AN INVESTIGATION INTO THE IMPACT CHILDHOOD ABUSE MAY HAVE IN THE PRESENTATION OF NEGATIVE SYMPTOMS IN PATIENTS WITH FIRST-EPISODE PSYCHOSIS

By

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Introduction to the thesis

The thesis comprises three chapters, representative of my time here on the MRes in Clinical Psychology course. Each chapter addresses a particular topic, with the intention of both expanding and adding to current knowledge within the clinical field. This is then followed by an individual reflection of my time on placement as well as the skills learnt and developed.

The first chapter examines the presence of coeliac disease in older age, in addition to the areas of their life which may be affected (e.g. neurological problems, adherence to diet restrictions). Coeliac disease is an autoimmune disorder of the small intestine triggered by the consumption of gluten. Previously, the medical profession viewed coeliac disease as a childhood and young adult illness and consequently, the presence of symptoms in older adults was often overlooked (Freeman, 2008; Vilpulla et al., 2009). Thus, many secondary symptoms develop causing an array of problems (Freeman, 1995; 2008; Thomson, 2009). The understanding that coeliac disease can present in older people is still relatively new and therefore, little research has explored this domain. A literature review was conducted to explore available studies on this specific area to comprise a better understanding of what is already known and consequently, what areas need more attention.

My second placement examined the neurobiological and psychological overlap between autism and first-episode psychosis. Both disorders share multiple similarities in the symptoms that are presented in patients; for example, deficits in social skills and blunted affect (Dickson et al., 2011). To investigate the overlap between the two, an interview was conducted with patients diagnosed with psychosis. The second chapter centres on how the participants were recruited and the different stages this entailed. The format of this chapter follows that of a presentation, illustrating the continuous cycle of the recruitment process.

This firstly involves meeting with the early intervention teams and building up good relationships. From this, participants can be contacted and interviews arranged. Once completed, feedback can be given back to the early intervention services to help improve patient support.

The final chapter sought to examine whether childhood abuse and neglect influenced the presence of negative psychotic symptoms. Prior to a psychotic episode, negative symptoms are known to occur, for example depression (Birchwood, Iqbal, Chadwick & Trower, 2000). However, it is unclear whether these symptoms impede less on an individual who has been exposed to an abusive childhood, or appear the same as those without childhood abuse (Kim et al., 2006; Ross et al., 1994). Subsequently, this area was chosen due to the contradictory findings in previous studies as well as to add to the childhood abuse-psychosis literature.

Reflection of the MRes in Clinical Psychology course

This course has enabled me to develop and expand valuable research skills and therefore, grow as a researcher. Both the taught modules and the practical placements have given me both the confidence and knowledge to guide me beyond university. Conducting a literature review during my first placement was a successful achievement and consequently, proved a useful skill when having to decide upon a concept to investigate for the final chapter. The final report is self-chosen and therefore, I felt empowered in my ability to first conduct a large, wide search of the current literature in the domain I wanted to research. More importantly, I felt competent in my ability to narrow my focus to centre on an achievable concept which could be explored. I felt the lessons and skills I learnt in the first placement helped hugely in achieving my aim for the final report.

Additionally, my second placement gave me the opportunity to work with vulnerable people, conduct clinical interviews and collect data that would later be used for my final study. By becoming involved with the early intervention services, I was able to see how a multi-disciplinary team worked. Alongside this, I learnt the importance of good rapport between both participants and clinical teams in order to enable successful recruitment.

Reflecting on my time here on the course, I am able to see how far I have developed in terms of a researcher. The practical placements have allowed me to witness and be a part of the core stages involved in the research cycle, including literature reviews to support study grants, recruitment processes, conducting research, conceptualising my own ideas and disseminating my findings through conferences, executive summaries and written reports. The taught aspect of the course provided me with the knowledge and the awareness needed to produce good quality work. Skills such as analysing literature papers and learning about the various types of qualitative analysis were both useful and necessary in the research world.

Throughout the course, I have made great use out of supervision and constructive feedback, using it to personally develop myself. Thus, the skills I have learnt on this course have helped improve my strengths and weaknesses, enabling me to complete this piece of work.

CHAPTER 1

COELIAC DISEASE IN OLDER AGE: A SYSTEMATIC REVIEW

Abstract

Introduction:

Recent medical advancements have revealed the influx of older aged patients receiving a diagnosis of coeliac disease (CD). Due to the diagnostic delay, secondary symptoms often occur coupled with common problems faced in later life (e.g. arthritis). There is limited research on the many factors which could be influenced by receiving a diagnosis of CD in older age, in addition to how it may present. Therefore, this systematic review examined all available literature on coeliac disease in older age.

Method and design:

A comprehensive literature search using six appropriate databases was undertaken. These were Embase, Health Management Information Consortium, Medline, Psychinfo, ScienceDirect, Web of Science. Key words relating to both CD and older age were used to identify suitable and relevant papers (e.g. gluten-free, geriatric). Older age was here defined as being over the age of 60 years old. This was then followed by a backwards and forward citation search. Selected studies which met the inclusion criteria were then subjected to a quality assessment which produced a total of 14 appropriate papers. The chosen instrument to measure the quality in this review was the established quality checklist produced by Kmet and colleagues in 2004. All papers were classified as possessing at least moderate levels of quality. The timeframe for this review was approximately two months.

Results and findings

On examining the selected papers, three themes were identified – Clinical presentation and gluten-free diet adherence (N=8); Associated conditions and complications (N=3); Neurological and cognitive decline (N=3). The first theme revealed similarities in the types of

symptoms reported between older and young people with CD. Despite this, the exact differences between the histological and clinical presentation between older and younger patients is still unknown. However, the assumption that older patients present more severely has been put forward. Papers revealed that older people generally adapted well to the new diet, adhering well.

The second theme highlighted how older people with CD were at an increased risk of suffering from autoimmune disorders and non-Hodgkin's disease. This could possibly have been due to the longer period of exposure time to gluten.

There were several conflicting findings found in the final theme centring on the effects CD may have on cognitive function and the potential development of dementia. Mixed findings revealed the uncertainty leading to inconclusive findings. Differences in methodology between current studies addressing this issue were a key reason for the disagreements found. Further research is needed to clarify and broaden knowledge on this relatively new area.

Introduction

Coeliac disease (CD), an autoimmune disorder of the small intestine, is activated by the consumption of gluten within genetically predisposed individuals. As a result, the small intestinal villi become inflamed and flattened leading to the malabsorption of many nutrients. The advancement in serological testing has led to an influx of individuals being diagnosed, presenting either asymptomatically, or with classical or atypical clinical manifestations (Mustalahti et al., 2002). Until recently, CD was often perceived as a young adult and childhood illness and, consequently, created diagnostic delay for those presenting with symptoms in older age (Freeman, 2008; Vilpulla et al., 2009). Currently, life-long adherence to a gluten-free diet (GFD) is the only known treatment for CD. By following this diet, the damaged villi are able to regenerate, alleviating symptoms and ameliorating long-term risks.

Removing gluten from one's diet can be extremely challenging due to the complexity of avoiding wheat, rye and barley based products (Kasarda, 1994), especially within Western foods; thus, gluten is ubiquitous. These primary grains found in cereals, breads, cakes, pasta and a majority of snack foods can be difficult to avoid. In addition, gluten is often used as a thickener, bulker or binder in everyday foods (e.g. sausages, soups/sauces, coatings on meats/fish, soy sauce) and medicines (Freeman, Lemoyne & Pare, 2002). Moreover, barley malt, often found in beer, corn and rice based foods, cannot be included (Zarkadas et al., 2006). Subsequently, adapting to a GFD may prove especially difficult to follow once lifetime dietary habits of consuming gluten-containing foods have been acquired (Vilpulla et al., 2011). Despite the improved accessibility of gluten-free food (GFF) and its availability on prescription for those with a confirmed diagnosis of CD (UK and other European countries),

adults often report problems with self-management, including lack of knowledge, poor labelling on products (Ukkola et al., 2012), difficulty identifying good quality GFF (Case, 2004; Zarkadas et al., 2006) and the increased cost of GFF (Lee, Zivin & Green, 2007; Stevens & Rashid, 2008). Nonetheless, older people have been shown to cope and adhere to a GFD as efficiently as the younger generation, gaining the same histological improvements (Casella et al., 2012a).

The initial presentation of CD and whether its severity among older individuals differs from younger generations is uncertain (Casella et al., 2012a; Gasbarrini, Ciccocioppo, De Vitis & Corazza, 2001; Mukherjee et al., 2010). Nevertheless, anaemia and deficiencies in iron, vitamin B12, folic acid and calcium are continuously reported in older people presenting with CD (Freeman, 2008; Hankey & Holmes, 1994; Vilpulla et al., 2011). In addition, those diagnosed later in life often suffer with dyspepsia (Casella et al., 2012a), thyroid disease (Freeman, 1995), neuropathy (Mukherjee et al., 2010), autoimmune disorders (including dermatitis herpertiformis) and gastrointestinal (GI) symptoms (Gasbarini et al., 2001). GI symptoms within older people with CD frequently include diarrhoea, abdominal pain and distension, often resulting in malabsorption, dehydration and malnutrition. This is of particular concern for the older individual as they may experience severe medical problems including unwanted weight loss, poor dentition and bone weakening (Thomson, 2009).

Several health problems have been associated with CD; for example, Freeman (1995) found lymphocytic gastritis (50%), lymphocyctic colitis (43%) and gall stones (20%) present among older people with CD. Additionally, the presence of non-Hodgkins Lymphoma (NHL) was found almost entirely limited to those aged 50 years and above (Casella et al., 2012a), complimenting previous studies in Italy (Catassi et al., 2002) and Europe populations

(Mearin et al., 2006). However, receiving a NHL diagnosis has decreased, indicating past findings were influenced by a cohort effect instead of a longer exposure time to gluten (Gao et al., 2009). This is supported by the widespread application of serological markers which has allowed for earlier detection, thus, earlier treatment.

CD has been found to effect bone structure, heightening the risk of bone fractures (Vasquez et al., 2000) and increasing the development of bone disease (Mukherjee et al., 2010). When compared to their younger counterparts, older people suffered from lower levels of albumin, calcium and vitamin D in addition to increased bone turnover, possibly accounting for the higher levels of osteoporosis and osteopenia found within this age group (Casella et al., 2012a). In addition, foot problems and the increased prevalence of falls are often reported within the older population. Tied with the presumption of weakened bones, accidental falls within older people with CD may place them at a heightened risk for serious injury (Rubenstein, 2006).

CD and its effect on neuropathy has long been explored, with the consensus being that it can lead to neural complications (Banerji & Hurwitz, 1971), particularly in terms of memory impairment (Collin et al., 1991). However, in the majority of cases, the effect of a GFD and/or vitamin supplementation has shown little improvements (Collin et al., 1991; Cooke & Holmes, 1984; Hadjivassiliou et al., 1996) and instead, only stabilisation of neurological disabilities (Hu, Murray, Greenaway, Parisi & Josephs, 2006). In regards to cognitive function, a link between age at onset of CD symptoms and deterioration of cognition has been identified (Casella et al., 2012b; Hu et al., 2006). This indirectly suggests that any effect CD has on cognition maybe more pronounced amongst older people due to the presumed longer exposure time to gluten (Casella et al., 2012b; Hallert & Astrom, 1983).

