil, 2024), so it is defined by a feature that is not its cause nor its effect. Moreover, as it is defined, no patient can have gastritis without having inflammation of the gastric mucosa and, just by having the latter, patients have gastritis. So,

inflammation of the gastric mucosa is necessary and sufficient for gastritis, and the latter is classified constitutively by current medicine.

RA, gastritis, and the examples posed by Fuller—i.e., chronic obstructive pulmonary disease (COPD), osteoporosis, lung cancer, myocardial infarction, and stroke—are only a few examples of diseases classified constitutively, but the list goes on and on[12].

As a defence of the constitutive analysis, I will now elaborate that the constitutive model does not entail the three problems of the aetiological model which I addressed in §2.1. In so doing, it will become clear that the list of diseases accommodated by a constitutive approach includes infectious diseases. As a part of my defence of the constitutive analysis, I will later show, in addition, that it is a more general analysis than the realisation analysis.

4.1 Aetiological classification vs constitutive classification

I will address the three problems of the aetiological classification I pointed out in §2.1, one by one. To recall, the first problem is that the aetiological classification is in tension with the present understanding of disease causation. Currently, indeed, many diseases are understood to have a variety of *non*-necessary causes at different levels of explanation, and causal relations between those causes and the diseases are largely explained based on statistical methods. So, as I pointed out in §2.1, it is hard to see how an aetiological approach to classification, requiring single, necessary defining causes, plays any role in classifying many diseases considered to be caused by a variety of non-necessary factors.

[12] Examples that I will provide through this section are CNCDs such as Sydenham's chorea, Parkinson's disease, Cushing's syndrome, diabetes, ischemic heart disease, atherosclerosis, as well as some infectious diseases such as malaria, cholera, and pneumonia. All of these are just a few examples of diseases currently classified constitutively in medicine.

However, in the constitutive approach, the causes of diseases are *not* relevant for classificatory purposes. Then, in the constitutive model, specific diseases need not be defined in terms of a *single*, necessary and universal cause to classify them, as they do in the aetiological model—nor do they need to be defined in terms of any other definite number of causes. Therefore, in contrast with the aetiological model, the constitutive model has no trouble in classifying diseases thought to be caused by several, non-necessary causes, so the latter is in *no* tension with the present understanding of disease causation. The constitutive model, then, does not entail the first problem of the aetiological classification pointed out in §2.1.

In order to show now that the constitutive model does not imply the second and third problems posed by the aetiological classification either, I should address the third problem first. As I elaborated in §2.1, such a problem is that the aetiological model allows misclassification of diseases. As I elaborated, (opportunistic) tuberculosis caused by a weakened immune system in patients with AIDS *could* be (mis)classified as the disease caused by HIV infection. That is because, assuming that diseases have only one necessary and universal cause, the aetiological, monocausal classification does not impose a constraint on which cause is to be employed to classify a disease. So, in the case just mentioned, the aetiological, monocausal classification allows an HIV infection, being a distal cause of tuberculosis, to be employed to define tuberculosis. Then, if the purpose of a model of disease classification is to classify diseases satisfactorily, the aetiological classification, with its monocausal tenet, simply does not accomplish its purpose, and it fails to be an adequate model of disease classification.

But, as Fuller observes (2017, p.13), if instead of defining tuberculosis monocausally it is defined constitutively, the misclassification problem does not arise. To see this, consider that, since the causes of the disease are not employed to classify diseases in a constitutive approach, trivially, tuberculosis could not be defined in terms of any of its causes, so it could *not* be defined as the disease caused by HIV infection—nor any other infection whatsoever—, avoiding the misclassification problem. Understood constitutively, tuberculosis is not defined in terms neither of its causes nor its effects and, for a bodily state to be a case of tuberculosis, it must be an *M. Tuberculosis infection* (or, more precisely an infection with some bacteria from the MTBC). The constitutive model, then, simply does not allow tuberculosis to be the disease caused by HIV—nor by any other factor.

Of course, the misclassification problem entailed by the aetiological classification could not only arise in the case of tuberculosis and AIDS, but also in any other case of opportunistic infections in which one of them distally causes the other by weakening the immune system. In any such case, the aetiological model allows the opportunistic infectious disease to be defined as the disease caused by the pathogen causing the non-opportunistic disease, leading to misclassification. But causes are not relevant for classification in the constitutive model and, thus, misclassifying opportunistic and non-opportunistic diseases given that they are defined in terms of their causes simply does not occur in the constitutive model. Then, a constitutive understanding of infectious diseases does not imply the third problem of the aetiological classification—i.e., the misclassification problem.

I will elaborate in the following subsection on further, important issues concerning the constitutive model and infectious diseases but, for now, we should note that the constitutive model does not entail the second problem of the aetiological classification either.

Such a problem states that the paradigmatic example of a disease classified aetiologically under the monocausal tenet, i.e., tuberculosis, is no longer so classified—it is, rather, classified by, e.g., the ICD in terms of four individually non-necessary causes. So, an aetiological classification does not accommodate this, once paradigmatic case. However, the constitutive model simply can accommodate tuberculosis: for such a model, the disease is classified as an infection with some bacteria from MBTC. Thus, the constitutive approach does not entail the second problem of the aetiological classification I pointed out in §2.1 either.

Then, the constitutive model does not entail any of the three problems posed by an aetiological classification. There are, however, some further issues to be discussed concerning infectious diseases and the constitutive model which I will discuss in the following subsection. Later, I will argue that the constitutive analysis is more general than the realisation analysis.

4.2 Infectious diseases

So far, the upshot of previous considerations is that *if* infectious diseases are understood constitutively, no misclassification is allowed. I will elaborate now that some infectious diseases—including tuberculosis—are *in fact* classified constitutively in current medicine by some sources but that, nevertheless, there is another group of infectious diseases which appear to be classified aetiologically at present. The arising question is how to account for the current classification of infectious diseases, which appears to be based on two models—the constitutive and the aetiological. Later, in this subsection, it will become clear that the best way of accounting for this state is to understand all infectious *constitutively*, even though

some of them have an apparent aetiological definition. As I will argue, this permits us to see the current classification of infectious diseases as based on a single, satisfactory model, instead of on two incompatible models, one of them being defective—the aetiological.

So, some infectious diseases, including tuberculosis, are *in fact* understood constitutively in current medicine by some sources. For instance, the MSD Manuals state that "[t]uberculosis is a chronic, progressive mycobacterial infection" (Nardell, 2022). Here, the disease is *not* defined in terms of its causes—nor of its effects—and, thus defined, patients without a mycobacterial infection (specifically, an infection with some bacteria from the MBTC) cannot have tuberculosis, and just by having one such infection, patients have the disease. Thus, under the definition above, a mycobacterial infection is necessary and sufficient for a bodily state to be a case of tuberculosis, and the latter is understood constitutively by the MSD Manuals.

Two other examples of infectious diseases understood constitutively by current medicine are malaria and cholera. I mentioned in §1 that the former is defined as "infection with *Plasmodium* species" (Marie & Petri, 2022). On the other hand, as the MSD manual states, "[c]holera is an acute infection of the small bowel by the gram-negative bacterium *Vibrio cholerae*" (Bush & Vazquez-Pertejo, 2022). So, these diseases are not classified based on what causes them—nor based on their effects—, and the features in terms of which they are defined are necessary and sufficient for them: in the case of malaria, as it is defined, no patient can have the disease without a *Plasmodium* infection and, by having the latter, they have malaria, whereas, in the case of cholera, no patient can have the disease without a *Vibrio cholerae* infection in the small bowel, and just by having the latter, they have cholera. So, current medicine has a constitutive understanding of some infectious diseases.

However, other infectious diseases appear to be classified aetiologically *at present*. Just as an example, mumps is defined by the ICD as "[a] disease caused by an infection with mumps virus" (WHO, 2022c). So, the disease is understood to be the *effect* of an infection with the mumps virus, based on which it is classified.

So, on the one hand, some infectious diseases are understood constitutively at present—e.g., tuberculosis, malaria, cholera—, and, on the other hand, others seem to be understood aetiologically—e.g., mumps. Given that, as I elaborated in §2.1, the aetiological model is defective—among other things because it allows the misclassification of diseases—, we might wonder how to understand the current situation of infectious disease classification. Let us look at two possible interpretations of it.

One interpretation is that current medicine employs two different models for classifying infectious diseases, i.e., the aetiological and the constitutive, which are incompatible between them: one classifies based on causes and the other does not. Further, in this interpretation, one of the models employed by medicine to classify infectious diseases is defective, i.e., the aetiological—it allows misclassification of diseases.

But a second interpretation of the current state of infectious disease classification is that, even though some infectious diseases appear to be defined aetiologically, they are to be understood constitutively. As Fuller suggests, aetiological descriptions of infectious diseases by current medicine can be seen as "rough characterizations rather than as formal definitions" (2017, p. 14). If we understand current infectious disease classification this way, we can view medicine as employing a single model for classifying infectious diseases, i.e., the constitutive, which *satisfactorily* accomplishes the purpose of adequately classifying those

diseases—for it does not imply the problem of misclassification posed by the aetiological model.

Clearly, then, if a general, *satisfactory* model of infectious disease classification is to be identified, we should opt for the second interpretation. This allows us to view current medicine as applying a single, satisfactory model of classification to infectious diseases, as opposed to viewing it as applying two distinct, incompatible models, with one of them being defective. So, those infectious diseases which are apparently defined aetiologically at present are best understood constitutively. Then, for instance, instead of taking it that mumps is the "disease caused by an infection with mumps virus" (WHO, 2022c), an alternative, constitutive definition could be that mumps is an infection with the mumps virus—or an infection with the virus *and* (some or all) characteristic symptoms (e.g., inflammation of the salivary glands).

Now, I elaborated in §4 that CNCDs are currently classified by the constitutive model. Later, in §4.1, I showed that the constitutive model does not entail the three problems of the aetiological model. Further, in this section, I argued that infectious diseases are best understood constitutively. So, the constitutive model of classification is best understood to be a model of classification for both infectious diseases and CNCDs. The upshot is, then, that an understanding of diseases—infectious or not—as being classified constitutively allows us to view current disease classification as based on a satisfactory model which recognises the contemporary understanding of disease causation, that accommodates all infectious diseases—including those that resist a monocausal definition at present—and which does not entail misclassification problems. Then, as a classification model, the constitutive model is

better than the aetiological. In the following subsection, I will argue that the constitutive analysis is better than the realisation analysis, for the former is more general than the latter.

4.3 The realisation analysis vs the constitutive analysis

In §3.1, I pointed out that the realisation analysis posits that diseases are realised in destructive (pathological) processes. In the identity sense of realisation, this implies that, according to this analysis, diseases are identical to their specific, pathological destructive processes. As I pointed out, this analysis seems to account for some cases of diseases such as gastritis correctly. In fact, as it is currently understood, gastritis appears to be identical to inflammation of the gastric mucosa—its specific, destructive process. In cases like this, the realisation analysis and the constitutive analysis are compatible. After all, if gastritis was identical to inflammation of the gastric mucosa, then having inflammation of the gastric mucosa would be necessary and sufficient for a bodily state to be a case of gastritis.

But, as I also pointed out, there are other diseases which are not clearly seen by medicine as identical to their related destructive process, such as Sydenham's chorea, Cushing's syndrome and Parkinson's disease. Cushing's syndrome is simply not seen as the same thing as hypercortisolism, and it is not clear that Sydenham's chorea and Parkinson's disease are viewed as identical to their respective pathological destructive processes—i.e., disruptions to CBGTC circuits and loss of dopaminergic neurons.

But all the diseases mentioned can be accommodated by a constitutive understanding. Recall that Sydhenam's chorea is "characterized by sudden onset chorea" with further symptoms being "slurring of speech and difficulty maintaining steady hand grip […] [a]nxiety, sadness, inattention, and obsessive compulsive thoughts and behaviors" (NORD,

2024). Being a form of chorea, Sydenham's chorea can be distinguished from the other forms because it develops after a streptococcal infection. So, those patients who do not have chorea and (some or all of) the other symptoms *specifically* following a streptococcal infection do not have Sydenham's chorea, and just by having the chorea and the other symptoms specifically following a streptococcal infection, patients have Sydenham's chorea. So, Sydhenam's chorea can be understood constitutively: it is not classified based on its causes nor its effects, and for a bodily state to be a case of the disease, it must involve chorea and other, characteristic symptoms specifically following a streptococcal infection.

On the other hand, recall that Cushing's syndrome is understood as "a constellation of clinical abnormalities caused by chronic high blood levels of cortisol" (Grossman, 2024) so, thus understood, those who do not have the clinical abnormalities—i.e., symptoms such as moon face and truncal obesity—*specifically* caused by high levels of corticosteroid hormones (hypercortisolism) cannot have the disease and, just by having the symptoms caused specifically by hypercortisolism, patients have Cushing's syndrome. Here, we should also note that the disease is not defined in terms of neither its causes nor its effects. In fact, although, in Cushing's syndrome, the relevant symptoms need to be *caused* by hypercortisolism, the disease is not defined as *the disease that causes* such and such symptoms". Then, Cushing's syndrome is understood constitutively by current medicine.

As to Parkinson's disease, we should note that it is the most common form of Parkinsonism, which is defined as "a clinical syndrome characterised by four cardinal features: rest tremor, muscular rigidity, akinesia [inability to voluntarily move the muscles] or bradykinesia [slow movement]" (WHO, 2024 G). Further, as I mentioned earlier, "the key pathology [of Parkinson's disease] is the loss of dopaminergic neurons that lead to the

symptoms" (Zafar & Yaddanapudi, 2023), so, considering that the disease is a form of Parkinsonism, patients who do not have parkinsonism (that is, characteristic symptoms) caused specifically by loss of dopaminergic neurons do not have Parkinson's disease and, by having parkinsonism caused specifically by loss of dopaminergic neurons, then patients have the disease. So, both Parkinsonism and loss of dopaminergic neurons are necessary and jointly sufficient for Parkinson's disease, and the disease can be accommodated by the constitutive analysis.

Thus, the constitutive analysis accommodates the cases of Sydenham's chorea, Cushing's syndrome, and Parkinson's disease, which are not adequately accounted for by the realisation analysis. Moreover, those diseases that are successfully accommodated by the realisation analysis in the identity sense are *ipso facto* accommodated by the constitutive analysis: for all the diseases—such as gastritis—which seem to be understood as identical to their specific pathology, the latter can be seen as necessary and sufficient for a bodily state to be an instance of the disease. Then, the constitutive analysis accommodates both the cases covered and non-covered by the realisation analysis in the identity sense of realisation, and the constitutive analysis is thus more general.

I pointed out in §3.2 that the realisation analysis in the *standard* sense does not account for ischemic heart disease, gastritis, diabetes, malaria and atherosclerosis, and also for no other disease which is currently defined in terms of its specific pathological, destructive process. In all these cases, the pathology of the disease (that is, the purported realiser) is necessary for the disease (the purported realised state), thus not having a genuine realisation relation—for such a relation is characterised by the realiser being (constitutively) sufficient (and explanatory) but *not* necessary for the realised property or state.

Based on the current medical understanding, though, ischemic heart disease can be understood constitutively as an inadequate supply of blood and oxygen to a portion of the myocardium; gastritis as inflammation of the lining of the stomach; diabetes as chronically elevated blood glucose levels caused by insulin deficiencies; malaria as infection with *Plasmodium*; and atherosclerosis as the formation of plaque inside the arteries. In all these cases, the features in terms of which the diseases are defined are neither their causes nor their effects, and such features are necessary and sufficient for the diseases. For instance, no patient can have ischemic heart disease if they do not have an inadequate supply of blood and oxygen to a portion of the myocardium, so it is necessary for the disease; and, just by having such an inadequate supply, patients have the disease, so it is sufficient for ischemic heart disease. A similar reasoning applies to the other examples.

Thus, the constitutive analysis accommodates all these cases which are not adequately accounted for by the realisation analysis in the standard sense of realisation. I mention that one difficulty of the realisation analysis in the standard sense is that, in all cases of diseases which are defined solely in terms of their specific pathological, destructive processes, there is no genuine realisation relation between the pathological process and the disease, for, in all these cases, the pathological process (that is, the purported realiser) is necessary for the diseases (that is, the purported realised state)—which simply does not fit a realisation relation.

But the constitutive analysis can accommodate all these diseases as well. Since they are defined solely in terms of their pathology by current medicine, then the relevant pathologies can be seen as necessary and sufficient for a bodily state to be a case of the

corresponding disease. Then, the constitutive analysis is more general than the realisation analysis in the standard sense as well.

So, the constitutive approach to classification does not entail the three problems posed by the aetiological approach, and the constitutive analysis is more general than the realisation analysis. Therefore, current disease classification is best understood constitutively, that is, as classifying specific diseases based on features which are neither their causes nor their effects, and which are necessary and sufficient for a bodily state to be a case of the disease.

A brief, final issue to be addressed is that some definitions of specific diseases could be a matter of dispute. For instance, the *Harrison's Principles of Internal Medicine* states that "[p]neumonia is an infection of the pulmonary parenchyma [the part of the lungs involved in adequate gas exchange]" (Mandell & Niederman, 2022), but another source states that "[p]neumonia is an umbrella term for a group of syndromes caused by a variety of organisms that result in infection of the lung parenchyma" (Jain *et al*, 2023). So, in the first definition, pneumonia can be understood as an infection in the lung parenchyma in a way that the latter is necessary and sufficient for pneumonia. But, in the second definition, an infection of the lung parenchyma is not by itself necessary and sufficient for the disease. Rather, both such an infection and characteristic symptoms (involved by the syndromes) appear to be necessary and jointly sufficient for pneumonia.

My point, however, is not to accurately define specific diseases, but to show that current classification is best understood constitutively. In fact, regardless of whether pneumonia is classified based on the relevant infection, or based on the relevant infection and symptoms, it is, nonetheless, constitutively classified, for features which are necessary and sufficient for it are provided which are neither its causes nor its effects. So, disputes

concerning definitions of specific diseases do not undermine the point that the best way to understand disease *classification* is constitutively.

5. A general model of medical classification

Drawing on Fuller's analysis, I argued in the previous section that current *disease* classification is best understood to be constitutive. In this section, it will become clear that classification of other medical conditions and ailments can also be understood constitutively, and this includes the current classification of psychiatric conditions. Then, medical classification in general is best understood to follow a single model, i.e., the constitutive. But I pointed out in the introduction to this chapter that current biological psychiatrists seek a change in psychiatric classification, from the current, purely symptomatic classification, to what they call a biomedical classification, which characterises psychiatric conditions as diseases. This search then seems to presuppose that there are, at least, two distinct ways of classifying in current medicine: (what I call) the symptomatic and the biomedical. Later in this section, I will provide a way of understanding this idea in light of the constitutive analysis, which implies that there is only *one* model for medical classification.

To begin with, let us note that medical conditions other than those considered diseases, e.g., syndromes, can also be understood to be classified constitutively. For instance, the *International Classification of Headache Disorders* (International Headache Society [IHS], 2018) states that migraine without aura is "[r]ecurrent headache disorder manifesting in attacks lasting 4–72 hours" (p. 18), and which fulfils certain other criteria (e.g., having nausea or vomit during headache, and having a unilateral location or pulsating quality—see IHS, 2018, p. 19). So, migraine without aura is neither classified based on its cause nor its

effects. Further, as currently understood, patients without a recurrent headache that has the features characteristic of the disease—e.g., a duration of 4-72 hours and leading to nausea—do not have migraine without aura, and just by having such a headache, patients do have migraine without aura. So, a recurrent headache with the characteristic features mentioned is necessary and sufficient for migraine without aura.

Further, other medical ailments which are not diseases nor syndromes can be understood as being classified constitutively by current medicine. Three examples are miscarriage, coma, and acne. The former is understood as "the loss of a pregnancy during the first 23 weeks" (NHS, 2024c); and "[c]oma is […] rigorously defined as an eyes-closed state of deep unconsciousness with an inappropriate response to stimulation that lasts for a prolonged period of time" (Huff & Tadi, 2023), whereas acne is understood to be "the formation of comedones, papules, pustules, nodules, and/or cysts as a result of obstruction and inflammation of pilosebaceous unit" (Keri, 2024). All these medical ailments are defined by features that are neither their causes nor their effects, and the features in terms of which they are defined can be understood as providing necessary and sufficient conditions for them.

So, diseases, syndromes and other medical ailments can also be understood to be classified constitutively by current medicine. An interesting issue is that this also applies to psychiatric conditions as they are classified at present. For instance, schizophrenia can currently be understood as being the cluster of symptoms established by the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) (e.g., delusions, hallucinations, diminished emotional expression) in the way established by the DSM (e.g., having them for at least six months) (see American Psychiatric Association [APA], 2013, p. 99). Thus understood, patients who do not have the characteristic symptoms in the way indicated by the DSM do

not have schizophrenia, and just by having those symptoms in the corresponding way, patients have the condition. So, having the characteristic symptoms as stated by the DSM is necessary and sufficient for schizophrenia. Then, schizophrenia can be understood to be classified constitutively at present. A similar reasoning, of course, applies to all other psychiatric conditions[13].

Then, the current classification in medicine *in general*, and not only that concerning diseases, can be understood constitutively.

5.1 Psychiatric classification and constitutive classification

As I elaborated in the introductions to this thesis and the current chapter, biological psychiatrists seek a change in psychiatric classification, from the current, symptomatic classification to a classification based on the biomedical model—as they call it. This seems to presuppose that there are, at least, two distinct models of classification in current medicine, i.e., what I call the symptomatic—according to which psychiatric conditions are characterised as syndromes—, and the biomedical—which, if developed, would characterise those conditions as diseases. However, I argued that medical classification in general is best understood to be constitutive, regardless of whether it concerns syndromes or diseases. A

[13] It is important to note that in cases such as migraine disorders and psychiatric conditions, the corresponding classification systems (i.e., the *International Classification of Headache Disorders* and the DSM) do not provide a *definition* of the conditions, but just a set of diagnostic criteria which, if fulfilled, grant a diagnosis. Then, in those classification systems, we lack a definition of migraines and psychiatric conditions independent from the diagnostic criteria. But, in these cases, diagnostic criteria simply *stipulate* that patients who fulfil criteria for a specific condition *do* have the condition—and not just fulfil the criteria for it. It is, in fact, not controversial that patients diagnosed with, say, (the syndrome of) schizophrenia based on current diagnostic criteria do instantiate a case of (the syndrome of) schizophrenia. So, they do have (the syndrome of) schizophrenia. (Although that is, of course, an issue independent of whether (the syndrome of) schizophrenia—or any other psychiatric condition—is a *manifestation* of an underlying neurological disorder, which has elicited controversy on which I will elaborate in Chapter II. At any rate, fulfilling the diagnostic criteria for schizophrenia grants that patients have (the syndrome of) schizophrenia, regardless of whether it is understood to be the manifestation of a specific neurological disorder). So, diagnostic criteria in these classification systems are to be understood as (constitutive) definitions of the conditions.

question that arises here, then, is how to understand biological psychiatrists' aspiration for a change in classification in light of the constitutive analysis, which implies that medical classification is best understood as following a *single* model.

To answer that question, it is worth noting that, underlying biological psychiatrists' quest for a change in psychiatric classification is the idea that (at least some) psychiatric conditions, characterised as *syndromes* at present, will be characterised as *diseases* once relevant knowledge is gathered—an idea on which I will extensively elaborate in Chapter II. So, the classification change sought implies the idea that (at least some) psychiatric conditions will come to be characterised as a type of medical condition distinct from a syndrome, i.e., as diseases. In other words, underlying the quest for a classification change in psychiatry is the aspiration that our understanding of (at least some) psychiatric conditions change, from one that considers those conditions as mere clusters of symptoms, to one that conceives of them as (neuro)biological factors[14] manifested by the symptoms which are the basis for their current classification.

So, I propose that the quest for a change in psychiatric classification be understood in light of the constitutive analysis as a quest for a change in the *characterisation* of psychiatric conditions—from syndromes to diseases—, rather than as a quest for the adoption of a different *model of classification* —i.e, the biomedical—for them. This implies that, if (at least some) psychiatric conditions come to be characterised as diseases, the model of classification applied to them would not change—it would remain the constitutive. However, if (at least some) psychiatric conditions come to be characterised as diseases in the future, the definitions of specific psychiatric conditions should change, from the current constitutive definitions

[14] Here, "biological factor" can be understood as designating either a biological process or a biological state.

citing only symptoms, to constitutive definitions of them citing biological factors known to cause the characteristic symptoms, thus reflecting the characterisation change.

It is important to note that there is currently no evident general pattern concerning the features of specific diseases that are to be cited in their (constitutive) definitions. For instance, many diseases such as gastritis are constitutively defined in terms of their specific pathological, destructive process, but others in terms of both their specific pathological processes *and* symptoms, such as Cushing's syndrome and influenza. Then, if psychiatric conditions come to be understood as diseases, their specific definitions *could* cite either only a biological factor *or* a biological factor and symptoms.

Then, more precisely, the quest for a change in psychiatric classification is best interpreted in light of the constitutive analysis as the aspiration for a change in the characterisation of (at least some) psychiatric conditions from syndromes to diseases, so that they come to be defined constitutively in terms of a biological factor *or* in terms of a biological factor and symptoms.

6. Conclusions

I surveyed three analyses concerning disease classification. All three of them are fundamentally based on description, but they also involve other elements. The aetiological analysis, in fact, attempts to describe the aetiological classification which was once actually employed with infectious diseases, and most of it consists of *explaining* how to best account for the monocausal tenet. The realisation analysis describes the way current medicine views diseases in light of the current understanding of disease causation (in terms of a pathology caused by a variety of causal factors at different levels of explanation which leads to

symptoms), and, beyond mere description, it attempts to elucidate certain metaphysical issues involved by disease classification—whether disease classification implies that diseases are realised in destructive processes. On the other hand, the constitutive analysis is mainly based on the description of the current CNCDs classification, but it exceeds mere description by arguing that an understanding of medical classification in general is best understood as constitutive. If medical classification is universally seen as constitutive, one can view medical classification as based on a single, coherent model that does not entail the problems posed by the aetiological classification and, further, one can explain disease classification with more generality as compared with the realisation analysis. Then, current medical classification is best understood as being constitutive.

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Chapter II

Biological and Integrationist Approaches to Psychiatry

I mentioned in the Introduction to this thesis that I will address, in Chapters III to VI, the main issues of this thesis, which relate to critiques against biological psychiatry posed by advocates of non-biological approaches. However, before doing that, I will focus in this chapter on the preliminary issue of what exactly distinguishes biological from non-biological approaches to psychiatric illness. A widely shared view is, of course, that the difference between them is evident: one attempts to develop a characterisation of psychiatric illness based on biology whereas, the other, a characterisation based on aspects other than the biological. This view does provide a broad summary of the difference between biological and non-biological approaches, but there is a range of nuances worth exploring in order to have a more precise and informative grasp of such a difference. The aim of this chapter is, then, to provide a precise and informative account of the difference between biological and non-biological approaches to psychiatric illness.

In fact, how psychiatric illness should be best approached is a fundamental matter of controversy in psychiatry. Traditionally, a *biological approach* has been implemented in the discipline, focusing on biological factors that could be associated with psychiatric illness. But, more recently, new trends attempt to incorporate psychological, cognitive, and social factors, in addition to biological ones—or a selection of any two or more of them—, into their explanations of psychiatric illness. I subsume these latter trends under the heading "integrationism"[15]—so they implement an *integrationist approach* to psychiatric illness. Biological and integrationist approaches are standardly understood to provide different

[15] A term that I borrow from Dan Stein (2021).

understandings of psychiatric illness, in a way that they are in tension with each other, so, in accounting for how they are different, I will focus in this chapter on elucidating the exact point of *conflict* between them.

Although it is clear that biological approaches aim at a biological characterisation of psychiatric illness and integrationist approaches at an integrationist one, explaining the exact point of conflict between those approaches is not a trivial task. Both of them admit biological, psychological, cognitive, and social factors—or a selection of some of them—in their explanations. For instance, an editorial in *The World Journal of Biological Psychiatry* states that "[i]f we define biological psychiatry by empirical methodology, then we could say that not only biological but also psychosocial parameters are a focus of biological psychiatry" (Hans-Jürgen Möller, 2001, p. 2). Further, by definition, integrationism involves biological factors in its explanations. So, to grasp the precise conflict between these approaches, a careful, detailed examination is required, beyond the mere assertion that one approach aims at a biological characterisation of psychiatric illness and, the other, at an integrationist one.

For reasons that will become apparent in due course, of the various respects in which biological and integrationist approaches differ, I will concentrate only on their respective understandings of psychiatric *classification* and *causation*, and of the *definition* of specific psychiatric conditions. So, in order to elucidate the precise conflict between those approaches, I will draw from available biological accounts a classificatory, a causal, and a definitional commitment that something like a *strong* version of biological psychiatry would endorse and, similarly, from available integrationist accounts, a classificatory, a causal, and a definitional commitment endorsed, in turn, by something like a *strong* version of integrationist psychiatry. It will become clear that the *classificatory* commitments of (strong)

biological and integrationist psychiatry are incompatible with one another, and so too are the causal and definitional commitments. Then, the exact point of conflict between these approaches lies in the incompatible commitments they endorse.

To be sure, although I will draw the *strong* forms of biological and integrationist approaches from available accounts, I do not attribute those forms, exactly as I will present them, to a specific author. The strong forms, however, are instructive of what it is to have a biological or integrationist approach to psychiatric illness. As I will elaborate in due course, specific biological and integrationist accounts endorse, in some or other version, some or all the classificatory, causal, and definitional commitments I will present, and they can be seen to fall under a spectrum with the strong forms of biological and integrationist psychiatry at its poles. In this understanding, as I will explain, specific accounts endorsing the most *biological* commitments in the exact versions I will present will be highly incompatible with accounts endorsing the most *integrationist* commitments in the exact versions I present, and two distinct accounts closer to the middle of the spectrum than to its poles would be compatible to some or other extent. So, the classificatory, causal, and definitional commitments provide a framework for understanding the conflict between biological and integrationist psychiatry's approaches to psychiatric illness.

In §1, I will address the debate motivating the development of integrationist approaches in psychiatry in response to the biological approach. I will also point out that, although it is a standard view that biological and integrationist psychiatry are in tension, usual ways of explaining how they differ from each other render those approaches compatible. However, at least some integrationist accounts have emerged as an approach to psychiatric illness alternative to the biological, not as complementary, so we might want to clarify the

exact point of conflict between them. For that purpose, I will elaborate in §2 and §3 on the biological and integrationist approaches to psychiatric classification and causation, and to the definition of specific psychiatric conditions, and I will present their respective classificatory, causal, and definitional commitments. It will become clear that each commitment of strong biological psychiatry is incompatible with the corresponding commitment of integrationist psychiatry.

Later, in §4, I will explain that the exact point of conflict between those approaches lies in the conflicting commitments they endorse, so that, despite apparent compatibility between those approaches, they provide fundamentally distinct understandings of psychiatric illness. I will then explain and illustrate with examples that specific accounts which do not endorse the strong versions of biological and integrationist psychiatry but variations of them can be seen to fall under a spectrum with the strong versions at its poles. Finally, I will provide brief concluding remarks in §5.

1. The debate

Psychiatrists have sought biological factors that could be associated with psychiatric illness for a long time, and a wide range of these factors have been posited to be associated with the psychiatric conditions classified by the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) and the *International Classification of Diseases* (ICD) over the years. However, an increasing number of criticisms have been raised against the outcomes of this enterprise of psychiatry in the last decades. The core of these criticisms is that, in the critics' view, evidence stemming from psychiatric trials has not established widely reliable associations between specific biological factors and specific psychiatric conditions.

Three main criticisms along these lines are as follows. First, it has been alleged that the outcomes of some studies disconfirm specific hypotheses that a specific factor is associated with a particular psychiatric condition or a psychiatric symptom. As an example, some authors believe that the influential hypothesis that imbalances of serotonin are associated with major depression is disconfirmed (e.g., Moncrieff, 2008, ch. 6; Moncrieff *et al*, 2022), for it has been allegedly observed that there is no difference in serotonin function between groups diagnosed with depression and "normal" groups.

Second, the outcomes thought to confirm some association between a biological factor and a psychiatric condition—or a specific symptom—by biological psychiatrists are gathered from studies that have been deemed by the critics not to be "well-designed studies with large samples and adequate controls, replicated successfully by other groups and not significantly contradicted by other findings" (The British Psychological Society [TBPS], 2018, p, 153). And, third, many critics have noticed that the findings are not specific. Just as an instance, although some genetic findings are well established in psychiatry, there is no single genetic variant or set of genetic variants associated *specifically* with a psychiatric condition[16]. All these criticisms can thus be summarised in Thomas Insel's (2014) claim that

> [s]o far, we don't have rigorously tested, reproducible, clinically actionable bio-markers for any psychiatric disorder. Genetic findings are statistical associations of risk, not diagnostic of disease; neuroimaging findings report mean group changes, not individual differences; and metabolic findings are not specific (p. 395).

[16] Hyman (2010) points out, for instance, that "[m]odern molecular genetic studies (currently most advanced for autism, schizophrenia, and bipolar disorder) indicate that no single genetic variant will prove either necessary or sufficient for any of these diagnoses […] and […] a very large number of genes in different combinations contribute to aggregate population risk of these and other mental disorders" (p. 162).

Based on criticisms of this sort against biological approaches in psychiatry, alternative approaches to psychiatric illness have emerged in the last decades both in psychiatry and in the philosophy of psychiatry. The most influential have been those that incorporate biological, psychological, cognitive, and social aspects, or a selection of any two or more of them, in their accounts of psychiatric illness. Following Dan Stein (2021, ch. 7), I label these alternative approaches as "integrationist", because they attempt to *integrate* any two or all aspects mentioned in their accounts. Examples of integrationist accounts that I deal with in this chapter are the *Research Domain Criteria* project (RDoC) (National Institute of Mental Health [NIMH], 2024a), the *Power Threat Meaning Framework* (PTM) (TBPS, 2018), accounts advocating the biopsychosocial model (e.g., Bolton & Gillet, 2019; Bolton, 2012; McConnell, 2020; Butler, 2019; Roache, 2020a, 2020b; and Kendler & Gyngell, 2020), and others.

Specific details of these accounts will be provided in due course. As a note, integrationist accounts are widely varied, and they endorse fairly different claims about psychiatric illness. However, I will provide in §4 a framework according to which the differing claims they make can be seen to fall under a spectrum so, by subsuming such varied accounts as RDoC and the PTM under the heading "integrationism", I do not mean that they endorse the same view of psychiatric illness.

Now, it is worth noting that there is a wide range of aspects concerning psychiatric illness that biological and integrationist accounts can approach differently. Just as an instance, consider psychiatric *explanation*. Biological approaches, of course, favour explanations of psychiatric illness in terms of biology. For example, Eric Kandel (1998)

proposes a framework for explaining psychiatric illness which is "designed to align current psychiatric thinking and the training of future practitioners with modern biology" (p. 460), and such a framework is based on five principles that "constitute, in simplified form, the current thinking of biologists about the relationship of mind to brain" (Kandel, 1998, p. 460). In Kandel's framework, all five principles concern the way *genetics* is related to the brain and behaviour (see Kandel, 1998, pp. 460-466) and, in light of that, authors such as Dominic Murphy (2006) have pointed out that, "[i]n this intellectual structure, other levels of explanation are […] given only a subsidiary role as characterizations of that which is to be explained in molecular [genetic] terms" (2006, p. 116).

But, on the other hand, integrationist approaches favour explanations of psychiatric illness in terms of all, or any combination of, aspects between the biological, psychological, cognitive, and social. An instance of this is RDoC, which might, at first glance, be thought of by some to be primarily focused on biology for, as its proponents state, "[t]he aim of RDoC is to provide data about basic biological and behavioral processes related to mental health and mental illness" (NIMH, 2024a). However, their proponents also claim that "[t]he aim [of RDoC] is to understand the nature of mental health and illness in terms of varying degrees of dysfunction in fundamental *psychological/biological* systems" (NIMH, 2024a; my emphasis), and the matrix of this research project involves five domains among which we find the *cognitive* and the *social processes*[17] domains. So, RDoC attempts to gather data

[17] To clarify, social processes in the context of RDoC involve *affiliation* and *attachment*, which are, respectively, "engagement in positive social interactions with other individuals" and "selective affiliation as a consequence of the development of a social bond" (NIMH, 2024b). Further, "Affiliation and Attachment are moderated by social information processing (processing of social cues) and social motivation" (NIMH, 2024b). So, although RDoC has a strong biological component, it focuses on social—psychological, and cognitive—aspects as well.

involving biological, psychological, cognitive, and social aspects to explain psychiatric health and illness[18].

We can see that these different approaches to psychiatric explanation involve some tension. Whereas biological approaches such as Kandel's seek to align psychiatry to biology by focusing on the genetic level in order to explain psychiatric illness, RDoC attempts to explain psychiatric illness in broader terms, focusing as well on psychological, cognitive, and social factors. So, one might think that biological and integrationist approaches are somehow incompatible with each other. After all, it is generally accepted that hard biological approaches—such as Kandel's—attempt to characterise psychiatric illness in a way conflicting with how non-biological approaches seek to characterise it. However, although the tension between these approaches seems to be clear, the question as to *what the exact conflict between these approaches is* is not trivial.

In fact, as Rebecca Roache (2020a) notes in describing the biopsychosocial model—another integrationist approach—, the latter "often involves little more than an acknowledgement that biological, psychological, and social factors are all relevant to understanding mental illness" (p. 6). But I mentioned in the introduction of this chapter that, according to an editorial in a biological psychiatry journal, "not only biological but also psychosocial parameters are a focus of biological psychiatry" (Hans-Jürgen Möller, 2001, p. 2). Then, so far, no conflict between biological and integrationist approaches is evident. Moreover, an advocate of the biopsychosocial model claims that "reductive biological

[18] Other examples of accounts attempting to provide integrationist explanations of psychiatric illness are the biopsychosocial model (e.g., Bolton & Gillet, 2019; Roache, 2020; Cecil, 2020); the *Power Threat Meaning Framework* (PTM) (TBPS, 2018); accounts such as Stein's (2021), O'Leary's (2021), Borsboom, Cramer, & Kalis' (2019); and Bolton's (2012), and Kendler & Gyngell's (2020) accounts, which I will address in more detail later in this chapter.

explanation provides tremendous insight" about psychiatric illness (Butler, 2019, p. 50) so, rather than a tension between biological and biopsychosocial approaches, some compatibility between them is apparent.

However, at least some integrationist approaches emerged as a *response* to the dominant biological approach in psychiatry—and not as complementary—so, one might want to clarify what the exact conflict between them is, rather than concluding that, after all, no tension occurs between them. So, in what follows, I aim to elucidate the exact point of conflict between biological and integrationist approaches to psychiatric illness. Some preliminary notes are in place before doing that, though.

I elaborated that *explanation* is one aspect that biological and integrationist psychiatry can approach differently, but various other aspects of psychiatric illness can be differently approached by them as well. Among those aspects, there is *treatment*, *ontology* of psychiatric conditions—whether they are, e.g., biological or psychosocial entities—, *classification*—whether psychiatric conditions are *syndromes* or *diseases*[19]—*causation*, and *definition* of specific psychiatric conditions. However, the latter three aspects, namely, classification, causation, and definition, greatly influence how biological or integrationist psychiatry should best approach the other aspects. For instance, if psychiatric conditions were *classified* as diseases (in the sense mentioned in Chapter I, of a cluster of symptoms with a specified *biological* cause), then it might be difficult to claim that they are merely psychosocial entities, as some integrationists might want to hold, and a characterisation of them as, at least partly, biological entities, would be in place.

[19] I will elaborate soon on this aspect in connection with my considerations concerning classification in Chapter I.

Also, if, for some reason, one believed that biological factors are the only relevant *causal* factors for psychiatric conditions, then psychiatric explanation could be satisfactory by focusing only on biological causal features, something which would not be the case if one believed that, say, cognitive and psychosocial factors are also relevant in the causation of psychiatric conditions. Or if specific psychiatric conditions were *defined* in purely biological terms, then they could hardly be characterised as psychosocial entities and, vice versa, if they were defined in purely psychosocial terms, i.e., based on psychological and behavioural symptoms—as it is, in fact, the case at present—the correctness of a characterisation of them as purely biological entities would not be obvious.

All these are just a few examples showing how specific approaches to classification, causation, and definition influence, to a great extent, specific approaches to, e.g., explanation and ontology of psychiatric conditions. On the other hand, as it will become clear later, classification, causation, and definition are deeply intertwined aspects of psychiatric illness. For these reasons, I will only concentrate on these latter aspects in accounting for the conflict between biological and integrationist approaches to psychiatric illness, an issue on which I will focus in what follows.

2. Biological approaches

The purpose of the current and the following sections is to extensively elaborate on the details of biological and integrationist approaches to psychiatric causation, classification, and definition in order to reach a better grasp of the exact point of conflict between those approaches. In addressing the mentioned aspects of psychiatric illness, I will draw on available biological and integrationist accounts. Nevertheless, those accounts come in a wide

variety, so I should select a few of them to accomplish the purpose of this chapter. In particular, I will only deal with biological approaches that more evidently conflict with integrationist approaches, and vice versa, drawing from each kind of approach a classificatory, a causal, and a definitional commitment. As I mentioned, however, I do not mean that all available biological and integrationist accounts endorse the mentioned commitments, and these can be understood to be held by *strong* forms of biological and integrationist psychiatry.

I will address psychiatric classification, causation, and definition as they are approached by biological psychiatry in that order in this section and, in the following section, the integrationist approach to these aspects.

2.1 Classification

Biological approaches to psychiatric illness generally endorse the idea that "what psychiatrists describe as "mental illnesses" are *diseases*" (Murphy, 2013, p. 967; my emphasis). To recall, as I pointed out in Chapter I, a disease is usually understood to be "a constellation of signs and symptoms for which there is a known physical cause" (Peterson & Keeley, 2015, p. 1). Notably, however, if we commit to this definition of disease, then, there would seem to be, by definition, no diseases among the psychiatric conditions classified by the DSM and ICD for, as I elaborated in §1, all of them are classified as syndromes[20]—that

[20] I elaborated extensively in Chapter I that, in general, medical classification is best understood to be constitutive and that, if one accepts this, *syndromes* and *diseases* are not classified differently—as biological psychiatrists think—, for *both* are classified constitutively. The difference between them, rather, simply lies in how they are *characterised*—which type of medical condition they are. In light of this, expressions in this chapter such as "psychiatric conditions are *classified* as syndromes—or as diseases" should be understood exactly as "psychiatric conditions are *characterised* as syndromes—or as diseases". It will become clear that, in this chapter, this is just a terminological issue.

is, as characteristic clusters of symptoms—, and no "physical" cause is (established to be) *known* for any of them.

So, how should biological psychiatry's idea that "mental illnesses" are diseases be understood? Basically, the idea is that, although psychiatric conditions in the DSM and ICD are classified as syndromes, at least some of them are caused by so far undiscovered, specific biological factors—an issue on which I will extensively elaborate in the following subsection. And, if that is the case, then, at least some psychiatric conditions, which are currently characterised as syndromes, in reality fit, in a way, the notion of a disease: they are clusters of symptoms with by physical causes—specifically, with biological causes, though so far unknown, so they are the sort of entities that would be classified as diseases if the biological causes of the clusters of symptoms were discovered. In other words, the idea is that at least some psychiatric conditions are, in reality, diseases, even though they are not currently so classified because the specific biological factors causing them have not been discovered.

An instance of this line of thought is Nassir Ghaemi's (2012). The author claims that, "in order to experience the advances that medicine achieved" (p. 52) in other areas,

> the first step would be to reclaim the Hippocratic tradition based on taking the concept of disease seriously. We could then hold that mental diseases are those conditions about which we now know (as with neurosyphilis), or will know (as with schizophrenia and manic-depressive illness), the specific biological abnormalities of the body and its organs which cause the illness (p. 52).

We can note in this passage that Ghaemi's idea is that we *will* know "the specific biological abnormalities of the body" that cause schizophrenia and manic-depressive illness—which

are currently characterised as syndromes—and, thus, that the latter are understood to be *diseases* even though there is no widely accepted evidence of specific biological abnormalities causing (the syndromes of) schizophrenia and manic-depressive illness. So, (strong) biological approaches in psychiatry hold a precise commitment that at least some of the entities they deal with—e.g., schizophrenia and manic-depressive illness—are the sort of entities that would be characterised as diseases in medicine if the latter identified their specific biological causes. It should be remarked that the biological approach to classification as I draw it from Ghaemi's view is *not* that, e.g., schizophrenia should be dealt with *as if it was* a disease, and then researchers should *explore* whether there is a biological factor specifically causing the schizophrenia syndrome. Rather, schizophrenia—and other conditions such as manic-depressive disorder—is assumed to *be* a disease, so, in biological psychiatrists' view, researchers *will know* the specific biological abnormality causing it—as in Ghaemi's quotation above.

So, the (strong) biological approach to psychiatric illness endorses a commitment that I call the "classificatory commitment" of biological psychiatry, which is, simply, as follows:

> CLASSIFICATORY COMMITMENT OF BIOLOGICAL PSYCHIATRY:
>
> some psychiatric conditions *are* diseases.

A brief final note is that, as it will become clear in the following subsections, this commitment is deeply intertwined with other two commitments concerning causation and definition endorsed by biological psychiatry.

2.2 Causation

So, biological approaches are committed to the idea that at least some psychiatric conditions are diseases. As I noticed, a disease is a medical condition that involves characteristic symptoms with a physical cause such as a specific biological factor. So, it might be clear now that, given that biological approaches in psychiatry think of psychiatric conditions as diseases, then they commit to the idea that at least some of those conditions—currently characterised as syndromes—are caused by specific biological factors, though the latter are currently widely unknown. In this subsection, I will elaborate on this approach to the causation of psychiatric conditions.

To begin with, it should be remarked that biological approaches in psychiatry have focused on finding biological factors that could be causes of psychiatric conditions. So, it is not uncommon that biological approaches "are committed to specific causal hypotheses in terms of abnormalities in underlying neurobiological systems, which are responsible for the observed patterns of signs and symptoms", as Murphy (2013, p. 967) claims regarding a specific form of biological approach—i.e., the "strong medical model" as I addressed it in Chapter I. Then, the biological approach to psychiatric *causation* is that psychiatric syndromes are caused by underlying brain and genetic abnormalities. In this chapter, however, I will only focus on *brain* abnormalities. To understand why, let us note that *genetic* abnormalities are generally thought of by biological psychiatry to be somewhat distal causes of psychiatric syndromes, in a way that genetic factors interacting with environmental factors to some or other degree lead to a brain abnormality which, in turn, leads to characteristic symptoms.

And, further, it will become clear throughout that integrationists accept the genetic contribution to psychiatric syndromes while rejecting biological psychiatry's take on the brain factors causing the syndromes. Then, biological and integrationist approaches admit genetic causes but diverge in their respective understandings of the *brain* factors causing psychiatric syndromes, as I will extensively explain in due course. Since the purpose of this chapter is to clarify the exact point of conflict between biological and integrationist approaches, I will focus only on biological causes at the level of the brain, for no tension is found between these approaches' understandings of biological causes at the genetic level.

To have a better grasp of biological psychiatry's take on psychiatric causation, I will now address some notions that should be included in our understanding of biological approaches to psychiatric causation, namely, the notions of *site*, *regularity,* and *specificity*. First, we should consider a biological psychiatry textbook stating that, in order to achieve the sort of classification sought by biological psychiatrists—i.e., one that classifies psychiatric conditions as diseases as I addressed it in the Introduction to this thesis—, "[w]e start out by asking not what is happening in the brain, but *where* in the brain is it happening?" (Trimble & George, 2010, p. 332; emphasis in the original). So, in searching for the causes of psychiatric conditions—currently characterised as syndromes—to later classify them as diseases, (strong) biological psychiatrists seek "the site of maximum neuroanatomical and neurophysiological change" (Trimble & George, 2010, p. 332) that causes a psychiatric syndrome.