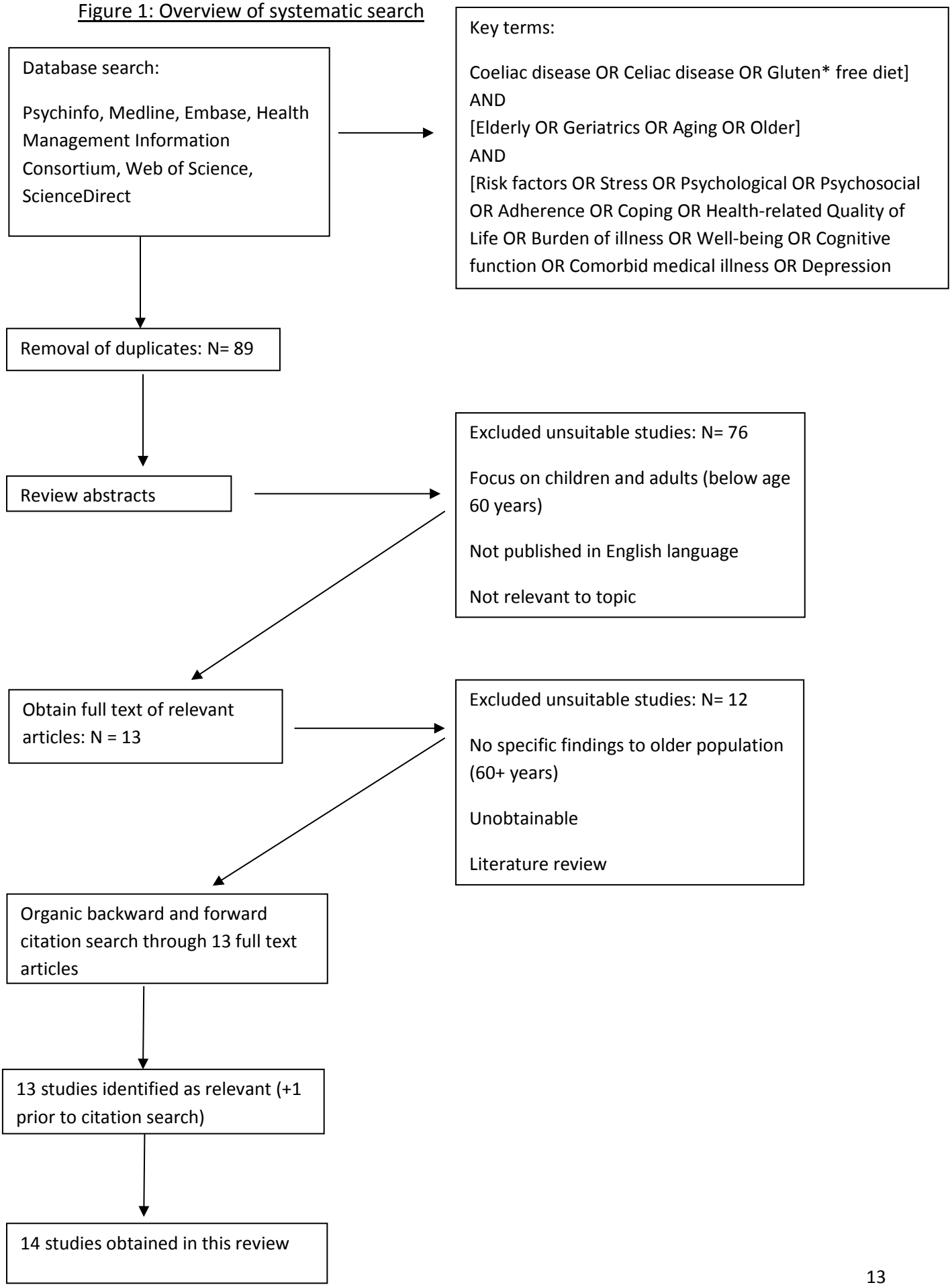
Overall, CD literature has predominantly focused on children and adults, neglecting the older generation. Due to the multitude of factors associated with old age and CD, it is important to understand and be aware of how living with CD in older age may present itself. Therefore, this systematic review aims to identify and examine all present research addressing CD in older age.

Method

Databases were searched using a variety of key terms to locate literature from 1946 to November 2013. The key terms were carefully selected to help find all existing literature on CD in older people. Thus, words revolving around the disorder, for example, gluten and the American version of spelling (celiac disease) were used. In addition, terms defining older age (over 60 years old) was used (e.g. geriatrics,elderly). Finally, key areas such as the social and psychological aspects which may be influenced by receiving a diagnosis were explored (e.g. stress; depression).

After removal of duplicate and unsuitable papers, one study remained. In addition to this, an organic backwards and forward citation search was conducted, generating a further 13 studies and thus, led to a total of 14 papers to review. The eligible papers were then put through an established quality assessment checklist for quantitative studies (Kmet, Lee & Cook, 2004). The process was completed by the researcher with any concerns being resolved with the help of the main supervisor. Scoring depended on how each study met each criterion (See Appendix 1 and 2): '2' – met the criterion entirely, '1' – partially met and '0' – not met at all. If a criterion was not relevant to the paper, it was excluded from the score. The calculation of the total sum involved adding the number of 'yes' responses, followed by the addition of the 'partials'. The summary score reflected the overall quality of the methodology for each paper, with the highest obtainable score being 22 (except Hankey & Holmes, 1994: 20). Studies were classified as high quality (score of 17 and higher), moderate quality (11-16) or low quality (10 or less) (Crist & Grunfield, 2012).

Figure 1: Overview of systematic search



Results

With the exception of two studies whose quality was moderate (Freeman, 1995; Hankey & Holmes, 1994), papers used here were classified as high quality. Papers were subsequently split into three categories:

1. Clinical presentation and GFD adherence (N =8)
2. Associated conditions and complications (N =3)
3. Neurological and cognitive decline (N =3)

Table 1: Summary of studies examining clinical presentation and adherence to a GFD

Authors, Date, Country	Study design	Sample	Age at diagnosis	Symptom duration before diagnosis	Primary aim	Presentation of CD	Adherence to gluten-free diet (GFD)
Casella et al., 2012(a) Italy	Retrospective cohort study: database from referrals to a CD clinic from 1990-2010.	Total Number= 1,225 Group A: N= 59 aged ≥65 years (M: 16; F: 43) Group B: N=1,166 aged 18-64 years (M:306; F:860) (Group B subdivided into 3 categories). Subgroup to measure effects of a GFD: Group A (older): n=43: spent 30 +/- 4months on GFD. Group B (younger): n=94: spent 29 +/- 1month on GFD.	Group A: 70.1 +/- 4.3 years Group B: 35.2 +/- 10.6		Compare CD in older and younger adults to assess effects of a GFD	Group A: lower prevalence of abdominal bloating; lower levels of calcium and vitamin D as well as higher prevalence of weight loss, dyspepsia, osteoporosis and IgA levels. Most prevalent CD-associated disease in both groups: thyroiditis; Biggest difference between groups: NHL diagnosis (Group A: 5.1%; Group B: 0.3%) T-scores significantly lower at baseline in Group A – suggests older age may confer limited additive risk to development of metabolic bone disease: take cautiously, lack of participants. Sample size in Group B significantly larger than Group A.	GFD did not significantly affect BMI in Group A. Group A can cope with GFD as efficiently as Group B and obtain same histological improvements Group A reported less symptomatic relief compared to Group B (69% vs. 95% respectively).
Freeman, 1995 Vancouver Columbia	Longitudinal study: 1982-1993. Review of patients' hospital and office records – details of presentation, medical history, adherence. Haematological and biochemical results also recorded.	30 CD sufferers aged 60+ years (M: 13; F: 17)			To review clinical findings of CD in over 60 year olds in a single institution and categorise the spectrum of associated clinical conditions.	Before initialising GFD: Weight loss (77%) and diarrhoea (73%) most common presenting factor. Anaemia (61%) and iron deficiency (47%) were also high. Associated clinical and pathological features: lymphocytic gastritis (50%), lymphocytic colitis (43%), small bowel ulceration (duodenum: 13%; Jejunal &/or ileal: 17%), DH (30%), hypothyroidism (27%) most common. 17% had lymphoma of small bowel malignancy	No reported findings.
Gasbarrini et al., 2001 Italy	Retrospective cohort study. Questionnaire Consecutively diagnosed during last 10 years in 10 Gastroenterology Units.	Total Number= 1,353 Group A: N= 60 aged ≥65 years CD patients (M: 16; F: 44). Group B: N= 1,293 aged <65 years (M: 378; F: 915).	Group A: Mean: 69.5 +/- 4.3 years. Group B: Mean: 36.8 +/- 5 years.	Group A: Mean: 17 +/- 19 years. Group B: Mean: 14 +/- 13.8 years.	Investigate the prevalence, the pattern of clinical presentation and the causes of death in elderly CD subjects.	Group A: greater frequency of presenting symptoms and lab abnormalities, except constipation. Group A: heart failure statistically higher (N=13) compared to average age, mean age of death 7 years earlier for males, 9 years for females. CD may be more pronounced, multisymptomatic due to longer duration in elderly and/or lesser ability for body to adapt Sample size in Group B significantly larger than Group A. to nutritional privation.	Group A: 11.6% refused GFD Group B: 16% refused GFD

GI: Gastrointestinal; BMI: Body Mass Index; DH: Dermatitis Herpetiformis

Table 1: (Continued)

Authors, Date, Country	Study design	Sample	Age at diagnosis	Symptom duration before diagnosis	Primary aim	Presentation of CD	Adherence to gluten-free diet (GFD)
Hankey & Holmes, 1994 England	Retrospective Cohort study: Hospital notes obtained including details of clinical presentation, family history, lab findings, compliance and response to GFD.	Total Number= 42 diagnosed after aged 60 between 1963 and 1991 (N=35 diagnosed in 1980+). 39 regularly reviewed in clinic (3 died). Sex: M:19; F:23		15/35 (excluding DH sufferers) attended medical services on several occasions: Mean: 28 years (6mnths-50years). 6 patients with GI symptoms: range: 9-50years.	To analyse an unselected series of CD patients aged 60 years and above, presenting to a District General Hospital.	Commonest symptom: GI symptoms, led to diagnosis in 25 patients. 19 complained of diarrhoea, abdominal pain and discomfort Remaining 6: bloating and flatulence. 10 reported no GI symptoms but presented with non-specific complaints of fatigues and lassitude, unexplained anaemia. DH led to diagnosis in 7patients.	GFD: 40/42 followed diet although 38 adhered strictly– these reported considerable improvement in well-being and resolution of symptoms. Weight, haematological and biochemical indices analysed at diagnosis and after 1 and 2 years on diet. All improved significantly to within normal range after 1 year of GFD – maintained after 2 years.
Lurie et al., 2008 Israel	Retrospective chart review in patients with CD over the age of 60 years. Eligible patients were reinterviewed	Total Number= 7 aged 60+ years (M: 3; F: 4). Ethnicity varied: 4 Ashkenazi origin, 3 Sephardic origin. Mean height and weight given. Gathered from gastroenterology clinic from 2003-2005.	Mean: 71.5 (61-86) years	Mean: 8 years +/- 2months to 9years. 3 participants reported lifelong symptoms.	Describe 7 case series of patients diagnosed with CD over the age of 60 years with varied presentations.	Most common presenting features were weight loss (n=4: Mean: 7.25kg; 5-12kg), iron deficiency anaemia (n=5), abdominal pain and diarrhoea (n=5). Elevated liver transaminases (n=2), severe early osteoporosis (n=2), folic acid deficiency (n=3). 1 patient reported 8 year history of severe peripheral neuropathy (MRI scan revealed white matter lesions in cerebral hemispheres- however, difficult to know whether attributed to CD or associated folic acid deficiency as white matter changes in elderly are common) and lifelong problems of migraines.	Initiation of GFD in patient with neuropathy: complete resolution of neuropathic symptoms and migraines (Follow-up not available). In 2 female patients, longstanding cognitive decline had significantly improved. GFD – significant weight gain (n=6).
Mukherjee et al., 2010 USA	Retrospective Cohort study: Clinical data reviewed from prospectively generated database at university-based referral centre	Total N= 274 <u>Group A:</u> N= 125 aged ≥65 years (Mean: M:54; F:71) <u>Group B:</u> N= 149 aged 18-30 years (M:31; F: 118) Only included biopsy confirmed. Highly selected sample in single centre – limited generalisability	<u>Group A:</u> Mean: 71.7 +/- 4.4 years. <u>Group B:</u> Mean: 25.4 +/- 3.6 years	<u>Group A:</u> Mean: 6.14 +/- 12.6 years <u>Group B:</u> Mean: 5.8 +/- 12.0 years [symptom duration similar]	Examine and compare CD in the elderly with young adults	Both groups presentation, clinically and histologically, were similar (including diarrhoea, anaemia, bone disease). No statistical significance in degree of villous atrophy. Group A: N=33 had 1+ autoimmune condition compared to Group B: N=28. Neuropathy (p=.023) and thyroid disease (p=.037) more common in Group A. DEXA scans revealed bone disease more common in Group A (61% vs 29% respectively). When compared to elderly non-coeliac patients – no significant difference in terms of z-scores (only for t-scores) – limitation: not same bone densitometry scanner used for everyone.	

DH: Dermatitis Herpetiformis; GI: Gastrointestinal

Table 1: (Continued)

Authors, Date, Country	Study design	Sample	Age at diagnosis	Symptom duration before diagnosis	Primary aim	Presentation of CD	Adherence to a gluten-free diet (GFD)
Stone et al., 2012 Australia	Cross-sectional study	Self-selected sample: N= 749 CD patients (M: 125; F: 622). Mean age: 49.71years (18-88 years).	Length of time with diagnosis: 93.78 months (1month-828months)		Three hypotheses to investigate the relative power of several variables to predict depression in people with CD.	Significant but very small, negative correlation between age and depressive symptomatology (shared variance less than 3%) 26.4% of patients scored above the depression cut-off (M-SDS: score of 37+). Negative relationship between comorbid medical illness and depression scores. Neither family history nor personal history of depression predicted depressive symptomatology.	98.1% following strict GFD at time of study.
Vilpulla et al., 2011 Finland	Longitudinal (2year) cohort study. Interviewed at baseline then 1 and 2 years after GFD. Screen-detected new CD patients from a cohort representing older Finnish population.	Original figure in 2002: 2815. After elimination, 35 participants were left. Sex: M:15; F:20 For GSRS and PGWB surveys, 110 age- and sex-matched control subjects collected from general population [CD not systematically excluded but reported no symptoms/family history].	Mean: 61 years (52-76) Does not state whether this was at diagnosis.		To establish whether CD should be rigorously searched for in people over 50 years of age and to evaluate subsequent dietary treatment.	10/35 had 1+ autoimmune disease. 10/35 had family history. Osteopenia found in 14 subjects; osteoporosis in 8. 8/35 had history of low-energy fracture (statistically significant vs general population: p<.01). Anaemia, iron, vitamin B12, folic acid and calcium deficient. Comments: Still insufficient evidence to advocate mass screening. Recommend active case finding in at-risk. No selection bias: taken from sample of another project with unrelated target of CD or abdominal disease.	GFD: 91% agreed to do it (3 died); 27 adhered strictly, 5 occasional transgressions. Diet had no obvious effect on BMI. QoL (PGWB) did not change during follow-up (but did not worsen) apart from improvements in well-being score. Comment: Rate of detection in Finland is relatively high, .9% already had diagnosis before screening process. Also, GFD is readily available here.

M-SDS: Modified Zung Self-Rating Depression Scale; GSRS: Gastrointestinal Symptom Rating Scale; PGWB: Psychological General Well-being Scale

Clinical presentation and adherence to a GFD

Clinical presentation:

Frequent symptoms often reported by older people with CD include a range of GI symptoms (e.g. diarrhoea, abdominal pain), alongside weight loss and weakness, bone disease, unexplained anaemia and deficiencies in calcium, vitamin B12 and folic acid (Casella et al., 2012a; Freeman, 1995; Hankey & Holmes, 1994; Lurie, Landau, Pfeffer & Oren, 2008; Mukherjee et al., 2010; Vilpulla et al., 2011). Whether the presentation of CD differs between ages, both clinically and histologically, is currently unknown. Two papers supported a similarity of presentation between patients over the age of 65 years and below the age of 65 years (Casella et al., 2012a; Mukherjee et al., 2010); however, Mukherjee et al. (2010) used a highly selected sample gathered from a single tertiary centre, thereby reducing generalisability. Surprisingly, Gasbarrini et al. (2001) reported higher severity in older people despite using a very similar sample to Casella et al. (2012a) who reported no difference. Nevertheless, the presumption that the older person with CD has been exposed to gluten for longer, coupled with a less adaptable body to nutritional deprivation, which possibly may result in multiple symptoms, is viable (Gasbarrini et al., 2001). In addition to this, older people are more likely to display autoimmune conditions (Mukherjee et al., 2010; Vilpulla et al., 2011), and for untreated coeliac individuals (typically much older) to be at an increased risk of heart failure (Gasbarrini et al., 2001).

Dietary Self-Management

Once gluten has been removed from the diet and the lining of the small intestine has healed, weight gain is possible (Hankey & Holmes, 1994; Lurie et al., 2008). However,

several studies have reported no significant effect for the GFD on a person's Body Mass Index (BMI) (Casella et al., 2012a; Vilpulla et al., 2011). Nevertheless, strict adherence and histological, haematological and biochemical improvements have been recorded (Casella et al., 2012a; Gasbarrini et al., 2001; Hankey & Holmes, 1994; Lurie et al., 2008; Stone, Storey & Hughes, 2012; Vilpulla et al., 2011), with additional improvements and/or complete resolution of neuropathy, migraines and cognitive decline (Lurie et al., 2008). Clinical indices have further been shown to reach within the normal range a year after commencing a GFD, with strict maintenance reported after 2 years (Hankey & Holmes, 1994). A statistical finding places symptomatic relief in an older individual much lower than that of a younger adult (69% vs. 95% respectively) (Casella et al., 2012a). Although disputed by Hankey and Holmes (1994), the lack of a comparison group within their study to compare age differences, may have impacted on results. Despite this, improvements in well-being have been found (Hankey & Holmes, 1994; Vilpulla et al., 2011), with quality of life remaining stable (Vilpulla et al., 2011) in addition to low levels of depression recorded within the older population (Stone et al., 2012).

Table 2: Summary of studies examining associated conditions and complications

Authors, Date, Country	Study design	Sample	Primary aim	Results	Comments
Gao et al., 2009 Sweden	Population-based case-control study	Total sample: 60,034 lymphoma sufferers (NHL, HL, CLL); N= 37,869 NHL (mean: 69years, interquartile range: 57-77). 236,408 frequency matched controls; 753,983 linkable first-degree relatives of patients and controls. 60% males in lymphoma patients. 54 NHL and 40 controls – personal history of CD. 76 NHL and 271 controls with coeliac family member	To calculate the secular trend of lymphoma risks within coeliac individuals.	Overall 5.4-fold increased risk for developing NHL (OR=5.35, 95% CI=3.56-8.06) but not HL or CLL. Risk of NHL higher for females although difference not significant. Association between CD and NHL more prominent in those under 65 years although not significant.	Heightened risk of NHL in those with CD, this is most prominent in first latency period (1-5years). However, this is declining. NHL risk increased 2-fold among those with a coeliac sibling (OR=2.03, 95% CI=1.29-3.19).
Meyer et al., 2001 North America	Cross-sectional Mailed survey out to obtain information from patients.	CD patients: 128 (M:23; F: 105) Mean age: 56years (21-83years). Males: mean: 59 +/-15years Premenopausal women: 39 +/- 9years (N=26) Postmenopausal women: 61 +/- 9years (N=79). Predominantly Caucasian. Claimed to adhere to GFD (mean duration: 9 +/-10years)	To examine osteoporosis in a North American adult population with CD.	Low bone mass and osteoporosis significantly less common in premenopausal women than in men and postmenopausal women. Osteoporosis present in 50% of men and 40% of postmenopausal women.	In 75%, BMD was below average for their age and in 46%, was more than 1 SD below norm. For every 1 SD decrease, relative risk of fractures increases by 1.5-2.9 (in Caucasian women). Patients with CD likely to be at increased lifetime risk for fractures.
Vasquez et al., 2000 USA	Cross-sectional study with a retrospective historical review through a personal interview, plus bone mineral density measurement.	Total Number = 330 <u>Group A:</u> CD N=165, 38patients aged 50+ years (M:22; F:143; Mean age: 40years, Range: 16-74years). All attended Malabsorption clinic of hospital. <u>Group B: Controls</u> N=165, 36people aged 50+ years (M:22; F:143; mean age: 41; range: 16-74)	To determine the prevalence of bone fractures and vertebral deformities in coeliac patients. To analyse the relationship between fractures and clinical data of patients.	By 70years old, 43% of coeliac patients presented with fractures (vs. 20% in controls). Osteoporotic fractures increase in frequency with age (higher prevalence in women and associated with minimal or moderate trauma).	No medical records of trauma events available hence, intensity of trauma unknown. Majority of fractures reported by coeliac patients occurred before diagnosis or in those who were non-compliant with the GFD (only 7% reported whilst on GFD).

NHL: Non-Hodgkin's Lymphoma; HL: Hodgkin's Lymphoma; CLL: Chronic lymphocytic leukaemia; SD: Standard Deviation; GFD: gluten-free diet

Associated conditions and complications

Associated conditions:

Thyroid disease and non-Hodgkins Lymphoma (NHL) are both commonly associated with CD, with a higher prevalence amongst older people (Casella et al., 2012a; Freeman, 1995; Gao et al., 2009; Mukherjee et al., 2010). Hypothyroidism (underactive thyroid gland) may delay receiving a diagnosis of CD due to the crossover in symptoms (e.g. constipation) (Freeman, 1995). Therefore, a diagnosis of hypothyroidism may precede a diagnosis of CD and hence, may appear more prominent in an older cohort of people with CD. Additionally, older people with CD possessed a 5-fold increased risk of contracting NHL in comparison to only 0.3% in 18-64 year olds, with risk being slightly higher in females (Casella et al., 2012a; Gao et al., 2009). Although only a small sample (n=30), Freeman (1995) highlighted the high incidence of malignant, clinical and pathological complications, thus demonstrating serious CD-associated problems (see Table 1). Surprisingly, the association between CD and NHL appeared more prominent (although not significant) within patients under the age of 65 years of age (Gao et al., 2009); however, this may result from early detection methods.

Bone Disease:

The malabsorption of key nutrients can result in the increase of bone disease in people with CD, particularly within older people (e.g. longer exposure to gluten) (Casella et al., 2012a; Meyer, Stavropolous, Diamond, Shane & Green, 2001; Mukherjee et al., 2010; Vasquez et al., 2000). However, age may only play a limited additive risk (younger coeliac vs. older coeliac) as no significant difference has been found between older coeliac and older non-coeliac patients (Casella et al., 2012a).Thus, CD may not be an independent risk factor for

the development of bone disease (Mukherjee et al., 2010). Conversely, postmenopausal women and their male counterparts are significantly more likely to have osteoporosis and a lower bone mass (Meyer et al., 2001). Furthermore, research found that 75% of people with CD had a bone mass density below their age-expected average, with 46% being one standard deviation below their expected norm, which indirectly increases their risk of bone fractures (Meyer et al., 2001). In accordance with these findings, Vasquez et al. (2000) reported 43% of people with CD over the age of 70 also presented with fractures (vs. 20% in controls). The absence of trauma medical records meant the intensity of trauma could only be partially considered; however, the frequency of osteoporotic fractures has been shown to increase with age, often resulting from minimal/moderate trauma (Vasquez et al., 2000). Interestingly, dietary self-management was found to reduce the risk of fractures, with only 7% of patients reporting incidents after treatment (Vasquez et al., 2000).

Table 3: Summary of studies examining neurological/cognitive decline

Authors, Date, Country	Study design	Sample	Primary aim	Results	Follow-up	Additional Comments:
Casella et al., 2012(b) Italy	Case-control study. Neuropsychological tests – 1 session, approx. 2hours GDS also given	Total Number= 36 Group A: CD N=18 (Mean: 75 +/- 4years) on GFD for 5.5 +/- 3years. Sex – M:8; F:10 Originally 32 Group B: controls N=18 Non-CD's admitted to hospital for minor clinical condition (Mean: 76 +/- 4years) Sex – M:8; F:10	To evaluate functional and cognitive performances in CD vs. control patients older than 65years.	Performance in several neuropsychological tests worse in Group A compared to Group B. Findings suggest: neurological manifestations of gluten intolerance include deterioration of cognitive function. No significant difference in GDS scores but Group A performed worse in tests requiring speed and attention, similar to scores usually found in elderly with depressive disorders.	Follow-up of GFD: 11patients: 6.7 +/- 3.7years – tested antibody negative 7patients: followed for 5.3 +/- 2.4years – tested intermittently t-TG antibody negative or positive during follow-up. No difference in cognitive performance between CD patients with persistent or intermittent negative t-TG antibody testing.	Cognitive performance worse in Group A despite prolonged gluten avoidance.
Frisoni et al., 1997 Italy	Case-control study	Total Number=57 Group A: AD 33 (M: 4; F:29) consecutive AD admitted to Alzheimer's Unit. Met all criteria for diagnosis. Mean: 77.9years (56-87years) Group B: Controls 24 (M:9; F:15)patients nonconsanguineous relatives (mostly spouses) without detectable cognitive deficit. Mean: 69.9years (55-84years)	To screen for CD in elderly patients with AD and compare this with elderly controls	Results indicate CD unlikely to be responsible for immune changes and to play a role in the pathogenesis of AD. CD in AD not more frequent than in controls		Group B had higher proportion of men than Group A – CD more common in females.
Hu et al., 2006 USA	Case series Mayo Clinic medical records from 1/1/1970 – 31/12/2005 electronically searched using set terms. Also conducted Short Test of Mental Status (STMS)	Total Number= 13 (M:8; F:5) with median age of cognitive impairment onset: 64years (45-79years). Divided into 2 groups: Group A: Onset of GI and cognitive symptoms separated by ≤1year Group B: Onset of GI and cognitive symptoms separated by ≥1year	To characterise the clinical, radiological and electrophysiological lab profiles and histological features of patients who developed cognitive impairment temporally associated with CD.	Most common cognitive complaint: amnesia N=12), followed by acalculia (N=7), confusion (N=6) and personality change (N=6). Group A: had lower average STMS score (24 vs. 32 respectively). 4 patients diagnosed as having coeliac dementia during their evaluation. 10/13 patients had gait ataxia, followed by peripheral neuropathy, myoclonus, seizures, headaches. Conclude: possible link (direct or indirect) between CD and cognitive decline.	10 patients deteriorated cognitively, 9 died of complications associated with progressive dementia. 2 patients improved cognitively with GFD (up to 10years). 1 patient remained neurologically stable with her cognitive deficits and ataxia 6months after gluten withdrawal.	5 patients developed simultaneous neurological and GI symptoms (median: 64 years, 59-79years). Mean age of GI complaint: 63years Diarrhoea most common symptom