In other words, biological causes of (at least some) psychiatric conditions have been understood by (strong) biological psychiatrists to be localised at a specific *site* of the brain—which can be a specific anatomical part, a specific neurotransmitter system, a specific

neuronal firing, or a specific region[21]—, though the exact sites associated with psychiatric syndromes have not yet been established. As I will elaborate in the following section, the commitment to a specific brain site by biological approaches is rejected by (strong) integrationists, and this is one of the main sources of conflict between these approaches.

But biological approaches have further presumptions concerning brain causes of psychiatric conditions. In fact, the biological factors sought by biological psychiatrists as candidate causes of psychiatric syndromes have been those that are distinctively shared by patients who have the same syndrome. David Kupfer and Darrel Regier (2011) point out that biological psychiatrists seek to develop a classification of psychiatric conditions in which "disorders are grouped by underlying pathophysiological similarities" (p. 673). According to the sought classification, all patients who share a certain pathophysiological feature such as a brain abnormality known to cause a characteristic cluster of symptoms would have the same psychiatric condition. Then, in biological psychiatry, biological factors causing psychiatric syndromes are expected to be biological *regularities*—that is, biological factors shared among patients.

An important issue is that the notion of a regularity is highly flexible. We might think e.g., that if biological factor *B* was the cause of a given psychiatric syndrome in just two patients, *B* could count as a regularity among those two patients. On the other hand, regularities can have bigger sizes, as in the case of diabetes, which is a common disease whose symptoms are caused by the widely shared biological feature of having constant,

[21] In fact, as it has been claimed regarding the search for causes of psychiatric syndromes, the "[m]ajority of […] efforts have been […] implicated with the hope that [*sic*] single brain *region/circuit* or […] a specific *neurotransmitter* might unravel one-to-one relationship with a disorder" (Venkatasubramanian & Keshavan, 2016, p. 4; my emphasis).

abnormally elevated blood glucose levels. What is noteworthy here is that, when biological psychiatrists search for the cause of a psychiatric syndrome, they do not seek a biological factor, say, *B* occurring only in one patient, such that *B* causes the syndrome in that one patient, nor do they seek something close to that. Rather, as Ahmed Samei Huda (2019) notes, in research trials seeking for causes of psychiatric syndromes,

> [t]he prevalence of a given factor is compared between participants who meet the criteria for a [psychiatric] condition and those who do not. If this factor is found to be much commoner in participants who meet criteria for a condition then this may indicate a causative relationship" (pp. 257-258).

So, biological factors which are widely shared among patients with a psychiatric syndrome are candidate causes of that syndrome. Thus, the biological approach to causation expects that biological factors that cause psychiatric syndromes are *wide biological regularities*. Of course, when a regularity becomes wide or small is a vague issue, but the point here is that biological traits which are shared by a handful of patients with a syndrome are *not* candidate causes of that syndrome for biological approaches to psychiatry. Then, in sum, the (presumed) biological causes of psychiatric syndromes are expected by biological psychiatry to be *wide regularities*.

A final issue is that, in searching for biological causes of psychiatric syndromes, biological psychiatrists have traditionally expected that the biological discoveries that they could make will "guarantee […] our […] nosological categories by ascribing to each clinical entity a biological correlation" (Schneckenburger, 2011, p. 11). In other words, the biological

factors causing psychiatric syndromes are expected by biological psychiatrists to specifically cause one syndrome, and not several of them.

Then, it is not only that biological psychiatrists commit to the idea that some psychiatric syndromes are caused by brain abnormalities, but their understanding of the (presumed) brain causes of those syndromes also requires those causes to occur at a single *site* in the brain—e.g., an anatomical part or a neurotransmitter system—, to be *wide regularities*, and to *specifically* cause a syndrome. In other words, (strong) biological approaches to psychiatry endorse the following

> CAUSAL COMMITMENT OF BIOLOGICAL PSYCHIATRY: some psychiatric syndromes are caused specifically by brain abnormalities in the form of wide regularities that occur at a single site in the brain.

To be noted here is that, although the commitment above focuses on (presumed) biological causes of psychiatric syndromes, biological psychiatry is not *in*compatible with those syndromes being also caused by psychological, cognitive, and/or social factors. I noticed earlier, for instance, that biological approaches explicitly acknowledge that psychosocial factors, in addition to biological factors, can be the focus of biological psychiatry. Further, the notion of a psychiatric syndrome does not entail any conceptual requisite that syndromes are to be caused by a single sort of factors and, for (strong) biological psychiatry's understanding of psychiatric causation, then, it suffices that one among the causes of psychiatric syndromes is a brain factor in the form of a regularity, occurring at a single site of the brain which specifically causes a syndrome.

A further note here is that the biological approach to *classification* is intertwined with the biological approach to *causation*. To see this, consider that, as implausible as it might sound for biological psychiatrists, if it was the case that psychiatric syndromes were *not* caused by biological factors such as brain abnormalities *at all* and, thus, the biological approach to causation—that psychiatric syndromes are caused by specific brain factors as explained above—was false, then, in the absence of a specific brain cause, psychiatric conditions, currently characterised as syndromes, would not fit the notion of a disease and, then, they could not be diseases. Then, the possibility that psychiatric conditions are diseases as stated by biological psychiatry's *classificatory* commitment depends on psychiatric syndromes being caused by specific brain abnormalities[22].

Finally, some accounts such as Murphy's (2009, 2013) and Phillips' (2015), which are, to some or other extent, sympathetic to the idea that psychiatric conditions are diseases, suggest that, at least in some cases, psychiatric syndromes are (partly) caused by cognitive or psychological abnormalities, instead of by brain abnormalities (as those described in the causal commitment above) (see footnote 5 in Chapter I). It is suggested that these cases would count as diseases as well, though rather than involving a brain abnormality causing characteristic symptoms, they would involve a cognitive or psychological abnormality causing the symptoms. In light of the considerations of this chapter, this sort of views could be seen as variations of the causal commitment above, as I will expand in §4.

[22] Although it might be a possibility that if a *genetic*, *wide regularity* was found to cause the symptoms of *specifically* one psychiatric condition, this condition fit the notion of a disease. This possibility, though, seems unlikely in the face of current evidence, for it shows genetic causes to be unspecific, as I pointed out in §1.

2.3 Definition

A matter of interest here is that specific psychiatric conditions are understood to be *defined* by the syndromes they are characterised in terms of (see §6 in Chapter I of this thesis). So, for instance, depression can be defined as the condition that occurs when patients develop characteristic symptoms (as stated by psychiatric diagnostic systems) such as constant low mood and feelings of hopelessness. But advocates of biological approaches to psychiatric illness have criticised this. Paul Meehl (1995), for instance, claims that definitions in terms of syndromes "ignore the fact that entities in the advanced specialties of medicine are not constructed like the DSM categories", and that, in those "advanced specialties", "the syndrome is taken as evidentiary, not as definitory (p. 267)". In Meehls' view, the "definition by syndrome only" in psychiatry "engenders a wrongheaded research approach, unlikely to payoff in the long run" (1995, p. 267).

The general idea here is that, according to biological approaches, the syndromes are manifestations of an underlying—so far unknown—biological abnormality or, as James Phillis (2015) explains, that the "mental or psychological symptoms always reflect an underlying biomedical condition" (p. 180). Biological psychiatry, then, seeks to define psychiatric conditions in terms of the underlying "biomedical conditions" rather than in terms of their manifestations—the syndromes. Thus, the current, symptomatic definition is seen by (strong) biological psychiatrists as provisional, being the result of the lack of knowledge about the biological abnormalities underlying the syndromes. Once the abnormalities are discovered, it is thought, psychiatric conditions will come to be defined in terms of them.

So, for instance, Robert Kendell and Assen Jablensky (2003) claim that "[p]sychiatry is in the position—that most of medicine was in 200 years ago—of still having to define most

of its disorders by their syndromes" (p. 9) and that "most psychiatric disorders […] are still defined by their clinical syndromes *because* their etiology[23] is still largely unknown" (p. 8; my emphasis). Based on a similar reasoning and, presuming that the brain causes of schizophrenia "will eventually be elucidated", Robert Kendell (1991) claims that "[s]ooner or later […] schizophrenia will come to be defined by its pathology rather than by its syndrome (p. 65). Here, we should recall the notion of pathology that I addressed in §3 of Chapter I. As I mentioned, "pathology" refers to a destructive biological[24] process which causes a characteristic cluster of symptoms.

So, biological psychiatry's take on the definition of specific psychiatric conditions is that at least some of them will cease to be defined in terms of their respective syndromes, and will come to be (re)defined in terms of a specific brain pathology—i.e., in terms of a brain abnormality that causes their characteristic symptoms—once said pathology is found. In other words, (strong) biological approaches to psychiatry endorse the following

> DEFINITIONAL COMMITMENT OF BIOLOGICAL PSYCHIATRY: at least some specific psychiatric conditions will be defined in terms of specific brain abnormalities.

Several issues are to be addressed in connection with this commitment. First, it is important to see that, in a strong biological approach to psychiatry, "brain abnormality" in the above commitment should be understood to be the same as in biological psychiatry's causal

[23] Note that "aetiology" here is employed just as a synonym of "cause" and not necessarily in the way I explained in Chapter I, of a compound of causes of a disease coming from different levels of explanation.
[24] Or cognitive, as I also explained in Chapter I—see footnote 5 in that chapter.

commitment (see §2.2). So, the abnormalities expected to define at least some psychiatric conditions in strong biological approaches are exactly the (presumed) brain abnormalities that, as biological psychiatrists commit, cause specifically at least some psychiatric syndromes—and which occur in the form of a wide regularity at a single site in the brain—but which psychiatrists have not yet discovered.

A second issue has to do with the constitutive analysis I elaborated on in Chapter I. As I argued, current medical classification, in general, is best understood constitutively, that is, as *defining* medical conditions for classificatory purposes in terms of certain factors which are necessary and sufficient for them, and which are not their causes—nor their effects. So, the first issue is that, if biological psychiatry sticks to the way medicine classifies currently, then the definitions of specific psychiatric conditions sought by the definitional commitment above will establish the brain abnormalities these conditions will be defined in terms of as necessary and sufficient for the conditions. So, if, for instance, schizophrenia comes to be defined in terms of brain abnormality *B* under the current model of medical classification, then *B* will be necessary and sufficient for schizophrenia.

A connected issue is that, if schizophrenia comes to be so defined—that is, in terms of a brain abnormality that causes it—, then one might think that schizophrenia will be defined in terms of its *cause*, thus not sticking to a constitutive model of classification but rather to something like an aetiological model (see §3 in Chapter I). As a first response to this, we should note that aetiological definitions of psychiatric conditions would be in the form of "schizophrenia is the disease *caused* by biological pathology *B*". However, I addressed in Chapter I the problems entailed by allowing definitions of this sort in medical classification—e.g., if the model of classification admits these definitions, it allows

misclassification of diseases. Then, the definitions of psychiatric conditions as required by the definitional commitment above could be in the form of "schizophrenia is brain abnormality *B*", which observes the constitutive model of classification.

Critics might think that, even if this latter sort of definition was provided, schizophrenia would, after all, be defined in terms of its cause—in the example, brain abnormality *B*, which causes schizophrenia. The problem with this line of thought is that it conflates two distinct stages of the understanding of schizophrenia. To see why, let us look at the sequence of relevant events that would lead biological psychiatrists to define a specific psychiatric condition in terms of its brain abnormality.

The picture is as follows. Currently, at time *T1*, psychiatric conditions are defined in terms of syndromes. So let us consider schizophrenia as it is defined now, in terms of the relevant syndrome, and call that syndrome *S*. According to the definition of schizophrenia at *T1*, then,

(DEFINITION 1):

schizophrenia is *S*

Let us suppose that, at the same time *T1*, *S* is caused by brain abnormality *B,* although, at time *T1*, *B* has not been discovered to cause *S*. Further, imagine that at a later time *T2*, psychiatrists do discover that *B* causes *S* and, following the DEFINITIONAL COMMITMENT OF BIOLOGICAL PSYCHIATRY, they define schizophrenia in terms of *B*, as follows:

(DEFINITION 2):

schizophrenia is *B*

What we should note here is that, given DEFINITION 1, *B* is a *cause* of schizophrenia at *T1*: since brain abnormality *B* causes syndrome *S*, and schizophrenia is defined exactly as syndrome *S*, then *B* causes schizophrenia. However, given DEFINITION 2, *B cannot* be seen as the cause of schizophrenia at time *T2*. That is because DEFINITION 2 states that schizophrenia is exactly brain abnormality *B*, so, conversely, brain abnormality *B* itself *is* schizophrenia according to DEFINITION 2—that is, schizophrenia is no longer just syndrome *S* at time *T2*. Then, brain abnormality *B*, being itself schizophrenia, cannot cause schizophrenia—brain abnormality *B* cannot cause itself. So, whereas at *T1* brain abnormality *B* can be understood as the cause of schizophrenia because the latter is just syndrome *S*, *B* can no longer be so understood at *T2* because schizophrenia is brain abnormality *B* itself at *T2*.

The line of thought according to which, if schizophrenia—currently defined as a syndrome—comes to be defined in terms of its brain abnormality it will be defined in terms of its cause conflates the understanding of schizophrenia at *T1* with the understanding of schizophrenia at *T2*. It is *only* at *T1* that brain abnormality *B* is a cause of schizophrenia because this condition is defined as the syndrome *S* at time *T1* but, at the time schizophrenia comes to be defined in terms of the brain abnormality *B*, then, *ipso facto*, schizophrenia comes to be exactly brain pathology *B* by stipulation of the definition, and *B* comes to no longer be a cause of schizophrenia. At *T2*, then, brain abnormality *B* is not a cause of

schizophrenia, but it is schizophrenia itself, and, *as conceived of at time T2*, this condition is *not* defined in terms of its cause.

A conceptual issue derived from possible re-definitions of psychiatric conditions such as the one I just presented is whether the new definition in terms of brain abnormality would pick out the very same condition that was once defined as a syndrome. Chapters V and VI of this thesis will extensively address this issue. As I will argue, in certain circumstances, definitions of psychiatric conditions in purely biological terms would, in fact, pick out the very same conditions previously defined in terms of psychological and behavioural syndromes.

But what is of interest now is that biological approaches are committed to the idea that some psychiatric conditions will be defined in terms of brain abnormalities, and this would not imply that, at the time these conditions came to be so defined, they would be defined in terms of their causes. Further, if re-definitions of psychiatric conditions occur under the current way of classifying in medicine, the relevant brain pathologies will be necessary and sufficient for the psychiatric conditions they define and, then, such a definition will be constitutive.

As a final note, it is worth mentioning that the biological approach to the *definition* of psychiatric conditions is intertwined with the biological approach to classification—i.e., that some psychiatric conditions, currently classified as syndromes, are diseases. As a matter of fact, if psychiatric conditions were *not* diseases, in a way that no specific brain abnormality was linked to them at all, then they could not be (correctly) defined in terms of brain abnormalities. So, whether psychiatric conditions come to be (correctly) defined in terms of brain abnormalities as biological psychiatrists seek depends on whether they are diseases. As

I also pointed out in §2.2, biological approaches' take on classification is, in turn, intertwined with biological approaches' take on causation. So, biological approaches' take on all three causation, classification, and definition are interconnected.

3. Integrationist Approaches

In this section, I will address psychiatric classification, causation, and definition as they are approached by integrationists. A classificatory, a causal, and a definitional commitment of integrationist psychiatry will be drawn from available accounts, and it will become evident that biological and integrationist psychiatry's commitments are incompatible with each other.

3.1 Classification

I elaborated in §2.1 that (strong) biological psychiatry endorses a classificatory commitment stating that (at least some) psychiatric conditions are diseases—though their specific biological pathologies have not been discovered and, for that reason, they are not currently classified as such. The purpose of this subsection is to understand (strong) integrationist psychiatry's contrasting classificatory commitment and, to do that, we should now focus on the way integrationism currently conceives of psychiatric syndromes.

Generally speaking, integrationists view the symptoms involved in psychiatric *syndromes* as a necessary aspect of psychiatric conditions. Let us look at an example. In arguing on how to implement the biopsychosocial model in psychiatry, Roache (2020b, p. 374) notices that patients can only be diagnosed with a somatic disorder such as cancer or chickenpox if a relevant biological factor is present—i.e., a certain tumour and a varicella-zoster virus infection, respectively. As Roache puts it, "the diagnosis of somatic disorders

[…] stand[s] or fall[s] […] with the presence or absence of certain biological factors" (2020, pp. 374-375). But Roache notes that, in contrast,

> [d]iagnosis of schizophrenia, like diagnosis of other mental disorders, stands or falls with the presence or absence of certain characteristic psychological and/or behavioural symptoms; [and] in this sense, reference to psychological and behavioural considerations is ineliminable in characterizing mental disorders (2020b, p. 375).

So, if, in Roache's view, reference to psychological and behavioural considerations is ineliminable from characterisations of psychiatric conditions, then the psychological and behavioural aspects of psychiatric conditions are a necessary aspect of them.

But, in addition to conceiving psychiatric symptoms as a necessary aspect of psychiatric conditions, integrationists generally believe that those symptoms should be captured by the diagnostic categories in classification systems of psychiatric illness. An instance of this view is Derek Bolton's (2012). The author has an understanding similar to Roache's concerning the role psychiatric symptoms play in psychiatric syndromes. For Bolton, in psychiatry, "especially in distress-related conditions such as anxiety and depression, the symptoms of distress are more constitutive of the illness [than in somatic medicine]" (2012, p. 10) because

> the mental phenomenology, and its immediate behavioral associations, and its interpretation in the social context, have a defining role in our concepts of mental illness, and it is likely that, whatever else we may want our diagnostic categories to capture, we want them to capture these phenomena […] capturing the surface phenomenology is

> likely to be expected from any psychiatric classification system, arguably as a primary adequacy criterion (2012, p. 10).

Then, since, in Bolton's view, the symptoms—that is, the "mental phenomenology"—forming psychiatric syndromes have a "defining role in our concepts of mental illness", then those symptoms should be captured by classification systems of psychiatric illness.

So far, however, the integrationist approach to classification is perfectly compatible with the biological approach to the same aspect. In fact, integrationists' approach to classification as I have presented it up to now just poses that psychiatric syndromes are necessary for psychiatric conditions and that those syndromes should be captured by classification systems of psychiatric illness. Nevertheless, all this does not rule out that psychiatric syndromes are caused by yet-undiscovered brain abnormalities as they were described in §2.2, and—here the link between biological psychiatry's causal and classificatory views becomes relevant—, if psychiatric syndromes were caused by such brain abnormalities, then psychiatric conditions would be diseases, as stated by biological psychiatry's *classificatory* commitment. In other words, the ideas that psychiatric symptoms are necessary for psychiatric conditions and that those symptoms should be captured by classification systems do *not* imply that psychiatric conditions are not diseases, and, then, so far, integrationist psychiatry and biological psychiatry are compatible in their understandings of psychiatric classification—biological psychiatry posits that psychiatric conditions are diseases, and integrationist psychiatry, as it is thus far presented, admits this.

However, integrationist accounts such as the *Power Threat Meaning Framework* (PTM) (TBPS, 2018) and some biopsychosocial accounts (e.g., Bolton, 2012) commit to psychiatric syndromes being caused differently, and this ultimately results in an integrationist

classificatory commitment which is *in*compatible with that of biological approaches, as I will briefly explain now. Just to recall, (strong) biological psychiatrists posit that at least some psychiatric syndromes are caused by brain abnormalities involving single sites, wide regularities, and specificity, as I elaborated in §2.2. Nevertheless, (some) integrationist accounts (e.g., PTM) take it that psychiatric syndromes are rather caused by brain factors occurring at several sites in the brain, and which involve non-specificity—a single factor causing several syndromes—, which implies that biological and integrationist approaches have a different understanding of brain factors that possibly cause psychiatric syndromes. I have elaborated on biological psychiatrists' views on this issue in §2.2, and I will extensively address the corresponding integrationist views in the following subsection (§3.2).

What is important now, though, is that, as I pointed out in §2.2, biological psychiatrists' idea that psychiatric conditions are diseases is linked to their commitment that at least some psychiatric syndromes are caused by brain abnormalities as they understand them, but, as conceived of by integrationists, brain factors that possibly cause psychiatric syndromes are *not* brain abnormalities like that. In light of this, then, (some) integrationists believe that the "use of mental illness diagnoses as if they […] capture meaningful and invariant individual-level diseases is difficult to justify" (Slade & Longden, 2015, p. 8). And, then, posing the lack of brain abnormalities as those sought by (strong) biological psychiatrists for psychiatric syndromes, (some) integrationist accounts reject that psychiatric conditions are diseases.

In sum, (some) integrationists conceive of psychiatric symptoms as a necessary aspect of psychiatric conditions, and they believe that those symptoms should be captured by classification systems of psychiatric illness. Further, (some) integrationists also reject that

psychiatric conditions are diseases. Then, if psychiatric conditions are not diseases—i.e., characteristic symptoms caused by specific pathology—, and the characteristic clusters of symptoms are a necessary aspect of them, and, further, according to (strong) integrationists, those clusters of symptoms are to be captured by classification systems of psychiatric illness, then psychiatric conditions are ultimately conceived of by (strong) integrationism as *mere* clusters of psychiatric symptoms—with no specific brain abnormality (understood as in §2.1) associated. In other words, (strong) integrationism endorses the following

> CLASIFICATORY COMMITMENT OF INTEGRATIONIST PSYCHIATRY: psychiatric conditions are mere behavioural, psychological, and cognitive syndromes.

3.2 Causation

It is clear now that integrationist accounts posit psychiatric conditions to be caused by a variety of factors at different levels of explanation. As an example, the biopsychosocial model "views mental illness as the result of a process which occurs over multiple causal levels" (Kendler & Gyngell, 2020, p. 42)—including the genetic, brain, psychological, cognitive, and social levels. On the other hand, it is also clear now that biological approaches focus specifically on the biological causes of psychiatric conditions. Nevertheless, I mentioned earlier that there is nothing in (strong) biological psychiatry's causal commitment that is incompatible with psychiatric conditions having a variety of causes at different levels of explanation—e.g., psychological, cognitive, and social—in addition to biological causes, as long as, in the compound of causal factors leading to a psychiatric condition, a brain abnormality as described in §2.2 is present. So, if the difference in approach between

biological and integrationist psychiatry is merely described in terms of biological psychiatry focusing only on biological causes of psychiatric syndromes and integrationism on more than biological causes, then there is ultimately no *in*compatibility between them—both biological and integrationist psychiatry would admit psychiatric syndromes have a variety of causes at different levels of explanation.

But, as I mentioned in the previous subsection, (some) integrationists do not believe psychiatric syndromes are caused by brain abnormalities as understood by (strong) biological psychiatrists. In this subsection, I will elaborate that, whereas (strong) biological psychiatry commits to wide regularities occurring at a single site of the brain specifically causing a psychiatric syndrome—as I noted in §2.2—, (strong) integrationist psychiatry commits to *small regularities* occurring at *several sites* of the brain which could cause more than one syndrome—so they are *non-specific*. The upshot will be that the point of conflict between biological and integrationist approaches to psychiatric *causation* lies, not in the fact that biological psychiatry focuses on biological causes of psychiatric syndromes and integrationism on more than biological causes but, rather, in the specific, incompatible understanding each of these approaches has of the causes of psychiatric conditions at the level of the brain.

As with biological approaches to psychiatric causation, I will address the notions of *site*, *regularity* and *specificity* as applied to biological causes of psychiatric conditions in that order in what follows. So, to begin with, I mentioned in the previous subsection that integrationist accounts such as the PTM and the biopsychosocial model reject the idea that brain factors that cause psychiatric syndromes are brain abnormalities as described in §2.2. PTM advocates, for instance, stress that "there are no consistent associations [of psychiatric

conditions] with any biological pathology or impairment" (TBPS, 2018, p. 151) and, in lack of evidence of biological pathology, the PTM commits to an understanding of brain factors in relation to psychiatric illness different from biological psychiatry's. Advocates of the PTM claim that

> even very simple [brain] functions and tasks frequently recruit entire systems operating in concert across multiple brain regions. Given this, we should not be surprised that there is no consistent evidence for simplistic explanations for distress that implicate particular neuroanatomical features in isolation, or which attribute it to deficits or excesses within single neurotransmitter systems. Explanations of this kind simply do not match the complex, dynamic reality of the functioning human brain in its ever-changing environmental milieu (TBPS, 2018, p. 155).

So, according to PTM advocates, simple brain functions such as remembering—the example posed by PTM (see TBPS, p. 155)—involve several sites of the brain. In this view, then, one might expect the complex brain functions involved in psychological symptoms of psychiatric conditions to encompass several sites of the brain, rather than "neuroanatomical features in isolation" or "single neurotransmitter systems". Notably, PTM's view entails that presumptions such as biological psychiatry's that a brain factor at a single site causes psychiatric distress "do not match the complex, dynamic reality of the functioning human brain". In other words, PTM's view is that, *in reality*, the brain leads to distress by

"recruiting" systems which operate across several brain sites, and not single brain sites as (strong) biological psychiatry presumes[25].

So, a picture which fits the (strong) integrationist approach to psychiatric causation just described is that brain factors that cause psychiatric syndromes occur *across* several neuroanatomical sites, several neurotransmitter systems, several regions, several neuronal firings, or a combination of some or all of these. In sum, an integrationist view inspired by PTM is that brain factors causing psychiatric syndromes—so far mostly unknown—occur across several sites of the brain.

I will now address the notion of *regularity*. Advocates of PTM note that "[i]n contrast to the specific biological causal mechanisms which support some medical disorder categories", the causation of psychiatric distress (including psychiatric syndromes) is "highly probabilistic, with influences operating contingently and synergistically. However, this does not mean that no regularities exist" (TBPS, 2018, p. 191). This means that, although integrationist accounts such as the PTM reject the idea that brain pathologies localised at single sites in the brain cause psychiatric syndromes, they still admit some regularities in the causation of psychiatric syndromes. But they claim that "these regularities are not […] fundamentally patterns in biology" (TBPS, 2018, p. 191).

The idea here is in two parts. First, in PTM's view, the regularities leading to mental distress (including that involved in psychiatric syndromes) can be of a nature different from the biological. As an example, poverty is a social factor shared among significantly many

[25]Beyond the PTM, the rejection that factors at a single site of the brain cause psychiatric syndromes can be implicitly found in other integrationist accounts of a biopsychosocial orientation, specifically in Bolton's (2012) and Kendler & Gyngell's (2020). For simplicity, however, I will not address these views here, and I will extensively elaborate on them in Chapter III in addressing a further issue in this thesis.

people with schizophrenia, so it might be considered a social regularity leading to its symptoms. Second, in PTM's view, factors coming from different levels, forming regularities, combine between them in subjects and lead to mental distress, including psychiatric syndromes (see TBPS, ch. 6). For instance, in a view inspired by the PTM approach, the syndrome of schizophrenia would result in patients from *both* their suffering from poverty and from, say, some genetic predisposition—and also from other relevant regularities—, with poverty considered as a social regularity and genetic predisposition as a biological regularity. (To be noted here is that this picture, as just described, involving various sorts of regularities interacting and leading to psychiatric syndromes, is also generally accepted by other integrationist accounts, especially biopsychosocial ones).

But it is worth noting that the idea that regularities causing psychiatric syndromes are not only biological, and that psychiatric syndromes result in patients from the interaction of regularities coming from different levels of explanation is *not* in tension with the biological approach to causation. In fact, as I mentioned earlier, biological psychiatry's causal commitment allows factors at different levels of explanation to be causes of psychiatric syndromes as long as, among the biological factors, there are brain abnormalities specifically causing those syndromes. This does not preclude the possibility that psychiatric syndromes are also caused by social or psychological regularities.

However, tension between biological and integrationist psychiatry can be found if we focus on regularities at the level of the brain. To see this, we should recall biological psychiatrists' idea that brain factors causing psychiatric syndromes come in *wide* regularities (see §2.2). It is noteworthy here that, in biological approaches to psychiatric illness, such an idea is entailed by biological psychiatry's *classificatory* commitment that psychiatric

conditions are diseases: given that a disease is a biological factor that causes characteristic symptoms, then, given a specific disease, its characteristic symptoms are caused, in *all* of its cases, by the very same biological factor. So, if one commits to the idea that psychiatric conditions are diseases, then, the characteristic symptoms of a specific psychiatric condition should be caused by the very same pathology—so far unknown—in all of its cases. This means that, if we commit to psychiatric conditions being diseases, then the characteristic symptoms of a specific psychiatric condition—understood as a disease—should be caused by a brain factor that is at least as widely shared as to be the cause of characteristic symptoms in *all* cases of that specific psychiatric condition. That is, the brain factor should be a (relatively) wide regularity.

Nevertheless, if one does not commit to the idea that psychiatric conditions are diseases and, instead, one endorses integrationists' *classificatory* commitment that those conditions are behavioural and psychological syndromes (as described in §3.1) while preserving the idea that these syndromes are (partly) caused by brain factors, then these brain factors should *not* necessarily be wide regularities. Since the notion of a syndrome does not require all of its cases to be caused by the same factor, then specific psychiatric syndromes could be partly caused by *small* brain regularities (more on this in a moment), rather than by wide regularities. So, if we take it that (strong) integrationism posits small brain regularities causing psychiatric syndromes instead of wide brain regularities as biological psychiatry does, then these approaches conflict.

Now, to better understand what small regularities are like, consider a psychiatric syndrome *S*, and several brain factors, say, *B1*, *B2*, and *B3*. That psychiatric syndrome *S* was partly caused by small brain regularities would mean that, among the varied causes of *S*, brain

regularity *B1* would be present in *some* cases of *S*, brain regularity *B2* in other cases, *B3* in other cases, and so on. This could mean either of two things: that (1) cases of *S* partly caused by *B1* would *not* be caused at the same time by *B2* nor *B3*, and cases of *S* partly caused by *B2* would not be caused by *B1* nor B3 at the same time, and so on; or that (2) some cases of *S* would be partly caused by a *combination* of any two or more among *B1*, *B2* or *B2*. In any case, the idea is that each of these brain factors would not be widely shared by patients with *S*, so those factors would be (relatively) small regularities. As a note, in the example just posed, I consider only three brain factors as small brain regularities but, as a matter of possibility, they could be many more.

In sum, (strong) integrationist psychiatry takes brain causes of psychiatric syndromes to be small regularities.

Regarding the notion of *specificity*, we should recall that, as I mentioned in §2.2, biological approaches to causation require single brain factors causing psychiatric syndromes to have causal specificity, that is, that a given brain factor causes only one syndrome, and not several of them. However, integrationists' take on the notion of causal specificity contrasts with this, for integrationists embrace non-specificity. To see this, consider Kendler & Gyngell's (2020) note that not only biological findings are not specific in psychiatry, but also social findings. They claim that "[f]or example, while childhood sexual abuse is a strong predictor of alcohol dependence, it is not specific. This environmental variable predisposes people to a wide range of pathologies" (pp. 40-42), and also that "[m]odels of other psychiatric disorders, such as depression, would yield very similar results" (p. 42).

But, instead of seeking to reach specificity in the future, Kendler & Gyngell's approach is to embrace this non-specificity, as well as other features of causes of psychiatric

syndromes generally disliked by biological psychiatrists, such as the little generality most single findings have (see Kendler & Gyngell, 2020, p. 40). Kendler & Gyngell's approach is that, based on available evidence, "we should not attempt to reduce psychiatric disorders to diseases with single clear aetiologies" (2020, p. 39), with "single clear aetiologies" meaning "single clear mechanisms" leading specifically to psychiatric syndromes—and having other features such as, e.g., generality. So, whereas non-specificity poses a problem for biological psychiatry, it is embraced and defended by integrationist accounts of a biopsychosocial orientation such as Kendler & Gyngell's. Then, an integrationist strong account based on Kendler & Gyngell's view commits to brain factors causing psychiatric syndromes being non causally specific.

In sum, (strong) integrationism is committed to the idea that a variety of factors at different levels of explanation—biological, psychological, cognitive, and social—cause psychiatric syndromes and that, among the biological factors, there are brain factors that occur at several sites of the brain, in the form of small regularities, being non causally specific. So, a strong version of integrationist psychiatry endorses the following

> CAUSAL COMMITMENT OF INTEGRATIONIST PSYCHIATRY: psychiatric syndromes are caused by a variety of biological, psychological, cognitive, and social factors and, among the biological factors, there are small brain regularities occurring across several sites of the brain, being non-specific to psychiatric syndromes.

An important issue here is that the causal commitment above does not impose a constraint on the sizes of *non*-biological regularities causing psychiatric syndromes—it admits wide as well as small non-biological regularities causing them. Further, there is also nothing in *biological* psychiatry's causal commitment that imposes some such constraint. On the other hand, both biological and integrationist psychiatry admit psychiatric syndromes are also caused by biological factors. So, the tension between biological and integrationist approaches' understanding of psychiatric causation does not lie in the sort of causes they admit—biological, psychological, cognitive, and social—, nor on the admitted sizes of *non*-biological regularities. Instead, as it can be derived from both biological and integrationist psychiatry's causal commitments, the point of conflict between these approaches concerning causation arises from the incompatible understanding each of them has of the causes of psychiatric syndromes specifically *at the level of the brain*: whereas (strong) biological psychiatry commits to wide regularities occurring at a single site of the brain specifically causing a psychiatric syndrome—as I noted in §2.2—, (strong) integrationist psychiatry commits to *small regularities* occurring at *several sites* of the brain which could cause more than one syndrome—so they are *non-specific*—, as I noted in this subsection.

3.3 Definition

To my knowledge, available integrationist accounts do not explicitly address the way specific psychiatric conditions should be defined in light of integrationist considerations about psychiatric causation and classification. However, a specific approach to the definition of particular psychiatric conditions is entailed by integrationist psychiatry's classificatory commitment. I elaborated in §3.1 that (strong) integrationist psychiatry endorses the idea that

psychiatric conditions are behavioural, psychological, and cognitive syndromes—rather than diseases. But if these conditions are *mere* syndromes, then they can only be defined *correctly* if they are defined as syndromes—that is, in terms of symptoms—, rather than, say, as diseases—that is, in terms of biological pathology or biological pathology and symptoms. Then, for coherence with integrationist psychiatry's classificatory commitment, specific psychiatric conditions should be defined only in terms of behavioural, psychological and cognitive symptoms. So, as entailed by integrationist psychiatry's classificatory commitment, a strong version of integrationism endorses the

> DEFINITIONAL INTEGRATIONIST COMMITMENT: Psychiatric conditions are only adequately defined in terms of behavioural, psychological and cognitive symptoms.

4. Biological and Integrationist approaches

I have drawn classificatory, causal, and definitional commitments of biological and integrationist approaches to psychiatry from some available accounts. In the context of this thesis, an account that held all three classificatory, causal, and definitional commitments of biological psychiatry exactly as I presented them is to be understood as endorsing a *strong biological approach* to psychiatric illness. Conversely, an account that held the exact forms I presented of the classificatory, causal, and definitional commitments of integrationist psychiatry is to be understood as endorsing a *strong integrationist approach*. I will elaborate later on how to understand accounts which endorse fewer of these commitments or variations

of them but, for now, the exact way the strong biological and integrationist approaches are in tension should be made explicit.

To begin with, we should consider *classification*. Strong biological psychiatry endorses the classificatory commitment that psychiatric conditions are diseases, that is, specific brain pathologies causing characteristic clusters of symptoms—with those pathologies not having yet been discovered. But, in contrast, strong integrationist psychiatry endorses the commitment that psychiatric conditions are mere behavioural, psychological, and cognitive syndromes, which implies that they are *not* diseases. So, biological psychiatry's classificatory commitment is *in*compatible with integrationist psychiatry's classificatory commitment, for the truth of the former entails the falsity of the latter, and vice versa—if psychiatric conditions are diseases, then they are not mere syndromes, and vice versa.

On the other hand, as regards *causality*, I explained that strong biological psychiatry endorses the causal commitment that some psychiatric syndromes are caused with specificity by brain factors in the form of a wide regularity occurring at a single site in the brain, whereas integrationist psychiatry endorses the commitment that psychiatric syndromes are caused by a variety of biological, psychological, cognitive, and social factors, with some of the biological factors being small brain regularities occurring across several sites of the brain, being non-specific to single psychiatric syndromes. Here, strong biological psychiatry's causal commitment is *in*compatible with integrationist psychiatry's causal commitment, for the truth of the former also entails the falsity of the latter, and vice versa—if the causes of some syndromes are brain factors in the form of a wide regularity occurring at a single site of the brain specifically causing single syndromes, then the causes of those very same

psychiatric syndromes are *not* brain factors in the form of small regularities that occur across several sites of the brain, and which cause more than one syndrome.

Finally, when it comes to the *definition* of specific psychiatric conditions, strong forms of biological psychiatry endorse the definitional commitment that at least some specific psychiatric conditions will be defined in terms of specific brain abnormalities, and strong forms of integrationism that psychiatric conditions are adequately defined in terms only of behavioural, psychological, and cognitive syndromes. Then, biological psychiatry's definitional commitment is incompatible with integrationist psychiatry's definitional commitment for, in a similar fashion as with the classificatory and the causal commitments, the truth of the former entails the falsity of the latter, and vice versa—if some psychiatric conditions were defined (correctly) in terms of biological pathology, then (not all) psychiatric conditions would be correctly defined in terms of behavioural, psychological, and cognitive syndromes.

Therefore, the exact point of conflict between strong forms of biological and integrationist psychiatry lies in the *in*compatible classificatory, causal, and definitional commitments they endorse. What this implies is that, despite the apparent *compatibility* between biological and integrationist approaches pointed out in §1, strong versions of these approaches endorse two fundamentally distinct conceptions of psychiatric illness. Now, not all available accounts of psychiatric illness with a biological or an integrationist orientation endorse the exact *versions* of the commitments I drew from some accounts and, also, not all available biological or integrationist accounts endorse *all* three commitments. So, one might wonder how to understand the way, say, a biological account which does not endorse the

strong biological approach conflicts with an integrationist account which does not endorse the strong integrationist approach.

To address this issue, I propose to understand the conflict between biological and integrationist psychiatry by thinking of a spectrum with the strong versions of biological and integrationist approaches at the extreme poles, and with accounts endorsing fewer than the three commitments, or variations of them, at some point in that spectrum. In this understanding, the more commitments among the classificatory, causal, and definitional *biological* commitments an account holds, and the more it endorses the exact versions I presented of those commitments, the closer it would be to the *strong biological pole* of the spectrum, and so on for accounts endorsing integrationist commitments. Further, in this understanding, accounts close to the strong biological pole would be highly incompatible with accounts close to the strong integrationist pole, and two distinct accounts closer to the middle of the spectrum than to the poles would be compatible to some or other extent.

To illustrate all this, let us consider two examples. The first example consists of one account close to the strong *biological* pole of the spectrum and another close to the strong *integrationist* pole, and it will become clear that these accounts are highly *in*compatible. The second example concerns two accounts closer to the middle of the spectrum than to its poles, and it will become evident that they are compatible. To begin with, the first example partly concerns Murphy's (2009, 2013) views. As I noted in §2.1, Murphy considers and discusses an understanding of psychiatric conditions which he calls the "strong interpretation of the medical model", to which I will refer, for short, as the "strong medical model". According to the strong medical model, "what psychiatrists describe as "mental illnesses" are diseases"

(Murphy, 2013, p. 967), so such a view endorses the CLASIFICATORY COMMITMENT OF BIOLOGICAL PSYCHIATRY—i.e., that at least some psychiatric conditions are diseases.

Moreover, the strong medical model is committed to "specific causal hypotheses in terms of abnormalities in underlying neurobiological systems, which are responsible for the observed patterns of signs and symptoms" (Murphy, 2013, p. 967) and, then, the strong medical model endorses the idea that psychiatric syndromes are caused by *brain abnormalities*—or, in the strong medical model's terminology, by abnormalities in *neuro*biological systems. Further, the strong medical model endorses the idea that, at least for some psychiatric conditions, a pathology "is common to all cases of a condition" and that, on this view, "all the people who share a diagnosis do so in virtue of having a common destructive process in their mind/brain" (Murphy, 2009, p. 113). So, the strong medical model also has it that brain abnormalities causing psychiatric syndromes are *wide regularities*—at least as wide as to be the basis for a psychiatric diagnosis in all cases of a given condition. In sum, the strong medical model commits to psychiatric syndromes being caused by brain abnormalities in the form of wide regularities, which is a variation of the CAUSAL COMMITMENT OF BIOLOGICAL PSYCHIATRY—which requires, further, that those abnormalities occur at a single brain site and have causal specificity.

Then, the strong medical model as discussed by Murphy explicitly endorses biological psychiatry's classificatory commitment and (a slightly different version of) biological psychiatry's causal commitment. Thus, the strong medical model as discussed by Murphy is close to the strong biological pole in the spectrum representing the conflict between biological and integrationist psychiatry, for it endorses some version of two commitments of biological psychiatry.

But consider now Kendler & Gyngell's (2020) view. The authors note that "[m]any in psychiatry are unhappy" with the current classification of psychiatric conditions provided by the DSM (2020, p. 40), which is based only on syndromes. According to Kendler & Gyngell, instead of embracing psychiatric classification based on syndromes, some authors who are unhappy with the DSM "believe [that] classifications should follow a 'hard medical model'" (2020, p. 40), which attempts to characterise psychiatric conditions in terms of syndromes that are caused by "single clear aetiologies" (Kendler & Gyngell, 2020, p. 39). So, basically, the hard medical model seeks to characterise psychiatric conditions as diseases.

But Kendler & Gyngell claim that a "move" from the current classification based on syndromes to a hard medical model "is not supported by the current state of psychiatric research" (2020, p. 40), and that current evidence suggests that "we should not attempt to reduce psychiatric disorders to diseases with single clear aetiologies" (2020, p. 39). Then, Kendler & Gyngell *reject* a project in psychiatry attempting to characterise psychiatric conditions as diseases. However, if those conditions are not to be characterised as diseases, then, Kendler & Gyngell's view must conceive of those conditions as mere syndromes—with no brain pathology as described in §2.2 associated. So, Kendler & Gyngell's view entails that psychiatric conditions are mere psychiatric syndromes, and that is simply the CLASSIFICATORY COMMITMENT OF INTEGRATIONIST PSYCHIATRY.

Further, Kendler & Gyngell emphasise that "[t]he risk factors for psychiatric disorders are sprinkled across multiple causal levels" (2020, p. 44), including the biological, psychological, and social levels. Then, their view endorses the idea that psychiatric syndromes are caused by a variety of biopsychosocial factors. Moreover, it is worth recalling that, in rejecting adherence to what they call the "hard medical model", Kendler & Gyngell embrace the lack of causal specificity, as I noted in §3.2. However, they also embrace the

lack of *generality* in causes of psychiatric syndromes, and this implies that they do not commit to the notion of wide regularities. To see this, note that, in illustrating that causes of psychiatric syndromes do not have generality, Kendler & Gyngell claim that "*ALDH* genetic variants […] are not generalizable, many people with alcohol dependence do not have these mutations" (2020, p. 42). This implies that ALDH variants are *not* shared among all patients with alcohol dependence, so those variants are not wide regularities for that condition. But Kendler & Gyngell simply embrace the lack of generality—thus also embracing the lack of wide regularities.

Then, assuming that embracing lack of causal specificity and generality implies commitment to the idea that, at least in some cases, causes of psychiatric syndromes lack causal specificity and are not wide regularities, as well as assuming that some of those causes occur at the level of the brain, then Kendler & Gyngell's view implies that psychiatric syndromes are caused by a variety of biopsychosocial factors which, at least in some cases, lack causal specificity and are not wide regularities. And this is just a variation of the CAUSAL COMMITMENT OF INTEGRATIONIST PSYCHIATRY—which requires, in addition to non-specificity and non-wide regularities, the rejection that brain causes of psychiatric syndromes occur at single sites of the brain.

Then, Kendler & Gyngell's account entails a commitment to the classificatory and (to a variation of the) causal commitment of integrationist psychiatry. Based on all this, then, Kendler & Gyngell's account is close to the strong integrationist pole in the spectrum representing the conflict between biological and integrationist psychiatry.

So, the strong medical model as discussed by Murphy is close to the biological psychiatry pole of such a spectrum, and Kendler & Gyngell's account is close to its strong

integrationist pole. What is to be noted here is that these accounts are highly incompatible: the strong medical model's idea that psychiatric conditions are diseases cannot be true if psychiatric conditions are, instead, mere syndromes, as Kendler & Gyngell's account holds, and vice versa. Further, psychiatric syndromes cannot be caused, at the same time, by brain factors in the form of wide regularities, as the strong medical model endorses, and—among other factors—by brain factors which are *not* wide regularities, which is entailed by Kendler & Gyngell's account. Then, the strong medical model's approach to classification and causation is *in*compatible with Kendler & Gyngell's approach to the very same aspects, and the medical model and Kendler & Gyngell's account, being close to the poles of the spectrum representing the conflict between biological and integrationist psychiatry, are highly incompatible.

But I will now present a second example which illustrates that two distinct accounts closer to the middle of the mentioned spectrum than to its poles are compatible to some extent. Suppose that account A only endorsed a variation of the CAUSAL COMMITMENT OF BIOLOGICAL PSYCHIATRY. Say this account committed to the idea that individual psychiatric syndromes are caused by several distinct brain abnormalities, with each brain abnormality giving rise to a sub-type of the condition—an idea which has gained growing acceptance in the last years (see Fang *et al*, 2022; Feczko *et al*, 2019; Seaton, Goldstein & Allen, 2001; Tabb, 2015). Then, account A would endorse the idea that psychiatric syndromes are caused by brain abnormalities in the form, say, of mid-sized regularities—rather than in the form of wide regularities, with one brain factor causing all cases of a psychiatric syndrome. Since account A would hold explicitly a variation of *only one* among the classificatory, causal, and definitional commitments, i.e., biological psychiatry's causal

commitment, then it would be closer to the middle of the spectrum representing the conflict between biological and integrationist psychiatry than, say, the strong medical model as discussed by Murphy—which endorses some version of two biological commitments.

But suppose that another account, say B, only endorsed the idea that specific psychiatric conditions should be defined, *at least partly*, as behavioural and psychological syndromes, such as it might be entailed by, e.g., Roache's (2020b) account addressed in §3.1—and which I will extensively address in Chapters V and VI. Account B would admit, then, that psychiatric conditions would be adequately defined either solely in terms of syndromes, or in terms of a syndrome and a certain biological factor—all account B requires is the relevant syndrome to be cited in the relevant definition. So, account B, then, would hold a variation of the DEFINITIONAL COMMITMENT OF INTEGRATIONIST PSYCHIATRY[26]—which states that psychiatric conditions are only adequately defined in terms of syndromes. Since account B would only endorse one of the three commitments of integrationist psychiatry, and it would endorse a variation of it, then it would be closer to the middle of the spectrum representing the conflict between biological and integrationist psychiatry than, say, Kendler & Gyngell's account—which endorses some form of two integrationist commitments.

What we should note is that theories A and B are compatible: it can be true at the same time that psychiatric syndromes are caused by brain factors in the form of middle-sized regularities—as account A holds—and that psychiatric conditions are correctly defined only if they are defined at least partly in terms of syndromes—as account B holds. For instance, it might be that, say, if schizophrenia was caused by several brain factors coming in middle-

[26]Although there is some vagueness here, for this could also be seen as a variation to *biological* psychiatry's definitional commitment. I will briefly address vagueness concerning the variation to the three commitments soon in this section.

sized regularities, then, it came to be defined in various subtypes, so that the definition of each subtype cited the relevant syndrome and the brain abnormality giving rise to that subtype. So, accounts A and B, being closer to the middle of the spectrum representing the conflict between biological and integrationist psychiatry than to the poles, would be compatible.

Murphy's, Kendler & Gyngell's views and accounts A and B as above illustrate my point that a theory which is close to the strong biological pole in the spectrum would be highly incompatible with a theory which is close to the strong integrationist pole, and that two distinct theories closer the middle of the spectrum than to its poles would be compatible. The examples I addressed also illustrated some variations to biological and integrationist psychiatry's commitments, but many other variations could also be introduced. Just as another instance relating to a causal commitment specifically, an account could endorse the idea that, say, psychiatric conditions are caused by brain abnormalities in the form of small regularities, localised at single sites of the brain, which is a variation to biological psychiatry's causal commitment—requiring brain abnormalities, *wide* regularities, and single brain sites.

A final issue is that some vagueness arises with respect to the possible variations of the classificatory, causal, and definitional commitments. I mentioned in §2.2 that certain accounts such as the strong medical model as discussed by Murphy allow that, at least in some cases, *cognitive* abnormalities are the causes of psychiatric syndromes (see 2009, pp. 113-114), instead of *biological* abnormalities. In this view, some psychiatric conditions would fit a variation of the notion of disease, being characteristic clusters of symptoms caused by a cognitive abnormality, rather than by a biological abnormality. If we endorsed this view,

then, among other ideas, we would hold the idea that psychiatric syndromes are caused in some cases by biological abnormality and, in others, by cognitive abnormality.

Notably, this idea can be seen as a variation to (strong) *biological* psychiatry's causal commitment, which states that brain pathology as described in §2.2 causes psychiatric syndromes. The variation is that, instead of only positing brain abnormalities as causes of psychiatric syndromes as biological psychiatry's causal commitment does, the strong medical model also posits *cognitive* abnormalities as causes of the syndromes. But this idea of the strong medical model can also be seen as a variation to integrationist psychiatry's causal commitment—which states that psychiatric syndromes are caused by a variety of factors at the biological, psychological, cognitive, and social levels, with some of the biological causes being brain factors as described in §3.2. The variation here is that, instead of positing, broadly, that psychiatric syndromes are caused, among other sorts of factors, by cognitive factors as integrationist psychiatry's causal commitment does, the strong medical model's idea *specifies* that those cognitive factors are *cognitive abnormalities*. So, it is not clear whether the medical model's idea that psychiatric syndromes are in some cases caused by cognitive abnormality is a variation of biological or integrationist psychiatry's causal commitments.

Nevertheless, the point of understanding the conflict between biological and integrationist psychiatry as a spectrum is not to be able to determine without vagueness whether a variation counts as a variation to some or other commitment. The idea is, rather, that accounts close to the poles of the spectrum will be highly incompatible, and two distinct accounts closer to the middle than to the poles will be compatible to some extent. Some vagueness as to whether a variation concerns one or another commitment does not preclude

us from understanding the conflict between biological and integrationist psychiatry in that way. Whether the strong medical model's idea that some cases of psychiatric syndromes are caused by cognitive abnormalities is seen as a variation to the biological or integrationist causal commitment does not preclude us from seeing that, being a variation to either of those commitments, such an idea would be closer to the middle of the spectrum than to either of the poles—for the poles are the commitments *without* variation—, and so it would conflict more with an account close to the poles than with another account in the middle of the spectrum.

5. Conclusions

In exploring whether biological and integrationist psychiatry are actually incompatible, I drew a classificatory, a causal, and a definitional commitment of strong biological and integrationist psychiatry from available accounts. As I showed, biological psychiatry's commitments are incompatible with integrationist psychiatry's commitments, so strong forms of these approaches are incompatible. The exact point of conflict between them lies in the conflicting commitments they endorse. Strong forms of biological and integrationist psychiatry, thus, endorse fundamentally distinct conceptions of psychiatric illness.

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CHAPTER III

Causal Commitments and Biological Definitions in Psychiatry. Beyond the Strong Biomedical Project

In Chapter II, I addressed biological psychiatry's search to define psychiatric conditions based on brain abnormalities for classification (§2.3). In the present chapter, I will counter a line of criticism against such a search. It will soon become evident that the discussion is framed in terms of whether definitions of psychiatric conditions based on brain *causes* can be achieved. Then, the discussion will appear to be whether an aetiological classification as I described it in Chapter I (§2) is attainable for psychiatric conditions. However, I have explained that such a classification is based on a defective model (Chapter I, §2.2) so, unless the aetiological model was accepted, the discussion in this chapter should be understood in non-aetiological terms. Then, at the end of this chapter, I will provide an interpretation of the discussion consistent with the *constitutive* model of disease classification that I defended in Chapter I (§4), elaborating on how such a discussion relates to the realisation analysis (Chapter I, §3) I addressed previously as well.

So, biological psychiatry seeks to define psychiatric conditions for classificatory purposes based on their brain causes. Criticisms have been raised against this, though. As I will explain, critics focus on the fact that diseases such as tuberculosis and syphilis, which are (supposedly) defined in terms of biological causes, *do* have "single, clear" biological causes, based on which they are defined. However, evidence has not proved that psychiatric conditions have single, clear biological causes. Instead, current findings suggest that several factors at different levels of explanation are causally related to those conditions. Then, in the (apparent) absence of single, clear biological causes, it is "unrealistic" or difficult to define those conditions in terms of biological causes—including those at the level of the brain. I

will counter this line of thought. After clarifying the best way to understand what a "single, clear" biological cause is, I will argue that definitions in terms of biological causes *could* be given to psychiatric conditions even if they did not have single, clear biological causes and rather they had, as current findings suggest, a variety of causes at different levels of explanation.

The plan is as follows. I will briefly elaborate on biological psychiatry's search to define psychiatric conditions based on their brain causes in §1. Later, in §2, I will present the critique that, since psychiatric conditions do not (seem to) have single, clear biological causes, then it is "unrealistic" or difficult to define them based on biological causes. As I will explain, the notion of a "single, clear" biological cause employed by the critics is problematic. It is based on the idea that diseases such as tuberculosis and syphilis have *only one* biological cause but, as I elaborated in Chapter I (§2), such an idea seems to be, strictly speaking, false. Diseases appear to have more than one biological cause—beyond infection with the relevant pathogen, tuberculosis and syphilis seem to be caused, e.g., by patients' lack of sufficient immunity to the pathogen, and by patients breathing oxygen. However, for reasons that will become apparent in §2, the notion of a single, clear biological cause should be re-interpreted rather than merely rejected, and the critics' claims should be addressed accordingly.

So, I will explore how such a notion should be best understood in §2.1. As I will argue, a single, clear biological cause for a psychiatric condition is best understood to be a single factor which is a *wide biological regularity* occurring at *single brain sites* with *causal specificity*, that is, a brain cause as required by the CAUSAL COMMITMENT OF BIOLOGICAL

PSYCHIATRY (see Chapter II, §2.2)[27]. Based on this, I will argue in §3 that definitions of psychiatric conditions in terms of their causes *could* be provided even if those conditions did not have biological causes of that sort. Since, as it will become clear, current evidence appears to be compatible with the CAUSAL COMMITMENT OF INTEGRATIONIST PSYCHIATRY (see Chapter II, §3.2)[28], I will argue in §3, more specifically, that psychiatric definitions based on biological causes could be provided even if this latter commitment was true, that is, even if brain factors in the form of non-wide regularities occurring at several brain sites with no causal specificity caused psychiatric conditions—jointly with other factors at different levels of explanation.

In §3.1, I will address some practical issues related to definitions based on biological causes and, in §4, the possible objection that my argument is based only on *a priori* considerations, while the issue at stake requires actual empirical evidence supporting the development of specific definitions based on biological causes. Later, in §5, I will explain how to understand the discussion concerning this sort of definitions in a way consistent with the constitutive model of disease classification, and I will also explain how the realisation analysis relates to the discussion. Finally, I will make some concluding remarks in §6.

1. Traditional Biological Definitions

I explained in Chapter II (§2.3) that specific psychiatric conditions are understood to be defined by the syndromes based on which they are classified. As an example, consider

[27] To recall, this commitment states that some psychiatric syndromes are caused specifically by brain abnormalities in the form of wide regularities that occur at a single site in the brain.
[28] To recall, this commitment states that psychiatric syndromes are caused by a variety of biological, psychological, cognitive, and social factors and that, among the biological factors, there are non-wide brain regularities occurring across several brain sites, being non-specific to psychiatric syndromes.

schizophrenia, which can be defined as the condition that occurs when patients develop characteristic symptoms (as stated by psychiatric diagnostic systems) such as delusions, hallucinations, and emotional withdrawal. I pointed out as well in Chapter II (§2.3) that biological psychiatrists have complained about this way of defining psychiatric conditions. Just to recall, Paul Meehl (1995), for instance, claims that definitions in terms of syndromes "ignore the fact that entities in the advanced specialties of medicine are not constructed like the DSM categories", and that, in those "advanced specialties", "the syndrome is taken as evidentiary, not as definitory (p. 267)".

I also pointed out in Chapter II (§2.3) that, traditionally, psychiatric syndromes—formed by behavioural and psychological symptoms—have been understood to be *manifestations* of underlying, so far unknown, biological abnormalities by biological psychiatry, and that the latter seeks to define psychiatric conditions in terms of those abnormalities for classification. In other words, biological psychiatrists seek a taxonomy of psychiatric illness in which (at least some) psychiatric conditions are classified based on underlying biological features in a way that those features define the conditions, instead of their symptoms. As an example of this line of thought, we can consider the "Biological Classification of Mental Disorders" (BeCOME project) (Brükl *et al*, 2020), a recent research project which is intended to "contribute to a novel taxonomy of mental disorders that integrates the underlying pathomechanisms into diagnoses" (p. 2), and which is aimed at "identify[ing] biology-based classes of mental disorders that improve the translation of novel biomedical findings into tailored clinical applications (p. 1)".

It is worth noting that, more specifically, the biological features based on which biological psychiatrists seek to define psychiatric conditions for classification are (yet

undiscovered) biological factors which allegedly *cause* psychiatric syndromes[29]. In particular, as Dominic Murphy (2009) points out, psychiatrists who seek a classification of this sort "look forward to a nosology [i.e., classification] based on pathological processes in brain systems" (p. 109). So, brain pathologies (or abnormalities[30]) have been sought for the purposes of classification. Then, for instance, Robert Kendell (1991) claims that "[s]ooner or later […] schizophrenia will come to be *defined* by its pathology rather than by its syndrome (p. 65; my emphasis). Let us call the definitions of medical conditions based on biological causes, sought for psychiatric conditions in biological psychiatry, "biological definitions".

An issue here is that, as I mentioned previously (Chapter II, §1), the causal hypotheses posited by biological psychiatrists so far are currently widely questioned and, then, claims that no one has "discovered the [biological] etiology [i.e., the causes] of mental disorders" (Whooley & Horwitz, 2013, pp. 80-81) are generally seen as non-controversial. In connection with this lack of knowledge concerning the biological causes of psychiatric conditions, then, biological psychiatrists have claimed that "[p]sychiatry is in the position—that most of medicine was in 200 years ago—of still having to define most of its disorders by their syndromes" and that "most psychiatric disorders […] are still defined by their clinical syndromes *because* their etiology[31] is still largely unknown" (Kendell & Jablensky, 2003, p. 8; my emphasis)—that is, because their (biological) causes are not currently known.

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[29] As I mentioned in Chapter II (§2.2), biological psychiatrists are generally "committed to specific causal hypotheses in terms of abnormalities in underlying neurobiological systems, which are responsible for the observed patterns of signs and symptoms" (Murphy 2013, p. 967), as it is exemplified by the strong medical model discussed by Dominic Murphy (2009, 2013).

[30] In the current literature, the terms "abnormality" and "pathology" are sometimes employed as synonyms and sometimes as conveying different meanings—with "abnormality" being usually employed as a statistical notion. As I have done previously in this thesis, however, I will employ these terms as synonyms in the present chapter, meaning a specific destructive biological state or process which leads to characteristic clusters of symptoms.

[31] Note that "aetiology" here is employed just as a synonym of "cause" and not in the way I explained in Chapter I, of a compound of causes of a disease coming from different levels of explanation.

Thus, the current classification of psychiatric conditions based on syndromes is seen by biological psychiatrists as provisional, being the result of a lack of knowledge concerning the brain abnormalities allegedly causing the syndromes. According to this line of thought, by allowing more time to researchers, they will end up finding the relevant brain abnormalities[32] and, once these are discovered, psychiatric conditions will come to be defined in terms of them. In sum, one of biological psychiatrists' aims is to provide biological definitions of psychiatric conditions for classificatory purposes when the abnormalities (supposedly) causing those conditions are discovered. This aim of biological psychiatry has, however, been criticised, as I will elaborate in what follows.

2. Against biological definitions in psychiatry

It should be noticed that biological psychiatry's attempts to define psychiatric conditions biologically have been traditionally understood as attempts to provide an aetiological classification for them such as the one I described in Chapter I (§2). This means that psychiatric conditions have been sought to be defined in terms of (supposedly existing) factors which are their only biological causes. In light of this, Hanna van Loo, Jan-Willem Romeijn, and Kenneth Kendler (2019) emphasise that "successes of monocausal disease models […] have been clear" (p. E-99) in cases of somatic diseases such as tuberculosis or Down's syndrome and, inspired by those successes, a "goal for classifications in psychiatry"

[32] Consider, e.g, Assen Jablensky's (2012) claims that "the typical progression of knowledge starts with the identification of the clinical manifestations (the syndrome) […] understanding of the pathology and etiology [including the biological causes] usually come much later" (p. 79), and that "molecular genetics and neuroscience will play an increasing role in understanding [the] etiology and pathogenesis" of psychiatric syndromes (p. 92), which shows his confidence that biological causes of the syndromes will be found.

is "to define diseases in terms of specific causes" (Van Loo, Romeijn & Kendler, 2019, p. E-100). Nevertheless, the authors claim that

> psychiatric nosology based on specific biological causes is probably an unrealistic goal for psychiatric disorders. At present, scientific evidence points [*sic*] into the direction that a complex developmental mix of biological, psychological and sociocultural risk factors are involved in causal pathways to psychiatric disorders as defined in the DSM, as opposed to single and/or specific biological causes (Van Loo, Romeijn & Kendler, 2019, p. E-100)

So, Van Loo, Romeijn & Kendler criticise biological psychiatry's search to define psychiatric conditions biologically by remarking on the picture of psychiatric causation suggested by current evidence: psychiatric conditions are caused, as present findings suggest, by a "mix of biological, psychological and sociocultural risk factors". In the authors' view, this is "opposed" to psychiatric conditions having "single and/or specific biological causes". However, as the authors understand this issue, single, specific biological causes are the sort of causes diseases in other areas of medicine are defined in terms of. For instance, tuberculosis and Down's syndrome are caused by an *M. Tuberculosis* infection and an extra copy of chromosome 21 respectively, and these are single, specific biological causes.

Then, in Van Loo, Romeijn & Kendler's view, the fact that psychiatric conditions have a variety of biological, psychological, and sociocultural causes, instead of single, specific biological causes as tuberculosis and Down's syndrome (supposedly) do, makes the search to define those conditions in terms of their biological causes "probably unrealistic". And, in response to this, the authors claim that "[d]isease definitions in terms of specific

causes are not the only potentially useful classifications for psychiatry" (Van Loo, Romeijn & Kendler, 2019, p. E-100), suggesting to pursue a different sort of classification in the discipline.

A remark will soon be made about Van Loo, Romeijn & Kendler's claims. But, for now, let us look at a further critique along the same lines. As I mentioned in Chapter II (§4), Kenneth Kendler and Christopher Gyngell (2020) note that "[m]any in psychiatry are unhappy" with the current classification of psychiatric conditions provided by the DSM (2020, p. 40), which is based only on syndromes. Kendler & Gyngell claim that critics who are "unhappy" with the current classification—among them, biological psychiatrists—"believe [that] classifications should follow a 'hard medical model'" (Kendler & Gyngell, 2020, p. 40), which seeks to classify psychiatric conditions based on "single clear aetiologies"[33] (Kendler & Gyngell, 2020, p. 39) as in the case of, e.g., syphilis—with a *Treponema pallidum* infection as its single, clear aetiology (see Kendler & Gyngell, 2020, p. 39).

However, I also noted in Chapter II (§4) that, according to Kendler & Gyngell, a "move" from the current classification to a hard medical model "is not supported by the current state of psychiatric research" (2020, p. 40), which rather supports the view that "risk factors for psychiatric disorders are sprinkled across multiple causal levels" (2020, p. 44), including the biological, psychological, and social. In Kendler & Gyngell's view, then, the variety of causes of psychiatric conditions makes "classification based on standard reductionist medical models difficult" (2020, p. 25), in a way that, based on current evidence, "we should not attempt to reduce psychiatric disorders to diseases with single clear

[33] Again, "aetiology" here is just employed just as a synonym of "cause".

aetiologies" (2020, p. 39). So, in other words, biological psychiatry's aim to classify psychiatric conditions based on biological causes, defining the former in terms of the latter, is not supported by current evidence according to Kendler & Gyngell, and that is because, instead of showing that psychiatric conditions are caused by "single clear (biological) aetiologies"—i.e., by single clear biological causes—as syphilis is, evidence suggests that those conditions are caused by a variety of factors at different levels of explanation.

Then, both Van Loo, Romeijn & Kendler's and Kendler & Gyngel's criticisms are based on the idea that psychiatric conditions having a variety of causes at different levels of explanation, and the alleged lack of single, clear biological causes for them, makes the definition of psychiatric conditions in terms of biological causes difficult or "unrealistic".

An important remark on these criticisms, however, is that the idea that medical conditions have *single* biological causes seems to be, strictly speaking, false. As I elaborated in Chapter I (§2), the lack of sufficient immunity to a pathogen and patients breathing oxygen can be considered biological causes of, say, tuberculosis and syphilis. Moreover, as I also mentioned in Chapter I (§2), Alex Broadbent (2009) notes that a variety of background conditions are part of the causal chain leading to cases of a disease[34]. Then, although, say, tuberculosis and syphilis are posed by the critics as examples of diseases defined in terms of their supposed *single* biological causes—i.e., the respective infections—those diseases are caused, strictly speaking, by more than a single (biological) cause. What this means is, simply, that it is not true that a disease given a biological definition is defined on the basis of a factor which is the only biological cause it has, for each disease has more than one

[34] As Broadbent (2009) notes, "[t]he patient would have to be well supplied with oxygen; the Earth would need to continue a peaceful orbit; hungry lions would need to be absent from the patient's vicinity" (p. 304), and so on.

(biological) cause. So, strictly speaking, a disease given a biological definition as in the aetiological model is actually defined based on one of its *various* biological causes.

This casts some doubt on the criticisms against biological definitions in psychiatry I explained earlier. As I mentioned, given the example of diseases currently defined biologically such as tuberculosis, which are understood by the critics to have single, clear biological causes, critics conclude that, since psychiatric conditions lack that sort of causes, then it is "unrealistic" or difficult to define these conditions based on biological causes. But, as I have pointed out, tuberculosis and any other disease defined biologically simply do not have only one, single (biological) cause, and they are still defined biologically. Then, not having only one, single clear biological cause, as in the case *both* of tuberculosis and psychiatric conditions, does not seem to preclude diseases from being so defined.

Nevertheless, this problem with the critics' view can stem from the defects of the aetiological model itself. As I explained in Chapter I (§2), such a model presupposes single, unique biological causes for medical conditions, even though these have more than one biological cause. Despite this problem, though, critics of biological psychiatry do seem to make a relevant point. They observe that current evidence seemingly supports that the way diseases such as tuberculosis and syphilis are biologically caused is *different* from the way psychiatric conditions are biologically caused, and that this difference, in their view, imposes a constraint on biological psychiatrists' aim to define psychiatric conditions biologically.

This criticism can be held even if tuberculosis or syphilis have, strictly speaking, more than one, single biological cause, so it is worth addressing the critics' claims. However, the difference between the way, e.g., tuberculosis and syphilis, on the one hand, and psychiatric conditions, on the other, are biologically caused is not immediately obvious, so it should be

clarified, and the critics' views addressed accordingly. To understand the mentioned difference, I will consider a further criticism against biological definitions in psychiatry in the following subsection, for it will allow us to grasp such a difference better.

2.1 Causes in medicine and psychiatry

In this subsection, I will explain a further criticism against psychiatric biological definitions and will later clarify the difference between how diseases such as tuberculosis and syphilis are biologically caused, and how psychiatric conditions are biologically caused. To begin with, Derek Bolton (2012) argues against biological psychiatry's aim to define psychiatric conditions biologically. In so doing, Bolton first considers—and later rejects—the view that a variety of factors at different levels of explanation lead to a "final common pathway" "implemented" in the brain which, in turn, causes psychiatric symptoms (see p. 9)[35]. This view considered by Bolton is illustrated by the "strong medical model" discussed by Murphy—which I addressed in Chapter I (§3)—, so, to better understand Bolton's claims, we can briefly look at the strong medical model. The latter takes it that

> we can distinguish between more remote and more proximate causes [of psychiatric conditions] […] Many factors can interact to produce the pathology that is common to all cases of a condition. On this view, all the people who share a diagnosis do so in virtue of having a common destructive process in their mind/brain (p. 113).

[35] In Bolton's own words, he considers the possibility that certain biological factors "may validate the classification system, by reducing the complex array of biopsychosocial causes to a single final common pathway, which is biological", in a way that "all the distant (early) biopsychosocial causes and the current psychosocial causes [of psychiatric conditions] must somehow be implemented in the brain" (2012, p. 9).

So, the strong medical model posits that a variety of factors cause a brain pathology which is common to all cases of a condition, and which leads to characteristic symptoms (see Chapter I, §3). Then, a final common pathway "implemented" in the brain can be understood as a brain pathology as described by the strong medical model—that is, a brain pathology caused by a variety of factors which, in turn, causes psychiatric symptoms. Bolton rejects this sort of views. He claims that "it is an empirical matter, not an a priori one, whether or not there is a final common pathway leading from multiple pathways to a single clinical syndrome" and that "[t]o date […] no or not many biomarkers of specific psychiatric syndromes have yet been found, despite looking" (2012, p. 10). Then, the author claims that "it looks implausible" to continue supposing that discoveries of final common pathways are "still on offer in psychiatry" (Bolton, 2012, p. 10).

Then, in the example of the strong medical model, Bolton's critique would be that discovering a pathology as that presumed by the strong medical model, so that psychiatric conditions are classified based on it, would "look implausible". Bolton is thus a sceptic that psychiatric conditions will be classified based on brain pathology—or, in his own words, based on a final common pathway implemented in the brain—, for, in his view, it looks implausible that something like that will be discovered. It follows scepticism that psychiatric conditions will be defined in terms of brain pathology—that is, in terms of a final common pathway—for classification. This is Bolton's criticism, and it helps us understand the difference between how diseases such as tuberculosis and syphilis are biologically caused, and how psychiatric conditions are biologically caused, as I will now elaborate.

To emphasise, the "final common pathway" in the brain that Bolton considers and rejects is just a brain pathology/abnormality[36]. And, as I elaborated in Chapter II (§2.2), *traditionally*, the features sought by biological psychiatry in brain abnormalities (supposedly) causing psychiatric conditions are that the abnormalities are *wide biological regularities* occurring at *single sites* of the brain, with *causal specificity*. These features are described by (what I call) the CAUSAL COMMITMENT OF BIOLOGICAL PSYCHIATRY. As I explained in Chapter II (§2.2), this commitment states that psychiatric syndromes are caused by wide biological regularities, that these occur at single sites of the brain—such as a single anatomical part, or a single neurotransmitter system, and so on—, and that they are causally specific, i.e., that a single biological factor causes only one psychiatric condition. Then, more specifically, the final common pathways in the brain that biological psychiatry has traditionally sought to classify and define psychiatric conditions are those described by biological psychiatry's causal commitment.

Here, it is worth noting that the causes of non-psychiatric diseases typically posed as examples of biologically defined diseases *do* have the features of being wide biological regularities occurring at single bodily sites with causal specificity. Let us look at an example. The cause based on which tuberculosis has been defined in the aetiological model is an infection with the bacterium *M. Tuberculosis*. As it is understood in the aetiological framework (see Chapter I, §2), such an infection is universally shared by patients with the disease, so having that infection is a wide biological regularity for tuberculosis. Further, the infection typically affects the lungs, so it affects a specific, single site of the body. Finally, in the aetiological understanding, the infection causes specifically tuberculosis and no other

[36] See footnote 30.

disease. So, the purported cause of tuberculosis, i.e., an *M. Tuberculosis* infection, is a wide biological regularity occurring at a single site of the body having causal specificity[37].

But, regarding psychiatric conditions, however, no brain abnormalities with these features have been discovered. Rather, as I elaborated in Chapter II (§1) and as critics of biological psychiatry usually remark, current findings show a variety of causal factors for those conditions, with biological findings usually being non-wide regularities and not having causal specificity (see Chapter II, §1). Moreover, critics have alleged that several sites in the brain are involved in the development of psychiatric distress (see Chapter II, §§3.1 and 3.2).

So, instead of supporting biological psychiatry's causal commitment—based on which biological psychiatry has aimed at psychiatric biological definitions—, current evidence seems to be rather compatible with the CAUSAL COMMITMENT OF INTEGRATIONIST PSYCHIATRY I presented in Chapter II (§3.2). This commitment states that psychiatric conditions are caused by factors at different levels of explanation such as the biological, psychological, cognitive, and social, and that, among the biological causes, there are brain factors in the form of non-wide regularities occurring at several brain sites, which do not have causal specificity. Then, based on current evidence, psychiatric conditions seem not to have "final common pathways" as described by biological psychiatry's causal commitment.

Here, we can return to the difference in how diseases such as tuberculosis and syphilis are biologically caused and how psychiatric conditions are biologically caused. Based on the

[37] Of course, the similarity between the causes of diseases such as tuberculosis and the causes sought by biological psychiatrists for psychiatric syndromes is not just a coincidence. As it has been widely noted, "[t]he 19th/20th-century biomedical disease paradigm [i.e., the aetiological model] was taken into the new psychiatry at the turn of the century" (Bolton, 2012, p. 9), and it was such a "biomedical disease paradigm" which motivated biological psychiatrists to seek biological definitions in psychiatry. In particular, such a motivation came from the successes allowed by biological definitions in the classification, treatment and prevention of diseases such as tuberculosis and syphilis—an issue on which I will elaborate in §3.1.

considerations above, I take it that such a difference is best understood as follows: diseases such as tuberculosis and syphilis, which are defined biologically for classificatory purposes, have among their causes biological factors which are wide regularities occurring at single sites of the body and which have causal specificity—such as, e.g., an *M. Tuberculosis* infection for syphilis—, whereas psychiatric conditions as they are currently classified do not have that sort of causes—in the view of the critics[38].

Given this interpretation, one can then understand the critics' claims as follows. Diseases such as tuberculosis and syphilis are defined in terms of just one of their biological causes, specifically, one that is a *wide regularity* occurring at *single bodily sites* with *causal specificity*[39]. But, as evidence suggests, psychiatric conditions lack biological causes of that sort, so it is "unrealistic" or difficult to define these conditions in terms of biological causes. Then, definitions based on biological causes for psychiatric conditions are ruled out by the critics. In the following section, however, I will argue that the lack of brain causes as required by biological psychiatry's causal commitment is not, by itself, an impediment to developing psychiatric biological definitions, and that these could be provided even if *integrationist* psychiatry's causal commitment was true. Later, I will address in §4 the possible objection that my argument is based only on *a priori* considerations, while the issue at stake requires empirical evidence supporting the development of specific biological definitions.

[38] Although some biological psychiatrists might argue, to the contrary, that psychiatric conditions do have something close to that sort of causes. For instance, Nassir Ghaemi (2012) claims that at least some psychiatric conditions will be "identifiable as [diseases] always have been, as *an abnormality of the body, often in an organ, which leads to a stereotypic syndrome presentation and a typical clinical course*" (p. 44; emphasis in the original).

[39] Instead of being defined in terms of a factor which is the only biological cause of the disease.

3. Biological definitions

I aim to show that the lack of biological causes for psychiatric conditions as the ones required by biological psychiatry's causal commitment is not an *a priori* nor a practical impediment to the development of psychiatric biological definitions. In particular, I will argue that those definitions could be developed even if integrationist psychiatry's causal commitment was true, that is, even if, among the varied causes of psychiatric conditions, these had brain causes which were not wide regularities, which occurred at several brain sites, and which caused more than one psychiatric syndrome. For this purpose, I will present an imaginary scenario and will build my argument based on it.

Before doing so, however, a note is in place. My point in this chapter is that psychiatric biological definitions can be provided even if integrationist psychiatry's causal commitment was true. Nevertheless, this does *not* imply that a psychiatric biological definition as the one I defend would coincide with only one of the psychiatric conditions classified by the DSM or ICD. That is, my argument implies that a biological definition could cut across two (or more) current diagnostic categories. This is a consequence, however, of the fact that the examples that I will be dealing with involve biological factors *without* causal specificity so, by definition, in those examples, a single biological factor causes more than one psychiatric condition—for this is a requirement of integrationist psychiatry's causal commitment. I will mention later, though, that biological definitions that coincided with single diagnostic categories could also be developed based on factors which had causal specificity but were non-wide regularities and occurred at several brain sites.

So, to begin with, consider the syndromes of depression and schizophrenia, and imagine that the following circumstances occur: suppose that childhood neglect, poverty,

discrimination, a certain cognitive deficiency, certain genetic predispositions, and abnormalities in three neurotransmitter systems, i.e., the dopaminergic, the glutamatergic, and the serotoninergic systems, were all established causes of both depression and schizophrenia.[40] Regarding the neurotransmitter systems, it might be, e.g., that they had complex relations in a way that, say, a deficiency or an excess in the production of a neurotransmitter affected the production of the others, and so on. Let us call the abnormalities in the neurotransmitter systems "the DGS abnormality" and suppose that, because of the workings of genetics, the DGS abnormality was developed only in patients with the relevant genetic predisposition *and* exposition to the social aspects mentioned[41]. On the other hand, imagine that only relatively few patients with depression and with schizophrenia had the DGS abnormality—let us say, just as an example, that about 20% of patients with depression had the DGS abnormality, and something similar for patients with schizophrenia. In addition, let us suppose that some patients with the DGS abnormality developed only depression, some others only schizophrenia, and some others both depression and schizophrenia.

The situation in this scenario is then one in which integrationist psychiatry's causal commitment is true for schizophrenia and depression: these are caused by a variety of factors

[40] In reality, all these factors have been correlated with the conditions. Regarding brain factors in particular, serotonin imbalances have been classically associated with depression, and dopamine and glutamate abnormalities with schizophrenia. Further, dopamine, glutamate, and serotonin haven been found to have some correlation with psychotic symptoms such as hallucinations and delusions, which are characteristic of schizophrenia (see, e.g., Stahl, 2018).

[41] In reality, as a matter of fact, dopamine production related with schizophrenia is thought to depend largely on environmental factors. As it is stated in a research review, "[r]esearch using healthy twin pairs has found evidence that environmental factors explain a substantial proportion of variation in normal presynaptic dopamine function" (Howes, McCutcheon, & Stone, 2015, p. 6). Indeed, dopamine abnormalities relevant to schizophrenia are thought to be "predominantly due" to factors other than genetic liability, which "account for 56% of the variance of presynaptic striatal dopamine function [which] is consistent with previous findings that striatal dopaminergic function is adaptive to environmental influences" (Stokes *et al*, 2013, p. 488).

at different levels of explanation, and a factor at the level of the brain, i.e., the DGS abnormality, is not a wide regularity—it is scarcely shared among patients with depression and schizophrenia—; also, such a brain factor occurs at several sites in the brain, for it "recruits" three distinct neurotransmitter systems; and, finally, the brain factor is not causally specific—it causes two syndromes. The question to be addressed now is whether a biological definition could be provided in this scenario.

I posit an affirmative response to this question. There is, in fact, no *a priori* impediment to including in the taxonomy of psychiatric illness a novel category defined in terms of the DGS abnormality. A novel condition in the scenario above could be named, say, "DGS disease" and it could be defined for classificatory purposes as *an abnormality in the dopaminergic, glutamatergic, and serotoninergic systems*—specifically, the DGS abnormality. Psychiatrists in this scenario, perhaps, might then separate the cases of depression and schizophrenia not caused by the DGS abnormality, making explicit that, in contrast with the cases caused by that abnormality, these other cases would still have an unknown biological cause. Maybe, the cases *not* caused by the DGS abnormality could simply be (re)named "depression syndrome" and "schizophrenia syndrome" to distinguish them from the cases caused by the DGS abnormality.

The point is that there is no *a priori* impediment for DGS disease to be included in the taxonomy of psychiatric illness, that it was defined in terms of the DGS abnormality, and that only patients who had the DGS abnormality had DGS disease. Then, such a psychiatric condition would be defined based on a specific biological cause[42]. In the following subsection, I will argue that there is also no practical, significant impediment for DGS disease

[42] Although this does not mean that DGS disease would be defined following the aetiological model, as I will explain in §5 of this chapter.

to be included in the taxonomy of psychiatric illness. However, some notes are in place before that.

It is important to note that biological factors forming non-wide regularities, occurring at several bodily sites, and lacking causal specificity in relation to syndromes—that is, biological factors similar to those required by integrationist psychiatry's causal commitment—have not individually precluded diseases from being defined biologically. For instance, regarding *non-wide regularities* causing a syndrome, consider the cluster of symptoms comprising excessive thirst, excessive need to urinate, and tiredness, which tend to cluster together and form a syndrome. Let us call this the "diabetes syndrome". The majority of its cases are caused by chronic hyperglycaemia—i.e., abnormally elevated blood glucose levels—, and these are cases of diabetes mellitus.

However, in *very rare* cases, the diabetes syndrome is caused by an endocrine abnormality which results from a dysfunction in a type of neurons called "vasopressinergic neurons", which leads to the abnormal release of fluids by the kidneys. These are cases of central diabetes insipidus, a disease unrelated to diabetes mellitus. It is worth noting that, since the diabetes syndrome is caused only in very rare cases[43] by an endocrine/neuronal abnormality as described above, then this abnormality is a *small* biological regularity for the diabetes syndrome as compared with hyperglycaemia, which causes the majority of diabetes syndrome cases.

[43] To see how rare are the cases of diabetes syndrome caused by the neuronal/endocrine abnormality as compared with those caused by hyperglycaemia, note that the prevalence of central diabetes insipidus has been estimated to be "about 0.004% of the global population" (Mutter *et al*, 2021, p. 1)—that is, about 215 thousand cases by 2021 worldwide—, while "the prevalence of diabetes in adults aged 20–79 years has more than tripled […] to 537 million (10.5% [of the global population]) today" (International Diabetes Federation, 2021, p. 2). Then, by 2021, there were about 215 thousand cases of diabetes insipidus worldwide, whereas there were 537 million cases of diabetes mellitus. So, cases of (what I call) the diabetes syndrome associated with diabetes insipidus are dramatically less than those associated with diabetes mellitus.

My point here is that, although the endocrine/neuronal abnormality is a relatively small regularity causing a syndrome, it has been employed in a biological definition. Central diabetes insipidus has been defined, in fact, as follows: [c]entral diabetes insipidus (CDI) is a clinical syndrome which results from loss or impaired function of vasopressinergic neurons […] impairing the synthesis and/or secretion of the antidiuretic hormone (Tomkins, *et al*, 2022, p. 2701). So, biological definitions have been developed in medicine based on biological causes of syndromes which form *non-wide* regularities.

On the other hand, consider diabetes mellitus. Currently, it is defined as follows: "[d]iabetes mellitus is impaired insulin secretion and variable degrees of peripheral insulin resistance leading to hyperglycemia" (Brutsaert, 2023). So, the disease is biologically defined in terms *both* of insulin dysfunction and abnormally elevated blood glucose levels (hyperglycaemia). Then, by itself, the fact that more than one site is involved in a disease—in this case, the function of producing insulin *and* having abnormally elevated blood glucose levels—has not precluded the development of biological definitions based on *more* than one bodily site[44].

Finally, the fact that a certain biological factor is non-causally specific in relation to syndromes has also not precluded the development of biological definitions. Consider, for instance, the symptoms of coughing, wheezing, having inflamed nasal passages or a stuffy nose and sinusitis, which form a syndrome. Let us call this the "respiratory syndrome".

[44] Recall that the notion of *site* is quite loose. As I mentioned in Chapter I (§2.2), the sites biological psychiatrists speculate that could be related to psychiatric conditions can be either abnormalities in a specific neuroanatomical part, or an abnormality in a single neurotransmitter system, or a specific pattern of neuronal firing, and so on. A site, then, can be understood merely as a specific anatomical part, feature, or function inside the body—as opposed to the whole body. Diabetes mellitus, then, involves, among other sites, the *function* of producing insulin (by the pancreas), and the *feature* of having certain amounts of blood sugar, and it is defined in terms of abnormalities in those sites.

Further, consider another cluster of symptoms comprising crampy abdominal pain, distension, reduced frequency of bowel motions, and loss of appetite, which is called "distal intestinal obstructive syndrome" (DIOS) (see, e.g., Mavilia & Pope, 2018). Despite being two very different syndromes, both the respiratory syndrome and DIOS can be caused—in the very same or different patients—by variants of the CFTR gene.

What is of interest here is that a single disease has been biologically defined based on the variants of the CFTR gene, despite the latter not having causal specificity in relation to the mentioned syndromes—the variants cause the two of them. The disease in question is cystic fibrosis, which is currently defined as follows: "[c]ystic fibrosis is an autosomal recessive disease caused by variants in the CFTR gene" (Grasemann & Ratjen, 2023). This example illustrates that the mere lack of causal specificity in relation to syndromes has not precluded the development of biological definitions in other areas of medicine.

Then, individually, the features of being a biological regularity which is not (relatively) wide, which occurs at several bodily sites, and which is non-causally specific in relation to syndromes allow biological definitions of diseases, as in the examples of central diabetes insipidus, diabetes mellitus, and cystic fibrosis, respectively. To be sure, it is difficult to find a disease defined in terms of a biological factor having all *three* features above. However, there is no constraint imposed by the notions of a non-wide biological regularity, of several bodily sites, and of lack of causal specificity, nor by the notion of a definition based on biological causes, that precludes a disease from being defined in terms of a biological cause which is a non-wide regularity occurring at several sites and which lacks causal specificity. As a matter of fact, an (imaginary) example of this is DGS disease, which I presented earlier. In what follows, I will argue that there would also not be a practical,

significant impediment for DGS disease to be included in the taxonomy of psychiatric illness in the circumstances of the scenario I proposed.

3.1 Practical issues

It is clear now that biological psychiatrists have traditionally sought the biological causes based on which they intend to classify psychiatric conditions to be large-sized regularities. This might, in part, be motivated by practical considerations. For instance, the wholesale development of diagnostic tests, medications, prevention and treatment plans for some diseases has been partly allowed by biological definitions based on wide biological regularities. If a disease such as, say, gastritis, is defined in terms of a wide biological regularity as *inflammation of the gastric mucosa* (Vakil, 2023), then, all and only patients suffering from said inflammation have the disease. This means that if a diagnostic test is sensitive to that inflammation, *all* cases of the disease can be diagnosed by employing the diagnostic test. Further, since gastritis is just inflammation of the gastric mucosa, treatments alleviating this inflammation would adequately apply to *all cases* of the disease. And, finally, if some measures are established to prevent the gastric mucosa from getting inflamed, then those preventative measures would apply to all instances of gastritis.

Biological psychiatry's search to define psychiatric conditions biologicaly has been motivated by the aspiration to achieve, in psychiatry, the sort of practical benefits just mentioned. As Bolton (2013) notes,

> [t]here is currently an extensive research effort in physical medicine to identify internal [bio]markers of disease processes reliably, to plan appropriate management, and early, to optimize prognosis under treatment, with progress in many areas. Similar benefits

> could accrue in psychological medicine, in psychiatry, if biomarkers could be identified (p. 446).

However, in the scenario concerning DGS disease, the DGS abnormality would *not* be a wide regularity for depression or schizophrenia, so this might be seen as a practical impediment to developing diagnostic tests, medications, and treatment and prevention plans for those conditions. For instance, a medication that targeted the DGS abnormality would not be a treatment for all cases of schizophrenia—for only some cases of the condition would be caused, in the imaginary scenario, by such an abnormality. Also, a test sensitive to that abnormality would not be, by itself, a standard diagnostic instrument for, say, depression, for, in the scenario I proposed, about 80% of patients with depression would *not* have the DGS abnormality.

However, the point of including DGS disease in the classification systems of psychiatric illness in the scenario I proposed is not to account for all cases of depression or schizophrenia. Instead, the category of DGS disease would only account for *all cases* of DGS abnormality. And, if a diagnostic test was developed that was sensitive to the DGS abnormality, then such a test could be employed as an instrument to diagnose *all cases* of DGS disease. Similarly, if some treatment successfully targeted the DGS abnormality, then it would be a treatment for all cases of DGS disease, and so on for preventative measures.

The point is that, although the DGS abnormality would be a non-wide regularity, occurring at several sites of the brain, lacking causal specificity in relation to depression and schizophrenia, the DGS abnormality could, nonetheless, be employed in a psychiatric biological definition, and there is no reason to believe that such a definition would preclude

the development of diagnostic tests, treatments, and prevention plans *for DGS disease* more than biological definitions in other areas of medicine do.

A further practical issue concerns a general worry about biological psychiatry. A very common critique against the latter is that an understanding of psychiatric illness merely in biological terms disregards important, non-biological factors leading to it, such as psychological and social risk factors. DGS disease as in the scenario I posed is defined in purely biological terms, so the mentioned critique might be thought to apply to it. However, although some diseases are defined biologically in other areas of medicine, they are not explained, treated, or prevented merely in biological terms—as I will illustrate in a moment—and, as in the case of those diseases, a definition such as that of DGS disease, being purely biological, can allow a variety of non-biological factors to be acknowledged in explanations, treatments, and prevention plans for it. Then, the general understanding of DGS disease needs not be merely biological, and it needs not disregard non-biological, relevant factors just because the disease is defined biologically[45].

To illustrate this, consider diabetes mellitus, which, as I mentioned earlier, is biologically defined as insulin impairment leading to hyperglycaemia (Brutsaert, 2023). Though the disease is defined in purely biological terms, the "Standards of Care in Diabetes" of the *American Diabetes Association* (2022) acknowledge that "social determinants of health […] contribute to health care and psychosocial outcomes and must be addressed to improve *all* health outcomes" (p. S11; my emphasis). Among the social factors currently known to contribute to the development of diabetes—specifically, type 2 diabetes—are socioeconomic status, neighbourhood and physical environment, and social context (see Hill-

[45] I will deal extensively with this issue in Chapter IV. In particular, I will argue that defining psychiatric conditions biologically does not commit explanations of those conditions to be biologically *reductionist*.

Briggs *et al*, 2021). So, for instance, regarding socioeconomic status, it is currently known that "[t]he higher a person's income, the greater their educational attainment, and the higher their occupational grade, the less likely they are to develop T2DM [type 2 diabetes mellitus]" (Hill-Briggs *et al*, 2021, p. 260). Then, current explanations of diabetes—specifically type 2 diabetes—involve not only biological factors but also psychosocial factors, even though the disease is defined in purely biological terms.

Furthermore, the Standards of Care in Diabetes describe the disease as "a complex, chronic condition requiring continuous medical care with *multifactorial* risk-reduction strategies beyond glucose management" (p. S1; my emphasis). That is, the Standards of Care advise the implementation of *psychosocial* interventions aiming to treat and prevent (the preventable types of) diabetes. Those interventions target, but are "not limited to attitudes about diabetes […] general and diabetes-related mood stress and/or quality of life, available resources, and/or psychiatric history" (American Diabetes Association [ADA], 2022, p. S79). Psychological assessment and treatment are also recommended to manage the disease (see ADA, 2022, ch. 4). All this illustrates that non-biological interventions are employed to treat and prevent diabetes, even though it is defined in purely biological terms. Then, even though it is thus defined, the disease is explained, treated and prevented beyond biology.

So, such as diabetes is not merely understood biologically even though it is thus defined, DGS disease as in the scenario I proposed could be understood beyond its biological features despite being defined solely in biological terms. DGS disease would in that scenario be biologically defined in terms of dopamine, glutamate, and serotonin abnormalities, but a variety of close and distant factors such as childhood neglect, poverty, and discrimination could be acknowledged in explanations of it. Moreover, recommended management plans

for the disease could include medications targeting the DGS abnormality and relevant psychosocial interventions. Regarding the latter, psychotherapy and the withdrawal of social stressors, or any other psychosocial intervention targeting the psychosocial factors known to cause the disease could be recommended to treat it. The point here is that acknowledging and managing heterogeneous causes of diseases is compatible with how medicine defines diseases biologically for classification currently. Then, an understanding of psychiatric conditions based on biological definitions needs not overlook relevant causal, non-biological factors.

A further, brief issue regarding the imaginary scenario I posed in §3 is that many cases of depression and schizophrenia would, in that scenario, not be caused by the DGS abnormality, so the question arises as to how those cases should be understood. For those cases, research intending to discover novel causal facts could simply continue to be carried out and, if relevant findings were made, novel biological definitions could be developed. So, for instance, in case a brain lesion B was found to cause a subset of, say, schizophrenia cases, a novel disease category could be included in the classification systems of psychiatric illness, defining a disease based on brain lesion B, and so on. Of course, whether there would be several biological variants of schizophrenia or depression does not undermine my claim, which is only that biological definitions could be developed in psychiatry even if integrationist psychiatry's causal commitment was true.

A final issue is that the example of DGS disease cuts across two categories of psychiatric illness, i.e., depression and schizophrenia. As I mentioned earlier, that is because the scenario I posed is stipulated to involve a *lack* of causal specificity so, by definition, the biological cause in my example causes more than one psychiatric condition. Nevertheless, if

DGS abnormality as in the scenario I posed was causally specific, even though it still was a non-wide regularity occurring at several brain sites, it could be employed in a biological definition. Let us think of a slight variation to the scenario I posed in §3, and suppose that the DGS abnormality was among the causes of schizophrenia but not depression or any other psychiatric condition. Thus, the DGS abnormality would be causally specific in relation to schizophrenia. In this circumstance, a novel category could be included in the taxonomy of psychiatric illness, being a sub-type of schizophrenia. This category could define a sub-type called, e.g., "DGS schizophrenia", as *an abnormality in the dopaminergic, glutamatergic, and serotoninergic systems*—specifically, the DGS abnormality.

Psychiatrists in these circumstances, perhaps, might then separate the schizophrenia cases not caused by the DGS abnormality from those caused by it. Maybe, the cases of schizophrenia not caused by the DGS abnormality could simply be (re)named "schizophrenia syndrome" to distinguish them from the cases related to the DGS abnormality, and the schizophrenia syndrome would simply form a sub-type of schizophrenia. Finally, practical and *a priori* considerations similar to those I explained regarding DGS disease could be applied to DGS schizophrenia. Then, biological definitions based on non-wide biological regularities occurring at several brain sites could correspond to only one category of psychiatric illness as well.

I will address a possible objection to my argument in the following section.

4. An objection

I anticipate a two-part criticism against my argument, and it is as follows. First, it defends psychiatric biological definitions merely based on *a priori* considerations—specifically,

based on the idea that those definitions are possible in the scenario I posed in §3. However, critics might claim, the issue at stake does not only concern the possibility that biological definitions were provided in psychiatry. As elaborated in §1 and §2, the critics' view is that psychiatry lacks biological definitions because discoveries supporting the development of those definitions are not currently available. So, not only the *possibility* of defining psychiatric conditions biologically is at stake in the discussion, but also whether relevant *findings* support biological definitions.