*GDS: Geriatric depression scale; GFD: Gluten-free diet; AD: Alzheimer's Disease; GI: Gastrointestinal

Neurological and cognitive decline

Older people with CD often report amnesia, acalculia, confusion and changes of personality, offering support for CDs effects on neurological manifestations including the deterioration of cognitive function. For example, older people with CD performed worse in a range of neuropsychological tests compared to non-coeliac age-matched controls (Casella et al., 2012b). Furthermore, the existence of a specific neuropsychological profile in people with CD has been proposed due to the selective conservation of memory (Casella et al., 2012b) and consequently, separating it from other cognitive disorders. This interlinks with the lack of support shown for an association between CD and Alzheimer's disease (AD) (Frisoni et al., 1997) as their neurological profiles differ, with the latter focusing heavily on memory impairment (Casella et al., 2012b). Despite this, patients have been known to be diagnosed with coeliac-related dementia (Hu et al., 2006: 11% of people with CD) and neuropathy (Table 1: Lurie et al., 2008). However, certain methodological discrepancies may have contributed to these findings, for example, the absence of a control group in Hu et al. (2006) study. Without a comparable baseline to measure, it is unclear whether CD potentially caused dementia or if the two illnesses occurred independently.

The effects of a GFD on cognitive function are uncertain; several studies have shown gluten removal to stabilise and/or improve cognitive function and thus, demonstrate the positive outcome good dietary self-management may have (Hu et al., 2006; Lurie et al., 2008). In contrast, Casella et al. (2012b) findings contradicted this, reporting significantly lower scores on a range of cognitive performance tests, when compared to age-matched controls, after strict adherence to a GFD (Mean: 5.5years, +/-3years).

Discussion

Existing literature on CD in older age was examined. Similarly to a younger cohort, older people with CD adhered to a strict GFD and benefited from a range of improvements (e.g. clinical indices, well-being). An array of studies have shown consistent clinical characteristics commonly reported by older people (e.g. diarrhoea, anaemia) as well as the presence of one or more autoimmune conditions. Older people with CD were more likely to experience premature heart failure, in addition to receiving a diagnosis of NHL and hypothyroidism. Problems with cognition were also identified, leading to the suggestion of a specific neuropsychological profile differentiating CD from AD.

However, lack of research within the older population has inevitably led to the uncertainty of key areas. For example, contradictory results were reported in relation to severity and age for both clinical presentation and symptomatic relief. Moreover, several studies also disagreed on the presence of an association between CD and neuropathy (dementia and AD) and the effects of the GFD on cognitive improvement. The existence of limited mixed views on various issues can create a multitude of problems, including a lack of awareness by health professionals of the specific issues related to CD in older age. Therefore, it may be beneficial to address these unresolved matters involving symptomatic relief and differences in severity of clinical presentation. Additional evidence on whether cognitive deficits and neuropathological disorders are a by-product of CD would also be of use, potentially impacting various existing screening and diagnostic procedures. Furthermore, various key issues faced in older age have not been addressed in connection to CD. For example, an older coeliac patients' physical (e.g. visual loss: Brennan, Horowitz & Su, 2005; mobility problems: Rubenstein, 2006), social (e.g. social life, burden of illness), psychological (e.g.

stress of being a caregiver: Schulz & Beach, 1999; Vitaliano, 1997) and financial (e.g. cost of a GFD: Lee, Ng, Zivin & Green, 2007) difficulties. These issues should be further investigated to see how general problems experienced in old age may impact an individual living with CD (Belsky, 1984; Bonder, 1994).

Generally, studies consisted of a relatively small sample size (Mean: 59 older participants with CD [exception of Stone et al., 2012: 749 participants]), although this may simply reflect the lack of current research specifically aimed at older people with CD. Sample biases were a key issue within several studies due to the large presence of female participants (Frisoni et al., 1997; Stone et al., 2012); this is important to note as CD is more common in females with a ratio of 2:1 (Shah & Leffler, 2010). Therefore, an overrepresentation of females is more likely to skew the results and thus, result in unreliable findings. Frisoni et al. (1997) looked at AD in people with CD in a sample of 4 males and 29 females; however, AD is also more prevalent in females (Schmidt et al., 2008) and consequently, findings reported here are not representative of the general population. Although no link between CD and AD (both common in females) was documented, the relationship is still unclear in males. Future research should address this relationship. Stone et al. (2012) used a self-selected sample, biased to females, to look at depression. Both CD and depression (Belmaker & Agam, 2008) are more frequently diagnosed in females; hence, this overrepresentation of women may have influenced the small significant association found between CD and depression.

Retrospective cohort designs were commonly used by researchers within this review and consequently, relying on previous data collectors findings may have resulted in selection bias and/or misclassification/information bias. More importantly, only a minority of studies conducted a 'follow-up', with a further 2 studies adopting a longitudinal design (Freeman,

1995; Vilpulla et al., 2011); subsequently, the long-term impact of CD for older people remains unclear and therefore, could be addressed in future research.

Due to the lack of research using people over 65 years old, papers with patients aged 60 years and above were included (Freeman, 1995; Hankey & Holmes, 1994; Hu et al., 2006; Meyer et al., 2001 [excluding premenopausal women]). Studies documenting age-related differences were also reviewed, for example, Stone et al. (2012). Although in this study the mean age was 50 years old (Range: 18-88), results indicated that depression decreased with age. Similarly, Vasquez and colleagues (2000) who recruited patients aged 50 years and above, reported heightened characteristics within older participants (70 years old: 43% presented with fractures). This therefore, was considered valuable in expanding knowledge in older coeliac patients. However, life expectancy is continuously extending, thus, defining who is considered old becomes increasingly difficult. Future research may wish to address how people view and live with CD in various subgroups of older age (e.g. 65-74; 75-84; 85+years).

An overview of the available literature exploring CD in later life has been provided. This review provides the reader with a clearer understanding of factors and associated variables which differentiate older and younger adults with CD, in addition to suggested topics for future research. This paper illustrates key clinical symptoms, offering guidance on the detection of CD, in addition to valuable information on treatment effects. Therefore, this review presents the first initial step in understanding CD within an older cohort.

Reflective Summary

The aim of this placement was to conduct a systematic literature review to help provide a better understanding of the issues faced by older people living with coeliac disease (CD). This was a great learning curve for me as I previously had no prior encounters with either CD or conducting a systematic review and therefore, I felt I truly benefited with the choice of this placement. Throughout my placement, I was able to learn and develop valuable new skills as well as overcome areas I found particularly challenging.

My initial response to this placement was to develop a clearer understanding of what living with CD was like. For me, this phase was particularly interesting due to the element of researching such a new topic. Furthermore, I was granted access to a DVD illustrating real-life accounts of people with CD, and as a result, I gained a greater insight to problems I previously had not thought off. From this, my task was to conduct a systematic database search to examine all available literature on CD in older people. I found this stage of my placement particularly difficult as I struggled with the concept of selecting suitable papers required to compile a systematic review. Thus, I reported papers discussing both CD in older age as well as general problems encountered in old age.

I initially thought that this was acceptable if there was a presumed cross-over between the two topics. For example, older people experience visual loss and therefore, older people with CD may also suffer with this and subsequently, this may hinder their dietary self-management (reading small print on food products). However, my supervisor was able to help me understand that the types of papers within a systematic review must include studies which combine both aspects of the topic: CD in older age. This enabled me to

understand the initial requirements a systematic literature review needs to ensure I avoid repeating the same mistake in the future.

Another problem I encountered involved the act of searching databases, and despite my preconceived ideas on the ease of this task, my first few searches were unsuccessful. On reflection, I particularly struggled with using the correct search term abbreviations (e.g. AND/OR), in addition to successfully amending the limits for each key term. A reoccurring problem I faced was excluding certain age groups (e.g. children) but finding these exclusions still present in the results. Nonetheless, I was able to overcome this with the help of previous written notes and guidance on the internet, alongside consulting my supervisor.

At each supervisory meeting, set targets were agreed upon helping the course of the placement run smoothly and subsequently, allowing time within the meeting to be spent efficiently. Consequently, both my time management and organisation skills were further developed with each task being completed on time. For example, by agreeing to complete the quality assessment of the selected papers within the systematic review before the next meeting, results obtained and any concerns which may have arisen could be discussed in the meeting with my supervisor.

Completing this systematic review combined with regular discussions during supervisory meetings has granted me with a greater understanding of CD in older age. A personal achievement of mine from this placement was completing the database search and quality assessment of the selected literature as I felt this was particularly challenging for me. I feel I have achieved my initial placement goals and hope for a possible dissemination in a peer-reviewed journal.

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Appendix 1: Checklist for assessing the quality of quantitative studies (Kmet, Lee & Cook, 2004)

Criteria		Yes	Partial	No	N/A
1	Question/objective sufficiently described?				
2	Study design evident and appropriate?				
3	Method of subject/comparison group selection or source of information/input variables described and appropriate?				
4	Subject (and comparison group, if applicable) characteristics sufficiently described?				
5	If interventional and random allocation was possible, was it described?				
6	If interventional and blinding of investigators was possible, was it reported?				
7	If interventional and blinding of subjects was possible, was it reported?				
8	Outcome and (if applicable) exposure measure(s) well defined and robust to measurement/misclassification bias? Means of assessment reported?				
9	Sample size appropriate?				
10	Analytic methods described/justified and appropriate?				
11	Some estimate of variance is reported for the main results?				
12	Controlled for confounding?				
13	Results reported in sufficient detail?				
14	Conclusions supported by the results?				