In connection with that, the second part of the criticism goes like this. My argument does not prove that a biological finding supports a biological definition as that of DGS disease *at present*. Then, no findings seem to support psychiatric biological definitions anyway, regardless of whether those findings are as required by biological psychiatry's causal commitment—as biological psychiatrists traditionally sought—, or by integrationist psychiatry's causal commitment—as in the scenario I posed. Then, as critics have *already* pointed out, no findings support psychiatric biological definitions. Then, in a way, my argument does not advance the discussion.

My response to this possible objection is as follows. I acknowledge the importance of relevant findings for biological definitions and the apparent lack of findings supporting definitions such as that of DGS disease. However, the *a priori* point I defend, that biological definitions can be provided in a scenario like the one I posed in §3, *does* advance the discussion. My argument brings to light important considerations overlooked by critics of psychiatric biological definitions. Recall that their critique is that, since psychiatric conditions do not have single, clear biological causes, then a classification based on biological causes is "difficult" or "unrealistic" in psychiatry. We should note, though, that

such a critique presupposes that classification based on biological causes is constrained only to conditions having single, clear biological causes—otherwise, in the absence of the latter, classification based on biological causes would not be difficult or unrealistic, as they claim.

However, my argument shows that this needs *not* be the case. In contrast with the critics' understanding, my argument shows that a biological classification based on causes can encompass conditions—such as psychiatric conditions—which do not have "single", "clear" biological causes and, rather, do have heterogeneous causes at different levels of explanation, and which involve significant non-biological features like behavioural and psychological symptoms. Furthermore, my argument also illustrates that there is no in principle reason to believe that biological definitions of conditions of this latter sort cannot allow the same sort of benefits that traditional biological definitions such as that of syphilis allow (see §3.1).

Then, although my argument does not accommodate current evidence to define a specific psychiatric condition biologically, it illuminates the fact that biological psychiatrists are *not* constrained to find "single, clear" biological causes to achieve the purpose of defining psychiatric conditions biologically for classification—as critics assume. This is a novel outcome and, then, the discussion is not in the same state as it was prior to my argument.

A final note is that, if one accepts that medical conditions can be defined biologically for classification based on the sort of *a priori* considerations I make in this chapter, some conditions could be defined biologically in reality if relevant discoveries were made. Thus, although my argument concerns the mere possibility that biological definitions were provided in psychiatry, it could also lead to a practical consequence. This does not mean, of course,

that I claim biological psychiatry *should* aim at developing biological definitions of this sort, a claim for which different support should be provided.

5. Further remarks

The discussion concerning psychiatric biological definitions is framed in terms of the *aetiological model* of classification I discussed in Chapter I (§2), in which the (supposed) single, biological causes of diseases are employed to classify them. Such a model "was taken into the new psychiatry at the turn of the [20th] century" (Bolton, 2012, p. 9), and biological definitions began to be sought in psychiatry in an attempt to replicate the successes allowed by the aetiological model in other areas of medicine. Then, in discussing about psychiatric biological definitions, biological psychiatrists and critics often have the aetiological model in mind, and the discussion is then framed in aetiological terms.

However, I explained in Chapter I (§2.1) that the aetiological model of disease classification is defective. So, unless we were happy with a defective model, the discussion concerning psychiatric biological definitions should be understood in a non-aetiological way. As I argued in Chapter I (§4), medical classification in general is currently best understood to be constitutive, that is, as defining medical conditions for classification in terms of features which are necessary and sufficient for them, and which are not their causes or effects. Then, the discussion concerning psychiatric biological definitions should be understood *constitutively* instead of aetiologically, I will now elaborate on the constitutive interpretation of the discussion in this chapter.

The issue at stake in the discussion concerning psychiatric biological definitions is whether definitions of psychiatric conditions in terms of their biological causes are viable.

But "definitions in terms of causes" can be interpreted in two ways, i.e., the aetiological and the constitutive. To illustrate the two interpretations, let us first consider the following example. Suppose that biological factor *B* causes schizophrenia specifically, that *B* has been discovered, and that schizophrenia has been given a definition in terms of *B*. For the purposes at hand, it is irrelevant whether B is a wide regularity and whether it occurs at single brain sites.

In the aetiological interpretation, *B* as above is understood as the cause of the *psychiatric condition* schizophrenia, and the latter is defined as follows:

schizophrenia is the disease caused by biological factor B

The aetiological interpretation, thus, states that schizophrenia is exactly the disease which is the effect of *B*. So, assertions such as "psychiatrists seek to define psychiatric conditions in terms of biological causes" must be understood in this interpretation as saying that psychiatrists attempt to define those conditions as effects of single biological causes.

On the other hand, in the constitutive interpretation, *B* as above is understood as the cause of the *syndrome* of schizophrenia, that is, as the cause of the *symptoms* of the condition—rather than as the cause of the condition itself—, and schizophrenia is defined as follows:

schizophrenia is biological factor B[46]

[46] A constitutive definition could also cite symptoms, and not only biological factors. I will consider this possibility later in this section.

The constitutive interpretation states that schizophrenia is exactly *B*. In this interpretation, something is schizophrenia iff something is *B*, so *B* is necessary and sufficient for schizophrenia, without *B* being any of schizophrenia's causes or effects. Then, assertions such as "psychiatrists seek to define psychiatric conditions in terms of biological causes" must be understood as saying that psychiatrists attempt to cite, in the definitions of psychiatric conditions, a biological factor which is known to cause the *symptoms* of the condition defined.

Then, in the aetiological interpretation, a definition in terms of biological causes is one based on a biological cause of the psychiatric *condition* itself. But in the constitutive interpretation, a definition in terms of biological causes must be understood as one based on a biological cause of the *symptoms* of the psychiatric condition. This latter interpretation is consistent with the constitutive model of classification I defended in Chapter I (§4). If I am correct and current medical classification is best understood to be constitutive, then the discussion concerning psychiatric biological definitions should be understood according to the constitutive, rather than the aetiological interpretation.

Now, the scenario I posed in §3 is more complex than the example of schizophrenia and biological factor *B* above, for the DGS abnormality does *not* have causal specificity, and it defines DGS disease nonetheless. However, such a scenario should also be viewed constitutively. In a constitutive interpretation, the DGS abnormality should be understood as a cause of the *symptoms* of schizophrenia and depression, and a novel psychiatric condition is defined as follows:

DGS disease is DGS abnormality

The constitutive interpretation states that DGS disease is exactly DGS abnormality and, in this interpretation, something is DGS disease iff something is DGS abnormality. Then, the DGS abnormality is necessary and sufficient for DGS disease, and the abnormality is neither one of the causes or effects of DGS disease. So, although DGS disease is defined based on biological causes of psychiatric conditions, it is classified constitutively rather than aetiologically.

A further question is whether the realisation analysis I addressed in Chapter I (§3) applies to psychiatric conditions defined biologically as DGS disease. According to the realisation analysis, diseases have an aetiology which causes a pathology, and the latter causes characteristic symptoms. Further, this analysis posits that the pathology realises the diseases. I pointed out as well that "realisation" appears to be understood as *identity* in this analysis, although that term also has a distinct, standard sense. As I will explain now, diseases such as DGS disease can, in fact, be understood to have an aetiology, a pathology, and symptoms, and they are adequately seen to be realised by their pathology in the identity sense of realisation, but not in the standard sense. However, I will also point out that a constitutive understanding of diseases like DGS disease is more general than the realisation analysis and, in that sense, the constitutive approach is preferable.

To recall, in the scenario I posed in §3, social factors such as childhood neglect, poverty, and discrimination, and biological factors such as genetic predispositions and the DGS abnormality are found to cause symptoms of depression and schizophrenia. Further, in this situation, the novel DGS disease is defined as *an abnormality in the dopaminergic, glutamatergic, and serotoninergic systems*—specifically, the DGS abnormality. So, in this

scenario, the social factors and the genetic predispositions above can be considered the *aetiology* of DGS disease, and the DGS abnormality its *pathology*—i.e., the destructive process specifically associated with the condition. In this understanding, the interaction of the social and biological factors mentioned leads to the development of the DGS abnormality which, in turn, leads to symptoms. As a note, in this scenario, symptoms can, in some cases, be those of depression, in other cases those of schizophrenia, and yet in other cases a combination of both in the very same patients. The point is that a psychiatric condition defined biologically like DGS disease can appropriately be seen to have an aetiology, a pathology and symptoms.

Regarding whether the relevant pathology can be understood to realise the condition, let us look first at the *identity* sense of realisation. I mentioned that DGS disease is defined as DGS abnormality in the scenario I posed. One might see this definition as establishing the identity of DGS disease, so that the latter is identical to the DGS abnormality. Understood in this way, DGS disease is then realised by its pathology—i.e., the DGS abnormality—in the identity sense, for the former is identical to the latter. I will address later, though, a slight variation of the scenario I posed, in which DGS disease is *not* realised by its pathology in the identity sense, even though the relevant definition remains constitutive. For now, let us look at the standard sense of realisation.

The standard sense I explained in Chapter I (§3.2) is that, in a realisation relation, the realis*er* property or state is constitutively sufficient, not necessary, and explanatory for the realis*ed* property or state. In the scenario I proposed in the present chapter (§3), the candidate realis*er* state or property is the DGS abnormality, and the candidate realis*ed* state or property, DGS disease. Then, the question here is whether the DGS abnormality is constitutively

sufficient, not necessary, and explanatory for DGS disease. To be noted, though, is that the definition of the disease as being DGS abnormality implies that no patient without the abnormality has the disease, so the DGS abnormality is *necessary* for DGS disease. Then, the former and the latter do not have a genuine realisation relation for, as I explained in Chapter I (§3.2), in a genuine realisation relation, the realiser is not necessary for the realised property or state. Then, DGS disease is not realised by the DGS abnormality in the standard sense of realisation.

A disease defined biologically such as DGS disease can thus be adequately seen as realised by its pathology in the identity sense of realisation, but not in the standard sense. Moreover, I pointed out above that DGS disease can also be correctly viewed as having an aetiology, a pathology, and symptoms. So, excluding the standard sense of realisation, the realisation analysis applies to diseases defined biologically such as DGS disease.

A further issue is important, though. I noted in Chapter I (§§ 3, 4.3, 5.1) that some definitions of diseases citing a biological factor in current medicine also cite relevant *symptoms*. For instance, the MSD Manuals state that "[c]ushing syndrome is a constellation of clinical abnormalities caused by chronic high blood levels of cortisol or related corticosteroids", with "[t]ypical symptoms and signs includ[ing] moon face and truncal obesity […] and thin arms and legs" (Grossman, 2024). Then, the definition of Cushing syndrome cites both an underlying biological factor—high blood levels of cortisol and related corticosteroids—and symptoms. And, although it is not clear what motivates physicians to define a condition only in terms of underlying biological factors or in terms of underlying biological factors and symptoms, it is clear that definitions of the latter sort are employed in current medicine.

Then, it is a possibility that DGS disease was defined, in the scenario I posed in §3, as *an abnormality in the dopaminergic, glutamatergic, and serotoninergic systems causing depression and/or schizophrenia symptoms*. If we understand this definition as establishing the identity of DGS disease, then this disease would be identical to the depression and schizophrenia symptoms *as caused* by the DGS abnormality. Then, it would not be the case that DGS disease would be identical to (only) the DGS abnormality and, conversely, it would not be the case that DGS abnormality, in itself, would be identical to the disease. So, in this case, the pathology of DGS disease, i.e., the DGS abnormality, would *not* realise the disease in the identity sense of realisation. Further, based on the definition of DGS disease citing symptoms as above, no patient without the abnormality (and symptoms) has the disease, so the abnormality would be necessary for the disease, and DGS abnormality would also not realise DGS disease in the standard sense of realisation—for, in a genuine realisation relation, the realiser is not necessary for the realised thing.

What is of interest here is that, for diseases defined biologically, the idea that diseases are realised by their pathology applies only if we understand realisation as identity, and in the particular case that only the relevant pathology is cited in the definition of the disease. For cases in which a biological definition cites both pathology and symptoms, diseases are not adequately viewed as being realised by their pathology—in either sense of realisation. However, a definition citing both pathology and symptoms could still be *constitutive* for, in a definition such as that of DGS disease citing its symptoms, both the abnormality and the symptoms are necessary and jointly sufficient for the disease, and they are neither its causes or effects[47]. So, in contrast with the realisation analysis, a constitutive understanding

[47] Note that the features cited in definitions of medical conditions determine whether they can be understood to be realised by their pathology. Although conditions such as schizophrenia are defined in terms of syndromes at

accommodates both cases—the one in which diseases are biologically defined solely in terms of pathology, and the one in which they are defined in terms of pathology and symptoms.

Then, as I argued in Chapter I (§4.3), from a classificatory point of view, the constitutive understanding of diseases is more general than the realisation understanding of them, and the discussion concerning psychiatric biological definitions can be best interpreted constitutively rather than in terms realisation—or in aetiological terms as well.

6. Conclusions

It is clear at this point that biological psychiatry has traditionally sought to define psychiatric conditions based on biological causes *as required* by biological psychiatry's causal commitment. I call the search to define those conditions in that way, the "strong biomedical project". So far, evidence has not supported biological psychiatry's causal commitment so, consequently, it has also not supported the strong biomedical project. But my argument shows that something like a "moderate biomedical project", attempting to define psychiatric conditions in terms of brain causes as required by *integrationist* psychiatry's causal commitment would be viable.

My argument, thus, provides an important insight into the discussion: the strong medical project is not promising, but this does not imply that biological psychiatry's search to define psychiatric conditions based on their brain causes should be abandoned, for such a search is compatible with brain factors being the sort of factors required by *integrationist*

present, one might think of those conditions as being realised (in either sense of realisation) by an unknown pathology—to be discovered. So, definitions in terms of syndromes allow the possibility that the conditions are realised by their pathology. However, if the pathology and symptoms of a condition come to be cited in the definition, the disease is not adequately viewed to be realised by its pathology (in either sense of realisation), as I explained based on the case of DGS disease.

psychiatry's causal commitment, which seems to be consistent with current evidence. Then, although the biological causes of psychiatric syndromes are not as they were traditionally expected, it is still possible to define psychiatric conditions biologically for classificatory purposes by implementing a moderate biomedical project.

Further, criticisms against psychiatric biological definitions are usually grounded on the idea that heterogeneous factors at different levels of explanation cause psychiatric syndromes. Nevertheless, as I argued, the search for psychiatric biological definitions is compatible with this. As I showed, psychiatric biological definitions for classification allow the integration of heterogeneous causal factors in explanations, treatment, and prevention plans for those conditions. Then, my argument shows that a usual critique against psychiatric biological definitions for classificatory purposes is not warranted.

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CHAPTER IV

Non-Reductionist Biological Definitions in Psychiatry

I have previously discussed biological psychiatry's search to develop psychiatric biological definitions for classification. As I explained earlier, a biological definition defines a psychiatric condition based on biological causes. In the present chapter, I will focus on whether *explanations* of psychiatric conditions would become biologically *reductionist* if they employed psychiatric biological definitions—in case these were developed. To a large extent, the discussion in this chapter hinges on the aetiological model of disease classification I addressed in Chapter I (§2). And, although I argued in Chapter III (§5) that biological definitions should be interpreted in terms of the *constitutive* model I defended in Chapter I (§4), I will elaborate my arguments in *aetiological* terms in this chapter to avoid the risk of changing the subject. By the end of this chapter, however, I will explain how my arguments apply if biological definitions are understood constitutively instead of aetiologically.

This chapter, more specifically, concerns psychiatric biological definitions and *explanatory reductionism* (ER). The latter is the most widely discussed reductionist view, and it states that explanations of the psychological manifestations of psychiatric conditions can be *adequately* stated in terms only of biological factors such as brain or genetic abnormalities—that is, that the psychological manifestations can be *reduced* to biological factors. As I will elaborate in due course, a common presumption among the critics of biological psychiatry is that, in searching for biological definitions, biological psychiatrists commit to ER—for those definitions are, in a way, considered as purely biological accounts of psychiatric conditions.

This presumption is usually taken for granted and its truth implies detrimental consequences for biological psychiatry. That is because ER is standardly rejected at present. So, if the search for psychiatric biological definitions was committed to ER, then it could be construed as a search for *prima facie* objectionable accounts—i.e., accounts of psychiatric illness solely in biological terms, which are now standardly rejected. Further, if the search in question is committed to reductionism, then this search is subject to the criticisms that have been advanced against reductionism. However, there are reasons to doubt that this presumption, generally taken for granted, is true. That is because, as I explained earlier in the thesis, current biological psychiatry acknowledges that non-biological factors are relevant in psychiatric explanations, something which a reductionist account would not do.

In fact, I will argue in this chapter that the quest for psychiatric biological definitions does *not* commit to ER and that psychiatric non-reductionist explanations based on biological definitions can be achieved. Then, the search for biological definitions does not further reductionist explanations, and complaints against ER do not apply to it. My arguments, then, contribute to correcting the generalised perception that biological psychiatry's project of defining psychiatric conditions biologically is reductionist.

In §1, I will elaborate that the quest for psychiatric biological definitions—understood in terms of the aetiological model—has been thought to commit to ER. Later, in §2 and §3, I will show that, as a matter of fact, it does not currently do so and that non-reductionist psychiatric explanations can be achieved based on psychiatric biological definitions. I will conclude by remarking, in §4, that my arguments also apply to those definitions understood *constitutively*.

1. Biological Definitions and Explanatory Reductionism

I have explained previously in this thesis that biological psychiatry seeks to develop definitions of psychiatric conditions based on their biological causes for classification. However, these definitions have been understood to be biologically *reductionist* by critics, something which is usually considered contentious in approaching psychiatric illness nowadays. In this section, I will explain how reductionism has been understood in psychiatry, and it will become clear why biological definitions have been thought to be reductionist. Nevertheless, I will argue in later sections for a non-reductionist understanding of psychiatric biological definitions.

To begin with, reductionism has been characterised in different ways in the literature but, in this chapter, I will only focus on *explanatory reductionism* (ER), the most widely discussed reductionist view. Though named in slightly different ways, ER has been discussed by, e.g., Radden (2004); Schaffner (2013, p. 1003); Murphy (2006); Borsboom, Cramer & Kalis (2019); Roache (2019); Bublitz (2020, p. 343); and Butler (2019, p. 46). It states that explanations of the psychological manifestations of psychiatric conditions such as delusions, hallucinations, low mood, and so on, can *adequately* be expressed solely in terms of biological factors like brain or genetic abnormalities. In other words, ER states that the psychological manifestations of psychiatric conditions, occurring at a higher level of explanation, are to be *reduced* to brain or genetic factors, occurring at a lower level of explanation.

A paradigmatic example of a reductionist account is Erik Kandel's (1998), which I mentioned in Chapter II (§1). As I pointed out, Kandel's account proposes a framework for explaining psychiatric illness "designed to align current psychiatric thinking and the training

of future practitioners with modern biology" (p. 460). I also mentioned that such a framework is based on five principles that "constitute, in simplified form, the current thinking of biologists about the relationship of mind to brain" (Kandel, 1998, p. 460), and that those principles concern the way *genetics* are related to the brain and behaviour (Kandel, 1998, pp. 460-466). So, since Kandel's framework is genetically centred, and it is aimed at explaining psychiatric illness, then it presupposes that the psychological manifestations of psychiatric illness can adequately be explained in genetic terms—and, in fact, that they *are to be* so explained.

At this point, it is worth noting that ER, on the one hand, and the search to define psychiatric conditions biologically, on the other, have been thought to be deeply intertwined. As I will explain in what follows, a widely shared idea is that ER implies the possibility of defining psychiatric conditions biologically and that, in defining psychiatric conditions biologically, biological psychiatrists would commit to ER. In other words, it has been thought that ER and the search for psychiatric biological definitions imply each other.

In fact, on the one hand, Denny Borsboom, Angélique Cramer, and Annemarie Kalis (2019) point out that ER "implies the possibility of constructing a biological *definition* of and diagnostic protocol for the identification of mental disorders" (p. 3; my emphasis). Then, *reductionist* accounts of psychiatric conditions have been seen as implying the development of *biological definitions*, for those accounts would define the conditions in biological terms.

On the other hand, the search for *biological definitions* in psychiatry has been thought to stick to *reductionism*. For example, consider Kenneth Kendler's & Christopher Gyngell's (2020) account. As I explained in Chapter III (§2), the authors claim that current evidence does not support psychiatric classification to be based on what they call the *hard medical*

model, "where illnesses are linked to a single clear aetiological mechanism" (Kendler & Gyngell, 2020, p. 40). So, in other words, psychiatric classification based on "single clear aetiological mechanism", that is, based on biological causes, is not supported by evidence according to the authors and, consequently, neither are psychiatric biological definitions—for these are put in terms of "single clear" aetiological mechanisms, which have not been found so far. Then, Kendler & Gyngell claim that "we should not attempt to *reduce* psychiatric disorders to diseases with single clear aetiologies" (2020, p. 39).

What is worth noting here is that, in criticising hard medical *classification*, they refuse attempts to *reduce* psychiatric conditions to "diseases with single clear aetiologies", as if developing a biological classification inevitably implied the development of a reductionist account. The idea here is that psychiatric biological definitions for classification would supposedly *reduce* the symptoms of a psychiatric condition to the biological factor defining that condition. Then, in searching for psychiatric *biological definitions*, biological psychiatrists are seen to stick to *ER*, for they seek to provide something like an account of psychiatric conditions in purely biological terms as required by ER.

Then, ER and the search for psychiatric biological definitions have been thought to imply each other. A further example of this line of thought is Herbert Harris' and Kenneth Schaffner's (1992) view. The authors note a growing tendency to incorporate genetic knowledge into psychiatric explanations. Then, they address the possibility of explaining psychiatric conditions reductively, in genetic terms. In doing so, they claim that

> [g]reat conceptual simplification can be obtained by the reduction of diverse symptom complexes to single molecular entities. The temptation to think about diseases in this reductionistic way is especially great when it represents a significant advance in our

> understanding of the basic neurobiology of mental illness. We may therefore see the emergence of *new classification schemes* such as 'G protein disorders' or 'serotonin receptor diseases' (Harris & Schaffner, 1992, p. 144; my emphasis).

What is of interest here is that, as it appears, the authors believe that a consequence of a reductionist understanding of psychiatric illness is "the emergence" of new classification schemes; specifically, the emergence of a biological classification in psychiatry—and, consequently, of biological definitions for the classification of psychiatric conditions[48]. So, in the authors' view, a *reductionist* explanation implies the *biological definition* of psychiatric conditions. But the change from the current classification based on syndromes to a psychiatric biological classification that could be allowed by new genetic knowledge is described by the authors as implying "[r]eductionistic shifts in the [psychiatric] classification" (Harris & Schaffner, 1992, p. 127). Then, a biological classification, implying the *biological definition* of psychiatric conditions, is understood to be committed to *reductionism*.

All these are just some examples that ER and the search for psychiatric biological definitions have been viewed as implying each other. This has been a widely shared assumption but, to my knowledge, it has not been explicitly put into question. But it is worth examining it, for, although it has generally been taken for granted, there are reasons to doubt that it is true. As I have explained earlier in various places—e.g., Chapter II (§1)—current biological psychiatry acknowledges that non-biological factors are relevant in psychiatric explanations, something which a reductionist account would not do. So, scrutiny is here

[48] Harris & Schaffner claim, in fact, that "[t]he analysis of the genetics of mental illness is likely to disclose new information about the underlying mechanisms of diseases that will warrant modification of existing classification. This would represent a movement away from a purely descriptive classification toward a *causal classification* of mental illness" (1992, p. 144; my emphasis).

required to determine whether ER and the search for psychiatric biological definitions imply each other, as it is generally taken for granted. This will be the focus of the rest of this chapter.

An important issue here is that, if the quest for biological definitions implied ER, this would bring detrimental consequences for biological psychiatry. Mainly, that is because ER is currently highly discredited both by biological psychiatrists and their critics. In fact, it is nowadays widely accepted that there is much more to know about psychiatric conditions than their biological determinants. Kendler & Gyngell note, for instance, that, as current evidence points out, "we need to look beyond just genes when explaining psychiatric illness" (2020, p. 39). Further, a variety of psychological and social factors have been causally linked with psychiatric illness, so these, non-biological factors are expected to be incorporated in psychiatric explanations[49]. Then, explanations of psychiatric conditions in purely biological terms as required by ER would simply disregard significant non-biological factors, thus not being adequate explanations of psychiatric illness.

So, on the one hand, ER is highly discredited and, on the other, the search for biological definitions has been understood to commit to ER. Then, biological psychiatry's search for psychiatric biological definitions could be construed as a search for *prima facie* objectionable accounts—if it was, in fact, committed to ER, biological psychiatrists would then be seeking purely biological accounts of psychiatric conditions, which are currently standardly rejected. Nevertheless, I will argue in what follows that the search for psychiatric biological definitions does not commit to ER, and that *non*-reductionist explanations based

[49] Some social and psychological factors linked to psychiatric illness have been "social class and poverty; income inequalities, unemployment; childhood neglect and sexual, physical and emotional abuse; sexual and domestic violence; belonging to subordinate social groups; war and other life-threatening events; bullying, harassment and discrimination and significant losses such as loss of a parent in childhood" (The British Psychological Society, 2018, p. 92).

on biological definitions can be achieved. As a consequence, biological psychiatry's search to define psychiatric conditions biologically, properly construed, does not further reductionist explanations of psychiatric illness, and complaints against ER do not apply to such a search.

2. Non-reductionist Biological Definitions I

In the remainder of this chapter, my strategy is to construct a non-reductionist approach to psychiatric biological definitions. To do so, I will consider three important characterisations and critiques of ER, namely, Dominic Murphy's (2006), Rebecca Roache's (2019), and Borsboom's, Cramer's & Kalis' (2019). In each case, I will show that the search for psychiatric biological definitions does not commit to ER as individually characterised by those authors and, consequently, that their critiques against ER do *not* apply to those definitions. Then, psychiatric *non*-reductionist explanations based on biological definitions can be achieved. I will deal with Murphy's critique in this section, and with Roache's and Borsboom, Cramer & Kalis' in §3.

2.1 Murphy's Critique

In this subsection, I will focus on showing that psychiatric biological definitions do not imply ER as it is characterised by Murphy (2006). In the following subsection, I will show that Murphy's criticisms against ER do not apply to psychiatric biological definitions, properly construed. To begin with, let us consider Murphy's claims that

> [m]any theories of reduction expect higher-level generalizations to be restated in terms of lower-level ones. In many cases, too, the expectation is that if the higher-level

> generalizations cannot be restated in lower-level terms, then the higher-level theory will be replaced by a lower-level one (p. 108).

To be noted here is that the higher-level generalisations that "many theories of reduction" expect to be restated in terms of lower-level generalisations are simply those concerning the psychological and behavioural manifestations of psychiatric illness—which are expected by those theories to be restated in terms of brain or genetic abnormalities. I will elaborate soon that the theories of reduction mentioned by Murphy imply ER but, as it will become clear, they also involve two other interrelated forms of reductionism—although, in Murphy's account, these forms are not explicitly mentioned and are not called the way I call them. As I understand Murphy's characterisation of theories of reduction, these involve *causal reductionism*, (the already familiar) *explanatory reductionism*, and *normative explanatory reductionism*.

Roughly, *causal reductionism* is the view that specific conditions—in this case, psychiatric ones—have "sole or chief" genetic causes, as I will explain in detail in a moment. Further, as it is now clear, *explanatory reductionism* states that psychological and behavioural manifestations of psychiatric illness can adequately be explained in purely biological terms—in particular, in theories of reduction as characterised by Murph, in purely *genetic* terms. Finally, *normative explanatory reductionism* is the view that those manifestations *should* be so explained. Let us first look at them in detail.

Consider *causal reductionism*. Murphy notes that "[m]any [reductionist] theorists regard molecular, and other genetic, explanations as more fundamental than higher-level explanations" (2006, p. 109). Then, reduction theories seek to restate the (supposedly) less fundamental explanations concerning higher-level, psychiatric manifestations, in lower-

level, genetic terms, which are considered more fundamental. Here, Murphy notes that a fundamental explanation could be understood as "the identification of the sole or chief [biological] cause of a condition" (2006, p. 109). So, in other words, a fundamental explanation of a psychiatric condition seeks to explain that condition in terms of its supposed "sole or chief" biological cause.

I will address the notion of a "chief" cause in a moment, but it is now important to note that, for fundamental explanations to be achieved, *causal reductionism*, i.e., the idea that specific conditions—in this case, psychiatric ones—have sole or chief genetic causes, should be true. If causal reductionism was false about psychiatric conditions and they did not have sole or chief biological causes, then fundamental explanations, expected to be based on sole or chief biological causes, could not be achieved. So, *causal reductionism* is required by the fundamental explanations sought by reduction theories.

Regarding the notion of a chief cause, it is hard to find a precise definition in Murphy's account, but the author provides a clue in claiming that "paradigmatic fundamental explanations are genetic because [in] single-gene disorders typically […] the gene has its customary effects almost regardless of the state of other parts of the system" (2006, p. 109). So, a chief biological cause can here be understood, as in Murphy's account, as a biological cause which has "its customary effects almost regardless of the state of other parts of the system". The important thing here is to note that theories of reduction as characterised by Murphy require *causal reductionism* as described above.

Regarding *explanatory reductionism*, it is worth noting that, since theories of reduction as in Murphy's characterisation commit to causal reductionism, then they seek explanations of psychiatric illness specifically at the *genetic* level, so psychological manifestations of

psychiatric conditions are expected to be adequately explained "in molecular terms"[50]. Then, theories of reduction require that the higher-level, psychological manifestations of psychiatric conditions can be adequately explained in terms of lower-level, genetic factors. So, in addition to causal reductionism, theories of reduction require *explanatory reductionism*.

Finally, let us address *normative explanatory reductionism*. Consider that, if causal reductionism and explanatory reductionism were true, so that psychiatric conditions did have "sole or chief" genetic causes and they could be explained in terms of those causes, then it would be reasonable to require a normative principle that psychological manifestations of psychiatric conditions *should* be explained in terms of the lower-level, genetic causes. Explanations in terms of factors at other levels would disregard the *sole* cause of psychiatric conditions, or they would disregard a cause leading to psychiatric conditions almost regardless of the state of other parts of the system—that is, their chief causes. In contrast, explanations in terms of sole or chief genetic causes would accurately address those causes. So, as Murphy notes

> [t]he reductionist impulse tells us that the explanatory theory [of psychiatric illness] we develop *should* draw on the resources of the very small – if not by employing microreductive concepts, then at least by employing molecular ones (2015, p. 56; my emphasis).

[50] As Murphy points out, in reductionist accounts, "explanations of psychopathology will occur at only one level of analysis, and […] nonmolecular factors will be relegated to a subsidiary, heuristic role in explanation: "biological psychiatry" looks for molecular explanations of mental illness. In this intellectual structure, other levels of explanation are neglected or given only a subsidiary role as characterizations of that which is to be explained in molecular terms" (2006, p. 117).

Then, theories of reduction as characterised by Murphy require *normative explanatory reductionism*, which is the idea that behavioural and psychological manifestations of psychiatric illness *should* be explained in terms of genetic causes.

Then, reduction theories as characterised by Murphy require three distinct forms of reductionism: causal reductionism, explanatory reductionism, and normative explanatory reductionism. I will show in what follows that biological definitions, psychiatric or not, do not require causal reductionism to be true. Further, I will also argue that biological psychiatry's search for biological definitions does not commit to explanatory reductionism and normative explanatory reductionism. Then, it does not stick to any of the three reductionisms above.

So, to begin with, let us consider causal reductionism and biological definitions in psychiatry. Recall that the former states that specific conditions—in this case, psychiatric ones—have "sole or chief" genetic causes. As I will elaborate now, in general, the development of biological definitions in medicine does not require causal reductionism to be true. To see this, consider tuberculosis as defined in the aetiological tradition, that is, as *the disease caused by an M. Tuberculosis infection*. It should be clear now that, although it is defined based on a single biological factor, i.e., the relevant infection, the disease is not *only* caused by such a factor. Rather, it is also caused by distal factors such as the lack of sufficient immunity to the pathogen and infected patients' breathing oxygen—as well as by many other factors in the background conditions—, as I mentioned in Chapters I (§2) and III (§2). Then, it is simply not true that tuberculosis has a *sole* cause, whether genetic or not. Yet it is defined biologically.

But one might think that tuberculosis has a "chief" genetic cause as understood in Murphy's characterisation of reduction theories, that is, a genetic cause which has "its customary effects almost regardless of the state of other parts of the system". In fact, as it has been noted, "there is increasing evidence to suggest that this disease [tuberculosis] […] reflects host genetic vulnerability" (Abel *et al*, 2014, p. 5), so genetics might play a chief role for tuberculosis. However, it has also been pointed out that "the precise nature of the genetic factors involved remains largely unknown" (Abel *et al*, 2014, p. 5). Then, it is currently *un*known whether tuberculosis has a "chief" genetic cause as described above: in general, "the precise nature" of genetics as related to tuberculosis is unknown. What this means is that it *might* be false that tuberculosis has a chief genetic cause—we simply do not currently know—and, yet, it is defined biologically.

So, on the one hand, it is false that tuberculosis has a *sole* cause—whether genetic or not—and, on the other, it is unknown whether it has a *chief* genetic cause—so it might be false that it does. Nevertheless, the disease has been defined biologically. Then, it is not required from diseases that they have sole or chief genetic causes to be defined biologically. This means that biological definitions do not require the truth of *causal reductionism*. As a consequence, there is no in principle reason to believe that, to be developed, specifically *psychiatric* biological definitions require the truth of causal reductionism.

Let us now address *explanatory reductionism* and psychiatric biological definitions. To argue that the search for psychiatric biological definitions does not commit to explanatory reductionism as the latter is understood in the reduction theories characterised by Murphy, let us consider biological psychiatry's understanding of psychiatric explanations. I have previously remarked that, beyond genetics, evidence points to various factors at different

levels of explanation as causes of psychiatric conditions. In fact, current evidence suggests that psychological and social factors, in addition to biological ones, play a causal role in the development of those conditions[51]. This has been widely acknowledged in biological psychiatry. For instance, in describing recent psychiatric biological approaches, Henrik Walter (2013) notes that "it is generally accepted that psychiatric disorders arise from a multitude of causes" (p. 2).

What is of interest here is that, as Walter claims in considering the current state of psychiatric evidence, in the "new biological wave in psychiatry", instances of psychiatric illness

> *cannot be fully explained* and thus understood if inter-level interactions […] are not taken into account. For example, it has been empirically shown that subjective explanations for depressive episodes by patients do not correlate with objective risk factors for depression […] a finding that makes it likely that explanations based on just a selection of levels (subjective experience and remembered behavioral events) do not explain depression well. The same can be said for simplified biological models of depression as a neuro- transmitter deficit that ignores many of the other levels (2013, p. 3; my emphasis).

What all this means is that, given the current state of psychiatric evidence and its acceptance by biological psychiatry, reductionist explanations which do not "take into account" the

[51] See footnote 49.

interactions between factors at different levels would be *in*adequate in accounting for those conditions. So, simply, psychiatric explanations focused solely on one level such as the genetic—as required by explanatory reductionism—would disregard non-genetic factors currently acknowledged by biological psychiatrists to cause psychiatric conditions. In other words, current biological psychiatry does not commit to the idea that psychiatric illness can *adequately* be explained in purely biological terms—in particular, in purely *genetic* terms as in the theories of reduction characterised by Murph. That is, current biological psychiatry is generally *not* committed to explanatory reductionism.

Now, Walter also notes that, in the current, "new biological wave in psychiatry", instances of psychiatric illness are expected to be "defined in part by the mechanisms that underlie and sustain them" (2013, p. 3). And, as it is clear now, those mechanisms are expected to be biological by biological psychiatry. For instance, advocates of Be-COME project (Brükl *et al*, 2020)—which I mentioned in Chapter III (§1)—claim that "[t]he overall aim of Be-COME is to contribute to a *biology*-informed taxonomy of mental disorders that points out the underlying disease mechanism" (Brükl *et al*, 2020, p. 21; my emphasis). All this illustrates that, despite current evidence showing psychiatric conditions to have "a multitude of causes" and that current biological psychiatry does *not* commit to explanatory reductionism, the search to define psychiatric conditions biologically remains alive in biological psychiatry.

So, current biological psychiatry seeks psychiatric biological definitions, but it does *not* generally commit to explanatory reductionism as in the reduction theories characterised by Murphy. Then, in searching for these definitions, biological psychiatry generally does not commit to reductionist explanations. In other words, biological psychiatry's search for

psychiatric biological definitions is not currently committed to explanatory reductionism. Illustrations of non-reductionist explanations based on psychiatric biological definitions will be provided in later sections.

But, for now, let us consider *normative explanatory reductionism* and psychiatric biological definitions. To be noted here is that, since current biological psychiatry generally does not commit to explanatory reductionism—as I explained above—, it simply does not stick to the normative reductionist principle that psychiatric explanations *should* be reductionist. In fact, as I pointed out in the introduction to Chapter II, an editorial in a biological psychiatry journal states that "[i]f we define biological psychiatry by empirical methodology, then we could say that not only biological but also *psychosocial* parameters are a focus of biological psychiatry" (Hans-Jürgen Möller, 2001, p. 2; my emphasis). So, current biological psychiatry does *not* commit to the idea that psychiatric conditions should be explained in purely biological terms, even though it seeks psychiatric biological definitions. Then, the search for those definitions is not committed to normative explanatory reductionism.

In sum, the search for psychiatric biological definitions does not require causal reductionism to be true, and it is not committed to explanatory reductionism and normative explanatory reductionism. Then, the search for psychiatric biological definitions does not stick to any of the three reductionisms involved in Murphy's characterisation of theories of reduction.

2.2 Murphy's criticisms

I will now argue that Murphy's criticisms against reduction theories would *not* apply to psychiatric biological definitions if these were developed. To do this, I will first explain that current evidence does not support those theories. Based on the lack of empirical support, as I will later elaborate, Murphy criticises reductionism by presenting a two-horn dilemma. Murphy notes that, in the face of the current state of evidence, reductionist accounts attempt to include non-biological levels in psychiatric explanations in a way that still preserves some focus on the genetic level. But, according to Murphy, in this case, reductionist biological theories "collapse into the biopsychosocial model" (Murphy, 2006, p. 120)—which is their rival view—, as I will explain soon. That is the first horn of the dilemma. Reductionist accounts can also simply remain purely biological. But, in doing so, these theories "develop an implausible fixation on molecular and genetic explanations" according to Murphy (2006, p. 120). That is the second horn of the dilemma. In Murphy's own words, then,

> biological [reductionist] approaches to psychiatry either collapse into the biopsychosocial model in an attempt to make room for nonbiological explanations […] or, if they try to remain biologically pure, they develop an implausible fixation on molecular and genetic explanations (2006, p. 120).

I will elaborate soon that neither horn of the dilemma would apply to psychiatric biological definitions if these were developed. But, for now, let us note that current psychiatric evidence does not support theories of reduction as characterised by Murphy. To begin with, causal reductionism about psychiatric conditions appears to be false in light of current evidence. As Murphy notes, psychiatric conditions "do not fit" the "picture" of having a sole or chief

biological cause (2006, p. 109). On the one hand, as pointed out by evidence, psychological and social factors, in addition to biological ones, play a causal role in the development of those conditions. Further, evidence also suggests that the effects of genes related to psychiatric illness largely depend on the environments patients are exposed to[52].

So, as it appears, psychiatric conditions are *not* determined genetically as causal reductionism requires. Instead of having a sole cause which is genetic, they are caused by various factors at different levels of explanation. And, instead of having genetic causes that have their effects "almost regardless of the state of other parts of the system"—that is, "chief" causes—, psychiatric conditions have genetic causes which depend on the state of other parts of the system—e.g., whether or not certain environments are present—to have their effects. Therefore, causal reductionism is not supported by current evidence.

A consequence of this is that explanatory reductionism and normative explanatory reductionism are also not supported by evidence. Given their various causes at different levels of explanation, psychiatric conditions could not, arguably, be *adequately* explained solely in genetic terms as required by *explanatory reductionism*. As I mentioned earlier, explanations stated merely in genetic terms would disregard relevant non-genetic causal factors. Further, since psychiatric conditions are caused by heterogeneous factors and not by sole or chief genetic causes, then, *prima facie*, a non-reductionist approach allowing heterogenous factors would be more appropriate in explaining them. So, *normative explanatory reductionism*, stating that explanations of psychiatric conditions should be

[52]For instance, as Kendler and Gyngell (2020) note, "[t]he causal effects of genes on psychiatric disorders appear in many circumstances to depend on the environment in which they are expressed. The same set of genes will have a different effect if they are expressed in an environment in which an individual is exposed to stressful life events, than if they are expressed in an environment free of stressful events" (p. 39).

reductionist, would conflict with current evidence. Then, the three reductionisms involved in theories of reduction as characterised by Murphy are not supported by current evidence.

In lack of empirical support—Murphy notes—, reduction theories face two possibilities: either they attempt to include non-biological levels in psychiatric explanations in a way that some focus on the genetic level is preserved, or they remain purely biological. In Murphy's view, neither of these possibilities works in favour of reduction theories, for the dilemma mentioned earlier arises. I will now explain the latter in detail and will elaborate, along the way, that neither horn of the dilemma would apply to psychiatric biological definitions if they were developed.

So, first, consider the possibility that reduction theories attempted to include non-biological levels in psychiatric explanations, in a way that some focus on the genetic level was preserved. The most obvious way to do this is to explain the contribution of genes to psychiatric conditions in terms of gene *expression*. In this view, certain genetic predispositions relevant to psychiatric illness get only expressed—that is, have the relevant effects—if relevant environmental or developmental factors are present—say, e.g., poverty or discrimination for schizophrenia. Understood in this way, factors at levels other than genetics can be acknowledged in psychiatric explanations and yet these can be understood to be *genetic*. That is because the presumption here is that psychological and behavioural manifestations of psychiatric illness can adequately be explained solely in terms of *gene* expression.

But Murphy notes that,

> if […] by "gene expression" [it] is [meant] "behavior, neuroanatomy or whatever else seems relevant," then [t]his picture is one in which our mental life is instantiated in the

> brain but is caused by psychological, social, and cultural factors and is explicable at several levels of explanation (2006, p.120).

In Murphy's view, the mentioned picture "is no different from the approach of the biopsychosocial model" (2006, p. 120), and this is a failure of reduction theories. To understand this criticism, let us note the difference between the biopsychosocial model and reduction theories in Murphy's account. The author claims that "[t]he difference between schools of thought [i.e., biological reductionist theories and the biopsychosocial model] depends on whether one kind of explanation is fundamental" (Murphy, 2006, p. 115). In other words, reduction theories seek explanations in terms of "sole or chief" genetic causes because those explanations are considered *fundamental*—as I explained above. This implies that those theories expect higher-level generalisation to be restated in terms of lower-level, genetic generalisations. In contrast, the biopsychosocial model does *not* seek fundamental explanations. This model recognises that "mental illness can be caused by an array of biological and cognitive factors" (Murphy, 2006, p. 12), and it allows those factors to be acknowledged in explanations *without* requiring generalisations at some level to be restated in terms of generalisations at another level.

However, in Murphy's view, accounting for psychiatric illness in terms of *gene expression* would result in a picture according to which "our mental life is instantiated in the brain" and it is caused by heterogeneous factors, being "explicable at several levels of explanation". But, as Murphy understands it, that is just the biopsychosocial approach. Then, according to the author, if reduction theories "attempt to make room for nonbiological

explanations" by focusing on gene expression, they collapse into their rival view, i.e., the biopsychosocial model. That is the first horn of the dilemma.

But that would not apply to psychiatric biological definitions if these were developed. As I explained in §2.1, current biological psychiatry does not commit to explanatory reductionism as characterised by Murphy. So, in that sense, it "makes room" for non-reductionist biological explanations. However, although biological psychiatry "makes room" for these explanations by allowing non-biological factors, a psychiatric biological definition would specifically employ a *biological* cause to define a condition. Then, despite psychiatric conditions being explained in terms of heterogeneous causes, a biological definition would *not* collapse into a biopsychosocial definition. So, the first horn of the dilemma faced by reduction theories, i.e., that if they attempt to make room for nonbiological explanations they collapse into a biopsychosocial approach, would *not* apply to psychiatric biological definitions if they were developed. In §3.1, I will illustrate a non-reductive explanation which is, nonetheless, based on a biological definition.

But let us now look at the possibility that, facing current evidence, reduction theories still remain purely biological. As it is clear at this point, this would require from those theories that higher-level generalisations should be restated in terms of lower-level generalisations. So, for instance, consider unemployment as a cause of depression. In a purely biological reductionist account, the causal contribution of the former to the latter should be explained in terms of, say, relevant neurotransmitters released and other neurochemical processes occurring in patients who get unemployed. These processes should be understood to trigger the activation of genes related to psychiatric illness. In this picture, explanations of unemployment causing depression in terms of, e.g., the distress experienced by the

unemployed individual or in terms of other psychological concepts should be restated in genetic terms.

In Murphy's view, attempts to re-state generalisations at one level of explanation in terms of another level "makes sense when levels of explanation are, putting it simply, different descriptions of the same causal process" (2006, p. 119-120). The author believes, though, that attempts to reduce unemployment to gene expression as in the example above are problematic in that "gene expression and long-term unemployment are different processes" (2006, p. 120). Murphy does not elaborate on what it means to be a process *different* from another. But one can intuitively tell that, e.g., the process involving the end of a job contract leading to long-term unemployment and the distress this might cause in an individual is a different process than that involving biochemical interactions which lead, through a series of biochemical steps, to the relevant genes getting expressed.

So, in Murphy's view, if reduction theories attempt to explain, e.g., long-term unemployment in terms of gene expression, those theories develop an "implausible fixation on molecular and genetic explanations", for molecular processes are simply different from the processes involved by unemployment. Then, in remaining purely biological, theories of reduction develop such implausible fixation. This is the second horn of the dilemma.

However, this would also not apply to psychiatric biological definitions if these were developed. To see that, consider the following claims, made in a biological psychiatry textbook:

> [w]e do need psychological and psychoanalytic concepts to wrap our minds around what is happening to people in emotional distress. And it is not just cognitive concepts that are needed but sufficiently well-resolved affective ones as well (Panksepp, 2004, p. 24).

This means that psychiatric explanations are expected by biological psychiatry to rely on psychological, cognitive, and affective concepts, in addition to biological concepts. So, in this view, e.g., unemployment could be considered in causal explanations of depression in terms of the distress it causes and in terms of other psychological concepts, and not as a process to be explained only in molecular terms by employing biological concepts.

A way in which a psychiatric biological definition could be employed in an explanation of that sort is as follows. Consider schizophrenia and suppose that it was *aetiologically* defined as *the disease caused by certain dopamine abnormality*[53]. Further, among its symptoms, consider delusions. One might imagine that the dopamine abnormality would be responsible for the mere ability of the brain to develop delusions. But the latter involve mental content: some patients have the delusion that, say, a family member has a plan to harm them, and others that they have a divine mission on earth. So, one might thus imagine that certain social environments and their psychological impact on patients, alongside certain genetic predispositions to develop the relevant dopamine abnormality, could specifically determine the particular mental *content* of the delusions in patients[54].

Let us suppose that patients who suffered child abuse were more prone to develop the persecutory delusion that a family member plans to harm them, and that patients who grew up in a context of extreme religious fanaticism were more prone to develop the grandiose delusion that they have a divine mission on earth. In this scenario, then, the genetic predisposition and the dopamine abnormality would be biological causes of delusions.

[53] To emphasise, I rely on an aetiological approach because the discussion on reductionism and psychiatric biological definitions is usually framed under the aetiological model of disease classification. I will expand in §4 on how to understand biological definitions constitutively, and will explain that my arguments also apply to those definitions, so understood.