Appendix 2: Results of the KMET quality framework checklist

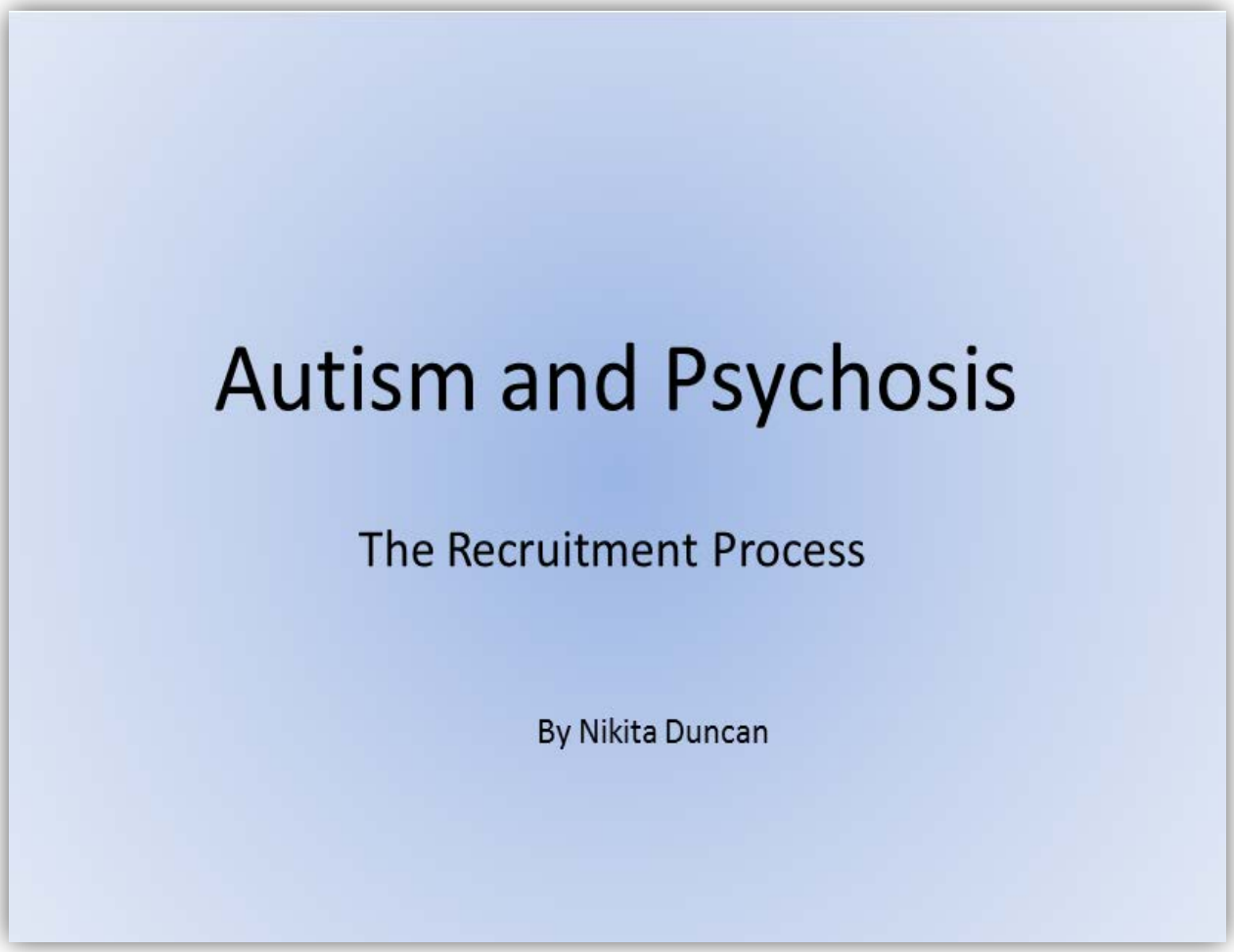
Each numbered criterion corresponds with the questions found in Appendix 1

Studies	KMET Checklist for assessing quality of quantitative studies - Criteria														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total
Casella et al., 2012(a)	Y	Y	Y	P	N/A	N/A	N/A	Y	Y	Y	Y	Y	P	Y	20/22
Casella et al., 2012(b)	Y	Y	Y	P	N/A	Y	Y	P	N	Y	Y	P	Y	Y	21/26
Freeman, 1995	Y	Y	Y	P	N/A	N/A	N/A	Y	N	N	P	Y	P	P	14/22
Frisoni et al., 1997	Y	Y	Y	Y	N/A	N/A	N/A	Y	P	Y	Y	P	P	P	18/22
Gasbarrini et al., 2009	Y	Y	P	P	N/A	N/A	N/A	Y	Y	P	P	Y	P	Y	17/22
Gao et al., 2009	Y	Y	Y	P	N/A	N/A	N/A	Y	P	Y	Y	Y	Y	Y	20/22
Hankey & Holmes, 1994	Y	Y	Y	Y	N/A	N/A	N/A	Y	N	P	N	N/A	Y	Y	15/20
Hu et al., 2006	Y	Y	Y	Y	N/A	N/A	N/A	Y	N	Y	Y	P	Y	Y	19/22
Lurie et al., 2008	Y	Y	Y	Y	N/A	N/A	N/A	Y	N	Y	Y	P	Y	Y	19/22
Meyer et al., 2001	Y	Y	P	Y	N/A	N/A	N/A	P	Y	Y	Y	P	Y	Y	19/22
Mukherjee et al., 2010	Y	Y	Y	Y	N/A	N/A	N/A	Y	Y	Y	P	P	Y	Y	20/22
Stone et al., 2012	Y	Y	P	Y	N/A	N/A	N/A	Y	Y	Y	Y	P	Y	Y	20/22
Vasquez et al., 2000	Y	Y	Y	P	N/A	N/A	N/A	Y	Y	P	Y	P	Y	P	18/22
Vilpulla et al., 2011	Y	Y	Y	Y	N/A	N/A	N/A	Y	Y	Y	Y	P	Y	Y	21/22

Y = Yes; P= Partial; N = No; N/A = Not applicable

CHAPTER 2

AUTISM AND PSYCHOSIS: THE RECRUITMENT PROCESS



Commentary:

Throughout my Spring and Summer placement, I have been involved in an exciting project which seeks to examine the neurobiological and psychological overlap between autism and psychosis. The placement was comprised of many different stages; however, today I would like to specifically share with you my experience and reflection of the recruitment phrase.

Autism and Psychosis

- What is autism? What is psychosis?
- Many areas overlap:
  - E.g. problems in socialisation, cognition and motor ability.
- Pre-1970's – terms used interchangeably
- The possibility of a continuum? (Craddock & Owen, 2010)

Autism ⟷ **Psychosis**

Commentary:

Autism is usually diagnosed in early childhood (Siegel, Pliner, Eschler & Elliot, 1988) and, individuals diagnosed, can present with a variety of symptoms including social withdrawal, communication impairment and obsessive behaviours (DSM-IV, American Psychiatric Association, 1994). A psychotic experience is often defined as a loss of contact with reality and may involve a variety of positive (e.g. hallucinations, delusions), negative (e.g. affective blunting) and secondary symptoms (e.g. depression, anxiety) (DSM-IV, APA, 1994). There are many traits which have been documented throughout the literature which illustrate a variety of similarities between the two disorders (e.g. Sheitman, Kraus, Bodfish & Carmel,

2004). For example, people with high-functioning autism can often become quite anxious when stressed, particularly if they have been asked to shift their attention. This experience can often appear thought-disordered and paranoid (Berney, 2000). This too can be seen in people with psychosis who experience conceptual disorganisation, paranoia, anxiety and the inability to handle pressure (Kay, Fisbein & Opler, 1987). Furthermore, both groups report deficits in social and neuro-cognition, motor ability, disorganised speech and negative symptoms (e.g. Dickson, Laurens, Cullens & Hodgins, 2011; Konstantareas & Hewitt, 2001; Leyfer et al., 2006). Meta-analyses have also revealed the presence of childhood deficits which mimic autistic traits in people prior to receiving a diagnosis of schizophrenia (Dickson et al., 2011). Similarly, findings from genetic research have been able to support the existence of an overlap between the two disorders (e.g. Vorstman et al., 2006).

Previously, autism was viewed as a core feature of schizophrenia (Bleuler, 1911), with some researchers believing autism to be the childhood predecessor to the later development of psychosis (Bender, 1947). Thus, although they are now conceptualised as two distinct disorders (Kolvin, 1971; Rutter, 1972), it is easy to see how they were previously viewed as one.

To help address the apparent association between the disorders, Craddock & Owen (2010) conceptualised the existence of a continuum. They argued that one end of the spectrum was predominantly influenced by neurodevelopment and the other end was to a higher degree, concerned with affective pathology. This illustrates how traits found in both disorders can exist on a spectrum, with an overlap existing in the middle. Moreover, documented research has highlighted the increased risk of developing psychosis in those

with autism (Petty, Ornitz, Michelman & Zimmerman, 1984), providing additional support to the conceptualised existence of a continuum.

Overview of Study

Aim: 'To investigate autistic traits in those with first-episode psychosis.'

Participants:

- 100 people with First episode psychosis (FEP)
- 30 matched controls
- Aged 16-35 years old

Method and Materials:

- Interviewer rated questions
- Self-report questionnaire
- MRI brain scan

Commentary:

Subsequently, our aim for this study was to investigate autistic traits in individuals with first-episode psychosis (FEP).

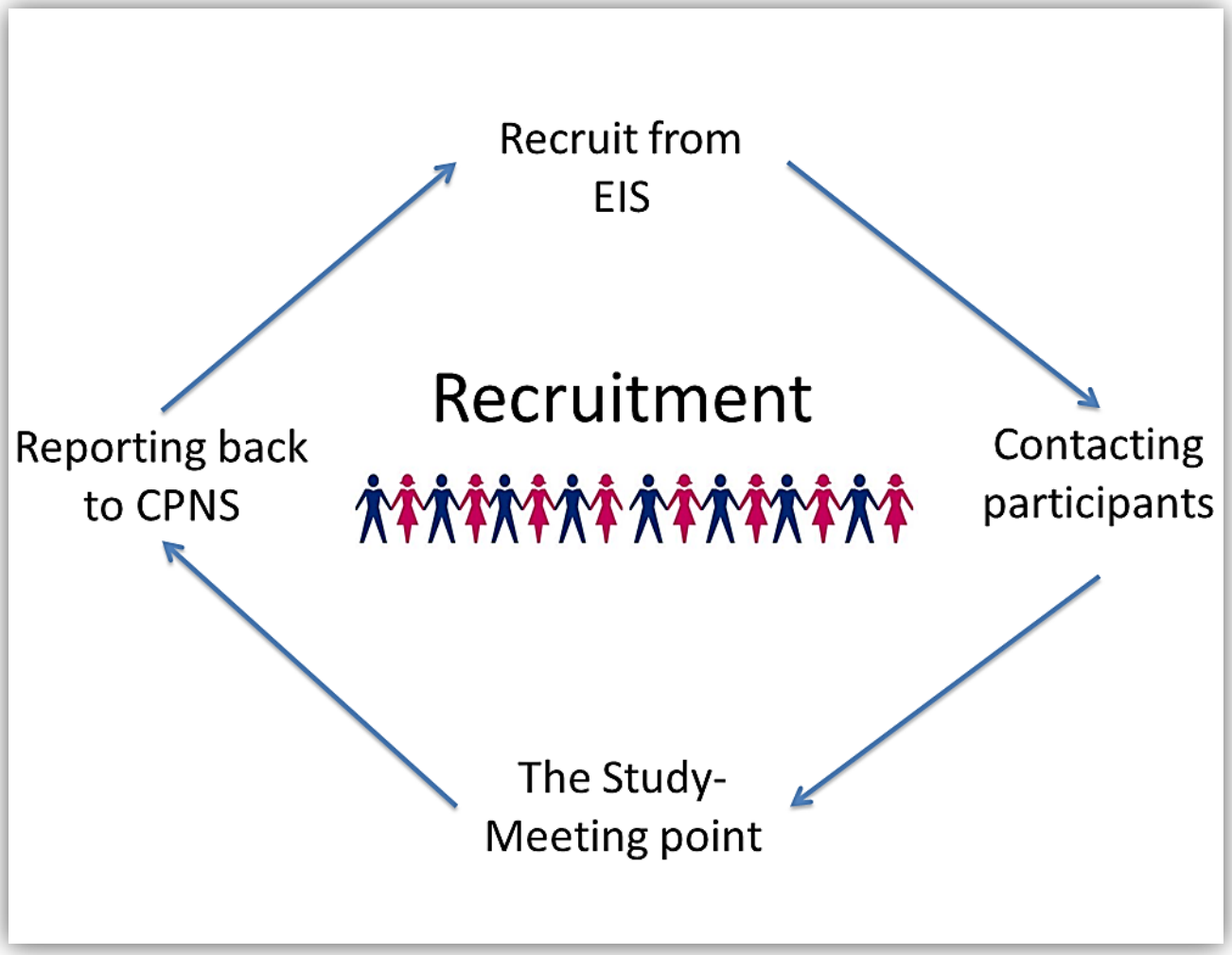
We recruited and interviewed one hundred people in touch with early intervention services (EIS) who were experiencing FEP. A subgroup sample of thirty people with FEP also participated in an MRI scan, and was matched to thirty healthy controls. Participants were aged 16-35 years.

The semi-structured interview lasted approximately one hour and thirty minutes. The interview used the Positive and Negative Syndrome Scale (Kay et al., 1987) which addresses

symptoms of psychosis over the last seven days. We then asked participants about their Quality of Life (Heinrichs, Hanlon & Carpenter, 1984) and their daily routine. This was followed by the Premorbid Adjustment Scale which focuses upon premorbid functioning (Cannon-Spoor, Potkin & Wyatt, 1982). Current functioning was also assessed through the Social and Occupational Functioning Assessment Scale (Goldman, Skodol & Lave, 1992) and the Personal and Social Performance Scale (Morosini, Magliano, Brambilla, Ugolini & Pioli, 2000).