[54] Here, I am employing a modified version of Jonathan Tsou's (2021) account stating that "biological mechanisms determine the general causal features of mental disorders (e.g., psychotic states, depressive states, manic episodes), while social mechanisms stabilize a more culturally-specific expression" (p. 18-19).

Further, child abuse, *qua* child abuse, considered in the face of the violence it involves and the psychological impact in patients exposed to it, would be a psychosocial cause of persecutory *delusions*. Along the same lines, extreme religious fanaticism would be a psychosocial cause of grandiose delusions.

Then, in this scenario, the development of symptoms in patients with a grandiose delusion could be explained as a consequence of the patient having a genetic predisposition to schizophrenia and having been exposed to extreme religious fanaticism. According to this explanation, those two elements would have led the patient to develop a dopamine abnormality, causing the ability of the patient's brain to develop delusions, and the specific exposition to extreme religious fanaticism would explain the content of the patient's delusion—that they have a divine mission on earth. An explanation along similar lines could also be provided for persecutory delusions.

What is important here is that, even if psychiatric conditions were defined biologically, biological psychiatry would not develop an "implausible fixation" on the genetic level, as illustrated by the example above concerning schizophrenia, a dopamine abnormality, and delusions. Psychiatric explanations are allowed by biological psychiatry to acknowledge *different* causal processes such as distress caused by childhood neglect leading to the delusion content of persecution, on the one hand, and gene expression leading to a dopamine abnormality, on the one other, without requiring the former to be restated in terms of the latter as reductionist accounts attempt to do.

Then, the second criticism in Murphy's horn dilemma would not apply to psychiatric biological definitions if these were developed and, as I argued earlier, neither would the first

criticism in that horn dilemma. So, Murphy's criticisms against reductionism do not apply to psychiatric biological definitions.

3. Non-reductionist Biological Definitions II

In this section, I will deal with ER as it is understood by Roache (2019) and Borsboom, Cramer & Kalis (2019). I will first show, in §3.1, that the search for psychiatric biological definitions does not imply ER as characterised by these authors and, later, in §3.2, that their criticisms against ER would not apply to psychiatric biological definitions in case they were developed.

3.1 Biological definitions do not imply ER

Roache (2019) provides a formulation of ER slightly different from my formulation. She claims that explanatory reductionism—which she calls "epistemic reductionism"—is "the view that facts expressed in psychosocial terminology can be replaced by facts expressed in biological terminology" (p. 221). That is just another way of stating the view that higher-level, psychological manifestations of psychiatric conditions can adequately be explained solely in lower-level, biological factors—which is my formulation of ER. As she claims, in a reductionist view, for instance,

> psychosis is just the occurrence of certain sorts of brain events, where 'just' implies that once you know all the relevant facts about brain activity, you know all there is to know about psychosis (p. 221).

I will elaborate in a moment that the search for psychiatric biological definitions does not commit to ER as understood by Roache but, for now, let us consider Borsboom, Cramer & Kalis's characterisation of ER. According to these authors, [e]xplanatory reductionism, in the context of mental health research, is the thesis that mental disorders can be explained in terms of biology" in a way that psychiatric explanations are developed "possibly by altering or correcting the description of higher-level phenomena along the road" (Borsboom, Cramer & Kalis, 2019, p. 2).

I will elaborate in a moment that the search for psychiatric biological definitions does not commit to this characterisation of ER either, but it is first worth noting that Roache's and Borsboom's, Cramer's & Kalis' characterisations of ER differ from Murphy's characterisation of theories of reduction. In contrast with the latter, the two former accounts do *not* understand ER as requiring sole or chief genetic factors to cause psychiatric conditions. Instead, those accounts focus on *brain* factors. Further, what is distinctive in Roache's understanding of ER is that it requires that "all there is to know" about the manifestations of psychiatric illness is some "relevant facts about brain activity". On the other hand, what is distinctive in Borsboom's, Cramer's & Kalis' understanding of ER is that, in their view, ER requires that psychiatric conditions "can be identified" with "neurobiological mechanisms and properties". In what follows, I will elaborate that the search for psychiatric biological definitions does not commit to ER as conceived of by either account.

First, let us consider Roache's understanding of ER. In the author's view, ER requires that all there is to know about the manifestations of psychiatric illness—such as, e.g., psychosis—"is just the occurrence of certain sorts of brain events". But it is important to

remark, as I previously did, that, although biological psychiatry currently seeks biological definitions, it acknowledges that non-biological factors cause psychiatric conditions (§2.1) and, further, it does not generally expect those factors to be explained in lower-level terms—such as in genetic terms (§2.2). So, it is clear that, for current biological psychiatry, which seeks biological definitions, there is much more to know about psychiatric conditions than just their biological determinants.

In searching for biological definitions, then, biological psychiatry does *not* commit to Roache's distinctive understanding of ER that all there is to know about psychiatric illness is the occurrence of certain brain events. (In other words, for current biological psychiatry, although a psychiatric condition was defined in terms of a biological factor only, there would be much more to know about the condition than the biological factor it was defined in terms of).

An illustration of what a psychiatric explanation based on a biological definition but which acknowledged heterogeneous causes could look like was partially provided in previous passages of this subsection. Recall the example in which schizophrenia symptoms were caused by a dopamine abnormality and the condition was defined in terms of such an abnormality. As I explained earlier, if it was defined aetiologically as *the disease caused by a dopamine abnormality*, explanations of it could, nonetheless, acknowledge the development of the dopamine abnormality as a consequence of relevant genetic, social, and psychological factors. In such an explanation, schizophrenia, so defined, would be understood to have heterogeneous risk factors.

Now, this might seem strange at first glance. After all, the aetiological definition of schizophrenia as the *disease caused by a dopamine abnormality* suggests that schizophrenia

is caused *only* by such an abnormality. Then, it might strike us as strange that, admitting such a definition, an explanation of schizophrenia acknowledged a *variety* of causes for the condition. However, we should note that tuberculosis, the paradigmatic example of a disease defined aetiologically, admits causal explanations that acknowledge a variety of heterogeneous factors. In a collection on major infectious diseases, Barry Bloom and colleagues (2017) state that "[t]uberculosis is an infectious bacterial disease caused by Mycobacterium tuberculosis" (p. 223)—an aetiological definition for the disease. Further, they mention a variety of risk factors for the disease such as having HIV or AIDS, occupation, diet, socioeconomic status, smoking, certain genetic predisposition, and others (see Bloom *et al*, 2017, pp. 246-248). Further, as Peter Davies (2005) claims in a review article, it is currently widely accepted that "[s]usceptibility to tuberculosis is multifactorial and complex" (p. 44).

Then, defined aetiologically, tuberculosis is explained as a result of an *M. Tuberculosis* infection and the interaction of many other biological and non-biological factors. So, although an aetiological definition seems to suggest that a disease is caused only by the factor it is defined in terms of, heterogeneous explanations of diseases defined aetiologically are allowed. This includes schizophrenia as defined aetiologically in the example above. My point, at any rate, is that biological psychiatry's search for biological definitions does not commit to Roache's distinctive understanding of ER that all there is to know about psychiatric manifestations is the relevant brain events.

Consider now Borsboom's, Cramer's & Kalis' take on ER. Their distinctive understanding is that ER requires psychiatric conditions to be identified with a set of "neurobiological mechanisms and properties, possibly by altering or correcting the

description of higher-level phenomena along the road" (2019, p. 2). The authors do not provide an example of how an "alteration" or "correction" of a higher-level description by a lower-level description would look like, but they seem to mean something like the following. Suppose that a dopamine abnormality, poverty, and discrimination caused schizophrenia. In this situation, the causal contribution of the social factors to schizophrenia could initially be described in psychosocial terms. For instance, in terms of the social meanings poverty and discrimination involve, and in terms of the psychological effects the relevant social factors have on patients.

However, in this situation, following ER as understood by Borsboom, Cramer & Kalis, this description would have to be "altered" or "corrected" at some point by descriptions made solely in terms of the relevant dopamine abnormality, in a way that these replaced the psychosocial descriptions. Nevertheless, biological definitions of psychiatric conditions do not require the correction or alteration of higher-level descriptions. As I have illustrated above with the example of the aetiological definition of schizophrenia, biological definitions are compatible with explanations of psychiatric conditions that acknowledge the causal contribution of psychosocial factors understood *qua* psychosocial factors, and not as factors which were to be later stated in biological terms. Then, the search for psychiatric biological definitions does commit to descriptions of higher-level phenomena having to be corrected or altered by descriptions of lower-level phenomena. Then, such a search does not commit to ER as understood distinctively by Borsboom, Cramer & Kalis.

So, biological psychiatry's search for biological definitions does not commit to either Roache's or Borsboom's, Cramer's & Kalis' understanding of ER.

3.2 Criticisms against reductionism do not apply to biological definitions

I will elaborate in this subsection that Roache's and Borsboom's, Cramer's & Kalis' criticisms against ER would not apply to psychiatric biological definitions if these were developed. I will first present the criticisms, and will later address them one by one. Roache (2019) claims that

> the question of whether someone is suffering from a mental disorder cannot […] be settled without reference to the patient's experiences and behavior; that is, to psychosocial phenomena. Such psychosocial phenomena are a central—if not the most important—aspect of clinical data used in psychiatric diagnosis. It is difficult to see how reliance on such data might be eliminated without radically reconceptualizing current views about mental illness (p. 221).

So, Roache believes that the patients' experiences and behaviours involved in their symptoms are "a central—if not the most important—aspect" of psychiatric diagnoses. Since ER aims at accounts explaining psychiatric illness in terms solely of *biological* factors despite symptoms, Roache's criticism is that reductionist explanations would disregard such a central aspect.

On the other hand, Borsboom, Cramer & Kalis believe that psychiatric symptoms are best explained in terms of "causal and intentional relations, which can only be made sense of by taking both the content of mental states and the world outside the patient's head into consideration" (2019, p. 9). ER, though, aims to explain psychiatric symptoms solely in *neurobiological* terms. So, these authors claim that "it is highly unlikely that the symptomatology associated with psychopathology can ever be conclusively explained in

terms of neurobiology" (2019, p. 10). Borsboom's, Cramer's & Kalis' criticism is, thus, that explanations based on ER are highly unlikely to be conclusive.

However, neither Roache's nor Borsboom's, Cramer's & Kalis' criticisms would apply to psychiatric biological definitions if these were developed. To address both criticisms, let us recall the scenario I presented in §2.2, in which a dopamine abnormality causes schizophrenia, persecutory delusions are linked with child abuse, and grandiose delusions with extreme religious fanaticism. Suppose that, in this scenario, schizophrenia was defined in terms of the dopamine abnormality and consider the group of patients who develop the dopamine abnormality *and* grandiose delusions.

Regarding Roache's criticism, we should note that, in the scenario above, the very fact that patients developed a delusion could be understood as a result of patients having the dopamine abnormality. Nevertheless, reliance on the patients' *symptom* of having a grandiose delusion would allow psychiatrists to explain schizophrenia in these patients by noting that their delusion would be a result of exposition to extreme religious fanaticism. Then, despite schizophrenia being biologically defined, its explanation could in the case of these patients rely on the relevant symptoms. An explanation along similar lines could be developed regarding persecutory delusions. This illustrates that reliance on data concerning symptoms would not need to be eliminated if biological definitions were developed so, in contrast with reductionist explanations, explanations based on biological definitions need not disregard symptoms. Then, Roache's concern about ER would not apply to these definitions if they were developed.

Now, regarding Borsboom's, Cramer's & Kalis' criticism, it is important to note that a biological definition of schizophrenia as in the scenario above allows explanations of

psychiatric symptoms that "take into account" the content of mental states in psychiatric symptoms and "the world outside the patient". Recall that the symptom of having a grandiose delusion in the scenario above could be explained in two parts, one being the development of the relevant dopamine abnormality, responsible for the mere fact that the patient has a delusion, and the other being the exposition to extreme religious fanaticism, responsible for the specific content of the delusion—that the patient has a divine mission on earth. Then, the symptom of having a grandiose delusion could be explained beyond the neurobiological process of abnormally releasing dopamine. It could also be explained in terms of "the world outside the patient"—i.e., a context of extreme religious fanaticism—, and in terms of the mental content of the symptom—i.e., that patients have a divine mission on earth.

Then, a biological definition of schizophrenia in terms of the dopamine abnormality admits explanations of its symptoms as those defended by Borsboom, Cramer & Kalis. Hence, explanations based on psychiatric biological definitions could be at least as likely to be *conclusive* as explanations of symptoms in terms of the content of mental states and "the world outside the patient"—which the authors defend. So, Borsboom's, Cramer's & Kalis' criticism that it is highly unlikely that reductionist explanations of psychiatric symptoms will be conclusive would also *not* apply to psychiatric biological definitions—at least no more than it would apply to the explanations they defend—if those definitions were developed.

Then, neither Roache's nor Borsboom's, Cramer's & Kalis' criticisms would apply to those definitions.

4. Final remarks

My arguments in this chapter have been developed in a context in which what I call "biological definitions" are usually understood in terms of the aetiological model of disease

classification (Chapter I, §2). However, the aetiological model is defective and current medical classification, in general, is best understood to be constitutive (Chapter I, §2 and §4). Hence, unless a defective model was accepted, biological psychiatry's quest for biological definitions should be understood as a search for *constitutive*, instead of aetiological, definitions. The question arises, then, as to whether my arguments in this chapter apply if biological psychiatry's quest for biological definitions is so understood. As I will elaborate in what follows, they do, so such a quest does not commit to ER even if biological definitions are understood constitutively.

To see that, it is important to recall that a biological definition is just a definition in terms of biological causes. Also, we should remember that the expression "definitions in terms of causes" can be understood *aetiologically* or *constitutively*, as I explained in Chapter III (§5). In an aetiological understanding, a definition is in terms of causes because it cites a biological factor which is considered the *cause* of the *disease* itself. Instead, in a constitutive understanding, a definition is in terms of causes because it cites a biological factor considered as the *cause* (or *causes*) of characteristic *symptoms* of the disease. And, in a biological definition understood constitutively, the biological cause (of the relevant symptoms) is necessary and sufficient for the disease, without being one of the disease's causes or effects[55].

So, recall the imaginary scenario I posed in §2.2 and §3.2, in which a certain dopamine abnormality causes (the syndrome of) schizophrenia. Let us call the dopamine abnormality "D". In an aetiological understanding, in which D is considered to be the cause of the disease itself, a definition as follows is provided: schizophrenia is *the disease caused*

[55] Recall, though, that a constitutive definition could also cite symptoms. However, I will focus in this section on constitutive definitions citing only a biological factor, for they are *prima facie* more prone to be considered reductionist.

by D. But, in a constitutive understanding, in which D is taken to be the cause of the *symptoms* of schizophrenia, a definition as follows is provided: *schizophrenia is D*, in a way that D is necessary and sufficient for schizophrenia.

My arguments against the presumption that the quest for psychiatric biological definitions commits to ER apply if we understand biological definitions constitutively as above. That is because they are largely based on the idea that current biological psychiatry generally acknowledges a diversity of causes for psychiatric conditions, that it admits non-biological concepts in explanations, and that, anyway, it seeks biological definitions, as I elaborated throughout. Thus, in searching for biological definitions—whether aetiological or constitutive—, biological psychiatry does not commit to ER.

In fact, since current biological psychiatry acknowledges a diversity of causes for psychiatric conditions, even if it sought *constitutive*, instead of aetiological, biological definitions, it would not require that those conditions are caused by "sole or chief" genetic causes—that is, it would not require the truth of causal reductionism (§2.1)[56]. Nor it would commit to ER or normative explanatory reductionism[57] (§2.1, as well). Then, if current biological psychiatry sought *constitutive* biological definitions, it would not commit to reduction theories as accounted for by Murphy. Further, in acknowledging a variety of causes for psychiatric conditions, biological psychiatry does not commit to the idea that all there is to know is relevant brain factors (§3.1), and this does not depend on whether it seeks aetiological or constitutive biological definitions. No commitment to Roache's specific take on ER is required in seeking constitutive biological definitions, then.

[56] Just to recall, causal reductionism is the idea that psychiatric conditions are caused by "sole or chief" causes. See §2.1.
[57] That is, to recall, the view that explanations of psychiatric conditions should be reductionist.

On the other hand, since current biological psychiatry admits non-biological concepts in its explanations, it does not require psychiatric explanations at higher levels to be "altered" or "corrected" by lower-level explanations (§2.2 and §3.1). Again, this does not depend on whether it seeks aetiological or constitutive definitions. Then, no commitment to Borsboom's, Cramer's & Kalis' specific take on ER is required in seeking constitutive biological definitions. Then, a quest for constitutive biological definitions is not committed to ER in either of the three characterisations I addressed in this chapter.

Now, suppose that the constitutive definition mentioned above that *schizophrenia is D*—i.e., a certain dopamine abnormality—was provided. I noted throughout that current biological psychiatry allows non-reductionist explanations so, schizophrenia, defined constitutively as being D, could be explained in non-reductionist terms as much as schizophrenia defined aetiologically in §2.1 could. Then, although schizophrenia was explained in terms of factors at several levels of explanation—including the biological, psychological and social—, its constitutive definition as above would remain purely biological. That is, such a definition would *not* collapse into a biopsychosocial definition. So, Murphy's criticism against ER in the first horn of the dilemma he poses (see §2.2), that if theories of reduction attempt to make room for nonbiological explanations they collapse into a biopsychosocial approach, would not apply to constitutive biological definitions.

Moreover, in explanations of schizophrenia in terms of biological, psychological, and social factors, the latter two sorts of factors could be incorporated *qua* psychological and social factors—not as factors to be replaced by lower-level facts. That is because, generally, current biological psychiatry does not require higher-level explanations to be re-stated in lower-level terms, as I elaborated earlier. Then, in providing biological constitutive

definitions, biological psychiatry would not develop an "implausible fixation" on the molecular level. Hence, Murphy's criticism against reduction theories in the second horn of the dilemma he presents would also not apply to constitutive biological definitions.

Now, recall the scenario in which a dopamine abnormality causes schizophrenia, persecutory delusions are linked with child abuse, and grandiose delusions with extreme religious fanaticism (§2.2). I remarked in §3.2 that, in that scenario, the very fact that patients developed a delusion could be understood as resulting from the dopamine abnormality. Also, I pointed out that the patients' *symptom* of having, e.g., a grandiose delusion, would allow psychiatrists to explain schizophrenia in these patients in terms of their delusions being a result of exposition to extreme religious fanaticism. Then, explanations of the condition could rely on the patients' symptoms. But this applies regardless of whether schizophrenia is defined aetiologically as in the example I addressed in 3.2 or constitutively as being D. Patients with schizophrenia defined constitutively could have grandiose delusions as much as patients with schizophrenia defined aetiologically, so explanations of those delusions could rely on the symptoms in any case. Then, psychiatric explanations based on constitutive biological definitions could rely on symptoms, and Roache's concern about ER would not apply to them.

Finally, I elaborated in §3.2 that an aetiological definition of schizophrenia admits explanations of its symptoms as those defended by Borsboom, Cramer & Kalis—that is, explanations referring to both the "world outside the patient" and the mental content involved in psychiatric symptoms. But *constitutive* biological definitions admit that as well. If schizophrenia was defined aetiologically as *the disease caused by D* or constitutively as being D, and grandiose delusions were one of its symptoms, the mere capacity to have delusions

could anyway be explained by reference to the dopamine abnormality, and the *content* of the delusion—having a divine mission on earth—by reference to extreme religious fanaticism in the "world outside the patient".

So, either definition allows explanations of schizophrenia to account for the relevant symptoms in terms of "the world outside the patient"—the context of extreme religious fanaticism—and in terms of the symptom's mental content—having a divine mission on earth. Then, Borsboom's, Cramer's & Kalis' criticism against ER does not apply to biological definitions, whether aetiological or constitutive.

Therefore, the quest for psychiatric biological definitions does not commit to ER regardless of whether those definitions are understood aetiologically or constitutively, and the criticisms against ER addressed would not apply to either aetiological or constitutive biological definitions. Then, the quest for (aetiological or constitutive) biological definitions in psychiatry does not further reductionist explanations.

As a final note, I should remark that, to my knowledge, no systematic, explicit argument has been raised against the specific view I *defend* that biological psychiatry's quest for biological definitions does not commit to ER. Examination of this view has, nonetheless, turned out fruitful. First, it is important to note that there is no systematic argument against the view I defend because the opposite view, i.e., that biological psychiatry's quest for biological definitions *commits* to ER, has generally been taken for granted. Then, the merit of my arguments, if they are correct, is to carefully elaborate that this latter, widely shared assumption—which is generally taken for granted—is not true. This contributes to correcting the generalised perception that biological psychiatry's project of defining psychiatric conditions biologically is reductionist.

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CHAPTER V

Purely Biological Psychiatric Conditions

A purely biological account (PBA) of a disease defines this disease in terms of a biological factor *B* in such a way that *B* is necessary and sufficient for the disease.[58] As I will elaborate in the following section, where I will also provide examples of PBAs, these are not rare in medicine. However, for reasons that will soon become apparent, no PBAs of psychiatric conditions, such as schizophrenia or depression, have been developed. These conditions are rather characterised as syndromes comprising behavioural and mental symptoms such as delusions, hallucinations, and emotional withdrawal.

Notably, some concerns have been raised in philosophy against the mere possibility that PBAs of psychiatric conditions could be developed. Broadly, critics contend that, since those PBAs would rely on relevant biological factors instead of on relevant behavioural and mental symptoms, then those PBAs would pick out biological conditions that would allegedly be *different* from the conditions that are currently characterised as syndromes in psychiatry, which are the major focus of concern for psychiatrists at present. If true, this line of thought would imply that, if PBAs were developed in psychiatry, psychiatry would simply miss the point as to its current, major focus of concern.

In this chapter, though, I will counter that line of thought by showing that PBAs of psychiatric conditions would pick out the very same conditions that are defined in psychiatry

[58] A PBA can be understood in a constitutive framework: it is just a definition of a disease in terms of the biological factor that causes its *symptoms*, such that the biological factor is necessary and sufficient for the disease, without said biological factor being one of the *disease*'s causes or effects. In other words, a PBA is just a biological definition understood in the constitutive, rather than aetiological, interpretation I explained in Chapter III (§5)—specifically, one which cites only the biological cause of relevant symptoms, but not the symptoms themselves. I employ the term "purely biological account" because the argument I address in this chapter employs it.

in terms of syndromes.[59] Then, if those PBAs were developed, psychiatry would not miss the point as to its current, major focus of concern.

In §1, I will present some examples of PBAs in medicine and will elaborate on why PBAs have not been developed in psychiatry. Further, I will present the critiques to the very possibility that those PBAs were developed. To my knowledge, there are four authors supporting this line of thought, viz. Rebecca Roache, in her (2019) and her (2020); Walter Sinnott-Armstrong & Jesse S. Summers, in their (2020); and Hanna Pickard, in her (2009). Nevertheless, in this chapter I will address only the argument that Roache advanced in her (2019): in Chapter VI I will discuss Roache's (2020), Sinnott-Armstrong's & Summer's (2020), and Pickard's (2009).

In §2, I will reconstruct Roache's contention, and advance an argument against it. In §3, I will respond to possible objections to my argument, and, in §4, I will make final remarks about this argument. Finally, in §5, I will discuss how my argument's conclusion bears upon a number of indirect criticisms raised against the possibility of finding PBAs in psychiatry.

1. PBAs in medicine and psychiatry

Definitions of diseases for classificatory purposes in terms solely of biological factors are common in current medicine. For instance: the *International Classification of Diseases* (ICD) defines gastritis as follows: "[g]astritis is an injury of gastric mucosa that involves epithelial damage, mucosal inflammation, and epithelial cell regeneration except for any epithelial defect" (World Health Organization [WHO], 2022).

[59] It is important to note that the arguments that I will present in this and the following chapters apply only to biological factors which are wide biological regularities and possess causal specificity in relation to the relevant syndromes. That is because the arguments I address are thus formulated, as it will become clear throughout.

Further, under the current definition of the disease, no patient could have gastritis without at the same time having the relevant injury of gastric mucosa, and, hence, this injury is necessary for the disease. Moreover, merely by having an injury of the gastric mucosa as described by the ICD, patients have gastritis, and thus the former is sufficient for the latter. Then, the injury of gastric mucosa as described by the ICD, which is known to cause the observable signs and symptoms of the disease, is necessary and sufficient for gastritis, and this disease is defined in terms of it.

Let us call accounts of this kind—accounts according to which a biological factor is necessary and sufficient for a disease—"purely biological accounts" (PBAs) of diseases. Other examples of diseases given a PBA by current medicine are pancreatitis, syphilis, and COVID-19. In fact, their outward signs and symptoms are caused, respectively, by inflammation of the pancreas, by a treponema pallidum bacterial infection, and by a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. And, further, these biological factors are necessary and sufficient for the diseases whose signs and symptoms they cause, for no patient could have those diseases without having developed the corresponding underlying biological factor, and, just by developing the latter, patients have the diseases—even though some patients could develop no symptoms.[60]

The biological factor employed in a PBA is usually the biological factor that is thought to cause the symptoms of the relevant condition. Nevertheless, no PBAs of

[60] The underlying biological causes of observable signs and symptoms can also be *only* necessary—and not sufficient—for some diseases. For instance, while patients could not have asthma in absence of inflammation of the airways—which shows that the latter is necessary for it—, it intuitively seems that such an inflammation does not suffice for patients to have the disease, for the characteristic symptoms—such as shortness of breath or a tight chest—appear to be necessary for asthma as well. As it happens, in fact, it seems odd to claim from a patient who never experienced shortness of breath or a tight chest that they have asthma. In any case, only PBAs of psychiatric conditions have been a matter of dispute in philosophy, so I will only focus on them in this chapter.

psychiatric conditions such as schizophrenia or depression have been developed so far. This lack of PBAs in psychiatry is due to the fact that there is no consensus in the discipline as to whether its best biological posits are based on proven causal relationships between specific biological factors and the symptoms of psychiatric conditions.[61] The best regarded of those posits is that certain dopamine and glutamate abnormalities are associated with schizophrenia, but it is still a matter of controversy whether those abnormalities are *causes* of that condition—understood as a syndrome, that is as a mere cluster of *symptoms*.[62] Further, the authors of a recent systematic review think that the outcome of the review challenges the longstanding hypothesis in psychiatry that low serotonin levels cause depression, by showing that there is no systematic association between that biological factor and the condition (Moncrieff et al, 2022). Other biological findings in the discipline are also well-accepted not to reliably establish a causal relationship between a biological factor and a psychiatric syndrome.

So, in lack of knowledge concerning the (presumed) specific biological causes of psychiatric conditions (understood as syndromes), researchers have not been able to develop PBAs of the latter, and have rather characterised those conditions as syndromes comprising distinctive clusters of behavioural and mental symptoms such as depressed mood, delusions, or hallucinations.

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[61] This is a widely acknowledged problem in current psychiatry, and it is usually referred to as the lack of biological validation of the diagnostic categories of mental disorder. Insel (2014), Poland (2015), and The British Psychological Society (2018, ch. 5)—among many others—have elaborated on this issue.

[62] In an extensive review, Howes, McCutcheon, & Stone (2015, p. 6) claim that it is not clearcut that the dopamine abnormalities associated with schizophrenia are a trait marker of it, which means that those abnormalities are not proven to cause the condition. Also, in another review, Kruse & Bustillo (2022, p. 10) claim from the glutamate abnormalities associated with schizophrenia that the extent to which they involve causal mechanisms for the condition is not clear. These claims just reflect the generalised endorsement in psychiatry of the idea that a causal relationship between the relevant dopamine and glutamate abnormalities and schizophrenia is not reliably established as a *causal* relationship.

But, as James Phillips (2015, p. 179) claims, "[t]he "official" way of classifying in psychiatry is biomedical. Psychiatric disorders and diagnoses are expected to follow the model of the rest of medicine". Then, biologically oriented psychiatrists aspire to follow "the model of the rest of medicine", where biologically-based accounts of diseases—including PBAs of them—are abundant. Advocates of biological approaches in psychiatry, in fact, believe that

> the typical progression of knowledge starts with the identification of […] (the *syndrome*) and the deviance from the "norm"; understanding of the pathology and etiology [that is, the causes of the syndrome] usually come much later (Jablensky, 2012, p. 79).

Thus, biologically oriented psychiatrists aim at making progress in the discipline in such a way that the current characterisation of psychiatric conditions as syndromes is intended to be abandoned in the future, when they discover the (presumed) specific biological causes of psychiatric conditions, and when, as a consequence, they develop biologically based characterisations of those conditions.[63]

Of course, psychiatrists will achieve that aim only in case specific biological causes in fact underlay psychiatric syndromes, and in case they were able to discover those causes, all of which is still to be settled. Nevertheless, the mere possibility that psychiatrists developed PBAs of psychiatric conditions has been taken with reservation in philosophy.

[63] In fact, the current characterisation of these conditions is seen as a problem in the discipline. In a psychiatric companion, Johnstone & Lawrie (2010) note that (my emphasis), diseases in areas of medicine other than psychiatry "are now defined at a more fundamental level than the clinical syndrome and there are usually clear, qualitative differences in aetiology [that is, the causes] even between disorders with similar syndromes […] *The problem is posed* […] not by psychiatric disorders per se, but by disorders which are still defined by their clinical syndromes" (p. 13).

Broadly, critics of biological approaches in psychiatry believe that, since those PBAs would rely on biological factors instead of on relevant behavioural and mental symptoms, those PBAs would pick out biological conditions that would allegedly be *different* from the conditions that are currently characterised as syndromes in psychiatry. It follows, from this line of thought, that, in case those PBAs were developed, psychiatry would simply miss the point as to its current, major focus of concern.

As I said earlier, in order to criticise this line of thought, I will address, in this chapter, Roache's arguments exclusively. Other arguments instantiating the same line of thought I will address in Chapter VI.

2. Roache's argument

Rebecca Roache (2019) claims that

> the question of whether someone is suffering from a mental disorder cannot, at least in our current medical framework […] be settled without reference to the patient's experiences and behavior; that is, to psychosocial phenomena. Such psychosocial phenomena are a central—if not the most important—aspect of clinical data used in psychiatric diagnosis. It is difficult to see how reliance on such data might be eliminated without radically reconceptualizing current views about mental illness […] A purely biological account of (say) schizophrenia stands or falls depending on how it is reflected by clinical data; that is, inter alia, by the patient's account of his or her experiences and/or by his or her behavior. To see this, imagine a biological account of schizophrenia that allowed the in-principle possibility of categorizing as schizophrenic people who experienced none of the usual psychological or behavioral symptoms, or of excluding

> from its categorization people who experienced those symptoms. *We might reasonably deny* that such an account employs the term 'schizophrenia' to refer to the same phenomenon to which today's psychiatrists refer using that term (p. 221, my emphasis).

Let us unpack this argument. First, it is important to remark that the purely biological account proposed to be imagined by Roache should characterise schizophrenia as a condition occurring only when patients develop a certain biological factor, say *B*. In that way, such an account would allow, as Roache's argument requires, that some *a*symptomatic patients were "categorised" as having schizophrenia—those who did not have symptoms but who developed *B*—, and that some symptomatic patients were categorised as not having the condition—those with symptoms but without *B*. Thus, in accordance with this account, there would be no other way for asymptomatic patients to be diagnosed with schizophrenia than to develop *B*, which shows that this factor would be necessary for the condition. Moreover, according to the very same account, just by developing *B* patients would have schizophrenia, which shows that *B* would be sufficient for it. Therefore, the account proposed by Roache is an instance of the kind of PBAs that I have described earlier, for, according to it, a specific biological factor—*B* in this case—is necessary and sufficient for a medical disorder—that is, for schizophrenia.

Now, Roache claims that the patients' experiences and behaviours involved by the symptoms of schizophrenia are *psychosocial* phenomena. Then, she notes that cases of the psychiatric condition in the absence of those psychosocial phenomena—i.e., asymptomatic patients with schizophrenia—would be allowed by the relevant PBA, as much as it would allow cases of those psychosocial phenomena in absence of the condition—symptomatic patients without schizophrenia. This seems to show that the relevant psychosocial

phenomena would not be captured by the term "schizophrenia" as employed in the relevant PBA. A PBA of schizophrenia would, by contrast, capture a *biological* phenomenon.

Further, the relevant psychosocial phenomena are considered by Roache to be "a central—if not the most important—aspect of clinical data used in psychiatric diagnosis" at present. Then, based on the assumption that these central aspects of psychiatric diagnosis would not be captured by "schizophrenia" in a PBA, Roache concludes that "we might reasonably deny that a purely biological account of schizophrenia would refer to the same phenomenon referred to by current uses of the term "schizophrenia"". This, of course, implies that, according to Roache's conclusion, "schizophrenia" in a PBA would refer to a *different* phenomenon than the phenomenon psychiatrists refer to at present by employing that term. Only thus, in fact, it might be reasonable to *deny* that a PBA of the condition in question would refer to the phenomenon that we currently call "schizophrenia", as Roache claims. The author makes very similar considerations in a later work (2020, p. 375), broadly reaching the same conclusion.

In what follows, though, I will argue that her conclusion is unwarranted. My contention is that, contra Roache, it is in fact reasonable to assert that "schizophrenia" as employed in a PBA of the relevant condition would as a matter of fact refer to the same phenomenon referred to by uses of that very term by psychiatrists at present.

2.1 Response

To begin with, let us recall that, in building her argument, Roache claims that "it is difficult to see" how reliance on current psychiatric data—of which "the patient's experiences and behavior" are a "central" component in her view—"might be eliminated without radically

reconceptualizing current views about mental illness". This suggests that Roache believes that psychiatrists might not rely on current psychiatric data—at least not on data concerning "the patient's experiences and behavior"—in developing a PBA of schizophrenia. Presumably, that would be because psychiatrists would be only focused on seeking the relevant biological factors in carrying out such a task.

Nevertheless, in reality, a PBA of schizophrenia could hardly be developed without relying on those data. That is because, for biological psychiatrists to develop such an account, they should first seek biological factors that could be associated with the behavioural and mental aspects that the condition is currently characterised in terms of. But, to do that, psychiatrists would need to rely, of course, on current data concerning, at least, which patients actually have—or had—the relevant symptoms, so that the presumed biological causes of those patients' syndrome were searched for. To be sure, that means that biological psychiatrists would, in fact, need to rely on data concerning which patients developed the "experiences and behaviour" relevant to schizophrenia in building its PBA.

We can thus see that the positing of that PBA would only result *in reality* from the fact that biological psychiatrists achieved their ambition of discovering the (presumed) biological, stable cause of the schizophrenia syndrome. And, since Roache's argument involves a PBA of the condition we now call "schizophrenia", then, the biological factors that could be cited by the PBA in case it was developed could only be those biological factors that were proven to cause the syndrome of schizophrenia.

Thus, let us suppose that, based on new, highly reliable findings linking certain dopamine and glutamate abnormalities with schizophrenia, biological psychiatrists established that those abnormalities in fact *cause* that syndrome, and then characterised

schizophrenia in purely biological terms as the condition occurring only when patients develop those dopamine and glutamate abnormalities. This would result in a PBA of schizophrenia according to which the dopamine and glutamate abnormalities are necessary and sufficient for the condition. Let us call the hypothetical scenario where this occurs the "biological scenario", and let us also contrast that scenario with the current, actual state of knowledge in psychiatry, which I will henceforth call "non-biological scenario".

Since in the biological scenario researchers develop the PBA of schizophrenia based on evidence consistently linking dopamine and glutamate abnormalities with cases of the schizophrenia syndrome, then, in that scenario, the schizophrenia syndrome is conceived of as the customary result of patients developing those abnormalities—just as the cluster of symptoms consisting of polydipsia, polyuria, and tiredness is currently conceived of as the customary result of untreated diabetes mellitus, which is—according to the relevant definition in the MSD manuals—an impaired insulin secretion and variable degrees of peripheral insulin resistance leading to hyperglycaemia (Brutsaert, 2023).

It is thus clear that psychiatrists in the *biological* scenario naturally say, of psychiatrists in the non-biological scenario, that they use "schizophrenia" to refer to the condition that occurs only when dopamine and glutamate are abnormally produced, but lack the relevant biological knowledge concerning the causes of the symptoms of that very condition. From the perspective of the biological scenario, then, there is nothing suggesting that psychiatrists in the non-biological scenario use "schizophrenia" to refer to a condition different from the condition that psychiatrists refer to in the biological scenario. Therefore, "schizophrenia" in the PBA developed in the biological scenario refers to the same condition that psychiatrists refer to at present.

The case of diabetes is illustrative of my argument, so I will now elaborate on it. Eighteenth-century physicians had already identified the characteristic way in which its symptoms cluster together, but they had not discovered the relevant underlying cause of them. But physicians nowadays assume that, when their 18th-century counterparts employed the term "diabetes" to refer to a condition primarily characterised in terms of symptoms, they in fact referred to the same condition that is currently characterised in purely biological terms as the condition that occurs when patients develop insulin deficiencies leading to hyperglycaemia.

As a matter of fact, as Elizabeth Lane (2009) has elaborated in an extensive study on the history of this disease, the term "diabetes" referred in the 18th century to a condition that involved the characteristic symptoms of polyuria, polydipsia, and tiredness, and which was linked with the urine of patients having a "wonderfully sweet [and] a honeyed taste" (p. 86). Further, the prominent assumption was held in 18th-century medicine that consuming foods with high amounts of carbohydrates was harmful to patients who had the disease called "diabetes". As Lane explains, physicians of the time found "rice and potatoes as problem foods for diabetics, urging abstinence from everything starchy or floury" (p. 127). Also, some physicians suspected that "the pancreas might be the site of the disease" (p. 131), and others pointed out "the significance of acetone and other ketones discharged in the acute stages of diabetes" (p. 138).

It is here of crucial importance to remark that, as relevant historical evidence shows, standardly, when patients in the 18th century were diagnosed with diabetes, they were diagnosed with a condition that was conceived of as involving polydipsia, polyuria, tiredness, sweet taste of urine, and problems with starchy and floury foods, which was associated with

ketones “discharged in the acute stages of diabetes”. “Diabetes”, thus, in the 18th century, referred to a condition having all these features.

Leaving that aside for a moment, it is also important to note that, currently, it is well established in medicine that insulin deficiencies leading to hyperglycaemia cause the characteristic symptoms and the characteristic sweet taste of urine in cases of diabetes. Further, it is known at present that carbohydrates, contained in foods such as rice and potatoes, are metabolised and transformed into glucose, which is released into the bloodstream, and that this fact could explain why foods with high amounts of carbohydrates were “problem foods for diabetics” as they were understood by 18th-century physicians. Also, it is currently a piece of well-established knowledge that certain cells of the pancreas produce insulin, and that the latter regulates glucose levels in blood, by enabling cells to absorb the glucose. Moreover, diabetic ketoacidosis, a condition involving the release of ketones into the bloodstream is currently known to be a common complication of untreated diabetes.

Then, the historical evidence concerning cases of a disease called “diabetes” in the 18th century fits well with current knowledge concerning the mechanisms involved in diabetes and its complications, in a way that, altogether, the former and the latter strongly support the assumption that patients said to have diabetes in the 18th century, in fact, had the condition that contemporary medicine has given a PBA and which we call “diabetes”. Thus, the latter term referred, in the 18th century, to the condition we nowadays refer to by employing that very term, and we naturally say that physicians in the 18th century used the term “diabetes” to refer to the condition that occurs only when patients develop insulin

deficiencies leading to hyperglycaemia—as it is already clear from the perspective of contemporary medicine.

This real case illustrates a transition from a non-purely biological account of a disease into a PBA. Originally, the disease in question was characterised on the basis of symptoms—polydipsia, polyuria, tiredness, etc.—and on the basis of a marker that is not considered reliable nowadays—i.e., sweet taste of urine, which, current physicians know, can be caused not only by diabetes but also by Maple syrup urine disease, medications, and supplements, or even by dehydration. In contrast, the disease accounted for by the PBA of diabetes at present is characterised as occurring only when patients develop insulin deficiencies leading to hyperglycaemia. But, in spite of the diverging characterisations, it is clear that the non-purely biological account and the PBA concern the very same condition, which we refer to at present by employing the term "diabetes".

Then, a PBA of the condition we currently call "schizophrenia" could be developed in accordance with current medicine in a similar way as the PBA of diabetes was developed. For instance, there is evidence available at present that antipsychotic medications, blocking dopamine receptors in the brain, are effective in a significantly large number of patients with schizophrenia. Such evidence, together with evidence stemming from in vivo imaging studies, and evidence gathered from post-mortem observations, is consistent with the claim that dopamine and glutamate abnormalities are associated with schizophrenia (see Howes, McCutcheon, & Stone, 2015), even though causality is not proven unequivocally.

So, *if* the biological scenario occurred in reality, and schizophrenia were given a PBA relating to dopamine and glutamate abnormalities, then psychiatrists in that scenario would naturally infer that the condition that they call "schizophrenia", and is characterised in purely

biological terms, is the same as the one that was characterised as a syndrome in the non-biological scenario. Hence, despite the diverging characterisations between scenarios, "schizophrenia" refers to the very same condition in both scenarios. Contra Roache, then, it is in fact reasonable to assert that "schizophrenia" in the relevant PBA refers to the very same phenomenon that is referred to by current uses of the term.

In the following section, I will address two possible objections to my argument.

3. Objections

3.1 First objection. Biological phenomena vs psychosocial phenomena

In order to reject my claim that "schizophrenia" refers to the same phenomenon in both scenarios, critics might assert that, by using that term in the biological scenario, psychiatrists refer to a *biological* phenomenon—the dopamine and glutamate abnormalities—, whereas psychiatrists in the non-biological scenario—that is, actual psychiatrists—refer to the characteristic syndrome—understood to be a *psychosocial* phenomenon in Roache's view. Thus, critics might contend that "schizophrenia" refers to *two* distinct phenomena in the two scenarios that we are considering.

However, this contention is ultimately implausible. Suppose first that the biological scenario, in fact, occurs in the near future in reality at time *T*, and that it results from several discoveries that confirm a causal relationship between dopamine and glutamate abnormalities, and cases of the condition we now call "schizophrenia". At *T*, then, schizophrenia comes to be characterised as the condition that occurs when the brain abnormally produces the neurotransmitters in question. Now, consider the class *S* of patients diagnosed with schizophrenia prior to *T* and who survived after *T*. Here, the question arises

as to whether patients in *S* will remain diagnosed with schizophrenia after *T* under the new, purely biological, characterisation of the condition. The answer is clear: only those patients in *S* who developed dopamine and glutamate abnormalities should remain diagnosed with schizophrenia. Let us call this subclass of patients, who have both the syndrome and the dopamine and glutamate abnormalities, *S'*.

Now, suppose that Roache's assumption is true that psychiatrists in the biological scenario refer to a phenomenon that is different from the one that actual psychiatrists refer to. This assumption implies that, after *T*, when psychiatrists in the biological scenario claim that patients in *S'* have schizophrenia as it is defined in the relevant PBA, these psychiatrists refer to a phenomenon (condition) different than the one that they labelled "schizophrenia" prior to *T*.

The patients in *S',* we have seen, are those that were diagnosed with schizophrenia prior to *T,* and retained their diagnosis after *T*. Consequently, the patients in *S'* have (or had) the symptoms of the syndrome that we call "schizophrenia" at present: that they have these symptoms is the reason why they were diagnosed with schizophrenia prior to *T*. Now, the patients in *S'* remain diagnosed with schizophrenia after *T*. If the psychiatrists in the biological scenario use "schizophrenia" to refer to a condition that is different from the syndrome in question, then the striking conclusion follows that patients in *S'* have *two* distinct conditions, both labelled "schizophrenia": a syndrome diagnosed prior to *T*, and dopamine and glutamate abnormalities, diagnosed after *T*.

But this conclusion is implausible. In my thought experiment, the patients in *S' retain* their diagnosis of schizophrenia precisely because psychiatrists after *T* believe that the phenomenon that they called "schizophrenia" before *T* is a part of the *same* phenomenon they

call schizophrenia after *T*. Hence, *S'* patients after *T* are diagnosed not with two distinct conditions but only with one.

To see this point more clearly, consider the very beginnings of the COVID-19 pandemic. At that time, many patients developed flu-like symptoms that were more severe or pernicious to the patients' health than the familiar flu. On the basis of their peculiar symptoms, these patients were suspected to have a new disease. Let us say, then, that these patients had a novel flu-like syndrome. Soon after, a novel virus associated reliably with these cases was discovered, and the novel flu-like syndrome was given a PBA[64]. Diagnostic tests were developed, and patients were tested for the virus. Surely, among the very first patients who had one such test performed, there were some who had the characteristic flu-like symptoms at the very time when the test was performed. After some of these patients tested positive, however, these patients were *not* said to have two conditions—the flu-like syndrome and the SARS-CoV-2 infection.

Since it was discovered that a SARS-CoV-2 infection caused the symptoms comprised by the syndrome, it was immediately assumed that the syndrome and the infection were both part of a single phenomenon, i.e., COVID-19. For biological psychiatry, seeking "disorders and diagnoses rooted in biomedical pathology" (Phillips, 2015, p. 179), discovering a biological, stable cause of the syndrome of schizophrenia would be analogous to discovering that a SARS-CoV-2 infection caused the new flu-like syndrome. That is, if it was established that, say, dopamine and glutamate abnormalities cause the schizophrenia syndrome—with its characteristic behavioural and mental states—, then the abnormalities

[64] No patient could have COVID-19 without having a SARS-CoV-2 infection, and, just by having the latter, patients have COVID-19—such as in the case of asymptomatic COVID-19 patients. Then, that infection is necessary and sufficient for the disease.

would explain the development of the syndrome, and this, in turn, would show that both the abnormalities and the syndrome form one *single* phenomenon, not two distinct phenomena. Hence, the supposition that the abnormalities and the syndrome are distinct is not warranted.

Thus, in regard to the first objection, it is important to note that the syndrome of schizophrenia and the dopamine and glutamate abnormalities might appear to be separated phenomena only if they are considered to be unrelated. Nevertheless, once we realise that, in the biological scenario, the former causes the latter, it comes as natural from the perspective of psychiatry—which aspires to follow current medicine—to think of the syndrome and the abnormalities as forming one single phenomenon—as natural as it is for us think of the flu-like syndrome and the SARS-CoV-2 infection as forming one single phenomenon.

Yet, critics might claim that having psychiatric symptoms such as delusions or emotional withdrawal is different than, say, having a headache, sore throat and fever. The latter might be thought to be biological phenomena, and, in that sense, it would be easy to accept that they form a single disease with the underlying SARS-CoV-2 infection, which is a biological phenomenon as well. But psychiatric symptoms are alleged to be *psychosocial* phenomena, and critics might contend that, *prima facie*, in light of their different nature, these symptoms could not form one single phenomenon with the dopamine and glutamate abnormalities.

But consider the following symptoms: impaired judgment, disorientation, confusion, behavioural changes, delusions, hallucinations, loss of memory—which might involve forgetting the names of close family members—, obsessive or repetitive behaviour, and frequently getting lost. All these symptoms are present in various psychiatric conditions—including schizophrenia—, and they involve the patients' experiences and behaviours as

much as the schizophrenia symptoms of delusions, hallucinations, and emotional withdrawal. Thus, under Roache's view, the former group of symptoms must be considered psychosocial phenomena as well.

Nevertheless, it is currently uncontroversial that impaired judgment, disorientation, confusion, and so on, are all caused in Alzheimer's disease by the development of amyloid-β plaques and neurofibrillary tangles. Further, it is also uncontroversial that those symptoms—which must be characterised as psychosocial phenomena under Roache's view—and the brain factors—which are a biological phenomenon—form one *single* condition, i.e., Alzheimer's disease. In fact, the opposite claim, i.e., that Alzheimer's disease is in reality two distinct conditions—brain factors on the one hand, and the cluster of symptoms on the other—fits poorly with contemporary medical discourse regarding that disease, and it is, therefore, implausible. Hence, there is no *prima facie* reason to believe that psychiatric symptoms, allegedly being psychosocial, could not form one single phenomenon with dopamine glutamate abnormalities in the biological scenario.