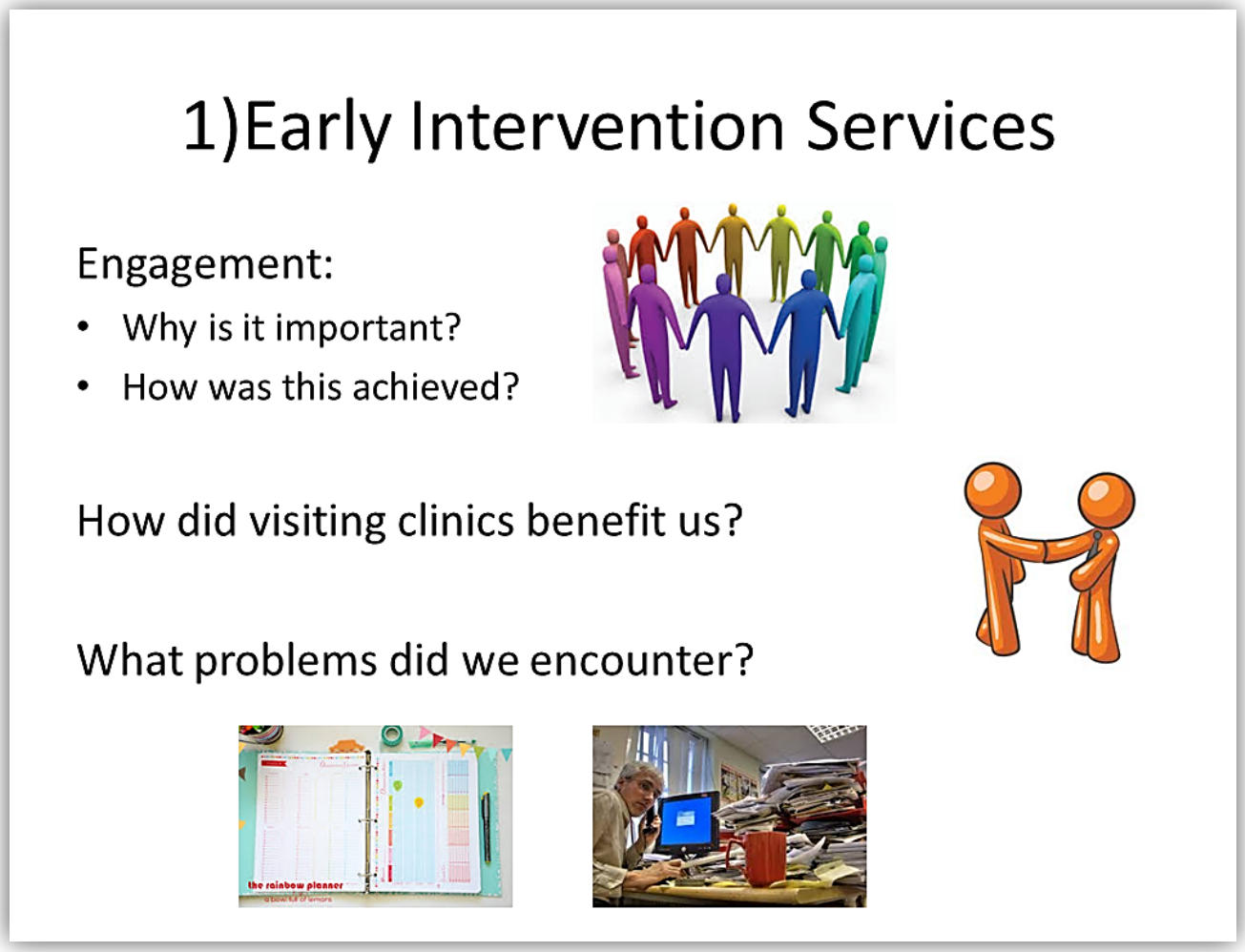
After the interview, participants were asked to complete the self-report questionnaire, taking approximately thirty minutes. The questionnaire used the Autism Quotient (Baron-Cohen, Wheelwright, Skinner, Martin & Clubley, 2001), the Brief Childhood Trauma Questionnaire (Bernstein et al., 2003), the Social Interaction Anxiety Scale and the Social Phobia Scale (Mattick & Clarke, 1998), the Beck Hopelessness Scale (Beck, Weissman, Lester & Trexler, 1974) and the Suicide Behaviours Questionnaire-Revised (Osman, Bagge, Gutierrez, Konick, Kopper & Barrios, 2001).

Those who agreed to participate in the MRI brain scan were assessed to ensure they were safe to proceed. To do this, control participants were first screened using the Structural Clinical Interview for DSM disorders screening tool (First, Spitzer, Gibbon & Williams, 2002). This was important in order to rule out any occurrences of mental illness, past or present, in the control group. After, both control and patient group were asked to fill out the standard health and safety questionnaire, enquiring about any medical problems, operations or metal devices fitted within the body. The brain scan lasted approximately 45 minutes and aimed to capture structural scans, resting state functional images and a brain spectroscopy.



Commentary:

Our recruitment process was a continuous cycle. We visited the EIS in Birmingham and Solihull Mental Health Trust (BSMHT) to recruit participants who were interested in the study. This was then followed by contacting and meeting the participants to conduct the study. Finally, we reported back to the EIS to help keep the participants Community Psychiatric Nurses (CPN's) informed and up-to-date on their client.



Commentary:

The success of this initial stage relied heavily upon our ability to engage with the EIS service. These services are over researched and therefore, the clinical teams may be more reluctant to part from their patient lists. Hence, it was important for us to build a good rapport with the services to show that we valued their input in participant recruitment. We showed this by visiting the services weekly, allowing them to become more familiar with ourselves and consequently, viewing us as extended members of their teams (as opposed to distant researchers). This led to being able to attend clinics and meet and recruit participants there, as opposed to contact over the phone.

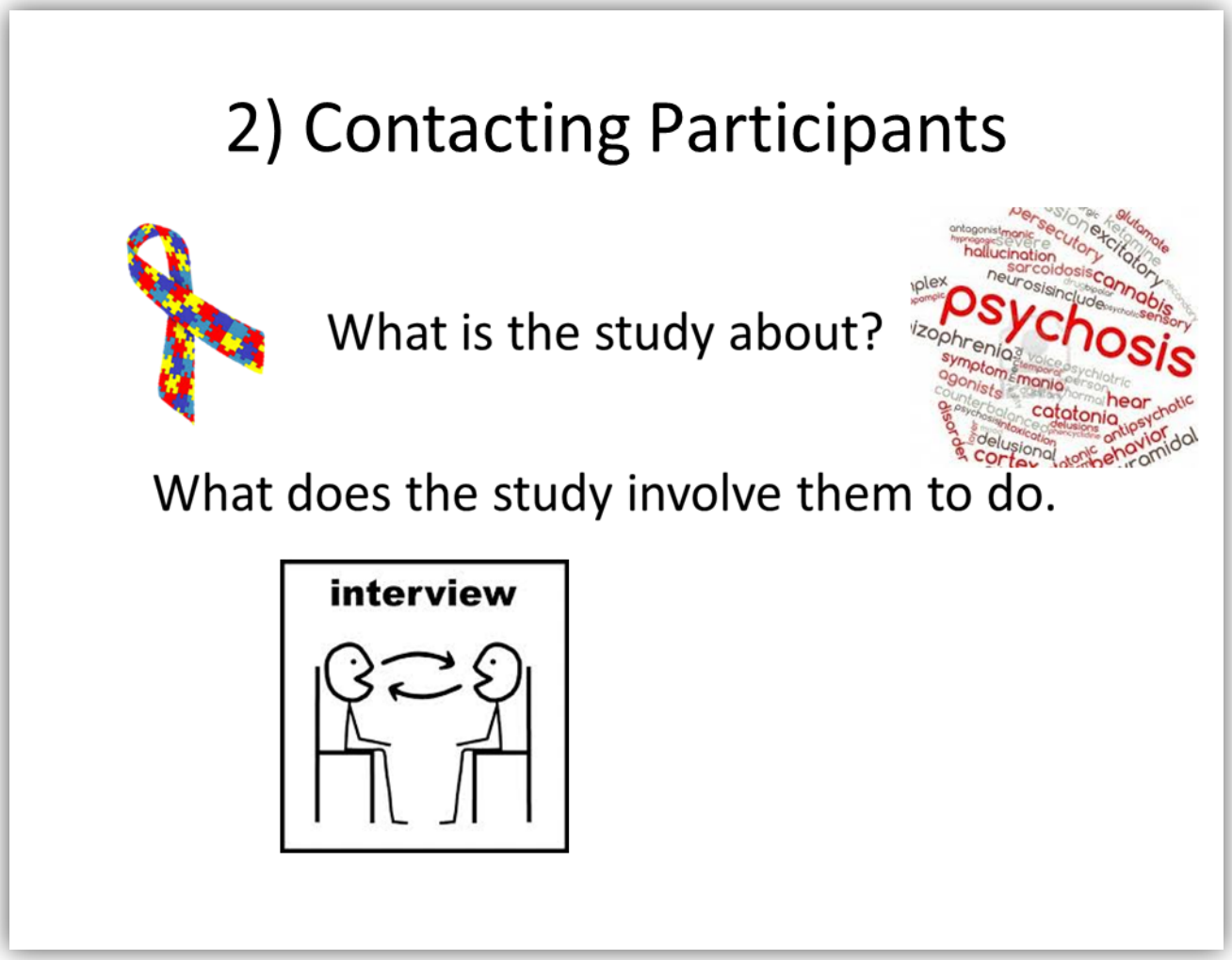
Nevertheless, this stage was accompanied by several problems. CPNs were often understaffed and overloaded with patients, consequently having little time to sit and discuss their case load with us. To overcome this, we needed to be flexible around their work timetable. Additionally, due to their busy schedules, CPNs often forgot to approach their patients about our study which impacted on the pace of our recruitment. However, visiting the services helped to remind the CPNs and therefore, sped this process up.

Commentary:

Our initial contact with the participant (whether it be in person or on the phone) was just as important as meeting the Early Intervention teams and so we needed to create a good impression. Receiving a call from an unsaved number can often be daunting, especially to individuals experiencing severe mental illness. Therefore, it was important to first introduce ourselves to put the participant at ease.

Commentary:

It was also important to establish whether the participant was able to talk or if they preferred us to call back at a more convenient time. We wanted to establish this as participants may be out in public or with friends or work colleagues who are unaware of their mental illness. Again, by asking this question, we were able to ensure the participant felt relaxed and at ease.



Commentary:

Participants possessed various levels of knowledge on what the current study involved depending on how much information they had been given by their CPN; thus, we provided a brief overview to what the study was investigating and what it would involve. This allowed the participant to make an informed decision on whether they would like to participate.

Reaching and contacting the participants was the main difficulty experienced throughout this stage. In some instances, their phone number would either go to voicemail or simply no longer connect. This was difficult to overcome and therefore, we approached the situation in various ways. Our first method involved trying to contact the participant at varying times

of the day and week. If this was unsuccessful, we then checked to see if we had up-to-date contact details for them and enquired as to whether there were any alternative phone numbers that we could try (e.g. home phone).

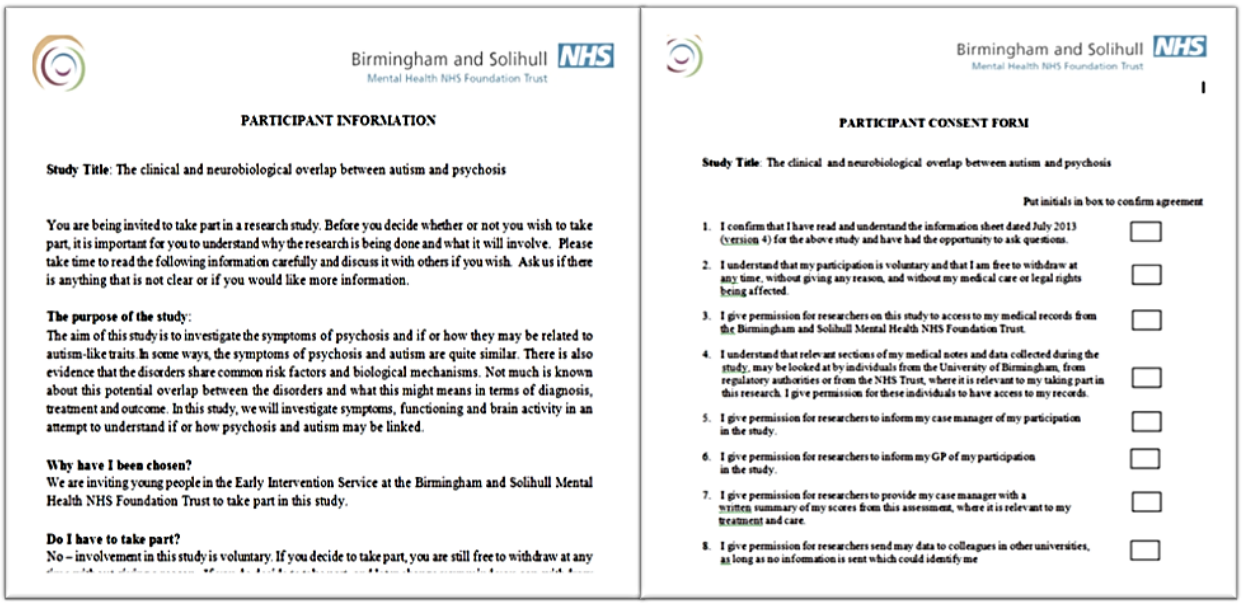
3) Meeting Participants

UNIVERSITY OF BIRMINGHAM

Commentary:

Once a date for the study was agreed, we then met the participant, whether that be at the University of Birmingham or at their home.