The first possible objection to my argument is, in sum, not compelling.

3.2 Second objection. Symptomatic and asymptomatic schizophrenia

The second objection to my argument is that it might strike us as strange to say from *a*symptomatic patients that they have schizophrenia, and from symptomatic patients that they do *not* have it, as a PBA of this condition would allow. I will first consider the case of asymptomatic patients with schizophrenia. In fact, under a PBA of this condition, patients who did not develop the characteristic symptoms but who developed the associated biological factor would be diagnosed with schizophrenia. The reasoning against my argument here is

that it seems odd to attribute schizophrenia to an asymptomatic patient given that this condition is currently characterised on the basis of its symptoms. Surely—it might be alleged—a symptomless state must correspond to a very different phenomenon than the phenomenon reflected by a symptomatic state. Thus, "schizophrenia" in the non-biological scenario, capturing syndromes, refers to a different phenomenon than that very term in the biological scenario—where it captures a symptomless, biological phenomenon.

But it is important to note that, as I argued in the previous section, once a PBA of a disease is developed in medicine, both the underlying cause of the outward symptoms and the symptoms themselves become to be understood as forming one single phenomenon—just as it occurred, for instance, in connection with the SARS-CoV-2 infection and the relevant flu-like syndrome, which together form COVID-19. A further issue is also important. Consider again the case of diabetes. At present, it is accepted that mild, but still abnormal, high levels of blood glucose that are constant, when untreated, might *not* cause symptoms in patients, and that many other patients with those abnormal levels develop the symptoms when untreated. But there is no controversy as to whether *a*symptomatic patients who develop constant, elevated blood glucose levels have diabetes: they simply do. And, of course, symptomatic patients who also have those blood glucose levels have that condition as well. Thus, "diabetes" currently captures symptomatic and *a*symptomatic presentations of constant, abnormally high levels of blood glucose.

Now, 18th-century physicians in fact claimed from patients with the characteristic symptoms that they had diabetes, but, in lack of relevant causal knowledge and of the corresponding PBA of the disease, they were completely unaware that asymptomatic patients could develop insulin deficiencies leading to hyperglycaemia, and, therefore, they could *not*

have claimed, of *a*symptomatic patients with insulin deficiencies leading to hyperglycaemia, that they had the disease. Then, "diabetes", as employed in the 18th century, captured *only* symptomatic presentations of the condition.

Further, consider that, if an 18th-century physician claimed from an asymptomatic patient that they had diabetes, their colleagues could have accused her of using the term "diabetes" to refer to a phenomenon different from that which other physicians referred to. But if it turned out that the asymptomatic patient in question developed insulin deficiencies leading to hyperglycaemia, we would say, from our contemporary point of view, that the 18th-century physician was not referring to a phenomenon different from the phenomenon referred to by their colleagues—regardless of how strange this might have sounded for these colleagues the at that time.

We can thus draw a lesson from the diabetes case. If a PBA of schizophrenia was developed in the biological scenario in a similar fashion as the PBA of diabetes, the relevant syndrome and the dopamine and glutamate abnormalities would be conceived of as forming one *single* phenomenon in the biological scenario, and this phenomenon could have both asymptomatic and symptomatic presentations—just as both diabetes and COVID-19 have the two sorts of presentation. This implies that, if a PBA of schizophrenia was developed, a symptom-less state would correspond to the same phenomenon as a symptomatic state caused by dopamine and glutamate abnormalities, as long as the symptom-less state was underlain by these abnormalities, too. Thus, in the biological scenario, asymptomatic and symptomatic cases of dopamine and glutamate abnormalities would both be instances of the phenomenon called "schizophrenia".

Of course, given our current characterisation of schizophrenia as a syndrome, the contention that patients could have this condition without symptoms sounds *at present* as strange to us as the claim might have sounded, for 18th-century physicians, that an asymptomatic patient had diabetes. But, from the perspective of the biological scenario, such a contention would nevertheless be as natural as it is nowadays for us to claim that 18th-century physicians lacked relevant knowledge, and that the possibility of asymptomatic cases of diabetes was seen as strange by them because, as they employed the term "diabetes", they could only capture the symptomatic presentations of insulin deficiencies leading to hyperglycaemia.

Thus, from the perspective of the biological scenario, it would be natural to claim that psychiatrists in the non-biological scenario can only pick out the *symptomatic* presentations of dopamine and glutamate abnormalities; but it would be clear, in this scenario, that those abnormalities also have *a*symptomatic presentations, and that both presentations are captured by the term "schizophrenia"—just as the term "diabetes" captures symptomatic and asymptomatic presentations of insulin deficiencies leading to hyperglycaemia.

Then, "schizophrenia" in the biological scenario refers both to some symptomless states, and to the symptomatic states that the term refers to in the non-biological scenario. Therefore, the term refers to the very same phenomenon in both scenarios—and thus this part of the second objection to my argument falls.

I will now consider the other part of this objection. Under a PBA of schizophrenia, patients who do not develop the biological factor associated with the condition cannot be diagnosed with it—even if they have the characteristic symptoms of schizophrenia. The reasoning against my argument here is that, given the current characterisation of that

condition as a syndrome, it would be odd not to say of a patient who has these symptoms that they have schizophrenia. In fact, current psychiatrists would claim of all patients with the relevant syndrome that they have schizophrenia; and, since in the biological scenario some of these patients turn out not to have schizophrenia, then "schizophrenia" refers to two distinct conditions in the two distinct scenarios—or so the objection goes.

Nevertheless, the fact that some symptomatic patients turn out not to have schizophrenia in the biological scenario does not undermine my argument. To see that, let us consider the COVID-19 case again, and note that, at the very beginning of the pandemic, the novel flu-like syndrome "including fever, malaise, dry cough, and dyspnea" was initially called the "Wuhan pneumonia […] because of the area [of the first outbreak] and pneumonia symptoms" (Liu, Kuo & Shih, 2020, p. 328). On the other hand, let us note that a flu-like syndrome not caused by a SARS-CoV-2 infection might have the same outward appearance as the COVID-19 symptoms. Probably, therefore, at the very beginning of the pandemic, physicians who employed the term "Wuhan pneumonia" picked out, in some occasions and inadvertently, cases of flu-like syndromes that were not caused by a SARS-CoV-2 infection. Then, as it is clear from our current point of view, they picked out *non*-COVID-19 cases and labelled them with the term "Wuhan pneumonia". Despite the existence of these cases, however, it is uncontroversial that the available PBA of COVID-19 refers to the same condition as the term "Wuhan pneumonia".

Nowadays, then, patients with the characteristic symptoms of COVID-19 who do not have a SARS-CoV-2 infection are not considered to have the disease—regardless of whether these cases were labelled with the term "Wuhan pneumonia" at the very beginning of the pandemic. And, conversely, physicians at that time might have employed the term "Wuhan

pneumonia" to pick out cases of the characteristic, novel flu-like syndrome, and some of those cases—those not caused by a SARS-CoV-2 infection—are not considered cases of COVID-19, as it is understood at present. Still, "Wuhan pneumonia", as employed at the very beginning of the pandemic, refers to the very condition we now call "COVID-19".

In the biological scenario, we have seen, some patients with the characteristic symptoms of schizophrenia, but without the relevant abnormalities, are considered not to have schizophrenia. However, I have argued that this does not imply that "schizophrenia", as employed currently, refers to a condition that is different from the condition referred to by a PBA in the biological scenario. In fact, the existence of symptomatic patients without a diagnosis of schizophrenia in the biological scenario shows, at most, that the syndrome of schizophrenia has several causes: dopamine and glutamate abnormalities, and other causes. Nevertheless, this does not imply that "schizophrenia" in the two scenarios that we are considering refers to two distinct phenomena.

Then, neither the first nor the second part of this objection to my argument undermine said argument. Therefore, the contention that "schizophrenia" in a PBA refers to a condition different from the condition referred to by current uses of that term is not warranted; and, consequently, Roache's claim is not warranted either that "we might reasonably deny that a purely biological account of schizophrenia would refer to the same phenomenon referred to by current uses of the term "schizophrenia"".

4. Final remarks on Roache's argument

Roache believes that "reference to psychological and behavioural considerations is ineliminable in characterizing mental disorders" (2020, p. 375). Since she also believes that

the development of PBAs of psychiatric conditions such as schizophrenia would *not* rely on those aspects, then, she claims that "[u]nfortunately for advocates of the biomedical approach […] it is unrealistic to hope that a purely biological account of mental disorder is possible" (p. 376). Roache's claim thus implies the assumption that PBAs of mental disorder are *not* possible. She does not elaborate more on this claim, but seems to support it by asserting that the condition accounted for by a PBA of schizophrenia "is not exactly the same disorder to which psychiatrists currently refer using the term 'schizophrenia'" (2020, p. 375), where the latter disorder is characterised on the basis of behavioural and mental symptoms.

Notably, Roache's assertion amounts to saying that—to use my example—dopamine and glutamate abnormalities are "not exactly the same disorder" as the syndrome we call "schizophrenia". I assume such an assertion is grounded on the idea that dopamine and glutamate abnormalities are a *thing* different from a cluster of mental and behavioural symptoms. But it is clear that the cluster of symptoms of having a sore throat, fever, and chills is not the same thing as a *mere* replication of SARS-CoV-2 viruses, but the former and the latter are nonetheless understood by physicians to form one single disorder, i.e., COVID-19. So, contra Roache, the assumption that dopamine and glutamate abnormalities are a thing different from the relevant syndrome does not imply that it is impossible to develop a PBA of schizophrenia. All that is required for such a PBA to be possible is that both the dopamine and glutamate abnormalities and the syndrome might be *components of one single disorder*. They are the same thing is not required.

Now, suppose that schizophrenia was proven to be caused by an underlying biological factor and that a PBA was developed on the basis of that biological factor. From the contemporary medical point of view, there is no *a priori* reason to believe that the condition

characterised by that PBA could *only* be composed of the relevant biological factor, and not of the syndrome it causes as well. Then, it is clearly *possible* that the condition characterised by that PBA was formed by the biological factor and by the syndrome that it causes. This means that the condition picked out by that PBA could include the mental syndrome. Thus, contra Roache, PBAs of mental illness are in fact possible.

My arguments in this section show that, in fact, in case a PBA of schizophrenia was developed, it would pick out exactly the same condition that is currently characterised as a syndrome and called "schizophrenia". Contra Roache, then, the most *reasonable* outcome to expect in case such PBA was developed is that it would, in fact, refer to the very same phenomenon as current, actual psychiatrists refer to.

5. Further Criticisms

There are other criticisms that indirectly target the mere possibility that PBAs could be developed in psychiatry. These criticisms are largely based on the idea that the behavioural and mental symptoms involved in psychiatric conditions are fundamentally different from the biological factors that could possibly be associated with psychiatric conditions (see, e.g., The British Psychological Society, 2018, p. 156). The reasoning here is that, given that psychiatric conditions would be defined in biological terms according to PBAs of them, then the fundamentally different behavioural and mental components of those conditions would be disregarded.

Consider, for instance, this claim by Tim Thornton (2020) (emphasis in the original):

> [s]uppose that innovations in neuroscience, molecular biology, and brain imaging were to lead to discoveries concerning the neurological underpinnings of familiar psychiatric diagnostic classifications of psychopathology. Suppose, further, that a future neuroscience identified some neurologically very similar states, which caused (or were identical with) no mental distress or suffering but which, on the basis of the neurological similarity, were proposed as asymptomatic forms of the previous diagnostic categories. Assuming that these were not predictive of mental distress or suffering, such a proposal would not, I suggest, mark a triumph of neuroscientific psychiatry. Rather, it would amount to psychiatry losing its primary focus on *mental* illness (p. 235).

The scenario proposed by Thornton involves PBAs of psychiatric conditions for, in fact, only if a certain biological factor was sufficient for one of these conditions, the possibility would arise of there being asymptomatic presentations of that condition—those of patients with the mentioned biological factor—, as Thornton proposes us to imagine. Also, an asymptomatic patient with a psychiatric condition could only have that condition in case they developed the relevant biological factor, and, then, the latter would be necessary for the condition. The criticism here is that this scenario, allowing for asymptomatic forms of psychiatric conditions, would amount for psychiatry to lose "its primary focus on *mental* illness".

The possibility of PBAs being developed in psychiatry has also been indirectly criticised based on other, closely related, reasons. It has been thought that the personal experience of the symptoms involved by those conditions would be overlooked by biologically based accounts of them—including (what I call) PBAs. For instance, Jennifer Radden (2004) claims that "[a]s a result of an increasingly narrow vision for what is relevant in explaining schizophrenia, important aspects of the schizophrenic's personal experience are

left out of this so-called biological psychiatry" (p. 371). Further, psychiatry's aspiration to develop biological accounts of psychiatric conditions—including PBAs—has been criticised on ethical grounds, for it is argued that this biological approach to psychiatric illness disregards subjectivity, thus objectifying patients (see, e.g., Bublitz, 2020).

In sum, indirect criticisms against psychiatric PBAs are that the development of PBAs in psychiatry would lead the latter to lose "its primary focus on mental illness", to dismiss the symptoms of psychiatric conditions and the personal experience of them, and to objectify patients. In developing those PBAs, psychiatry would then miss the point as to its current, major focus of concern.

I believe, though, that this line of thought is unwarranted. I have contended that PBAs of psychiatric conditions pick out the very conditions that psychiatrists currently characterise as syndromes. If my contention is right, then purely biological psychiatry would be concerned with those syndromes no less than current, non-biological psychiatry. After all, even though Alzheimer's disease is nowadays given a biologically-based account, the relevant cluster of symptoms is still a major focus of concern for physicians. There is thus no *a priori* reason to believe that a biologically-based psychiatry, including PBAs, would dismiss the patients' symptoms—at least no more than current physicians dismiss the symptoms of patients with Alzheimer's disease.

In light of this, since a purely biological psychiatry would in fact be concerned with the relevant syndromes—as much as current medicine is concerned with the symptoms of Alzheimer's disease—there is no good reason to believe that the relevant mental aspects of psychiatric conditions, altogether with the personal experiences involved by them, would be overlooked in a purely biological psychiatry *more* than they could be overlooked by current psychiatry. Moreover, there is also no good reason to believe that a purely biological

psychiatry, relying mainly on biological accounts of psychiatric conditions, but still concerned with the symptoms, would "objectify" patients more than current psychiatry could do it. Then, the indirect criticisms against psychiatric PBAs made by The British Psychological Society (2018), Thornton (2020), Radden (2004) and Bublitz (2020), are unwarranted.

6. Conclusions

My response to Roache's argument addresses the schizophrenia case specifically. However, the idea that a PBA of a psychiatric condition would pick out the very condition that is characterised as a syndrome at present can be applied to PBAs concerning psychiatric conditions in general—as long as these PBAs are developed by relying on discovered biological causes that underlie the signs and symptoms of the relevant psychiatric condition, and, thus, as long as they are developed in accordance with current medicine.

The idea that, in the biological scenario, patients with both the underlying biological cause and the syndrome are diagnosed with *two* distinct conditions fits poorly with contemporary ways of characterising diseases in medicine. The idea that, e.g., a symptomatic patient with Alzheimer's disease has, in reality, *two* diseases (a syndrome and a compound of amyloid-β plaques and neurofibrillary tangles) simply does not correspond to the ways in which diseases are characterised by current medicine. Symptomatic patients with relevant symptoms and the compound of amyloid-β plaques and neurofibrillary tangles have just *one* disease, i.e., Alzheimer's.

This and other considerations I made in response to Roache's argument show that the claim is untenable that PBAs of psychiatric conditions do not pick out the conditions that are currently characterised as syndromes. Roache's conclusion is, therefore, unwarranted.

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CHAPTER VI

Could Psychiatric Conditions Be Defined Biologically?

As in Chapter V, the focus of this chapter is the line of thought according to which, if purely biological accounts of psychiatric conditions were developed, the conditions picked out by these definitions would be distinct from the psychologically defined conditions that constitute the major focus of concern for psychiatrists at present. In this chapter, I employ, for the most part, the term "purely biological definition" instead of "purely biological account" to stick to a more neutral terminology, for I will deal with arguments different from that in Chapter V. At any rate, a *purely biological definition* of a disease is just one that defines this disease in terms of a biological factor *B* in such a way that *B* is necessary and sufficient for the disease in question.[65] In Chapter V, I discussed a version of the line of thought above, formulated by Rebecca Roache (2019); in this chapter, I will address another three versions, developed, respectively, by Walter Sinnott-Armstrong & Jesse S. Summers (2020), Hanna Pickard (2009), and Rebecca Roache (2020).

I will argue, in short, that these three versions are unsound. My contention is that, if purely biological definitions of psychiatric conditions were developed, they would in fact pick out exactly the same conditions that are picked out by the corresponding psychological definitions. As it will become clear throughout, as in Chapter V, the discussion in this chapter concerns a *conceptual* issue, viz., whether biological definitions of psychiatric conditions

[65] A purely biological definition can be understood in a constitutive framework as much as a PBA. As a matter of fact, a purely biological definition can be understood as a definition of a disease in terms of the biological factor that causes its symptoms, such that the biological factor is necessary and sufficient for the disease, without said biological factor being one of the *disease*'s causes or effects. In other words, it is just a biological definition understood in the constitutive, rather than aetiological, interpretation I explained in Chapter III (§5)—specifically, one which cites only the biological cause of relevant symptoms, but not the symptoms themselves.

could pick out the psychologically defined conditions that are currently the major focus of concern for psychiatrists. Accordingly, the separated—although closely related—, empirical issue of whether purely biological psychiatric definitions are *likely* to be provided falls outside the scope of this chapter.

I will address Sinnott-Armstrong & Summers', Pickard's, and Roache's argument in §1, §2, and §3, respectively, and will make some final remarks in §4.

1. Sinnott-Armstrong & Summers's argument

Sinnott-Armstrong & Summers (2020) contend that biological factors that could possibly be correlated with depression are not "constitutive or definitive" of it, "even if they are causal or explanatory" (p. 87). (As it will become clear, on Sinnott-Armstrong's & Summers' view, being constitutive or definitive of a condition is the same as being necessary for that condition.) In arguing for their contention, Sinnott-Armstrong & Summers present what I take to be two distinct arguments, which I call "the psychological argument" and "the real depression argument", respectively. I will present both arguments in this subsection, and will address them separately in §1.1 and §1.3. I will argue, simply put, that both of these arguments are unsuccessful.

So, to begin with, it is important to note that, in Sinnott-Armstrong's and Summers' (2020) view, being constitutive or definitive of a condition concerns

> what is essential to the mental illness rather than […] what causes, explains, or treats it […] A claim about what […] constitutes (or defines or is essential to) a mental illness tells us what is necessary for that condition to be the particular mental illness it is rather

> than some other mental illness or no mental illness. When a condition is constituted or defined by a complex set or a conjunction of traits, nothing can possibly be an instance of that condition if any of those traits is missing (p. 85-86).

Further, Sinnott-Armstrong & Summers illustrate their notion of being constitutive or definitive of a condition by relying on the following example: claiming, for instance, that substance dependence is constituted by certain psychological traits and by some abnormal brain activity implies, the authors maintain, that "an individual patient [who] has all of the psychological traits of people with substance dependence but lacks that abnormal brain activity […] does not really have any substance dependence" (p. 86). Clearly, then, under Sinnott-Armstrong and Summers' notion, that a certain factor is constitutive or definitive of a condition means that the factor is *necessary* for that condition, so that, in the absence of this factor, the condition cannot occur.

Now, Sinnott-Armstrong's & Summers' *psychological argument* departs from a thought experiment according to which it is established that "99% of people with a certain biomarker (such as a pattern of neural activity)" develop depression, and also that 99% of patients with the relevant symptoms have the biomarker (p. 87). Further, they claim that, in this hypothetical scenario, a patient who develops the symptoms of depression but who does not have the biomarker does nonetheless "have the mental illness of depression" (p. 87). They then also contend that, "[c]onversely, a person who has that biomarker but who lacks any depressed feelings, thoughts, or actions would *not* have the mental illness of depression" (p. 87; emphasis in the original). In supporting their reasoning, they consider the case of "someone with the biomarker who smiles and laughs, is energetic and sociable, and says, 'Life is great. I am so happy'". According to the authors, "[w]e might not understand what is

going on in this case, but we would not suspect the mental illness of depression" (2020, p. 87).

The authors conclude that "these intuitions suggest that the psychological aspects of depression—the depressed feelings, thoughts, and actions—are what constitute or define the mental illness of depression", and that "[i]n contrast, the biological aspects or correlates of those psychological aspects are not constitutive or definitive of depression, even if they are causal or explanatory" (2020, p. 87). Thus, the conclusion of the psychological argument is that biological correlates are not constitutive or definitive of depression even if they are causal or explanatory—which is equivalent to the claim that biological correlates are not necessary for depression.

Importantly, though, Sinnott-Armstrong and Summers allow for the possibility that the term "depression" "might […] come to refer to all and only people with [the] biomarker, regardless of their psychological symptoms" (p. 87). This would only happen, however, if depression was given a purely biological definition in terms of the biomarker. And, under such a definition, no patient without the biomarker could have the condition. Then, if the term "depression" came to refer to all and only patients with the biomarker, as Sinnott-Armstrong & Summers allow, that biomarker would be necessary for depression.

To make this possibility compatible with the conclusion of the psychological argument, which is exactly the opposite, Sinnott-Armstrong & Summers advance the real depression argument. As derived from the thought experiment they posit, it is clear, in their view, that defining depression in terms of a biomarker "is not the way we would define or diagnose depression now", and, therefore, that "there are no grounds now to claim that such a biomarker would be a discovery about 'real' depression" (p. 87). The authors do not elaborate

on what they mean by "real depression", but it seems that what they mean is "what depression really is". Consequently, the conclusion of the real depression argument can be interpreted as the contention that the discovery of a biomarker that could be cited in a biological definition of depression could not be claimed to constitute a discovery about what depression really is—i.e., a condition constituted and defined, according to Sinnott-Armstrong and Summers, by "depressed feelings, thoughts, and actions".

If the discovery in question cannot be claimed to be a discovery about what depression really is, it must be because real depression is a condition *different* from the condition that would be called "depression" in the scenario where "depression" applies to all and only those patients who have the relevant biomarker. That is: from Sinnott-Armstrong's and Summers' argument it follows that a condition defined biologically, in terms of the biomarker itself, might well be called "depression" but would not be real depression, and, therefore, it would be different from the condition defined psychologically in terms of "depressed feelings, thoughts, and actions"—which is the real depression. In sum, therefore, Sinnott-Armstrong's and Summers' argument entails that the condition picked out by the biological definition in question ought to be distinct from the condition picked out by the relevant psychological definition.

I will respond to Sinnott-Armstrong and Summers' arguments in the following subsections.

1.1 Response to the psychological argument

Let us consider the conclusion of the psychological argument: the relevant biological correlates are not constitutive or definitive of depression, even if they are causal or

explanatory. To my mind, Sinnott-Armstrong's and Summers's conclusion is best interpreted along the following lines: biological factors are not constitutive or definitive of what depression *really* is, regardless of the way it is diagnosed at present[66]. In what follows, I will assume that this is the right way to interpret Sinnott-Armstrong's and Summers' conclusion, and I will argue that the conclusion is unwarranted.

Let us look again into Sinnott-Armstrong & Summers' argument. They claim, recall, that, in their thought experiment, only patients with the relevant symptoms have depression, regardless of whether these patients had the relevant biomarker: someone with the biomarker who smiles and laughs, the authors maintain, is *intuitively* free of depression. This claim implies that, *intuitively*, someone in the thought experiment who does not have the relevant depressed feelings, thoughts, and actions does not have depression. So, in Sinnott-Armstrong's and Summers' view, their thought experiment reveals that our "intuitions suggest that it is not any biological factors, but the psychological aspects of depression—the depressed feelings, thoughts, and actions—that constitute or define the mental illness of depression" (2020, p. 87).

It should be clear at this point that it is by way of an appeal to intuitions that Sinnott-Armstrong and Summers draw their conclusions. To my mind, however, this reliance on

[66] Note that, currently, only patients who develop the characteristic symptoms—which involve the "depressed feelings, thoughts and actions" claimed by Sinnott-Armstrong and Summers to be constitutive or definitive of depression—can be diagnosed with the condition. That is because depression is currently defined psychologically in psychiatry, only in terms of relevant psychological aspects. So, since depression is diagnosed only on the basis of symptoms, then, *trivially*, it is not diagnosed on the basis of any biological correlate, and, therefore, patients can in fact have depression without having a biological factor that could possibly be correlated with the syndrome of depression. Thus, if, in making their claim, Sinnott-Armstrong and Summers meant that, currently, biological correlates are not definitive or constitutive of depression, they would thus be making a trivial claim because depression is in fact currently diagnosed only on the basis of symptoms, so, it is attributed to patients independently of whether patients have some specific biological correlate. Trivially, then, biological correlates are not definitive or constitutive of depression *as it is currently diagnosed*. So, if Sinnott-Armstrong's and Summers' claim is to be taken as making a substantive, rather than trivial, claim, it should be interpreted as related to depression *regardless* of the way it is diagnosed at present.

intuitions is problematic. To show why it is so, consider the case of Alzheimer's disease. Currently, it is well established that amyloid-β plaques and neurofibrillary tangles are associated with the symptoms of this disease—which are well known to include loss of interest in activities, social withdrawal, mood swings, impaired judgment, disorientation, confusion, and loss of memory, among others. There is, therefore, a high correlation between certain biological markers and the cluster of psychological symptoms that is characteristic of Alzheimer's. Thus, the state of actual research concerning Alzheimer's disease is similar to the state of depression research in Sinnott-Armstrong's & Summers' thought experiment, where a high correlation between the syndrome of depression and a certain biomarker has been established.

Let us suppose that we want to defend that psychological symptoms are constitutive or definitive of Alzheimer's disease. In order to do so, we might draw inspiration from Sinnott-Armstrong's and Summers' arguments: we might claim that, intuitively, patients who have not developed any of the noticeable symptoms of Alzheimer's disease do not have the disease—even if they have the associated biological markers. Consequently, we might contend, the psychological symptoms of Alzheimer's disease are constitutive or definitive of that disease, for patients cannot have the disease if they have not developed said symptoms.

Current physicians, however, have discovered that many *a*symptomatic patients develop amyloid-β plaques and neurofibrillary tangles; and, in light of this,

> [d]uring the past decade, a conceptual shift occurred in the field of Alzheimer's disease (AD) […] Thanks to evolving biomarker research and substantial discoveries, it is now possible to identify the disease even at the preclinical stage before the occurrence of the

> first clinical symptoms. This preclinical stage of AD has become a major research focus. (Dubois *et al*, 2016, p. 294).

That is: important efforts are currently being made in medicine to establish criteria that could, in the future, allow physicians to diagnose Alzheimer's disease in *a*symptomatic patients with amyloid-β plaques and neurofibrillary tangles (see Driscoll & Troncoso, 2011; Hohman *et al*, 2016; Jia *et al*, 2019; Dubois *et al*, 2016; and Porsteinsson *et al*, 2021).

What is important to note here is that physicians have begun to attribute Alzheimer's disease to *a*symptomatic patients who develop amyloid-β plaques and neurofibrillary tangles. Consequently, the intuition that patients with amyloid-β plaques and neurofibrillary tangles but without symptoms do *not* have Alzheimer's disease simply clashes with the way that disease is coming to be characterised by physicians: for, according to these physicians, patients are perfectly capable of having Alzheimer's disease in the absence of symptoms. Hence, our intuitions concerning Alzheimer's are not reliable when it comes to establishing the way in which this condition might be *defined* and diagnosed.

As a matter of fact, physicians currently aspire to reach a point in the near future where Alzheimer's will be *defined* and diagnosed solely on the basis of the amyloid-β plaques and neurofibrillary tangles. Thus, ultimately, the way in which Alzheimer's, and diseases in general, turn out to be defined and diagnosed is a matter settled on the basis of the progress effectively made by the medical sciences, and *not* a matter settled *a priori* on the basis of mere intuitions.

Consequently, reliance on intuitions in connection with the definition and diagnosis of medical conditions is problematic: new knowledge in medicine might lead to conceptual shifts and to the development of patently counterintuitive, novel characterisations of a given

disease. Since depression is currently conceived of as a medical condition, relying on intuitions about it in a discussion about its possible characterisations might be as misleading as intuitions are in connection with Alzheimer's disease. It is undoubtedly possible that newly gathered medical data could lead to a conceptual shift concerning depression, and to the development of counterintuitive, new characterisations of the condition.

In summary, then, the psychological argument is built on a problematic reliance on intuitions concerning depression. The psychological argument is thus unwarranted, and Sinnott-Armstrong & Summers fail in showing that biological correlates are not constitutive or definitive of depression. I contend that, in order to settle the question of whether or not biological factors are constitutive or definitive of depression, we must rely on reasons independent of our intuitions. In the following sub-sections, I will elaborate on this contention, and I will argue that depression can in fact be given a biological definition.

1.2 Beyond intuitions

Let us consider again the conclusion of the psychological argument: the relevant biological correlates of depression are not constitutive or definitive of it *even if they are causal or explanatory*. This latter bit of the conclusion is striking because it goes plainly against the way in which medicine aims to define psychiatric conditions at present. And, as I will argue, once reliance on intuitions concerning depression is abandoned, the issue of whether biological correlates of depression are constitutive or definitive of the condition can be settled only by relying on the way medicine defines diseases. As I have insisted throughout my thesis, psychiatric conditions have been long expected to be defined in terms of their causes.

Since they are characterised as syndromes—i.e., mere clusters of symptoms—, then, simply put, their biological causes are causes of the relevant *symptoms*.

I have also note that what is understood to be the biological cause underlying the characteristic symptoms of a condition, when found in research, is usually established as a necessary—and, sometimes, also as a sufficient—component of the relevant disease. Then, the disease in question is defined in terms of the underlying biological cause of the characteristic symptoms. Recall, for instance, the case of gastritis, which is defined as an injury to gastric mucosa that causes the characteristic symptoms of gastritis—i.e., gnawing or burning ache or pain in the upper belly, nausea, vomiting, etc.

Though critics are pessimistic that the current DSM framework might allow biological psychiatrists to define psychiatric conditions biologically[67], it is still a *possibility* not ruled out in current psychiatry that the syndrome of depression is caused by a specific biological factor—just as the symptoms of gastritis are specifically caused by inflammation of the lining of the stomach. If depression is found to be so caused, biological psychiatrists could, following the "model of the rest of medicine", as they aspire to do, start diagnosing and defining depression on the basis of that specific biological factor. And, if they do, the relevant biological factor will become necessary for depression—that is, constitutive or definitive of it.

Thus, there are, beyond intuitions, grounds to settle the question of whether biological correlates are constitutive or definitive of depression. Those grounds are the following: current medicine standardly defines diseases in biological terms; and if a biomarker correlated with the syndrome of depression were found to cause depression, biological

[67] See critiques of this sort in, e.g., Demazeux & Singy (2015), Kapur, Phillips, & Insel (2012), and Insel (2014).

psychiatrists could develop a biological definition of depression in terms of the biomarker. In this scenario obtains, the biomarker might be established as necessary for depression: it might be established that patients cannot have depression without having the biomarker, and, consequently, the biomarker might be established as constitutive or definitive of depression. Whether or not this scenario obtains, though, is to be established empirically, not on *a priori* grounds.

Sinnott-Armstrong & Summers could try to respond to the above conclusion by way of the "real depression argument", but such response would fail.

1.3 The real depression argument

Sinnott-Armstrong & Summers (2020) say that the meaning of the term "depression" could change and "[…] come to refer to all and only people with [the] biomarker, regardless of [the absence or presence of any] psychological symptoms" (p. 87). This could occur, they say, if depression was given a biological definition—i.e., a definition in terms of a biomarker. The authors further claim that

> [o]ur project is neither prescriptive nor in opposition to such potential changes. Our only conclusion is that this is not the way we would define or diagnose depression now, so there are no grounds now to claim that such a biomarker would be a discovery about 'real' depression (p. 87).

This is what I call the "real depression argument". To make sense of this argument, we must regard it as an extension of the psychological argument. Recall that the psychological argument states, in short, that our intuitions dictate that patients with the hypothetical

biomarker associated with depression, but without the relevant symptoms, do not have depression. Then, allegedly, only the psychological symptoms of depression are constitutive or definitive of this condition, and, consequently, biological correlates are not constitutive or definitive of it. Based on the conclusion of the psychological argument, Sinnott-Armstrong & Summers further present the real depression argument, which states that defining depression in terms of a biomarker—i.e. defining "depression" so that it applies to all and only patients with that biomarker—"is not the way we would define or diagnose depression now" and, therefore, there are no grounds now to claim that such a biomarker would be a discovery about 'real' depression (p. 87).

As I explained above, the real depression argument entails that the psychological and the biological definitions of depression pick out two different conditions, viz. what the authors call "real depression"—i.e., a cluster of psychiatric symptoms—and a biomarker associated with those symptoms, respectively. From this it follows that, if a biomarker is discovered and used to define depression in terms of it, the resulting definition will not be a definition of "real depression" and, consequently, the discovery of the biomarker in question will not be a discovery concerning "real" depression.

The problem with the real depression argument is that, as I will show in what follows, there are in fact grounds *at present* to claim that the discovery of a biomarker associated with the psychological syndrome of depression would be a discovery concerning "real" depression.

The claim that this discovery would not be about real depression clashes dramatically with the standard practice of current medicine. To see this, consider the following symptoms: loss of interest in activities, social withdrawal, mood swings, impaired judgment,

disorientation, confusion, forgetting the names of close family members, and so on. These psychological symptoms tend to occur together in characteristic ways in some patients. Late 19th-century physicians called this specific cluster of symptoms "senile dementia", and sought the biological cause underlying those symptoms as they occurred specifically in older patients. Hence, research concerning senile dementia was, in the late 19th century, in a state similar to the present situation of biological research concerning psychiatric conditions, in the sense that biological psychiatrists currently seek, as physicians did in the 19th century, the biological causes underlying a characteristic clusters of symptoms.

Significant findings made public by Alois Alzheimer in 1906[68] helped to establish the compound of amyloid-β plaques and neurofibrillary tangles as a biological cause underlying senile dementia. And, currently, the particular form of what was called "senile dementia" that is caused specifically by the amyloid-β plaques and the neurofibrillary tangles is called "Alzheimer's disease" The plaques and tangles in question are constitutive or definitive of this disease. What is of interest here is that, in the standard practice of current medicine, it is uncontroversial that the discovery of amyloid-β plaques and neurofibrillary tangles underlying senile dementia was a discovery concerning what senile dementia *really* is, i.e., a disease whose characteristic symptoms are caused by amyloid-β plaques and neurofibrillary tangles, and was later given the name "Alzheimer's disease".

The fact that the discovery of amyloid-β plaques and neurofibrillary tangles is without controversy considered a discovery concerning what was called "senile dementia" is due to the fact that, as Hucklenbroich (2017) describes,

[68] For a history of Alzheimer's disease, see Assal (2019), and Yang *et al* (2016).

> [i]n the history of medicine and medical science, a typical pattern of discovery takes its course from primarily observing some single, isolated symptoms or clusters of symptoms, to secondarily lumping them together to typical constellations of symptoms called syndromes, to eventually identifying one disease entity by discovering the causal connection between them and thus identifying the consistent, unifying basis of all observed symptoms and findings in that syndrome (p. 795).

Then, under the standard practice of current medicine, once a group of symptoms *S* is observed to cluster together, the postulation is made that they form a disease entity *D*, which is presumed to be formed by *S* and a biological cause *C* which underlies *S*. Then, *C* is later sought in research, and, under this understanding, its discovery is, in fact, a discovery concerning *D*—for *D* is, from the outset, presumed to be composed of *S* and *C*.

In the case of depression, certain symptoms have already been observed to cluster together in characteristic ways, so the presumption is made by biological psychiatrists, in accordance with the standard practice of current medicine, that those symptoms form a disease entity that might include, in addition, a biological cause underlying those symptoms—recall the claim that psychiatric disorders are expected to be "rooted in biomedical pathology".

As I mentioned earlier, biological psychiatrists, in fact, seek the cause of the characteristic group of symptoms of depression, and, under this understanding, the discovery of their underlying biological cause would then be a discovery concerning *what depression really is*: the syndrome is hypothesised from the outset to be just one of the two components of a disease entity—viz. depression—formed by the symptoms *and by the biological cause underlying them*. So, a discovery of the latter would be a discovery concerning depression.

There are, then, grounds to claim at present that the discovery of a biomarker associated with the syndrome of depression would constitute a discovery concerning real depression. Sinnott-Armstrong's & Summers' contention that there are no grounds now to claim that the discovery of the relevant biomarker would be a discovery concerning real depression is simply false.

I have argued that both the psychological and the real depression arguments are unsound. It follows that a biological definition of depression would pick out exactly the same condition that the relevant psychological definition.

2. Pickard's argument

Hanna Pickard (2009) contends that the following two claims are compatible:

> first, that particular kinds of mental illnesses may prove to be valid scientific kinds, and second, that our concept of mental illness, as an overarching or generic category, involves a deviation from 'psychosocial, ethical, and legal' norms (2009, p. 85-86).

To understand these claims, let us note first that, currently, schizophrenia is, as all other psychiatric conditions are, defined psychologically. The psychological definition of schizophrenia picks out nothing other than a cluster of characteristic symptoms. Pickard (2009) states that the symptoms of schizophrenia—on the basis of which diagnoses of the condition are currently made—are "superficial or personal-level properties pertaining to psychological and physical functioning and behaviour, which are identified by psychiatrists through interview and observation" (p. 86). Then she invites us to imagine a biological scenario where psychiatrists find a correlation between those symptoms and certain brain

lesion, so that, "rather than using interview and observation" for diagnosis, psychiatrists perform a brain scan (p. 86).

In this scenario, Pickard maintains, psychiatrists would "test in the first instance for the underlying scientific property, not for the superficial symptoms" (p. 86). At this point, she instructs us to imagine a patient who, in the scenario that we are considering, has no symptoms at all, but develops the relevant brain lesion. Then Pickard asks whether this patient has schizophrenia. She claims that

> [w]e may be unsure, but, it seems at least possible that, given the conditions imagined in this thought experiment, our intuitions incline us to think that she does. For instance, we can easily imagine that she might be advised that the lesion should be operated on for preventative reason, lest it develop from 'latent' into 'full-blown' schizophrenia. But instead, suppose we ask: is this woman mentally ill? It seems our intuitions about this are entirely clear. She is not. We may in the end judge that she has schizophrenia, given the hypothesized discovery of its underlying, scientific property and its place in diagnostic procedures. But she is not mentally ill – any more than she is mentally disturbed, or mentally distressed, or mad, or crazy, or insane. She has no superficial or personal-level symptoms. She does not deviate from our 'psychosocial, ethical, and legal' norms (p. 87).

According to Pickard, therefore, the patient has schizophrenia but is not mentally ill. Then she draws a partial conclusion:

> [i]f we pry apart the superficial and the underlying scientific properties, our concept of mental illness tracks the former, even if our concepts of particular kinds of mental illnesses [such as "schizophrenia"] track or come to track the latter (p. 87).

Thus, in Pickard's view, particular mental illnesses like schizophrenia can prove to be valid scientific kinds: the "concept" of "particular mental illness", Pickard says, tracks a "scientific property" underlying the relevant syndrome. On Pickard's view, moreover, the behavioural and mental symptoms of schizophrenia involve deviation from psychosocial, ethical, and legal norms, and, since "mental illness" tracks those symptoms, then, a mental illness involves deviation from the mentioned norms. Hence, on Pickard's view, particular mental illnesses might prove to be valid scientific kinds, even though mental illness involves deviation from psychosocial, ethical, and legal norms.

In what follows, my only focus will be the partial conclusion quoted above. As a note, it is important to remark first that, in Pickard's thought experiment, asymptomatic patients who develop the relevant brain lesion might be diagnosed with schizophrenia. Consequently, in the thought experiment, schizophrenia has a biological definition that says that schizophrenia is a condition that occurs only when the relevant brain lesion is developed—independently of whether symptoms are present or not.

Pickard's intermediate conclusion involves two claims: that (1) concepts of particular mental illnesses, such as "schizophrenia", track the relevant underlying scientific properties; and that (2) the concept of "mental illness" tracks the superficial properties. The underlying scientific properties are just the biological factors reliably associated with specific conditions, whilst the superficial properties are the symptoms of specific conditions.

Now, in Pickard's view, the claim that "schizophrenia" tracks a valid scientific kind partly involves the idea that such a term "picks out a real and independently existing kind of thing, objectively distinct from other, perhaps superficially comparable, kinds of things" (2009, p. 89). So, suppose, for instance, that the cluster of symptoms characteristic of schizophrenia was caused by two completely unrelated biological factors: the brain lesion mentioned in Pickard's thought experiment, and an intoxication derived from a thus-far unknown dysfunction of the liver. Then, given the biological definition mentioned in the thought experiment, "schizophrenia" picks out the brain lesion only, but not the liver dysfunction that is superficially similar to this lesion.

Contrastingly, on Pickard's view, "mental illness picks out the relevant superficial properties, i.e., the relevant cluster of symptoms, regardless of whether it is caused by the brain lesion or to the liver dysfunction. Hence, according to Pickard, "schizophrenia" picks out *only* the underlying scientific property, whilst the superficial properties are picked out by "mental illness". It thus follows from Pickard's contention that a biological definition of schizophrenia picks out nothing other than the relevant underlying scientific property. In the following subsection, I will counter this entailment.

2.1 Response to Pickard's argument

Let us consider a slight variation of the thought experiment advanced by Pickard: imagine the case of a patient, different from the one devised by Pickard, who has the brain lesion associated with schizophrenia and develops the syndrome of schizophrenia. There are now two instances of the brain lesion: an asymptomatic one (proposed by Pickard) and the symptomatic one I just proposed.

If Pickard is right, then "schizophrenia", as it occurs in the definition involved in her thought experiment, picks out *only* the scientific property underlying the relevant symptoms—i.e., the brain lesion. Even in the case of the symptomatic patient, that is to say, the claim that the patient has schizophrenia is nothing other than the claim that the patient possesses the brain lesion in question: the claim says nothing whatsoever relating to the patient's symptoms.

Now, if a brain lesion was reliably associated with the syndrome of schizophrenia, and schizophrenia was defined in terms of that brain lesion, then, according to the standard practice of current medicine, schizophrenia would count as a disease entity—that is, as a medical condition composed of a syndrome and the underlying biological cause of that syndrome. On the other hand, when Pickard (2009) claims that "[t]he paradigm example of a kind of mental illness which might count as a *real illness* is schizophrenia" (p. 88; my emphasis) it is clear that she considers schizophrenia to be a medical condition. Consequently, in the thought experiment where a schizophrenia is associated with, and then defined in terms of, a brain lesion, schizophrenia forms a disease entity.

I have previously presented some considerations regarding the way disease entities are understood in medicine at present, but I will now elaborate more on this in order to show why Pickard's contention is unwarranted.

As I explained in Chapter I (§3), diseases are understood in current medicine to have a single biological (or cognitive) pathology (i.e., a certain destructive process common to all cases of the disease) which, in turn, leads to characteristic symptoms. Additionally, certain authors, like Hucklenbroich (2017), maintain that the symptoms of a disease are a part of this disease: under the current medical framework, Hucklenbroich says, "all symptoms and

pathological findings in a case of disease entity *D* are manifestations of *D* and, hence, parts of *D*" (p. 798). Despite this, though, Hucklenbroich claims that

> the different courses that are variants of […] [a] disease entity may be distinguished by their degree of severity […] There may even be courses without any symptoms or signs—so-called *bland*, *clinically silent*, or *inapparent* courses (Hucklenbroich, 2014, pp. 618-619; emphasis in the original).

Hence, although a disease has specific symptoms related to it, the development of the disease varies among patients to the extent that, in some cases, diseased patients do not develop symptoms at all. The lesson to learn from this is that disease entities are phenomena involving specific pathology, signs, and symptoms; that all of these are conceived of in current medicine to be components of the relevant disease entity—and not phenomena separated from it—; and that the presentation of the symptoms can be widely varied. Consequently, any term employed intentionally to designate a medical condition characterised under this disease entity model must pick out a phenomenon possessing all of these features. In other words, a genuine disease-entity term cannot pick out only an *asymptomatic* version of a pathology while excluding the symptoms—which are just manifestations of it.

Now, in Pickard's thought experiment, a specific biological factor is found to underlie the relevant syndrome and a purely biological definition is provided for schizophrenia. Under the standard practice of current medicine, then, schizophrenia, in Pickard's thought experiment, is to be understood to form a disease entity; and, accordingly, "schizophrenia", in the thought experiment, is to be understood as a disease-entity term. As I explained, even in the case of the *symptomatic* hypothetical patient of the hypothetical brain lesion, Pickard's

contention entails that "schizophrenia" picks out *only* the scientific property underlying the patient's symptoms—i.e., the brain lesion.

But this entailment clearly conflicts with the standard way in which genuine disease-entity terms work in current medicine and the disease-entity model, for those terms must pick out phenomena comprising pathology, signs, and symptoms, and not any one of these components in isolation. Hence, in current medicine, and according to the disease-entity model, if schizophrenia is characterised, in Pickard's thought experiment, as a disease entity, then "schizophrenia" is a disease-entity term, and it should not pick out merely the underlying scientific property of the disease. It must, instead, pick out the complete disease entity, that is, a phenomenon composed of pathology, signs, and symptoms. Pickard's contention is, thus, unwarranted.

Now, it might be claimed that, in the thought experiment, schizophrenia should *not* be given a characterisation as a disease entity "schizophrenia" should not be characterised as a disease-entity term. However, this claim simply clashes with current medicine and the disease-entity model. In the thought experiment, a specific biological cause is associated with a syndrome; and, according to current medicine and the disease-entity model, a syndrome associated with a specific biological cause ought to be characterised as a disease entity. There is, then, no reason to believe that schizophrenia, in the thought experiment, is not a disease entity.

Someone might contend, though, that "schizophrenia" is an *un*usual disease-entity term: a disease-entity term which, by contrast with other disease-entity terms, picks out only one isolated component of the relevant disease. But, under the conditions imagined in the thought experiment, there is no reason to believe that schizophrenia could be different in any

relevant way from other diseases, and, accordingly, so there is no reason, either, to believe that the term designating it should be an unusual in any way.

2.2 Final remarks on Pickard's argument

As I have mentioned, in Pickard's thought experiment, schizophrenia would be defined biologically, for it would be a condition that occurs only when patients develop the relevant brain lesion—regardless of whether they develop symptoms. And, as it is clear now, Pickard contends that the term "schizophrenia" would only pick out the relevant brain lesion, but not the relevant symptoms. This implies that the biological definition of schizophrenia in the thought experiment would pick out only the relevant biological factor but not the symptoms. On the other hand, schizophrenia is actually defined psychologically at present, and its psychological definition picks out exactly the relevant syndrome—that is all it currently picks out, in fact. Then, it follows from Pickard's contention that the biological definition of schizophrenia, picking out a biological factor but not the relevant symptoms, would pick out a condition *different* from the condition that the relevant, actual psychological definition picks out—i.e., the mere syndrome of schizophrenia.

As I argued, though, Pickard's contention is unwarranted, and the term "schizophrenia", being a disease-entity term in the thought experiment, would pick out the relevant biological factor and the relevant syndrome—in addition to the relevant aetiology and signs. Then, the biological definition of schizophrenia in the thought experiment, defining a disease entity, must pick out a condition comprising the relevant biological factor and the symptoms—plus the aetiology and the signs.