3) Meeting Participants



Birmingham and Solihull NHS
Mental Health NHS Foundation Trust

PARTICIPANT INFORMATION

Study Title: The clinical and neurobiological overlap between autism and psychosis

You are being invited to take part in a research study. Before you decide whether or not you wish to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

The purpose of the study:
The aim of this study is to investigate the symptoms of psychosis and if or how they may be related to autism-like traits. In some ways, the symptoms of psychosis and autism are quite similar. There is also evidence that the disorders share common risk factors and biological mechanisms. Not much is known about this potential overlap between the disorders and what this might means in terms of diagnosis, treatment and outcome. In this study, we will investigate symptoms, functioning and brain activity in an attempt to understand if or how psychosis and autism may be linked.

Why have I been chosen?
We are inviting young people in the Early Intervention Service at the Birmingham and Solihull Mental Health NHS Foundation Trust to take part in this study.

Do I have to take part?
No – involvement in this study is voluntary. If you decide to take part, you are still free to withdraw at any

Birmingham and Solihull NHS
Mental Health NHS Foundation Trust

1

PARTICIPANT CONSENT FORM

Study Title: The clinical and neurobiological overlap between autism and psychosis

Put initials in box to confirm agreement

1. I confirm that I have read and understand the information sheet dated July 2013 (version 4) for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected. ☐
3. I give permission for researchers on this study to access to my medical records from the Birmingham and Solihull Mental Health NHS Foundation Trust. ☐
4. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from the University of Birmingham, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
5. I give permission for researchers to inform my case manager of my participation in the study. ☐
6. I give permission for researchers to inform my GP of my participation in the study. ☐
7. I give permission for researchers to provide my case manager with a written summary of my scores from this assessment, where it is relevant to my treatment and care. ☐
8. I give permission for researchers send may data to colleagues in other universities, as long as no information is sent which could identify me ☐

Commentary:

Once met, the information sheet was discussed to help provide the participant with more information about the research, in addition to explaining the confidential nature of the study. The consent form was then given, with any questions about their participation addressed.

3) Meeting Participants

Administer interview:

- Provide a comfortable, relaxed atmosphere.
- Be open to symptoms
- Emergency situations

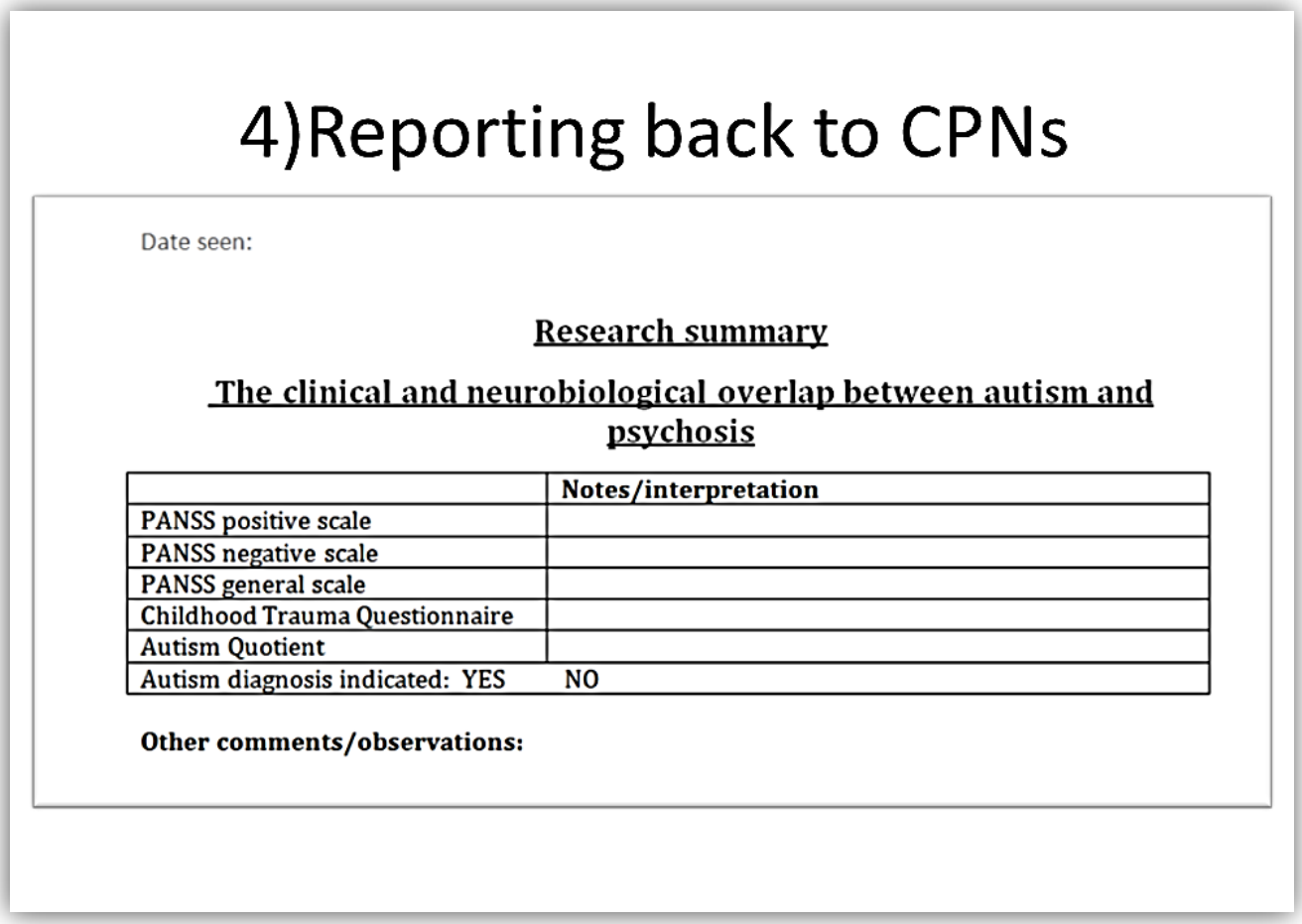
Most importantly, enjoy!

Commentary:

Throughout the interview, it was important to provide a comfortable and relaxed atmosphere, helping the participant to feel at ease. Due to the nature of the study, the questions asked by the interviewer may receive unusual responses. For this reason, it was important to be open to hearing an array of positive symptoms and to respond appropriately. Likewise, some participants may have experienced a host of negative symptoms and therefore, knowing how to handle these situations was beneficial. During the interview, the lone-working policy was followed and we understood what to do if sensitive information was disclosed (e.g. active suicidal plans).

Finally, the next step was to relax and enjoy conducting the interview! Not only was this part fun, it was also both informative and interesting!

4)Reporting back to CPNs



Date seen:

Research summary

The clinical and neurobiological overlap between autism and psychosis

	Notes/interpretation
PANSS positive scale	
PANSS negative scale	
PANSS general scale	
Childhood Trauma Questionnaire	
Autism Quotient	
Autism diagnosis indicated: YES	NO

Other comments/observations:

Commentary:

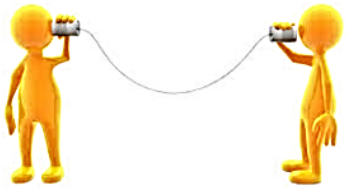
Once the interview ended (and if the participant had given consent for us to do so) we then developed a short summary for their CPNs. We provided feedback on a range of areas including their symptoms of psychosis over the past seven days and disclosure of any childhood trauma. This was followed by their score on the Autism Quotient and a yes/no indication of autism. In addition, we also had a box to include other comments and observations noticed throughout the interview (e.g. new family tensions or a positive act); again, this ensured the CPNs were kept up-to-date. On receiving these summaries, responses from CPNs have been positive, often expressing the usefulness of highlighting new symptoms or behaviours which they may not have been aware of. These individual

reports were our way of giving the early intervention teams something back, which additionally helped to maintain a good, stable relationship.

Overall Reflection

- What did I like?

- What did I learn?



- What would I do differently?

Commentary:

Upon completing this placement there have been many things that I have both learnt and enjoyed. I was able to develop an insight into how the EIS worked as well as visually experiencing how a multidisciplinary team function together. It was also fascinating to watch hand-over meetings between the CPNs and the psychiatrists, learning about how these are structured in addition to providing and contributing useful information back to various team members.

Conducting the interviews on my placement was another aspect which I enjoyed. It was a great experience to meet a magnitude of participants, all with varying symptoms and

presentations. I felt that I truly learnt a variety of skills; for example, being able to communicate with people who may be unresponsive or hyperactive. I also developed an understanding of how to be both patient and receptive to participants, followed by how to deal with unusual responses (e.g. experiencing delusions).

Although there were some difficulties in the recruitment process which I discussed throughout the presentation, I do believe that we conducted this stage in the best way possible. By going directly to the EIS's and talking with the CPNs, we were able to receive help on participant selection (e.g. capability of taking part). This was hugely beneficial and we avoided wasting time.

Overall, I feel that I have gained and developed many practical research skills throughout my placement. Being equipped with the ability to communicate effectively with a range of different audiences and structure my time around recruitment and data gathering has allowed me to further prepare myself for future work within the research field.

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CHAPTER 3

AN INVESTIGATION INTO THE IMPACT CHILDHOOD ABUSE MAY HAVE IN THE PRESENTATION OF NEGATIVE SYMPTOMS IN PATIENTS WITH FIRST-EPISODE PSYCHOSIS

Abstract

Introduction:

A large body of research centres on the relationship between childhood abuse and positive symptoms in psychotic disorders. In contrast, the role of both childhood abuse and neglect and its interplay with negative symptoms has been overlooked. Limited knowledge is known in this relatively new area and therefore, more information is needed to better understand this relationship.

Aims:

1. Is there a relationship between the presence of negative symptoms in first-episode psychosis and the past experience of childhood abuse?
2. Furthermore, is there a specific type of childhood abuse or neglect which leads to a stronger incidence of negative symptoms?
3. Did the presentation of negative symptoms in those who had experienced childhood abuse differ between genders?

Method and Design:

For this study, sixty-nine patients (Males: 50; Females: 19) were recruited from the Early Intervention Services. Participants ranged from 17-36 years old (Mean: 25.40 years; SD: 4.77) and were diagnosed with a range of psychotic disorders (63.8% diagnosed with psychosis). Data were taken from a larger study examining the neurobiological and psychological overlap between first-episode psychosis and autism. This study explored and analysed data collected from two scales which were taken from the larger study. Participants were interviewed using the Positive and Negative Symptom Scale (Kay et al.,

1987) and then completed the Brief Childhood Trauma Questionnaire (Bernstein et al., 2003). Analysis was only performed on these two scales.

Results and findings:

Factor analysis was first conducted to produce the 'negative symptom' cluster. This would then allow for further exploration into whether negative symptoms were effected by childhood abuse. However when run, the core assumptions needed for the analysis were not met. Therefore, a closely-matched sample from a previous study was felt appropriate (Emsley et al., 2003). The 'negative symptom' factor derived by the authors was adopted for this study. Upon exploring the data, no significant relationship was found between exposure to childhood abuse and the incidence of negative symptoms. However, emotional abuse and neglect were reported most frequently among the sample. The presentation of negative symptoms in those who had been abused during childhood did not differ between males and females. Limitations and future research are discussed.