Now, similar considerations as the ones I made in §1 concerning depression apply to the case of schizophrenia. Under the current framework in medicine, the syndrome of schizophrenia is hypothesised to be only one among various components of a disease entity, i.e., schizophrenia, which could also be formed by a biological cause underlying the syndrome. And, if it was, in fact, the case that a specific biological factor caused the syndrome of schizophrenia, and a biological definition was provided for schizophrenia as in Pickard's thought experiment, then such a definition would just be a new definition of the very same condition that was once defined in psychological terms on the basis of the syndrome. Such a definition would just cite a different component of schizophrenia. As I argued, this claim is supported by the fact that both the syndrome and the (presumed) biological factor that could possibly cause the latter are hypothesised *from the outset* to be both components of a single disease entity, i.e., schizophrenia.

Then, the biological definition of schizophrenia in the thought experiment would pick out exactly the same condition picked out by the current psychological definition of schizophrenia. Therefore, a biological definition of schizophrenia could pick out exactly the same condition that the relevant psychological definition picks out.

3. Roache's argument

A further argument stating that a biological definition of a psychiatric condition would pick out a condition different from the one that is picked out by the relevant psychological definition is Rebecca Roache's (2019; 2020). In dealing with it, I will draw on my responses to Sinnott-Armstrong & Summers' and Pickard's arguments. Let us see. Rebecca Roache (2020) claims that

> [a] diagnosis of a somatic illness such as cancer, chickenpox, or multiple sclerosis is not contingent on the patient's having certain sorts of subjective experiences, or on behaving in certain characteristic ways […] diagnosis of somatic disorders does not stand or fall with the presence or absence of certain experiences and behaviours. They stand or fall, instead, with the presence or absence of certain biological factors. This is not the case for psychiatric disorders. People who are not unhappy *ipso facto* do not suffer from depression; people who do not experience recurrent, intrusive thoughts or behaviours *ipso facto* do not suffer from obsessive–compulsive disorder; people who do not have unusual difficulties with performing intellectual tasks *ipso facto* do not have an intellectual disability; and so on. Psychological and behavioural considerations play a far more central role in determining whether or not someone has a mental disorder than they play in deciding whether or not someone has a somatic disorder (p. 375).

Based on that reasoning, Roache (2020, p.375) further claims that any "biological account of a mental disorder is correct only in so far as it picks out those people who suffer the relevant psychological and behavioural symptoms characteristic of that disorder" and that a biological account of schizophrenia that "*at least in principle*, enable[d] people to be diagnosed with schizophrenia even if they lacked any of the psychological or behavioural symptoms characteristic of schizophrenia" (emphasis in the original) would not describe "exactly the same disorder to which psychiatrists currently refer using the term 'schizophrenia'". Further, Roache (2020) claims that

> [d]iagnosis of schizophrenia, like diagnosis of other mental disorders, stands or falls with the presence or absence of certain characteristic psychological and/or behavioural

> symptoms; in this sense, reference to psychological and behavioural considerations is ineliminable in characterizing mental disorders[69] (p. 375).

I reconstruct Roache's argument as follows:

> [P1]: Diagnosis of mental disorders stands or falls with the presence or absence of certain experiences and behaviours. Therefore,
>
> [C1]: any account of a mental disorder, including those that involved biological knowledge, is *correct* only in so far as it picks out those people who suffer the relevant experiences and behaviours, which are involved in the characteristic symptoms of that disorder. And, therefore,
>
> [C2]: since purely biological accounts (PBAs) of schizophrenia—or of any other mental disorder—would allow *a*symptomatic cases of that disorder—or of any other mental disorder—and, thus, they would pick out the cases of some patients who *lack* the relevant psychological and behavioural symptoms, then PBAs of schizophrenia—or of any other psychiatric condition—would *not* be correct accounts of mental disorders[70]. Therefore,

[69] This claim is also made by the author on similar grounds in her (2019) work (p. 221).
[70] Note that, although this claim is not explicitly made by Roache, it necessarily follows from [C1]. That is because the latter states that *only* certain accounts of mental disorder, i.e., those that pick out (all and only) relevant symptomatic cases are correct. Necessarily, then, if [C1] was true, those accounts of mental disorder that did *not* capture (all and only) relevant symptomatic cases would not be correct, as I state in [C2].

[C3]: such PBAs, being not *correct*, would not describe exactly the same disorder to which psychiatrists currently refer using the term "schizophrenia"—or any other mental-disorder term.

Therefore,

[C4]: reference to psychological and behavioural considerations is ineliminable in characterising schizophrenia—or any other mental disorder.

In what follows, I will focus on showing that Roache's argument is not successful.

3.1 Response to Roache's argument

Let us consider [P1]: that diagnosis of mental disorders stands or falls with the presence or absence of certain experiences and behaviours—specifically, those involved in the relevant symptoms. That premise is true at present. But that is just due to the fact that psychiatric conditions are currently defined psychologically in psychiatry and that current diagnoses in the discipline are made only by observing the relevant symptoms in patients. This could change in the future, though.

Let us consider the case of Alzheimer's disease to see this. In the history of medicine, a diagnosis of Alzheimer's disease has stood or fallen depending on whether patients developed the relevant experiences and behaviours, e.g., loss of memory, agitation, confusion, mood swings, and so on, involved by the symptoms of the disease. Patients were not diagnosed with it in the absence of symptoms. But, as I elaborated in §1.1, current

physicians are currently working on the development of criteria that could enable them to diagnose *asymptomatic* forms of Alzheimer's disease. Then, it is likely that, in the not-so-distant future, Alzheimer's disease becomes to be diagnosed only on the basis of the biological factor associated, regardless of whether patients develop the relevant symptoms.

If this happened, a diagnosis of Alzheimer's disease would not "stand of fall" depending on whether patients developed the relevant behaviours and experiences. It would rather stand or fall only with the presence or absence of the relevant biological factor. Now, in spite of whether it is likely to occur in reality, it is a possibility that a specific biological factor was found to cause the syndrome of schizophrenia, and it could thus become to be diagnosed only on the basis of that biological factor, as much as Alzheimer's disease could in the future become to be diagnosed only by tracking the relevant biological factor in patients. And, if this possibility occurred in reality in the case of schizophrenia, then, diagnoses of this condition, as those of asymptomatic Alzheimer's disease, would not stand or fall depending on the symptoms.

So, purely biological diagnoses of psychiatric conditions such as schizophrenia are *possible*: if the syndrome of schizophrenia was found to be caused by a specific biological factor, then the condition could become to be defined on the basis of that biological factor and also diagnosed on the basis of that factor. And, in case that possibility occurred in reality in the future, diagnoses of that psychiatric condition would not stand or fall depending on the presence of the relevant experiences and behaviours[71]. Then, the fact that diagnosis stands or falls depending on the symptoms is *contingent* on the current characterisation of

[71] At this point, the reader might get a sense that my reply to Roache seems question-begging. It is not. I clarify this issue in footnote 9.

schizophrenia. Thus, Roache's claim that diagnosis of mental disorders stands or falls with the presence or absence of certain experiences and behaviours, as it stands, is incomplete: it should state that that is true only *at present*, and that that fact is contingent on the psychological characterisation of psychiatric conditions currently available.

Of course, Roache could attempt the move to claim that schizophrenia, as diagnosed biologically, would not be the same condition as the condition that is currently called "schizophrenia", so that purely biological diagnoses of what we now refer to by employing that term were not possible. But this would be begging the question. Let us see. The claim that schizophrenia, as diagnosed biologically, would be a condition different from what we now call "schizophrenia" is implied by [C3], for a purely biological diagnosis of schizophrenia would only be possible under a PBA of that condition, and [C3] states that such a PBA would not describe the same condition that we nowadays call "schizophrenia"—that is, [C3] implies the claim that a PBA of schizophrenia would pick out a condition *different* from the one we now refer to by employing the term "schizophrenia".

But, as it is clear, [C3] is derived in the argument as a *consequence* of premise [P1], altogether with conclusions [C1] and [C2]. So, the claim that schizophrenia, as diagnosed biologically, would not be the same condition as the condition currently called "schizophrenia" should *follow* from [P1], [C1] and [C2], and not be presupposed from the outset in [P1]. So, unless Roache wanted to make a question-begging reply, [P1] must state that diagnosis of mental disorders stands or falls with the presence or absence of certain experiences and behaviours *at present*, allowing the possibility that biological diagnoses of mental disorders could be developed in the future.

So, there could be accounts of psychiatric conditions involving purely biological diagnoses of them. In turn, this implies that there could be accounts of psychiatric conditions that did pick out cases of patients who lacked the relevant experiences and behaviours, i.e., those accounts supporting a diagnosis of the condition on the basis of the biological factor associated with it, which would result in that asymptomatic patients with the relevant biological factor should be diagnosed with, say, schizophrenia.

One important thing here is that accounts of that sort, that allowed purely biological diagnosis of psychiatric conditions, must be presumed to be *correct*. Consider again the biological account of Alzheimer's disease sought currently by physicians, according to which patients could be diagnosed solely on the basis of the associated biological factor. As derived from current medical parlance, physicians seek to develop criteria to diagnose asymptomatic forms *of that specific disease*, not criteria to diagnose a disease different from Alzheimer's, such that it involved amyloid plaques and neurofibrillary tangles, and which was asymptomatic—but that was not Alzheimer's disease. That biological account must be presumed to exactly concern Alzheimer's disease. Consequently, the biological account of Alzheimer's disease sought by physicians, if it was developed, must be presumed to be *correct*—it would really be about Alzheimer's.

Similarly, in case a biological factor was found to cause, say, the syndrome of schizophrenia, and new diagnostic criteria were developed for that condition, then, there is no *a priori* reason to claim that, in developing new biological diagnostic criteria, psychiatrists would seek to elaborate criteria to diagnose a condition *different* from schizophrenia. So, biological accounts of that condition, allowing a biological diagnosis of it, would be *correct*,

for they would be presumed to pick out the same condition previously diagnosed on the basis of symptoms[72] [73].

From this, it follows that [C1] is false. Recall that the latter states that any account of a mental disorder, including those that involved biological knowledge, is *correct* only in so far as it picks out those people who suffer the relevant psychological and behavioural symptoms characteristic of that disorder. But, as I have just argued, there could be accounts of a mental disorder that could be presumed to be correct even though they did not pick out some people who suffered the relevant psychological and behavioural symptoms characteristic of that disorder. Then, for current medicine, it is not the case that "any" account of mental disorder is correct *only* in case it picks out (all and only) symptomatic cases. Some accounts could be correct even if they pick out some asymptomatic cases—those accounts that were developed in case a biological factor was found to cause the syndrome of, say, schizophrenia, and according to which patients were diagnosed solely on the basis of that biological factor.

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[72] Note that, at this point in Roache's argument, the author could not deny this without begging the question: to reject the idea that there could be *correct* accounts of psychiatric conditions such as schizophrenia that did not pick out cases of patients who developed the relevant experiences and behaviours, Roache should reject that a biological diagnosis of schizophrenia would correctly pick out the condition we call "schizophrenia". But this claim, already implied in [C3], is to be proven by [P1], [C1], and [C2], not previously assumed*!*

[73] It is important to note that, exactly at this point, I am *not* arguing in favour of my general contention that biological definitions of psychiatric conditions could pick out the very same conditions picked out by the corresponding psychological definitions. My aim in this subsection is specifically to show that Roache's argument is not successful in light of the current medical understanding. It is thus *not* the case that, at this specific point, I *argue* that, since schizophrenia, as biologically defined, would be the same condition as schizophrenia as psychologically defined, then a biological account of schizophrenia would be correct. My only claim here is that schizophrenia could become to be diagnosed biologically—a possibility that Roache (2020) herself recognises in her footnote 15 (p. 375)—and that, in current medicine, the presumption must be made that such a biological account would be correct, for it would be presumed that biological schizophrenia would be the very same condition as psychological schizophrenia—as much as biological Alzheimer's disease would be presumed to be the very same condition as Alzheimer's disease as it is currently diagnosed. At this point, I do *not* assume that such a presumption is true. And, as a matter of fact, I will later argue in this section that there are reasons to suppose that such a presumption is true. So, I do not beg the question in dealing with Roache's argument.

So, unless Roache begged the question, it is a possibility not ruled out by premise [P1] and conclusion [C1] that diagnoses of schizophrenia did not stand or fall depending on the relevant symptoms, and, thus [P1] is true only *at present*. From this, it follows that [C1] is false, so, contrary to it, some accounts of psychiatric conditions could be assumed to be correct even if they did not pick out some relevant symptomatic cases.

Now, from all this, in turn, it follows that [C2] is also false. [C2] states that PBAs of mental disorders, which would allow *a*symptomatic cases of the relevant disorder and, thus, would pick out cases lacking the relevant experiences and behaviours, would not be *correct* accounts of mental disorders. But the truth of this claim depends, in Roache's argument, on the truth of [C1]: the latter implies that only those accounts that pick out relevant cases of symptomatic patients are correct. If [C1] was true, then, PBAs of psychiatric conditions, which would pick out cases lacking the symptoms, would not be correct, and, thus, necessarily, [C2] would be true. But, as I argued above, [C1] is false: not all correct accounts of mental disorders pick out only relevant symptomatic cases, for there could be some correct accounts that would pick out *a*symptomatic cases, as I elaborated above, so [C2] is simply false.

Consequently, [C3] is also false. That conclusion states that PBAs of psychiatric conditions would not describe exactly the same disorder to which psychiatrists currently refer by employing the relevant mental-disorder terms. However, since those PBAs would be developed on the basis of the discovery of a biological factor causing the relevant syndrome, then, [C1] and [C2], being false, do not preclude the possibility that a PBA of, say, schizophrenia would be correct, which means that it would pick out the relevant condition that was once diagnosed on the basis of symptoms. Recall that, in developing purely

biological diagnostic criteria for Alzheimer's disease, it is not as if physicians were attempting to pick out a condition *different* from Alzheimer's disease that was associated with the relevant amyloid plaques and neurofibrillary tangles.

Rather, they presume that the condition picked out by purely biological diagnostic criteria would exactly be Alzheimer's disease. Since those criteria stem from a characterisation in terms of a PBA—only if the disease is defined biologically it can be *diagnosed* in a purely biological way—, then a PBA would pick out the very same condition previously defined in other ways. The case of schizophrenia would be similar to that of Alzheimer's disease.

Now, let us recall that Roache (2020, p. 375) claims that "diagnosis of schizophrenia, like diagnosis of other mental disorders, stands or falls with the presence or absence of certain characteristic psychological and/or behavioural symptoms" and that, in that sense, she concludes that "reference to psychological and behavioural considerations is ineliminable in characterizing mental disorders"—[C4] in my reconstruction of her argument. But if by "characterising" mental disorders Roche means establishing diagnostic criteria and defining a condition—which is all she talks about in this respect in her argument—, then [C4] is simply false.

As I argued above, it is a possibility not successfully ruled out by Roache's argument that diagnostic criteria of, say, schizophrenia, changed and only included biological aspects. And those criteria specifically should depend upon a PBA of schizophrenia, which must be presumed to be correct. In turn, such a PBA could only be developed if schizophrenia was given a biological definition, which would exclude reference to relevant psychological and

behavioural considerations. Then, the latter are not "ineliminable" from diagnostic criteria nor from definitions of mental disorders, and [C4] is false.

Then, Roache's argument is not sound: it is a possibility not successfully ruled out by her argument that diagnoses of schizophrenia did not stand or fall depending on the relevant symptoms, and, thus [P1] is contingent on the current psychological characterisation of psychiatric conditions. From this, it follows that [C1] is false, and, consequently, that [C2] and [C3] are also false. Further, [C4] is simply false. The argument is, therefore, not compelling.

What is of interest to the general discussion of this chapter is that [C3], i.e., that a PBA of a psychiatric condition would not describe exactly the same disorder to which psychiatrists currently refer using the corresponding mental-disorder term is not warranted by Roache's argument. In fact, if Roache avoided begging the question, it is a possibility allowed by her argument that a PBA of a psychiatric condition such as schizophrenia was correct, and, then, that such an account described the very same condition that is currently characterised as a syndrome at present.

3.2 Final remarks on Roache's argument

As I argued in §3.1, [C3] must be presumed to be false. That is because it is a possibility that, in case a biological factor was found to cause the syndrome of schizophrenia, diagnostic criteria for schizophrenia could change and become purely biological. And, in fact, under that framework, there is no *a priori* reason to believe that the development of such biological diagnostic criteria would be intended to target a condition different from the condition we nowadays call "schizophrenia". Thus, the presumption should be made, under that

framework, that a biological account of schizophrenia developed on the basis of a biological factor that caused the syndrome of schizophrenia, and according to which that condition was diagnosed solely on the basis of the relevant biological factor, would be *correct*, for such an account would pick out exactly the same condition that is currently diagnosed solely on the basis of the relevant symptoms.

That presumption is important because, if it is true, then, necessarily, [C3]—i.e., that PBAs of psychiatric conditions would not pick out the conditions that are correspondingly defined psychologically at present—is false. So, the falsity of [C3] implies that PBAs of psychiatric conditions *could*, if developed, pick out the corresponding conditions diagnosed on the basis of symptoms. Further, since PBAs of psychiatric conditions involve biological definitions of them, then, if [C3] is false, biological definitions of psychiatric conditions, implied by those PBAs, could pick out exactly the very same, corresponding conditions that are currently defined psychologically, which supports my general contention in this chapter.

Let us call the presumption that a biological account of schizophrenia, involving purely biological diagnostic criteria for it, would be correct, "*P*". An important question here is, of course, whether *P* is true. I claim that it is so, in fact, exactly because of the way diseases are currently understood in medicine. Let us recall that disease entities are composed of pathogenesis, signs and symptoms. Further, when a new characteristic cluster of symptoms is observed, it is presumed that the cluster is primarily caused by a specific biological factor—i.e., the pathogenesis—, in a way that it is presumed that both the cluster of symptoms and its underlying biological cause are part of a disease entity, say *D*. Then, when the primary biological cause of the syndrome is found, *D* is, under the current aetiological framework, defined in terms of such a biological cause.

What is important here is that characteristic patterns of (behavioural and mental) symptoms have been observed by psychiatrists, and that at least some of those syndromes, such as schizophrenia, are presumed to be caused by a specific underlying biological cause—those syndromes are "expected" to be "rooted in biomedical pathology", as Phillips (2015, p. 179) puts it. And, under the disease-entity model, those syndromes must then be hypothesised to form a disease entity that could also possibly be composed of the presumed biological cause of the syndrome. So, for instance, under the disease-entity model, schizophrenia must be hypothesised to be composed of the syndrome and of its presumed, underlying biological cause. Then, if that biological cause was in fact found in the future, and schizophrenia was defined and diagnosed biologically, then it would be exactly the same condition—the same *disease entity*—that is currently defined and diagnosed psychologically.

So, since, from the outset, schizophrenia—as well as other psychiatric conditions—is hypothesised to form a disease entity, in case a biological cause was established to underlie the relevant syndrome, then the latter would be a component of that very same disease entity, and because of this, a biological definition and diagnosis of schizophrenia would pick out exactly the same condition that is currently picked out by a psychological definition, because both definitions would pick out the very same *disease entity*—though they would cite different components of it: the psychological definition would cite the syndrome, and the biological definition, the biological cause underlying the syndrome.

Then, as long as schizophrenia is conceived of as a medical condition, *P*—that is, the presumption that a biological account of schizophrenia, from which purely biological diagnostic criteria stem, would be *correct*—must be true precisely because of the very way schizophrenia—and other psychiatric conditions—is characterised from the outset, i.e., as

possibly forming a disease entity. Then, since *P* must be true, my claim is supported that biological definitions of psychiatric conditions could pick out exactly the same conditions picked out by the relevant psychological definitions.

In summary, as I argued, Roache's argument is unsound, and thus, not compelling. Further, because of the very way schizophrenia and other psychiatric conditions are characterised—as possibly forming a disease entity—, the presumption must be true that a biological account of schizophrenia, involving purely biological diagnostic criteria for it, would be *correct,* which contradicts Roache's claim that a PBA of schizophrenia would not pick out exactly the same condition currently referred to by the term "schizophrenia" by psychiatrists.

Since PBAs of psychiatric conditions imply biological definitions of them, and those PBAs could pick out the corresponding conditions currently defined as syndromes, then, if purely biological definitions were developed, those definitions could pick out exactly the same conditions that are currently defined psychologically.

4. Conclusions

So, as I have argued, the three arguments addressed in this chapter are unsuccessful. They fail to show that biological definitions of psychiatric conditions would *not* pick out the very same conditions picked out by their corresponding psychological definitions. Sinnott-Armstrong & Summers' psychological argument is based on misleading reliance on intuitions, and the conclusion of their real depression argument is simply false. Further, Pickard's contention that "schizophrenia" in a biological definition would pick out only the relevant underlying scientific property is unwarranted, for, if that term was a disease-entity

term, it should pick out more than just the relevant biological factor. Finally, Roache's argument does not successfully precludes that PBAs of psychiatric conditions would pick out the very same conditions that are currently diagnosed solely on the basis of symptoms.

So, purely biological definitions of psychiatric conditions that could possibly be developed would pick out exactly the same conditions that are defined psychologically at present. My contention, thus, stands, and psychiatric conditions could in fact be defined biologically.

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APPENDIXES

Putting scientific realism into perspective[74]

In this paper, we offer a brief overview of the debate between realism and anti-realism in the philosophy of science. On the background of that debate, we consider two recently developed approaches aimed at vindicating realist intuitions while acknowledging the limitations of scientific knowledge. Perspectivalists explain disagreement in science without giving up the idea that currently accepted scientific theories describe reality largely accurately: they posit the existence of different perspectives within which scientific claims can be produced and tested. The integrative approach instead encourages researchers to embrace pluralism: conflicting frameworks and methodologies can be integrated when new knowledge is gained. In the natural and human sciences, researchers sometimes behave as if perspectivism is true; at other times, they hope for a reconciliation between conflicting frameworks and believe that this can be achieved by progressively filling knowledge gaps.

Keywords: *scientific realism*; *instrumentalism in science*; *objectivity*; *truth*; *perspectival realism*; *integrative approaches*; *disagreement*; *scientific progress*.

1. Realism and anti-realism in the philosophy of science

A key philosophical question about science is how we can resolve a disagreement in science without giving up the idea that our current scientific theories are largely accurate descriptions of an external reality. In the first part of the paper, we introduce two philosophical positions, namely realism and anti-realism, and observe how both views have branched out in more

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radical and more moderate versions to respond to various objections and counterexamples. In the second part of the paper, we introduce perspectival realism and the integrative approach as exciting new forms of moderate realism. We discuss how they account for disagreement in science, considering two examples, one in physics and one in psychiatry.

Philosophical realism is a view that encompasses both claims about what there is (metaphysical claims) and claims about what we can know as human beings with limited cognitive capacities (epistemic claims). You step out in the garden and observe a big cat sitting on the wall. Now take your observation: 'There is a big cat on the wall.' If you are a realist, you believe that in the world there are objects (such as a cat and a wall) and properties (such as being big) that exist independently of whether you can observe them or think about them. Even if you did not see the big cat on the wall, the cat would still be there, sitting on the wall, and would still be a big cat.

The philosophical realist is also committed to the idea that our perceptual capacities are a good guide to what there is in the world: this does not mean that we can infallibly know about the objects and properties around us by trusting our senses. Of course, we can be subject to hallucinations. Other factors can also affect the reliability of our perceptual processes and the veridicality of our perceptual states: for instance, the cat may look bigger than it is if the cat is next to a mouse. However, the realist is committed to the idea that, by and large, our experience gives us a good reason to believe that things are out there in the world and are roughly as we experience them: if we see a cat and hear a miaow, then there is a miaowing cat out there.

Against realism, sceptics argue that we do not know whether the information we receive through our senses is a good guide to what there is in the world. That is because we

can imagine scenarios in which what we take to be real is completely illusory, without us realizing the extent of the illusion. Hilary Putnam, for instance, discusses the brain in a vat hypothesis: suppose a mad scientist has removed your brain from your skull and managed to keep your brain alive. In a lab, the mad scientist has arranged for your now-disembodied brain to receive electrical impulses that offer the same stimulation your brain would receive if you experienced objects and properties in the world (Putnam 1982). So, your brain has the visual experience of there being a big cat on the wall, but there are no cats, no walls, and no 'you', apart from your electrically stimulated brain. This may seem a very far-fetched scenario, but the central idea is compelling: we could be in a situation where, based on our experiences alone, we would not be able to tell whether anything exists out there, independent of us.

When we apply philosophical realism to science, we get scientific realism (Bortolotti 2008). This is the view that our current scientific theories describe and explain reality in a largely accurate way – one common way to capture the idea is to say that the theoretical statements in those theories are approximately true. How does scientific realism work? Just as you come to know that there is a big cat on the wall by trusting your personal experiences of seeing a cat and hearing a miaow, so you can come to know that oxygen is required for combustion to occur when you observe that the flame is extinguished soon after the candle is placed under a glass. The observation of the flame being extinguished confirms the explanation provided by the theory of combustion because the observation is successfully predicted by the theory.

Obviously, there are other explanations that could be put forward to account for the extinguished flame. And this is where a scepticism-inspired view comes in. According to

anti-realism about scientific theories, our current theories are useful to us by enabling us to make successful predictions about reality even if they did not describe and explain reality by and large accurately. And, for the anti-realist, we are not in a position to distinguish those theories that just enable successful predictions – and are just empirically adequate – from those that also describe and explain reality by and large accurately – and thus are approximately true.

How does anti-realism work? If you were a brain in a vat, you wouldn't know that you are a brain in a vat, because your perceptual experiences would be indistinguishable from the perceptual experiences you would have if you were not a brain in a vat. Similarly, you wouldn't know whether your theory is approximately true or merely empirically adequate because all you would have to judge the theory by is the predictions it makes. The theory that oxygen is needed for combustion to occur is confirmed by the observation that the flame is extinguished soon after the candle is placed under a glass. But all we can say is that the theory is empirically adequate: that is, our observation has not disconfirmed it. Whether the theory is also true is a further question that cannot be answered by observation alone.

Scientific anti-realism is supported by a series of arguments aimed at showing that empirical adequacy is all we can hope for. This erodes our confidence in the approximate truth of our current scientific theories. One such argument is the pessimistic meta-induction: the history of science teaches us that we ended up replacing all our previous theories when we realized that they did not describe and explain reality accurately (Laudan 1981). Isn't it overwhelmingly likely that our current scientific theories will also be replaced one day? Then, why should we believe now that they describe and explain reality accurately?

Scientific realism is defended by a series of arguments aimed at showing that it is plausible to believe in the approximate truth of scientific theories. One such move is the no miracles argument (Boyd 1989): we all agree that science has been overwhelmingly successful, and the accuracy of scientific theories is the best explanation for the success of science. In other words, the only explanation for the success of science that doesn't turn such a success into a miracle is that scientific theories are approximately true. If the theories were not approximately true, how else could we explain their continuing to enable successful predictions?

2. Types of realism and anti-realism

Not all anti-realist positions are the same, and even realism has branched out in various forms depending on how it reacted to the challenges posed by the sceptics. What differs across these views is the understanding of the role of scientific theories and the assessment of their capacity to provide objective knowledge about the world surrounding us.

One popular view is instrumentalism about science: the basic notion is that we should understand theories as tools we use to predict events, and not as accurate descriptions or explanations of reality that can be true or false. So, we should not believe theories, but accept them. When we believe that a big cat is on the wall or that oxygen is necessary for combustion, we commit ourselves to the truth of those statements – that is, we commit to the world being as the statements say it is. But if the sceptical challenges succeed in eroding our confidence, then we may no longer commit to the truth of there being a big cat on the wall or of oxygen being necessary for combustion. We merely accept that the big cat is on the wall based on our perceptual experience; and we accept that oxygen is necessary for combustion

based on our empirical observations. This means that there is no further commitment on our part about reality being the way those statements say it is.

For the instrumentalist, the theory of combustion is a useful tool for predicting the behaviour of candles, but we would need to make a leap of faith to claim that the theory also describes and explains reality accurately. In particular, we would need to commit to the existence of entities that we cannot experience with our senses unless we are aided by instrumentation. For instance, we would need to believe that things like oxygen, which we cannot observe with our naked eyes, exist. Rather than making that leap of faith, we can merely accept the theory as a useful tool, leaving open the possibility that in the future a more precise tool will become available, leading to further successful predictions.

'Selective' forms of realism have been proposed to respond to the sceptical challenges, among which the most influential have been structural realism and internal realism. On these accounts, the basic realist intuition that scientific theories are approximately true is still endorsed but there is also an acknowledgement that scientific theories are limited as a means of attaining objective knowledge about reality.

Structural realism holds that scientific theories do not necessarily tell us about the nature of reality (e.g. what light is), but instead provide information about the underlying structure of reality (e.g. how light travels) (Worrall 1989). That would explain why competing theories are structurally very similar. Compare Fresnel's theory of light with Maxwell's. For Fresnel, light is made up of particles and moves through an elastic solid; for Maxwell, light is made up of waves and moves within an electromagnetic field.

F) Light is made up of particles

M) Light is made up of waves

The theories compete with one another and (F) and (M) cannot be both accurate descriptions of reality, as their descriptions of light conflict. However, both theories can accurately predict many observations about optics. For the structural realist, both theories get something right: they have correctly identified relationships between optical phenomena which means that they describe the structure of reality correctly if not its nature.

Although structural realism has been a very influential view, there are two main objections to it. First, it is not clear that for any scientific theory it is straightforward to distinguish content (nature) from form (structure), and the distinction seems necessary if structural realism is to be a genuine alternative to scientific realism (Psillos 1995). Second, it is not clear that all instances of scientific change involve different accounts of the nature of reality and a structural continuity between competing theories (Chakra- vartty 2004): isn't how the theories capture the structure of reality also amenable to revisions?

Internal realism can be described as a compromise between scientific realism and instrumentalism about scientific theories (Putnam 1982). Take a simple question: How many objects are there in the dining room? If you are doing particle physics, you may answer by counting molecules. If you are setting the table, you may answer by counting chairs. What is the right way of answering the question? In a sense, both answers get things right relative to the appropriate conceptual scheme. For Putnam, there are things out there in the world, but how we describe and explain them is not independent of our minds, because the concepts we use to describe and explain them are a product of our minds.

We cannot describe and explain reality without using concepts, such as 'chair', 'molecule', 'wave', and 'particle', and which concepts we choose will affect what we come to state and believe about reality. You are not wrong when you answer the question how many

objects there are in the dining room by counting chairs, even if your answer is different from that of the particle physicist. You and the particle physicist provide different answers because you have different interests, and apply a conceptual scheme that reflects those interests.

Although internal realism offers a compelling picture of how different conceptual schemes carve up reality, it may not help us decide whether one conceptual scheme does a better job than another at describing reality accurately. Is Maxwell's theory of light better than Fresnel's? Internal realism won't tell us that Maxwell's theory describes reality better because we lack a direct, neutral access to reality from which to evaluate the accuracy of the two competing theories. But we can tell whether Maxwell's theory has a better predictive success because internal realism can discriminate between conceptual schemes on the basis of how coherent and useful they are.

Perspectival realism acknowledges the existence of competing ways of carving up reality (perspectives) without giving up the possibility of comparing and evaluating those ways of carving up reality (Massimi 2018). This is prima facie a very attractive view. It combines the benefits of scientific realism – by salvaging the intuition that the- ories get things right – and those of other 'selective' forms of realism – by denying the foot-stamping (Fine 1984) and context-independent nature of some versions of scientific realism. We are going to discuss perspectival realism in more detail in the next section, as it is an immediately appealing and increasingly influential approach.

3. Perspectival realism and disagreement in physics

Just like scientific realism, also perspectivism is a view about what there is and how we come to know it, embracing the notion that there is a reality independent of us, whilst rejecting the

objectivity of scientific knowledge. Michela Massimi presents the goal of the perspectivist very clearly:

> [O]ne can accept and fully endorse that scientific inquiry is indeed pluralistic and that there is no unique, objective, and privileged epistemic vantage point without necessarily having to conclude that perspectives shape scientific facts or relativize truth (Massimi 2018, page 170).

What is a perspective? According to Massimi, a perspective is 'a scientific practice, including the epistemic claims, methodological resources, and justification endorsed by a scientific community'. In particular, a practice comprises:

> (i) the body of scientific knowledge claims advanced by the scientific community at the time; (ii) the experimental, theoretical, and technological resources available to the scientific community at the time to reliably make those scientific knowledge claims; and (iii) second-order (methodological-epistemic) claims that can justify the scientific knowledge claims advanced (Massimi 2018, page 152).

On a metaphysical level (which concerns itself with what there is out there in the world), perspectivism acknowledges that there is a reality out there, independent of our perspective on it. This is what enables us to say that a theory gets things right. So, with respect to what there is, perspectivism is a legitimate form of realism. On the epistemic level (which concerns itself with our capacity to know reality), however, perspectivism argues that our capacity to attain knowledge about reality is mediated by our perspective. So, on what we can know,

perspectivism counts as a selective form of realism, by claiming that our access to reality is constrained by our being situated in the world at a particular time and in a particular place.

For an understanding of perspectivism in science, it is important to highlight that all aspects of a scientific theory and of making science (what we claim to know, which experiential resources we have, and our methodological commitments) can vary across perspectives. However, epistemic standards are relatively stable. What are epistemic standards? Epistemic standards are the norms we use to assess scientific theories and may include simplicity, explanatory scope, and accuracy (Massimi 2017). The idea is that, if we are faced with two ways of interpreting the evidence that seem equally supported by our experiments so far, we may decide to opt for the interpretation that has some further advantages over the alternative: maybe the simplest one, the one that fits the best with other things we know, or the most elegant one.

Such epistemic standards can take different forms across different perspectives, but their stability enables us to compare scientific theories and ways of doing science from the standpoint of our current perspective. Even if our methods change and the things we believe to be true change across perspectives, the relevance and power of accuracy, simplicity, elegance, and coherence as epistemic norms remain stable. This enables com- parisons and assessments, although these won't be delivered from an entirely neutral or objective standpoint. In sum, according to perspectival realism, a pair of apparently conflicting scientific claims can both be true: from the perspective of Maxwell's theory of light, light is made up of waves; from the perspective of Fresnel's theory of light, light is made up of particles. This is because each perspective comes with its rules for determining the truth of

scientific statements. However, within our perspective, we can compare Fresnel's theory with Maxwell's theory on the basis of how simple, elegant, and coherent they are.

So how does perspectival realism account for disagreement in science, that is, differences in perspectives that are simultaneously available? Massimi (2018) proposes a refined version of perspectival realism, focusing on what it means to be dependent on a perspective. Massimi illustrates her notion of perspective-dependence with the following example:

(a) Water is a liquid with viscosity.

Allegedly, claim (a) poses a challenge for realism because it seems to be true according to hydrodynamics but false according to statistical mechanics, as Massimi explains. According to hydrodynamics, water is a fluid, and, consequently, has fundamental properties like viscosity. Therefore, (a) is true for hydrodynamics. But statistical mechanics treats water as a collection of discrete molecules, and, consequently, water has no viscosity. Therefore, (a) is false for statistical mechanics.

The problem for realists is to decide whether it is hydrodynamics or statistical mechanics that accurately describes the nature of water. But does scientific realism as such have the resources to solve this problem? Remember that scientific realism holds that currently accepted scientific theories are (largely) accurate descriptions of reality. If two of those theories conflict with each other, then they cannot be both accurate descriptions of reality, and we need to give one up. But this would be a self-refuting move for realism – since both theories are currently accepted scientific theories.

Massimi's perspectival realism offers a solution to this problem by distinguishing between context of use and context of assessment. Each perspective acts as a context of use

– which is the context from within the scientific statement is made and where the rules for determining the truth of scientific statements are formulated. Each perspective also acts as a context of assessment – which is the standpoint from which scientific statements from other (previous or competing) perspectives are assessed in terms of how adequately they are performing.

If the context of use is hydrodynamics, (a) is true; if the context of use is statistical mechanics, (a) is false. But we can appeal to statistical mechanics as a context of assessment. An assessor could say: viscosity is a property of water from the perspective of hydrodynamics, and it 'still features in statistical mechanics, but this time as a derivative property (i.e. as the property of momentum transport across laminae of mean flow)' (Massimi 2018, 354). That is, from the perspective of statistical mechanics as the context of assessment there is no conflict between the statements of hydrodynamics and statistical mechanics, because (a) as uttered in hydrodynamics remains true when it is assessed from the perspective of statistical mechanics.

This is an appealing solution to the problem of disagreement in science, but one concern is that the assessor, as conceived of by Massimi, would have to gain access to more true statements than a practitioner of hydrodynamics, and to more true statements than a practitioner of statistical mechanics—the assessor would have to gain access to the statement that viscosity is a derivative property of a collection of molecules of water. Precisely because of this additional knowledge, the assessor can connect claims coming from hydrodynamics and from statistical mechanics, integrating the two successfully. That is, the context of assessment seems to be the perspective of physics as a whole, and not statistical mechanics

in isolation from the other perspectives. The assessor would indeed ground the claim that (a) is true in wider knowledge about physics and be able to claim that:

(b) Water is a collection of discrete molecules that, as a collection, behaves as a liquid – which entails that it has viscosity.

Now, (b) is a true statement according to current physics, which dissolves the apparent conflict between statistical mechanics and hydrodynamics. Even for the practitioner of statistical mechanics, it is true that water has viscosity—but viscosity is not a property relevant to the study of water within the perspective of statistical mechanics. In other words, statement (b) displays a fuller and more accurate description of water than (a).

Let's consider another example. What can we do when the disagreement involves scientific statements that are not uncontroversial in the scientific field? It is usually accepted that, according to the general theory of relativity, nothing within spacetime travels faster than light. But quantum mechanics has identified a striking phenomenon called 'entanglement', which implies that information of the state of a physical system travels instantaneously between two entangled systems – that is, that the information travels faster than the speed of light. Both theories are widely accepted in physics because of their empirical success. For instance, quantum mechanics, it is often said, is the most accurately predictive theory humans ever produced. And, indeed, both theories are currently the main theories in physics, where general relativity accounts for very big objects, and quantum mechanics for extremely small objects.

Then, it would seem that from current physics we can infer that:

(c) Nothing travels faster than the speed of light in spacetime.

(d) It is not the case that nothing travels faster than the speed of light in spacetime.

To preserve credibility, realists should be able to account for such tensions in physics, explaining how we can interpret them in a realist way. One could say that in physics we lack a piece of knowledge that would enable us to choose between (c) and (d) or otherwise resolve the conflict between them. We currently do not know what that piece of knowledge is, but future empirical research and the further development of existing theories will increase the chance for us to gain the relevant piece of knowledge.

This reflects the attitude physicists take when they face conflicts between general relativity and quantum mechanics. For one of the main aspirations in physics is to develop a theory that unifies both of those theories, something like a theory of 'quantum relativity'. We can take it that such a unifying theory, once developed, would rule out either (c) or (d) or explain the apparent conflict between them, and do the same for other significant conflicts between quantum mechanics and general relativity. Indeed, it is the thought that conflicts between the theories can be solved by a unified theory that motivates the development of such a theory.

4. Perspectival realism and disagreement in the mental health sciences

Should scientists take the same attitude towards conflicting claims in the human sciences? An analogous situation to the one concerning the general theory of relativity and quantum mechanics in physics can be found in psychiatry. Because psychiatry is a medical field grounded in sciences that are less mature than physics, the controversial claims are not reserved to low-level empirical statements but extend to higher-level statements about what makes something an entity that can be investigated within that field (see e.g. Fellowes 2021).

In particular, there are controversies about what counts as a psychiatric disorder, and about how to conceive psychiatry itself. Due to the conceptual nature of these disagreements, it may appear that a perspectival approach would be particularly well suited to address them.

Take the following statements:

(e) What makes something a mental disorder is that it is a biological dysfunction.

(f) Itisnotthecasethatwhatmakessomethingamentaldisorderisthatitisabiological dysfunction.

Statement (e) can be inferred from the perspective of biological psychiatry. Statement (f) follows from the perspective of social psychiatry.

Biological psychiatry posits that at least some of the conditions classified as mental disorders are biological dysfunctions. This is a dominant perspective in psychiatry, and it is a stance clearly influenced by the status of other areas of medicine, in which diseases are understood as biological dysfunctions. In psychiatry, though, such an assumption remains controversial, for the consensus is that, although there are many good candidates of biological factors that could be associated with some psychiatric conditions, up to now it has proven challenging to reliably associate biological factors with some of the diagnostic categories of mental disorder.

Some researchers aspire to find those biological factors that could validate diagnostic categories, in hope of being able to further define psychiatric conditions in terms of the biological factors associated with them. Such as Down's syndrome is currently associated with having an extra chromosome 21, biological psychiatrists hope that, say, schizophrenia will be associated with a certain biological factor. In sum, biological psychiatry endorses (e).

On other conceptions of mental disorders, conditions could not be classified as disorders without considering behavioural aspects and values. For instance, the symptom-

based conception implies that what makes something a mental disorder is a pattern of behaviour. Social psychiatry has a broader view of mental disorders: social, psychological, and environmental factors are crucial for the development of such disorders. What makes something a mental disorder for social psychiatry is that it is associated with a certain combination of social, psychological, and environmental factors. In sum, social psychiatry endorses (f).

A few years ago, a new research project was launched in order to attempt to gain new knowledge about mental health from various domains, including the biological – genetics, molecules, cells, and physiology – and the psychological – behaviour and self-report. It is the Research Domain Criteria project (RDoC). RDoC's aim is to 'understand the nature of mental health and illness in terms of varying degrees of dysfunction in general psychological/biological systems' (NIH, 2022). Given the current lack of biological validation of the diagnostic categories, and the problems this carries, RDoC advocates consider that

> [i]t is essential to find a way to increase knowledge concerning the biological, physiological, and behavioral components and mechanisms through which multiple and interacting mental health risk and protective factors operate–a research framework that does not rely on disorder-based categories (NIH, 2022).

As we can see, researchers' attitude towards conflicting claims in psychiatry varies. Sometimes, biological and social psychiatry are seen as so different from each other that the only option we have when we are faced with the choice between two conflicting claims is to say that each is true according to one of the competing perspectives. But in frameworks like

the RDoC, the assumption is that researchers lack relevant knowledge at present, knowledge that once gained, will allow them to resolve the dispute between the claims.

This idea is exemplified by Dan Stein's integrative approach. Stein (2021) takes it that biological psychiatry and social psychiatry are two frameworks 'guiding the future of psychiatry' (181). The author recognizes that there is an apparent conflict between these frameworks—that the former attempts a biological characterization of the domain of mental health and illness, whereas the latter is rather socially and psychologically oriented. A perspectival approach would dictate that, depending on the perspective one takes, one or the other characterization would be the correct conception of mental health and illness. However, Stein argues that each framework involves research 'gaps'. As Stein puts it:

For clinical neuroscience, a major gap in psychiatry is that our diagnostic systems are not aetiologically based and that our treatments are not sufficiently personalized [...] For global mental health, on the other hand, a major gap in psychiatry is underdiagnosis and undertreatment (Stein 2021, 182).

Stein's idea is that psychiatry will make progress by advancing research in each framework:

> [for] clinical neuroscience [psychiatry] will advance by understanding how brain mechanisms lead to symptoms, by developing biomarkers that are useful for diagnosis and treatment stratification, and by developing treatments that address those mechanisms that are involved in a particular individual's symptoms [...] [for] global mental health [...] psychiatry will advance by understanding the social determinants of mental disorders, by developing interventions that are feasible and acceptable across the world, by scaling these up for delivery by nonspecialized health workers (Stein 2021, 182).

Stein proposes an integrative approach to psychiatry that recognizes that psychiatry has a range of gaps; that advances in psychiatry require both discovery and implementation research, that clinical neuroscience and global mental health can join forces to drive such research forwards, aiming for a personalized public health that addresses more precisely a range of individual and social determinants of mental illness. (182–183, our emphasis).

Facing the conflict between biological and social psychiatry, Stein's attitude is that mental health researchers should gain knowledge from each framework in order to further integrate such knowledge into a unified, non-conflicting conception of mental health and illness. Importantly, we can also note that the ultimate perspective sought by the integrative approach is the one of psychiatry as a whole – that is, the perspective of the body of knowledge in psychiatry.

Thus, disagreement in physics and psychiatry illustrates that, in some instances of conflicting scientific claims, the attitude scientists take is that the conflicting claims can both be true, but according to different perspectives; in other instances, the attitude is to integrate the competing approaches as much as possible and recognize the existence of knowledge gaps that will be filled when further facts are discovered.

5. Conclusions and limitations

In this paper, we offered a brief overview of the debate between realists and anti-realists. Both are concerned with whether science can deliver objective knowledge of reality and whether currently accepted scientific theories represent the world in a largely accurate way. We also provided a quick update on the realism debate by discussing two recent proposals made by perspectivists and integrationists about how to address disagreement in science.

According to perspectivism, scientists view the world from a given perspective. When the perspectives differ significantly, the claims scientists commit to within a perspective can clash with the claims that are regarded as true from another perspective. According to the integrative approach, there is a clear tendency among scientists to pursue the development of a coherent body of knowledge within each science, and the explicit or implicit goal is to avoid committing to conflicting statements by pursuing relevant new knowledge. Knowledge gaps at our present time are seen as a powerful motivation to pursue further research and not as problems for a realist conception of science.

This perspectival and the integrative approaches can work at various levels of generality and in distinct fields, from whether water has viscosity to whether biological dysfunction is what characterizes mental disorders. However, how perspectivism and the integrative approach can be successfully applied to specific instances of disagreement is a challenging question that deserves further investigation.

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En contra del compromiso causal de la psiquiatría biológica[75]

Se le llama 'psiquiatría biológica' a la vertiente de la investigación psiquiátrica que busca establecer asociaciones estables entre condiciones psiquiátricas y factores biológicos específicos. La búsqueda de tales asociaciones está motivada por lo que llamo el "compromiso causal" de la psiquiatría biológica, que es la presunción de que factores biológicos específicos son las causas principales de las condiciones psiquiátricas. En este artículo argüiré que dicho compromiso es una presunción implausible sobre esas condiciones, pues la mejor evidencia psiquiátrico-biológica disponible no lo respalda y es dudoso que la evidencia futura lo hará.

Biological psychiatry seeks to establish reliable associations between specific biological factors and psychiatric conditions. The search for such associations is motivated by the presumption that the major causes of psychiatric conditions are specific biological factors. I call such a presumption the "causal commitment of biological psychiatry". In this paper, I will argue that the causal commitment is an implausible presumption, for the best available evidence does not support it, and it is unlikely that future evidence will do it either.

Palabras clave: *filosofía de la psiquiatría*; *causas biológicas*; *condiciones psiquiátricas*; *psiquiatría*; *psiquiatría biológica*.

1. Introducción

Se le llama 'psiquiatría biológica' a la vertiente de la investigación psiquiátrica que busca establecer asociaciones estables entre condiciones psiquiátricas[76] tales como la esquizofrenia

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[76] Algunas propuestas teóricas disputan la idea de que las condiciones clasificadas por el 'Manual Diagnóstico y Estadístico de los Transtornos Mentales' (American Psychiatric Association, 2014) deben tener el estatus de enfermedades (véase, por ejemplo, Bortolotti, 2020, o The British Pychological Society, 2018). Para eludir la presunción de que dichas condiciones son enfermedades utilizaré sistemáticamente el término, más bien neutral,

y la depresión, por un lado, y factores biológicos específicos, por el otro. Como elaboraré más adelante, la búsqueda de tales asociaciones está motivada por la presunción de que las causas *principales* de las condiciones psiquiátricas deberían de ser factores biológicos específicos—mayormente desconocidos hasta ahora. Llamo a esta presuposición el 'compromiso causal' de la psiquiatría biológica.

Este compromiso tiene gran influencia en la psiquiatría actual y, además, ha sido prominente a lo largo de la historia de la disciplina. Por ello, evaluar su pertinencia es una tarea apremiante. Mi intención es mostrar que el compromiso causal de la psiquiatría biológica es, ultimadamente, una presunción implausible sobre las condiciones psiquiátricas. Como argüiré, la razón es que, por un lado, la mejor evidencia psiquiátrico-biológica disponible no respalda al compromiso causal; y, por otro lado, es altamente dudoso que la evidencia futura lo hará. Mis consideraciones sugieren que factores de tipo biológico tanto como factores de tipo social-ambiental son causas *igualmente* significativas de las condiciones psiquiátricas.

En el apartado §2 mostraré que la psiquiatría biológica de hecho sostiene el comprimiso causal descrito. Más adelante, en el apartado §3, elaboraré mi crítica. La psiquiatría biológica ha sido amplísimamente replicada, por lo que es importante destacar la forma en que mi contribución al debate es inédita y sustanciosa. Dedicaré el apartado §4 para esa tarea. Finalmente, presentaré de forma breve mis conclusiones en el apartado §5.

2. La psiquiatría biológica y su compromiso causal

Los investigadores en psiquiatría se han dedicado por mucho tiempo a buscar factores biológicos que estén específicamente asociados con las condiciones psiquiátricas clasificadas por el 'Manual Diagnóstico y Estadístico de los Trastornos Mentales'[77] ('DSM' por sus síglas

de 'condición psiquiátrica' para referirme a ellas, en lugar de usar otros términos más comunes como 'desorden mental', 'enfermedad psiquiátrica', o 'trastorno mental'.

[77] Existen otros sistemas de clasificación de las enfermedades que incluyen a las condiciones psiquiátricas, tales como la *International Classification of Diseases*. Sin embargo, el DSM es la clasificación de condiciones psiquiátricas más influyente en nuestros días, por lo que solo me enfocaré en estas últimas tal como aparecen en él.

en inglés) (American Psychiatric Association, 2014), tales como la esquizofrenia[78] y la depresión. Esta vertiente de la investigación psiquiátrica ha sido llamada 'psiquiatría biológica', y ha logrado algunos avances significativos. Destaca especialmente el caso de la esquizofrenia, que ha sido asociada con anormalidades en la producción de los neurotransmisores dopamina y glutamato en ciertas zonas del cerebro de forma consistente en diversos estudios. Además, se ha mostrado que el desarrollo de esa condición en los pacientes está significativamente vinculado con herencia genética. En el apartado §3 abordaré en detalle la evidencia que muestra tales vínculos.

Sin embargo, la situación al respecto de otras condiciones psiquiátricas es menos alentadora para la psiquiatría biológica. Por ejemplo, la idea de que niveles bajos de serotonina en el cerebro están asociados con la depresión ha sido altamente influyente en la disciplina, pero una revisión sistemática muy reciente arroja que

> "las principales áreas de investigación sobre la serotonina no proveen evidencia consistente de que hay una asociación entre serotonina y depresión, y tampoco apoyo para la hipótesis de que la depresión está causada por actividad o concentración reducida de la serotonina" (Moncrieff *et al*, 2022, p. 1).[79]

Además, múltiples artículos de investigación establecen que sus resultados confirman una asociación entre un factor biológico y una condición psiquiátrica específica—o un síntoma de ella—, pero, en su contra, se alega con frecuencia que esos artículos normalmente no son "estudios bien diseñados con muestras grandes y controles adecuados, que estén replicados

[78] La evidencia parece apoyar que ciertos factores cerebrales están asociados con la esquizofrenia. Por ello, se ha considerado ocasionalmente a esta condición como una neurológica en lugar de una psiquiátrica (ver, e.g., Liberman & Corrigan, 1992), es decir, como una enfermedad del cerebro y no como una enfermedad mental. No está claro, sin embargo, que las enfermedades mentales no sean *al mismo tiempo*, ultimadamente, enfermedades del cerebro (para una discusión al respecto ver, e.g., Fagerberg, 2022). Además, "los avances recientes en neurociencias hacen insostenible en este momento saber dónde trazar con precisión la línea entre las enfermedades neurológicas y las psiquiátricas" (Baker, Kale & Menken, 2002, p. 1468) (mi traducción, el original es como sigue: "recent advances in neuroscience make it untenable at this time to know precisely where to draw the line between neurological and psychiatric disorders"). A la luz de estas consideraciones y, en la medida en que la esquizofrenia está incluida en el DSM, tomaré a esta condición como una *psiquiátrica*. En cualquier caso, que mi argumento sea correcto no depende de si la esquizofrenia es psiquiátrica o neurológica.

[79] Mi traducción. El original es como sigue: "The main areas of serotonin research provide no consistent evidence of there being an association between serotonin and depression, and no support for the hypothesis that depression is caused by lowered serotonin activity or concentrations. Some evidence was consistent with the possibility that long-term antidepressant use reduces serotonin concentration".

exitosamente por otros grupos, y que no sean significativamente contradichos por otros hallazgos" (The British Psychological Society, 2018, p. 153).[80]

Este tipo de críticas no son infrecuentes, y las quejas involucradas por ellas se pueden resumir en la afirmación de Jeffrey Poland (2015) de que "la investigación ha tendido a producir hallazgos que son negativos, no replicables, inconsistentes, débiles, no específicos o no interpretables" (p. 26).[81] De esta manera, los esfuerzos de la psiquiatría biológica, vistos de forma global, han sido relativamente estériles.

Sin embargo, la aspiración de la psiquiatría biológica no ha sido abandonada. Para apreciar esto último, es importante entender que la pretensión de encontrar factores biológicos que se asocien específicamente con las condiciones psiquiátricas tiene su origen en la idea de que dichas condiciones son enfermedades. De hecho, como lo indica James Phillips (2015),

> "La manera "oficial" de clasificar en psiquiatría es biomédica. Se espera que los desórdenes y diagnósticos psiquiátricos sigan el modelo del resto de la medicina, con desórdenes y diagnósticos psiquiátricos arraigados en patología biomédica. Idealmente, el modelo alcanzaría diagnósticos válidos, médicamente fundados" (p. 179).[82]

Vale la pena indicar que, en la medicina biomédica, el estándar con respecto a la relación entre factores biológicos y enfermedades es que ciertos factores biológicos están vinculados de forma específica con una enfermedad—y solo con esa—, y que los primeros definen a las últimas. Por ejemplo, ciertas formaciones anormales de proteína en el cerebro llamadas "placas amiloides" y "ovillos neurofibrales" están asociadas específicamente con una de las formas de demencia, a saber, la enfermedad de Alzheimer. Notablemente, otras formas de demencia no se vinculan con las placas amiloides y los ovillos neurofibrales, sino con factores cerebrales diferentes—e.g., los cuerpos de Lewy. Así, la enfermedad de

[80] Mi traducción. El original es como sigue: "well-designed studies with large samples and adequate controls, replicated successfully by other groups and not significantly contradicted by other findings".
[81] Mi traducción. El original es como sigue: "research has tended to produce findings that are negative, non-replicable, inconsistent, weak, non-specific, or uninterpretable".
[82] Mi traducción. El original es como sigue: "The "official" way of classifying in psychiatry is biomedical. Psychiatric disorders and diagnoses are expected to follow the model of the rest of medicine, with psychiatric disorders and diagnoses rooted in biomedical pathology. Ideally, the model would achieve discrete, medically founded, valid diagnoses".

Alzheimer es exactamente la forma de demencia asociada con placas amiloides y ovillos neurofibrales.

De esta forma, en su aspiración a concordar con "el resto de la medicina", la psiquiatría biológica ha presumido que un factor biológico debería de estar asociado específicamente con una de las condiciones psiquiátricas—y no con varias—en una forma análoga a como las placas amiloides y los ovillos neurofibrales están asociados con la enfermedad de Alzheimer. En la misma línea, además, se esperaría que el posible factor biológico asociado con una condición psiquiátrica fuera establecido como la 'característica definitoria'[83] de dicha condición.

Esta manera de pensar con respecto a las condiciones psiquiátricas podría parecer obsoleta para quienes están familiarizados con la investigación psiquiátrica contemporánea. Sin embargo, la caracterización de esas condiciones como enfermedades ha motivado aun recientemente la búsqueda de posibles factores biológicos individuales que estén asociados con ellas de forma específica, a pesar del árido estado en el que se encuentra la investigación psiquiátrico-biológica actual.

La idea de los investigadores es que, a pesar de que padecemos de una gran falta de conocimiento biológico, caracterizar a las condiciones psiquiátricas en términos de síndromes tal como se hace en el presente—esto es, como patrones característicos de síntomas—facilitará la adquisición de nuevo conocimiento biológico:

> "Primero, la progresión típica del conocimiento comienza con la identificación de las manifestaciones clínicas (el síndrome) y la desviación de la 'norma'; el entendimiento de la patología y de la etiología usualmente vienen mucho después […] En la actualidad, la enfermedad de Alzheimer, […] con demencia como su manifestación clínica, morfología cerebral específica, patofisiología tentativa y con causas al menos parcialmente conocidas, es una de las pocas condiciones en la clasificación psiquiártica que están ya definidas por su patología en lugar de su síndrome […] la esquizofrenia, sin embargo, es mejor descrita como un síndrome" (Jablensky, 2012, p. 79).[84]

[83] Este término es tomado de Kendell & Jablensky, 2003, p. 8.

[84] Mi traducción. El pasaje es como sigue: "First, the typical progression of knowledge starts with the identification of the clinical manifestations (the *syndrome*) and the deviance from the "norm"; understanding of the pathology and etiology usually come much later […] Today, Alzheimer's disease, […] with dementia as its clinical manifestation, specific brain morphology, tentative pathophysiology and at least partially understood

Así, la búsqueda de asociaciones estables entre al menos algunas condiciones psiquiátricas y factores biológicos específicos no cesa. Más específicamente, esa búsqueda consiste en realizar estudios en los que

> "La prevalencia de un factor dado se compara entre los participantes que reúnen los criterios para una condición [psiquiátrica] y aquellos que no. Si se encuentra que este factor es mucho más común en los participantes que cumplen los criterios para la condición, entonces esto puede indicar una relación causal" (Samei Huda, 2019, pp. 257-258).[85]

Entonces, cuando los investigadores encuentran el mismo factor biológico en muchos pacientes con la misma condición psiquiátrica pero no en individuos sin la condición—esto es, cuando encuentran alguna *regularidad* biológica asociada con la condición—, ese factor se entiende como una posible causa de la condición psiquiátrica. Por ello, la mejor caracterización del proyecto de la psiquiatría biológica que consiste en buscar asociaciones entre factores biológicos y condiciones psiquiátricas es que dicho proyecto consiste en la búsqueda de las *causas* biológicas de esas condiciones.

Ahora, en la medicina en general hay una tendencia a entender las causas biológicas de las enfermades como sus causas más importantes. Tomemos como ejemplo la concepción contemporánea de la diabetes tipo 2. En situaciones normales, el páncreas produce insulina—una hormona que permite la entrada de la glucosa sanguínea en las células. En la diabetes tipo 2, la insulina producida por este órgano es de baja calidad, o no es producida en absoluto. Además, en los casos de esta enfermedad, las células presentan resistencia a la insulina, lo cual dificulta aún más la entrada de la glucosa sanguínea a las células, por lo que esta última

causes, is one of the few conditions in psychiatric classifications that are already defined by their pathology rather than their syndrome […] Schizophrenia, however, is still better described as a syndrome".

[85] Mi traducción. El pasaje original es así: "The prevalence of a given factor is compared between participants who meet the criteria for a [psychiatric] condition and those who do not. If this factor is found to be much commoner in participants who meet criteria for a condition then this may indicate a causative relationship".

sustancia se mantiene disponible en grandes cantidades de forma constante en el torrente sanguíneo.

Por otro lado, es ampliamente aceptado que factores tales como tener estrés y una vida sedentaria, y consumir grandes cantidades de carbohidratos—esto es, factores relacionados con el estilo de vida, el ambiente y la salud mental—contribuyen causalmente a la diabetes tipo 2. Sin embargo, la concepción médica estándar es que la insulina de baja calidad y la resistencia a la insulina son las causas más importantes de los constantes niveles elevados de glucosa en sangre. Las causas biológicas de las enfermedades, así, son las más importantes desde la perspectiva biomédica.

En la medida en que, como se indicó previamente, la psiquiatría biológica aspira a estar en línea con el modelo biomédico del resto de la medicina, se infiere que las regularidades biológicas que posiblemente se asocien con las condiciones psiquiátricas se entenderán como las causas más importantes de ellas, es decir, que se tomarán como sus causas *principales*. De hecho, Robert Kendell (1991) afirma que "[l]os psiquiatras y los genetistas están firmemente convencidos de que han demostrado que los factores genéticos juegan un papel *principal* en la etiología de la esquizofrenia" (p. 70-71)[86], donde por "etiología" se refiere a las causas biológicas de esa condición.

En suma, pues, el proyecto global de la psiquiatría biológica está fundado en la presuposición de que:

> COMPROMISO CAUSAL: Las causas principales de las condiciones psiquiátricas son regularidades biológicas específicas—mayormente desconocidas en el presente—que subyacen a los síntomas.

Es importante notar que, a la luz del árido panorama en el que se encuentra la investigación psiquiátrico-biológica presente, el compromiso causal descrito es una *presunción* que orienta la investigación, y no una hipótesis confirmada con evidencia robusta. Esto permite que el

[86] Mi traducción. El pasaje original es así: "Psychiatrists and geneticists are firmly convinced that they have demonstrated that genetic factors play a major role in the etiology of schizophrenia". Yo añadí las cursivas en el pasaje traducido.

compromiso causal sea objeto de disputa teórica. En efecto, en las siguientes secciones argüiré en contra de él.

3. En contra del compromiso causal

Afirmo que el compromiso causal de la psiquiatría biológica es una presunción implausible sobre las condiciones psiquiátricas. Esto es porque, como mostraré en §3.2, la mejor evidencia biológica disponible en el presente no respalda tal compromiso y, además, como lo abordaré en §3.3, es altamente dudoso que la evidencia futura lo hará.

3.1 *Consideraciones preliminares*

Un asunto preliminar es el de qué se puede querer afirmar con que una causa es la *principal* de una condición. Al esclarecer esta cuestión debe capturarse la idea de que las causas biológicas son, en algún sentido, más importantes que otro tipo de causas con respecto a las condiciones psiquiátricas. Esto es porque tal idea está presupuesta por la psiquiatría biológica al aspirar a concordar con el modelo biomédico del resto de la medicina, tal como lo abordé anteriormente. Encuentro que cualquiera de las siguientes dos alternativas captura dicha idea:

(a) Que ciertas regularidades biológicas son necesarias y suficientes, o necesarias, o suficientes, para las condiciones psiquiátricas; o,
(b) Que ciertas regularidades biológicas incrementan la probabilidad de padecer las condiciones psiquiátricas más de lo que lo hacen otro tipo de factores—tales como los psicológicos o los sociales—por sí solos.

La tarea de evaluar si la evidencia psiquiátrico-biológica apoya al compromiso causal, entonces, consistirá en determinar si los factores biológicos que—según los investigadores—están asociados con las condiciones psiquiátricas son causas *principales* de ellas en cualquiera de los sentidos (a) o (b).

Debido al espacio limitado, no puedo realizar un estudio exhaustivo de la evidencia biológica sobre las condiciones psiquiátricas, por lo que me enfocaré solo en la que se relaciona con la esquizofrenia. Después de todo, como lo diría Jaak Panksepp (2004),

"[t]ípicamente, la esquizofrenia ha sido el "estándar de oro" con base en el que nuestro entendimiento de los desórdenes psiquiátricos será juzgado" (p. 20).[87]

Abordaré, así, la evidencia que respalda la idea de que hay vínculos causales entre ciertos factores de tipo cerebral y genético, y la esquizofrenia. Comenzaré primero con los factores cerebrales y procederé después con los genéticos.

3.2. *La dopamina*

Hay dos eminentes hipótesis que vinculan a ciertos factores cerebrales con la esquizofrenia, a saber, la hipótesis de la dopamina y la hipótesis del glutamato. Solo me concentraré en abordar la primera, pues el estado de la investigación con respecto al glutamato está significativamente menos avanzado que el de la dopamina.[88]

De acuerdo con la hipótesis de la dopamina,

> "Los síntomas positivos y los desorganizados (e.g., psicosis, pensamiento desorganizado) están causados por actividad excesiva de la dopamina en la vía mesolímbica […] En contraste, los síntomas negativos (e.g., abolición, retraimiento) están causados por actividad deficiente de la dopamina en la vía mesocortical" (Tsou, 2021, p. 12).[89]

Es decir, queda postulado que cierta producción anormal de la dopamina causa la esquizofrenia. Para que aquella sea una causa principal de esta, tal anormalidad debería

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[87] Mi traducción. El original es: "[t]ypically, schizophrenia has been the "gold standard" by which our understanding of psychiatric disorders will be judged".

[88] De hecho: "la medida en que [las anormalidades del glutamato] representan mecanismos causales en lugar de compensaciones o consecuencias de déficits cerebrales más fundamentales no está claro. Además, estas anormalidades glutamatérgicas no se correlacionan con componentes importantes de la enfermedad, tales como síntomas positivos o negativos, o déficits cognitivos […] un modelo glutamatérgico tiene todavía un valor heurístico para guiar la investigación futura sobre la esquizofrenia" (Kruse & Bustillo, 2022, p. 10). Esta es mi traducción. El pasaje original es como sigue: "the extent to which [glutamate abnormalities] represent causal mechanisms as opposed to compensations or consequences of more fundamental brain deficits is not clear. Furthermore, these glutamatergic abnormalities do not correlate with important components of the illness, like positive or negative symptoms or cognitive deficits. […] a glutamatergic model still has heuristic value to guide future research in schizophrenia".

[89] Mi traducción. El original es: "positive and disorganized symptoms (e.g., psychosis, disorganized thought) are caused by excessive dopamine activity in the mesolimbic pathway […] By contrast, negative symptoms (e.g., avolition, flat affect) are caused by deficient dopamine activity in the mesocortical pathway".

cumplir con alguno de los siguientes supuestos, en concordancia con (a) y (b) tal como los describí en §3.1:

> CONFIRMACIÓN DE (a)(DOPAMINA): que la anormalidad en la producción de la dopamina relacionada con la esquizofrenia sea necesaria y suficiente, o necesaria, o suficiente, para dicha condición; o,
>
> CONFIRMACIÓN DE (b)(DOPAMINA): que la anormalidad en la producción de la dopamina relacionada con la esquizofrenia incremente la probabilidad de desarrollar la condición más de lo que otros tipos de factores relevantes—e.g., de tipo social-ambiental—, por ellos mismos, lo hacen.

Comencemos a evaluar si anormalidades de la dopamina son necesarias o suficientes para la esquizofrenia. Lamentablemente, no es difícil notar cómo ese *no* es el caso, pues para que tal anormalidad fuera necesaria o suficiente para la condición, esta última debería estar definida en términos de aquella—tal como, por ejemplo, la enfermedad de Alzheimer está definida como la demencia asociada con placas amiloides y ovillos neurofibrales.

Hasta ahora, sin embargo, la evidencia no ha sido suficiente para que los investigadores definan a la esquizofrenia en términos de las anormalidades de la dopamina, pues, a pesar de las consistentes asociaciones entre ellas y la condición, no ha quedado plenamente establecido que esas anormalidades de hecho están involucradas en los procesos causales de la esquizofrenia (ver, e.g., Howes, McCutcheon, & Stone, 2015, p. 6).

A la luz de esta situación, supongamos que un paciente desarrollara síntomas característicos de la esquizofrenia en concordancia con los criterios diagnósticos del DSM, de manera que fuera correctamente diagnosticado con ella. Debido a que en el presente esa condición no está definida en términos de anormalidades de la dopamina, es concebible que los síntomas del paciente en cuestión fueran causados por otro factor biológico[90] y, así, su

[90] Efectivamente, se piensa que algunos síntomas que ocurren característicamente en la esquizofrenia—tales como las alucinaciones, los delirios y el retraimiento emocional—están causados por factores cerebrales diferentes a la dopamina y al glutamato en otra condición psiquiátrica, a saber, la psicosis inducida por substancias. Por ejemplo, el entendimiento contemporáneo es que las alucinaciones que ocurren en casos de esta condición podrían estar causadas por la activación de los receptores 5HT2AR de la serotonina, en lugar de con receptores de dopamina o de glutamato (ver, e.g., Rolland *et al*, [2014]).

caso sería uno de esquizofrenia que no estaría asociado con la anormalidad de la dopamina, lo que muestra que esta última no es necesaria para la condición.

Por otro lado, supongamos que otro paciente tuviera anormalidades de la dopamina pero que no desarrollara síntomas francos que permitieran diagnosticarlo con esquizofrenia. Debido a que esta no está definida en relación con tal anormalidad, no basta tener la última para tener la condición, por lo que la anormalidad de la dopamina no es, tampoco, suficiente para la esquizofrenia.

De esta manera, la anormalidad en la producción de la dopamina no cumple con CONFIRMACIÓN DE (a)(DOPAMINA) y, en consecuencia, esa anormalidad no es una causa principal de la esquizofrenia en el sentido de (a).

Queda por evaluar si la producción anormal de la dopamina puede establecerse como la causa principal de la esquizofrenia en el sentido de (b). Una forma pertinente de determinar esto es comparar las siguientes dos probabilidades:

> [P1] la probabilidad de desarrollar la esquizofrenia dado que los pacientes *sí* tienen anormalidades de la dopamina pero que *no* tienen ninguna causa asociada con la esquizofrenia que sea de otro tipo—por ejemplo, ciertos aspectos sociales-ambientales; y,
>
> [P2] la probabilidad de desarrollar la esquizofrenia dado que los pacientes *no* tienen anormalidades de la dopamina pero que *sí* tienen una o varias de las causas de otros tipos asociadas con la esquizofrenia—por ejemplo, ciertos aspectos sociales-ambientales

Si resulta que [P1] es más alta que [P2], entonces la anormalidad de la dopamina se podría establecer como causa principal de la esquizofrenia, pues esto significaría que tal anormalidad incrementa la probabilidad de desarrollar la condición más de lo que factores de otros tipos, por sí mismos, lo hacen. Veamos si tal es el caso.

Consideremos [P1]. Para calcular esta probabilidad se requiere la existencia de casos en los que hay producción anormal de la dopamina sin exposición a factores de tipo social-ambiental relevantes para la esquizofrenia, es decir, pobreza (e.g., Burns, Tomita & Kapadia, 2014), inmigración (e.g., Malzberg & Lee, 1956, and Cochrane, 1977) y raza (e.g., National

Institute of Mental Health, 1994), entre otros. Como argüiré ahora, la mejor especulación sobre el valor de [P1] es que este es 0, pues la producción de la dopamina depende materialmente de aspectos sociales-ambientales, tal como mostraré. Por esto, no debería esperarse que casos de producción excesiva de dopamina *sin* exposición a aspectos sociales-ambientales relevantes en absoluto ocurran en la realidad. En lo que sigue mostraré eso y después abordaré [P2].

Tómese en cuenta que "[l]a investigación que usa pares de gemelos ha encontrado evidencia de que los factores ambientales explican una porción sustancial de la variación normal en la función presináptica de la dopamina" (Howes, McCutcheon, & Stone, 2015, p. 6).[91] Esto es, la producción normal de dopamina está vinculada con aspectos sociales-ambientales. De hecho, ellos

> "dan cuenta de un 56% de la variación en la función estriatal presináptica de la dopamina [lo cual] es consistente con hallazgos previos de que la función dopaminérgica estriatal es adaptativa a las influencias ambientales. Por ejemplo en los primates, la función dopaminérgica estriatal puede ser alterada por un cambio en la jerarquía social, y en los humanos la función dopaminérgica estriatal está asociada con el estatus social y con el apoyo social tal como es percibido" (Stokes *et al*, 2013, p. 488).[92]

En otras palabras, la producción normal de dopamina en el cerebro está mayormente influenciada por aspectos ambientales en lugar de por herencia genética. Esto sugiere que la producción *anormal* de la dopamina debe de estar conectada con influencias ambientales también.

[91] Mi traducción. El original es: "[r]esearch using healthy twin pairs has found evidence that environmental factors explain a substantial proportion of variation in normal presynaptic dopamine function".
[92] Mi traducción. El original es: "account for 56% of the variance of presynaptic striatal dopamine function [which] is consistent with previous findings that striatal dopaminergic function is adaptive to environmental influences. For example in primates, striatal dopaminergic function can be altered by change in social hierarchy, and in humans striatal dopaminergic function is associated with social status and perceived social support".

De hecho,

> "pocas variantes genéticas de riesgo implican directamente al sistema de la dopamina, lo que indica que es probable que la señalización aberrante de la dopamina se deba predominantemente a otros factores" (McCutcheon, Krystal, & Howes, 2020, p. 15).

Esto es, actualmente se piensa que las anormalidades de la dopamina asociadas con la esquizofrenia se deben "predominantemente" a factores diferentes que la herencia genética, esto es, a factores sociales-ambientales. En efecto, se encontró en un estudio que "las alteraciones patológicas en el cuerpo estriado límbico tanto en la esquizofrenia como en las adicciones más probablemente reflejan factores de riesgo ambientales específicos del individuo que factores genéticos de riesgo para esas condiciones" (Stokes *et al*, 2013, p. 489).

Lo que es importante para nuestra discusión es que esto sugiere de forma consistente que factores de tipo social-ambiental determinan, de alguna manera, cuánta dopamina se produce o no en el cerebro. Y cuando este produce un exceso de aquella, aparecerá la esquizofrenia. No es difícil ver, así, que la evidencia actual apoya la idea de que la producción de la dopamina *depende materialmente* de ciertos factores sociales-ambientales en una forma significativa.

Para dilucidar cómo afecta esa consideración a nuestra discusión, tómese el caso de la diabetes tipo 2. Podemos decir que la alta y constante disponibilidad de glucosa sanguínea en esa enfermedad en efecto depende materialmente de la producción de insulina de mala calidad y de que las células sean resistentes a la insulina. Es exactamente porque estas últimas dos cosas ocurren que la glucosa se acumula en el torrente sanguíneo. Esto significa que es materialmente inviable que un paciente con diabetes tenga niveles elevados constantes de glucosa sanguínea pero que *no* tenga insulina deficiente y resistencia a la insulina. Si el paciente no tuviera estos últimos, la glucosa sanguínea simplemente podría ser absorbida de forma normal por las células. Por eso, deberíamos esperar que la probabilidad de que ocurra en la realidad un caso de glucosa elevada sin insulina deficiente y sin resistencia a la insulina sea de 0—es decir, que no ocurra en la realidad.

Análogamente, así, debido a que la producción de dopamina depende materialmente de la interacción del paciente con factores sociales-ambientales—tal como lo apoya la

evidencia actual—, casos de dopamina excesiva asociados con la esquizofrenia *sin* exposición a factores sociales-ambientales relevantes en absoluto son materialmente inviables en la realidad, por lo que deberíamos esperar que la probabilidad de que casos como esos ocurran sea de 0.

Considérese ahora [P2]. Para calcular esta probabilidad se debe presuponer la existencia de casos en los que los pacientes son expuestos a aspectos sociales-ambientales relevantes pero que no desarrollan anormalidades de la dopamina. Supongamos que los síntomas de la esquizofrenia fueran únicamente causados por dichas anormalidades. Este sería un escenario favorable para la psiquiatría biológica, pues esta justamente intenta encontrar factores específicos que se asocien con las condiciones psiquiátricas de forma unívoca—así como las placas amiloides y los ovillos neurofibrales se asocian de forma unívoca con la enfermedad de Alzheimer.

Entonces, si la dopamina fuera una causa unívoca de la esquizofrenia, los pacientes sin anormalidades de la dopamina *no* podrían tener esquizofrenia en la realidad, porque ningún otro factor causaría, en este escenario, tal condición. Y, consecuentemente, la probabilidad de desarrollar esquizofrenia dado que los pacientes hubieran sido expuestos a factores sociales-ambientales relevantes pero que no desarrollaran niveles anormales de dopamina sería de 0, pues tales casos serían inviables en la realidad.

Así, como argüí antes, el valor a esperar para la probabilidad [P1] es de 0 y, bajo los supuestos recién establecidos, debemos considerar que el valor de la probabilidad [P2] también es de 0. [P1], en consecuencia, no es mayor que [P2]. Por lo tanto, la anormalidad de la dopamina no cumple con CONFIRMACIÓN DE (b)(DOPAMINA), y no es una causa principal de la esquizofrenia en el sentido de (b).

3.3 *Regularidades genéticas*

Actualmente está bien establecido que

> "Un gran cuerpo de datos recolectados de familias, gemelos y personas adoptadas a lo largo de muchos años ha respaldado consistentemente la contribución de un componente

> genético primordial y complejo en la propensión a la esquizofrenia y a los desórdenes del espectro de la esquizofrenia" (Riley & Kendler, 2005, p. 95).[93]

Es importante notar que la esquizofrenia no está asociada con una sola variación genética, sino que

> "PGC-II, el estudio más grande de asociación de genoma completo que ha investigado factores genéticos de riesgo para la esquizofrenia identificó previamente 128 variantes genéticas independientes asociadas con el riesgo de esquizofrenia" (Ohi *et al*, 2017, p. 1).[94]

Para que dichas variantes pudieran ser consideradas como las causas principales de las condiciones psiquiátricas, debería cumplirse alguno de los siguientes supuestos:

> CONFIRMACIÓN DE (a)(GENES): que las variantes genéticas relacionadas con la esquizofrenia sean necesarias y suficientes, o necesarias, o suficientes, para dicha condición; o,
>
> CONFIRMACIÓN DE (b)(GENES): que las variantes genéticas relacionadas con la esquizofrenia incrementen la probabilidad de desarrollar la condición más de lo que otros tipos de factores relevantes—e.g., de tipo social-ambiental—, por ellos mismos, lo hacen.

Comencemos a evaluar si las variantes genéticas de riesgo para la esquizofrenia son necesarias o suficientes para tal condición. Desafortunadamente, el mismo problema que impide que las anormalidades de la dopamina sean necesarias y suficientes para la esquizofrenia afecta a las variaciones genéticas. Esto es, dicha condición no está definida en

[93] Mi traducción. El original es: "A large body of data collected from families, twins, and adoptees over many years has consistently supported the involvement of a major, complex genetic component in liability to schizophrenia and schizophrenia spectrum disorders".
[94] Mi traducción. El original es: "PGC-II, the largest genome-wide association study investigating genetic risk factors for schizophrenia, previously identified 128 independent schizophrenia-associated genetic variants".

términos de ningún factor biológico, incluidas las alteraciones genéticas. Por eso, estas últimas no son necesarias ni suficientes para la condición.

De hecho, no todos los pacientes con esquizofrenia considerados en los estudios tienen las regularidades genéticas asociadas con ella, por lo que ninguna de las regularidades genéticas identificadas hasta ahora es necesaria para que los pacientes desarrollen esquizofrenia. Por otro lado, tener la regularidad genética no garantiza que se desarrolle la condición. Por ejemplo, los gemelos que son hijos de pacientes con esquizofrenia tienen la carga genética relevante, pero está bien establecido que no todos los gemelos hijos de mismos padres desarrollan la condición. O, como lo indica el National Health Service (2023) del Reino Unido: "tener esos genes no necesariamente significa que se desarrollará esquizofrenia".[95] En consecuencia, las regularidades genéticas asociadas con la esquizofrenia no son, tampoco, suficientes para que los pacientes la desarrollen.

Por lo tanto, no se cumple con CONFIRMACIÓN DE (a)(GENES), y las variaciones genéticas asociadas con la esquizofrenia no son causas principales de ella en el sentido de (a).

Pero aún puede evaluarse si CONFIRMACIÓN DE (b)(GENES) es el caso. Recordemos que para ser una causa principal de las condiciones psiquiátricas en el sentido de (b), los factores biológicos deberían incrementar la probabilidad de desarrollar la condición asociada más de lo que otro tipo de factores lo hacen.

Los hallazgos genéticos vinculados con la esquizofrenia, de hecho, permiten asegurar que es más probable que quienes tienen la regularidad genética desarrollen esquizofrenia en comparación con la población en general. Sin embargo, no hay nada en la evidencia que sugiera que quienes tienen las regularidades genéticas son más propensos, solo por eso, a desarrollar esquizofrenia *en comparación* con aquellos que tienen regularidades relevantes de tipo ambiental-social pero no genéticas. En este sentido, simplemente, no hay evidencia directa que apoye CONFIRMACIÓN DE (b)(GENES).

Sin embargo, no me concentraré a continuación en evaluar si las variantes genéticas incrementan la probabilidad de desarrollar esquizofrenia más de lo que otros factores, por sí

[95] Mi traducción. El original es: "It's more likely that different combinations of genes make people more vulnerable to the condition. However, having these genes does not necessarily mean you'll develop schizophrenia".

mismos, lo hacen. La razón es que hay un motivo más fundamental para rechazar que la evidencia genética confirma el compromiso causal. Esto es porque incluso el cumplimiento de CONFIRMACIÓN DE (b)(GENES) no sería un respaldo empírico para aquél. Veamos por qué.

Recordemos que hay al menos 128 variantes genéticas independientes asociadas con el riesgo de desarrollar esquizofrenia. Además, un asunto importante aquí es que

> "Datos […] recientes respaldan fuertemente que hay una coincidencia genética entre la esquizofrenia y el desorden bipolar, sobre los cuales se ha mostrado que comparten variantes poligénicas en común con muy pequeños efectos" (Gejman, Sanders & Duan, 2010, p. 12).[96]

Esto quiere decir que las variaciones genéticas vinculadas con la esquizofrenia no están asociadas *específicamente* con ella.

Así, la mejor evidencia genética en el presente respalda fuertemente una concepción de la esquizofrenia según la cual esa condición es causada, en conjunto, por una multiplicidad de variantes genéticas que pueden también causar el trastorno bipolar. Esta concepción es incompatible con la caracterización causal de la psiquiatría biológica sugerida por su compromiso causal, i.e., que una causa unívoca causa específicamente una condición psiquiátrica. Como vemos, nada cercano a solo *una* variante genética causa la esquizofrenia, y las variantes genéticas asociadas con ella no son tampoco específicas para tal condición, pues pueden también causar trastorno bipolar.

Así, aunque las 128 variantes genéticas asociadas con la esquizofrenia en conjunto incrementaran la probabilidad de que los pacientes desarrollaren esquizofrenia más que otros factores por sí solos—para lo cual, no obstante, no hay evidencia actualmente—y, así, se cumpliera con CONFIRMACIÓN DE (b)(GENES), el compromiso causal de la psiquiatría biológica no estaría respaldado si se tomaran a las 128 variantes genéticas como causas de la esquizofrenia. Esto es porque las condiciones psiquiátricas estarían asociadas con una diversidad biológica mucho mayor a la esperada por la psiquiatría biológica.

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[96] Mi traducción. El original es: "Recent […] data strongly support a genetic overlap between schizophrenia and bipolar disorder, which were shown to share polygenic common variants with very small effect sizes".

En suma, como he dado cuenta, la mejor evidencia no apoya que los factores asociados con la esquizofrenia a nivel cerebral ni a nivel genético son las causas *principales* de la esquizofrenia en el sentido de (a) ni en el de (b). Dado que la mejor evidencia disponible con respecto a la condición psiquiátrica mejor investigada no apoya al compromiso causal de la psiquiatría biológica, resulta implausible que la evidencia concerniente a otras condiciones psiquiátricas, con menos realce dentro de la investigación, lo haga. Por lo tanto, la evidencia actual no confirma que el compromiso causal de la psiquiatría biológica es verdadero.

Una objeción es que la evidencia en el futuro podría confirmar tal compromiso. A continuación, me dedicaré a replicar esa idea.

3.4 *Posible evidencia biológica*

Mi objetivo es contrarrestar el entusiasmo por la idea de que posiblemente la evidencia en el futuro confirmará el compromiso causal de la psiquiatría biológica. Aunque es cierto que esta idea no se puede rechazar *a priori* por completo porque, simplemente, es de hecho posible que ocurra lo que ella establece, hay razones de peso para dudar de que ese será el caso.

Para comenzar, retomemos la evidencia genética relacionada con la esquizofrenia. Es importante notar que, tal como se entiende en el presente, "el paradigma actual establece que tanto los factores genéticos como los ambientales son importantes en la génesis de la esquizofrenia"[97] (Petronis *et al*, 1999, p. 646). Esto significa que, en aquellos casos en los que los pacientes tienen las variantes genéticas relevantes se requieren, además, aspectos ambientales que desencadenen la activación de los genes asociados con la esquizofrenia.

Así, por un lado, el conocimiento genético actual apunta a que ciertas regularidades genéticas se podrían establecer como causa de la esquizofrenia y, por otro, tal conocimiento también apunta a que las regularidades genéticas requieren de factores de tipo social-ambiental para tener el efecto de causar, conjuntamente, la esquizofrenia. En consecuencia, la evidencia disponible señala que, en aquellos casos de esquizofrenia en los que se identifica la presencia de las variantes genéticas relevantes, los factores biológicos son al menos igualmente importantes que los sociales-ambientales. Esto es porque, en esos casos, los factores genéticos no son suficientes, por sí mismos, para causarla, mientras que la evidencia

[97] Mi traducción. El original es: "the current paradigm states that both genetic and environmental factors are important in the genesis of schizophrenia".

apunta a que esos factores *en conjunto* con los ambientales sí son suficientes para la esquizofrenia.

Que el conocimiento biológico mejor establecido tenga esas implicaciones puede entenderse en el sentido de que futuros hallazgos biológicos apoyarán, como lo hace la evidencia presente, la idea de que factores ambientales juegan un papel al menos igualmente importante que los genéticos con respecto a la esquizofrenia. Esto, desde luego, estaría directamente en contra del compromiso causal de la psiquiatría biológica, según el cual las causas biológicas tienen un papel *más* significativo que los factores no biológicos.

Por otro lado, como veremos a continuación, el conocimiento psiquiátrico actual, tanto biológico como no biológico, no nos da ninguna buena razón para creer que las causas de la esquizofrenia serán de tipo biológico sin una dependencia significativa de los factores sociales-ambientales.

De hecho, la evidencia *no* biológica actual apoya cada vez más la idea de que factores de tipo social-ambiental juegan un papel al menos igual de relevante que los biológicos con respecto a la esquizofrenia y a otras condiciones psiquiátricas. Como lo indica 'The British Psychological Society' (2018):

> "Hay un gran cúmulo de evidencia […] de que las circunstancias de vida de las personas juegan un papel principal en el desarrollo y mantenimiento de los problemas psicológicos, emocionales y comportamentales […] Entre los factores más importantes se encuentran: clase social y pobreza; desigualdad de ingresos, desempleo; descuido en la infancia y abuso sexual, físico y emocional; violencia doméstica y sexual; pertenecer a grupos sociales subordinados; la guerra y otros eventos que amenazan la vida; el 'bullying', el acoso y la discriminación, y pérdidas significativas tales como la pérdida de un padre en la infancia" (p. 92).[98]

[98] Mi traducción. El original es: "There is a great deal of evidence […] that the circumstances of people's lives play a major role in the development and maintenance of psychological, emotional and behavioural problems […] Among the most important factors are: social class and poverty; income inequalities, unemployment; childhood neglect and sexual, physical and emotional abuse; sexual and domestic violence; belonging to subordinate social groups; war and other life- threatening events; bullying, harassment and discrimination and significant losses such as loss of a parent in childhood".

Además, nada en la evidencia actual indica que la evidencia futura rebatirá la evidencia no biológica presente. Por lo tanto, si nos adherimos al estado actual del conocimiento psiquiátrico tanto biológico como no biológico, se puede notar que *no* hay razones de peso para esperar que la investigación futura arrojará causas biológicas principales para la esquizofrenia, tales que no requieran significativamente de factores sociales-ambientales para tener su efecto. Esto va en contra del compromiso causal de la psiquiatría biológica al menos con respecto a esta condición, la cual es una de las más investigadas actualmente.

Ahora, con respecto a la hipótesis de la dopamina, es importante notar que, como argüí previamente, la producción de esa sustancia parece depender materialmente de la interacción del individuo con su ambiente. Esto sugiere que consideraciones análogas a las de los factores genéticos de riesgo aplican a la producción anormal de la dopamina. Es decir, que, dada evidencia fuerte sobre la dependencia material entre producción anormal de dopamina y factores sociales-ambientales, es improbable que la evidencia futura arrojará que la dopamina no depende de tales factores. Esto va en contra del compromiso causal de la psiquiatría biológica, por lo que la adherencia a la hipótesis de la dopamina supone, al mismo tiempo, que el compromiso causal de la psiquiatría biológica con respecto a la esquizofrenia en particular será improbablemente confirmado por la evidencia futura.

Aunque esto último aplica específicamente en el caso de la esquizofrenia, la naturaleza de otras condiciones psiquiátricas tales como la depresión, empuja fuertemente a creer que los factores de tipo social-ambiental juegan un papel al menos igualmente significativo que los de tipo biológico, y que la evidencia futura confirmará esto en lugar del compromiso causal de la psiquiatría biológica. Después de todo, como se ha argüido convincentemente por Will Davies (2016), las condiciones psiquiátricas tienen componentes constitutivos que provienen de la relación del individuo con su ambiente.

Una objeción es que mis consideraciones dependen fundamentalmente del estado actual de la investigación psiquiátrica, pero la historia de la ciencia muestra que presuposiciones fundamentales de las ciencias pueden cambiar de forma radical de un momento a otro, por lo que el estado actual del conocimiento psiquiátrico no proporciona una garantía de que la investigación futura no confirmará el compromiso causal.

Pero es importante notar que los grandes cambios de paradigmas en las ciencias suelen implicar que partes cruciales de las teorías viejas se conservan en las teorías nuevas.

Presumiblemente, esto se debe a que al menos ciertos componentes de las teorías viejas son verdaderos. Por ejemplo, la genética mendeliana sigue siendo útil para entender el funcionamiento de la genética, a pesar de que en el presente dispongamos de desarrollos en la teoría genético-evolutiva.

De esta manera, si asumimos que los mejores resultados de la investigación psiquiátrica actual conllevan *verdad*, lo más probable es que sus resultados se mantengan, no que se refuten.

4. La crítica al compromiso causal y su lugar en el debate contra la psiquiatría biológica

La psiquiatría biológica ha sido amplísimamente criticada, y muchas de las críticas que se han hecho tienen algún grado de conexión con mi argumento en contra de ella. Así, la originalidad de mi contribución al debate sobre la pertinencia de la psiquiatría biológica podría no ser claro. Por eso, a continuación, mostraré cómo las críticas en contra de la psiquiatría biológica no atacan a su compromiso causal—y la mayoría ni si quiera lo abordan. Mi argumento es, entonces, inédito dentro del debate.

Uno de los asuntos más problemáticos dentro de la psiquiatría y de la filosofía de la psiquiatría es el papel que ha jugado el marco conceptual basado en el DSM con respecto a la caracterización de las condiciones psiquiátricas. La crítica aquí es que, en resumen, tal marco conceptual tiene "confiabilidad cuestionable en el campo [de la psiquiatría], constructos y validez predictiva cuestionables, definiciones fenotípicas pobres, heterogeneidad, comorbilidad [y] un precario concepto de trastorno mental" (Poland, 2015, p. 25).[99]

Sin embargo, debe notarse que estas críticas se enfocan en las deficiencias derivadas de la utilización del marco conceptual del DSM en la investigación, y no en el compromiso causal de la psiquiatría biológica. De hecho, en muchos casos, las críticas de este tipo están motivadas por aspiraciones biologicistas. Esto es, algunas de ellas proponen nuevos marcos conceptuales que puedan facilitar la adquisición de conocimiento biológico en psiquiatría.

[99] Mi traducción. El original es: "questionable reliability in the field [of psychiatry], questionable construct and predictive validity, poor phenotypic definitions, heterogeneity, comorbidity, [and] an unsound concept of mental disorder".

Un ejemplo de esto es el famoso 'Research Domain Criteria Project' del 'National Institute of Mental Health' de Estados Unidos.

En cualquier caso, nótese que el marco conceptual del DSM podría ser inadecuado para los fines de la investigación y esto, sin embargo, no descartaría que las causas principales de las condiciones psiquiátricas fueran regularidades biológicas. Así, este primer grupo de críticas no se dirige al asunto abordado por mi argumento en contra de la psiquiatría biológica, y tampoco lo ataca.

Otras críticas exigen que la psiquiatría biológica enriquezca su caracterización de las condiciones psiquiátricas incluyendo en ella aspectos psicológicos y sociales que puedan ser relevantes. Esto es, se pide que la psiquiatría aplique una perspectiva biopsicosocial en su investigación. Esto último, como lo indica la crítica

> "Puede ser utilizado como un medio para distinguir a la psiquiatría de otras áreas de la medicina y como un medio para demostrar que la psiquiatría no está puramente en la empresa de la investigación biomédica reductiva" (Broome, 2020, p. v).[100]

Sin embargo, la psiquiatría en general podría tener una perspectiva biopsicosocial en el sentido de que buscara identificar factores de riesgo de tipo psicológico y social—además de los biológicos—para las condiciones psiquiátricas, y eso no impediría que las causas principales de las condiciones psiquiátricas fueran regularidades biológicas específicas. Entonces, tampoco este influyente grupo de críticas aborda ni ataca al compromiso causal de la psiquiatría biológica.

Un tercer grupo de críticas se caracteriza por poner en cuestión que las condiciones psiquiátricas deban ser consideradas patológicas. Un ejemplo clásico es la crítica de Thomas Szasz (1974). Más recientemente, 'The British Psychological Society' (2018) ha rechazado la 'patologización' de los patrones de pensamiento y de comportamiento clasificados por el DSM. Pero nada en esas críticas está en contra del compromiso causal de la psiquiatría biológica. De hecho, nada impide que las condiciones psiquiátricas no sean patológicas y aun

[100] Mi traducción. El original es: "This can be used as a means of distinguishing psychiatry from other areas of medicine and as a means of demonstrating that psychiatry isn't purely in the business of reductive biomedicine".

así estén causadas principalmente por regularidades biológicas específicas—aunque quizá no por disfunciones.

Por último, se ha planteado la pregunta sobre en qué tipo de categoría ontológica caen las condiciones psiquiátricas. En un extremo, estas podrían ser 'géneros naturales'—de manera que la clasificación de las condiciones psiquiátricas estaría determinada por la naturaleza. En otro extremo, se propone que las condiciones psiquiátricas son 'géneros sociales'—o sea, que la clasificación de aquellas solo está determinada por las convenciones de los psiquiatras, sin algo en la naturaleza que imponga tal clasificación (ver Kincaid & Sullivan, 2014, para una panorámica del debate). Aquí, debe notarse que la forma estándar de proceder en este debate es argüir que las condiciones psiquiátricas caen en una u otra categoría según lo que los autores consideran que es respaldado por la evidencia. Por eso, el compromiso causal de la psiquiatría biológica no es atacado en estas discusiones.

Como he expuesto, entonces, las abundantes críticas a la psiquiatría biológica realizadas hasta ahora no han atacado a su compromiso causal, ni lo han abordado directamente.

5. Conclusiones

Como he argüido, la evidencia no confirma que el compromiso causal de la psiquiatría biológica es verdadero, y es altamente dudoso que hallazgos futuros lo harán. En consecuencia, dicho compromiso causal es una presunción implausible sobre las condiciones psiquiátricas. Esto sugiere que la perspectiva más prometedora con respecto a esas condiciones es una según la cual los factores de tipo biológico tanto como los de tipo social-ambiental son causas *igualmente* significativas de las condiciones psiquiátricas, y no que los factores biológicos son sus causas principales.

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