Introduction

Childhood abuse (CA) has been defined as involving all variants of abuse (physical, sexual, emotional abuse) and neglect (physical, emotional neglect), which occurred during childhood and adolescence. Thus, physical abuse has been defined as "bodily assaults on a child by an adult or older person that posed a risk of or resulted in injury". Sexual abuse involved "sexual contact or conduct between a child younger than 18 years of age and an adult or older person". Emotional abuse was described as "verbal assaults on a child's sense of worth or well-being or any humiliating or demeaning behaviour directed toward a child by an adult or older person". Emotional neglect, on the other hand, was seen as the "failure of caretakers to meet children's basic emotional and psychological needs, including love, belonging, nurturance and support". Similarly, physical neglect was defined as "the failure of caretakers to provide for a child's basic physical needs, including food, shelter, clothing, safety and healthcare" (Bernstein, Ahluvalia, Pogge & Handelsman, 1997; Bernstein et al., 2003).

Exposure to CA has been found to impact later life in a variety of ways. Deficits within cognitive functioning and memory have been well documented, highlighting difficulties in attention, abstract reasoning and executive functioning (Beers & De Bellis, 2002; Bremner et al., 2004; Mezzacappa, Kindlon & Earls, 2001; Navalta, Polcari, Webster, Boghossian & Teicher, 2006; Perez & Widom, 1994). Alongside this, the risk for developing psychological problems has been associated with CA; for example, post-traumatic stress disorder, anxiety, depression and psychosis (e.g. Scheeringa, Zeanah & Cohen, 2011). Up until recently however, little attention had been paid to the conceptualised link between CA and psychosis. Thus, this relatively new phenomenon has become increasingly popular to

examine, exploring whether an abusive childhood can act as an additive risk factor to the later development of psychosis (Brown, 1973).

Often defined as a loss of contact with reality, first-episode psychosis (FEP) is usually preceded by emotional and social difficulties such as depression and social anxiety (Birchwood, 2003; Birchwood, Iqbal, Chadwick & Trower, 2000; Poulton et al., 2000); victims of CA regularly report similar problems (Birchwood, 2003). Furthermore, a significant increase in the proportion of negative life events and CA are believed to occur in those prior to the onset of a psychotic illness (Bebbington et al., 1993). Findings from research have revealed high prevalence rates for various forms of CA (childhood sexual, physical, emotional abuse and neglect) in both adult and child patients with psychosis, potentially indicating the existence of a CA-psychosis link (e.g. Bebbington et al., 2004; Briere, Woo, McRae, Foltz & Sitzman, 1997; Goff, Brotman, Kindlon, Waites & Amico, 1991; Holowka, King, Saheb, Pukall & Brunet, 2003; Livingston, 1987; Read, Morrison & Ross, 2005; Swett, Surrey & Cohen, 1990; Uçok & Bikmaz, 2007).

Childhood abuse and psychosis

Much of the existing literature focused on individuals with schizophrenia, thus, relatively little attention was paid to individuals experiencing FEP. This created a selection bias of patients comprising of a poorer prognosis, who suffered from possible contributing medication effects as well as an increased risk of exposure to later abuse. Due to this, the focus turned to exploring the effects CA can have on symptomatology and outcome of prognosis in FEP patients. To investigate this matter further, a large-scale study involving 4045 patients who suffered with psychosis was conducted (Janssen et al., 2004). The findings emulated previous small-scale FEP studies, indicating that reported CA and neglect

could predict the development of psychosis in adulthood, particularly if the abuse was more severe. These robust findings were apparent even after controlling for numerous demographic variables and reported risk factors and subsequently, they concluded that CA predicted the development of positive psychotic symptoms.

In recent years, findings from researchers have highlighted how the experience of childhood sexual and/or physical abuse may influence the risk of developing FEP (Conus et al., 2010; Read et al., 2005). In addition, patients exposed to sexual and physical abuse as a child were found to have lower levels of functioning prior to symptom onset, followed by a longer duration of untreated psychosis. Despite this, when compared to patients without a trauma history, there was no significant difference in their age of psychosis onset. Therefore, there may be unaccounted variables which delay CA patients from initiating earlier treatment, such as not living in the family home (Addington, Van Mastrigt, Hutchinson & Addington, 2002).

Throughout the literature, childhood physical and sexual abuse has been viewed as powerful predictors in the development of a psychotic episode (Briere et al., 1997; Janssen et al., 2004; Shevlin, Dorahy & Adamson, 2007). However, other studies dispute this, claiming the presence of CA to hold no significant difference in the later development of psychosis. Such findings depict similar, if not decreased, prevalence rates of CA in individuals with psychosis when compared to healthy participants (Brown & Anderson, 1991; Cohen, Seeman, Gotowiec & Kopala, 1996; Friedman et al., 2002; Pribor & Dinwiddie, 1992; Ritscher, Coursey & Farrell, 1997; Wurr & Partridge, 1996). However, the supporting literature which found no significant link relied heavily upon data collected from official sources (e.g. Spataro, Mullen, Burgess, Wells & Moss, 2004). Thus, the data used may have

contained a higher amount of abused children who were removed from their environment at an earlier stage and consequently, benefited from receiving earlier treatment, help and support. Subsequently, children in these circumstances were at a lower risk of developing psychosis in adult life.

Another predictor which has also been shown to influence the likelihood of developing psychosis is trauma intensity (Kilcommons & Morrison, 2005; Mullen, Martin, Anderson, Romans & Herbison, 1993; Read, Perry, Moskowitz & Connolly, 2001; Schenkel, Spaulding, DiLillo & Silverstein, 2005; Shevlin et al., 2007). This has been illustrated in several studies; for example, experiencing multiple traumas during childhood has been proven to increase initial risk of psychosis and severity of later symptoms (Shevlin et al., 2007). Additionally, a dose-response relationship between trauma intensity and the risk of developing psychosis has been revealed (Janssen et al., 2004). Individuals were discovered to be five times more likely to develop psychosis if subjected to moderate levels of CA when compared to those without an abuse history. This pattern continued as the severity of abuse intensified, with an estimated 30 times greater chance of developing psychosis for those in the highest frequency category. Thus, the frequency of the trauma as well as the severity can influence the patient's prognosis.

Childhood abuse and symptomatology

Pre-existing research has been able to demonstrate how CA can affect the presentation of psychotic symptoms (e.g. Hammersley et al., 2003; Read et al., 2005; Uçok & Bikmaz, 2007). Large cross-sectional studies have reported higher levels of cognitive deficits and poorer psychosocial functioning in patients with a history of CA, which was reportedly maintained over time (Cusack, Frueh & Brady, 2004; Lysaker, Beattie, Strasburger & Davis, 2005; Read et

al., 2001; Rosenberg, Lu, Mueser, Jankowski & Cournos, 2007). Both CA and neglect have also been connected to an earlier age of onset (Schenkel et al., 2005), frequent relapses and an increased prevalence of psychiatric co-morbidities (e.g. anxiety, depression) (Bifulco, Brown, Moran, Ball & Campbel, 1998; Hirschfeld & Weissman, 2002; Rosenberg et al., 2007). Moreover, an exposure to CA has been associated with higher rates of suicidal thoughts and attempts (Christofferson, Poulsen & Nielsen, 2003), with the detection of CA viewed as a better predictor of suicide compared to depression (Read et al., 2001). Aside from this, dissociative symptoms have often been found in those exposed to CA too (Holowka et al., 2003; Kilcommons & Morrison, 2005; Kim, Kaspar, Noh & Nam, 2006; Lysaker, Meyer, Evans, Clements & Marks, 2001; Mulholland et al., 2008; Ross & Keyes, 2004; Schäfer et al., 2006; Schäfer et al., 2012; Spitzer, Haug & Freyberger, 1997; Vogel et al., 2009a; Vogel et al., 2009b).

More importantly, presenting with a history of CA has been found to influence the presence of positive symptoms (Janssen et al., 2004; Uçok & Bikmaz, 2007). Ross and colleagues (1994) highlighted some of the core symptoms displayed in people who report traumatic childhoods including: auditory hallucinations, ideas of reference, thought insertion, paranoid ideation, reading others' minds and visual hallucinations. In particular, the presence of hallucinations has been frequently reported in this clinical group (Read et al., 2005), with emphasis on experiencing a running commentary from voices (Kennedy et al., 2002; Read, Agar, Argyle & Aderhold, 2003; Ross, Anderson & Clark, 1994). Large-scale studies have also illustrated how childhood abuse and neglect can significantly increase the risk of experiencing hallucinations in all age categories (Hammersley et al., 2003; Read et al., 2003; Read et al., 2005; Uçok & Bikmaz, 2007; Whitfield et al., 2005). Additionally, Romme

and Escher (2006) revealed that 77% of people with a diagnosis of schizophrenia recognised the voice heard, disclosing that it related back to the abuse experienced in childhood. The presence of tactile hallucinations was also notably elevated in people who had received sexual and physical abuse; this was surprising as it is generally uncommon (Shevlin et al., 2007). Thus, positive symptoms, particularly hallucinations, seem to present strongly in those reporting CA.

Although the existence of positive psychotic symptoms has often been noted in the literature, negative symptoms have too been shown to occur (Kim et al., 2006; Read et al., 2005; Schenkel et al., 2005). To what extent the role of CA plays in negative symptomatology is unknown due to mixed findings; for example, a slightly lower amount of negative symptoms has been found in various childhood abuse subgroups when compared to controls (Goff et al., 1991; Ross et al., 1994). Conversely, other studies report no difference between patient and control groups (Famularo, Kinscherff & Fenton, 1992; Herman & Schatzow, 1987; Lysaker et al., 2001; Resnick, Bond, Mueser, 2003). Vogel et al (2011) conducted a study to further explore whether negative symptoms were increased in those who had experienced childhood abuse and neglect. The study revealed significant results which indicated a link between negative symptoms and CA. Furthermore, the researchers argued that higher levels of neglect (particularly physical neglect) posed a greater risk than childhood abuse. Nonetheless, there was a significant positive correlation between the presence of any childhood trauma and negative symptoms.

In the majority of cases, patients report the experience of depression in the prodromal phase (before the first psychotic episode) regardless of exposure to CA (Birchwood et al., 2000). Over half of patients commonly describe experiencing post-psychotic depression due

to a number of adjustment issues of receiving a diagnosis too (Birchwood, 2003). Therefore, this highlights the presence of a core negative symptom, which in many cases can run through the course of psychosis (pre- and post-psychosis). However, the literature is still unclear about the additive impact childhood abuse can have on negative symptomatology. Consequently, various suggestions have been put forward to try and decipher this relationship (e.g. Harrison & Fowler, 2004).

There are thought to be many variables which could influence the relationship between CA and FEP, for example gender. Females have been found to be at an increased risk of developing FEP when exposed to trauma, in particular, childhood physical and sexual abuse (Fisher et al., 2009). Prevalence rates identified suggest 30-60% of females with a schizophrenic spectrum disorder report childhood sexual abuse, which is a significant increase from males (25-30%) (Lysaker et al., 2005). However, childhood physical abuse was discovered to have a stronger and more robust effect for psychosis in women (Fisher et al., 2009). This was also supported by findings presented in the female control group, whereby women disclosed severe physical abuse along with higher rates of psychotic-like symptoms. Hence, this suggests the existence of a continuum model of psychosis, specifically in females (Johns et al., 2004). Despite females reporting higher levels of CA, it has been thought that males are in fact, more severely affected (Aas et al., 2011), with a higher display of negative symptoms, such as affective flattening (Carpenter & Kirkpatrick , 1988; Gur, Petty, Turetsky & Gur, 1996; Maric, Krabbendam, Vollebergh, de Graaf & van Os., 2003; Nasrallah & Wilcox, 1989; Preston, Orr, Date, Nolan & Castle, 2002; Ring et al., 1991; Schultz et al., 1997; Shtasel, Gur, Gallacher, Heimberg & Gur, 1992; Thorup, Waltoft, Pedersen, Mortensen & Nordentoft, 2007).

Although a relatively new area, the literature investigating the effects CA can have on psychosis has flourished and developed. The additive risk childhood abuse may have on the later development of psychosis has been the theme highlighted within the research field. Interestingly, CA has been shown to impact symptomatology, with specific traumas increasing the prominence of certain symptoms (e.g. tactile hallucinations, dissociative symptoms). In particular, the presence of positive symptoms has been thoroughly researched, with a strong emphasis on hallucinatory behaviour. Additionally, studies have explored the affect CA can have on cognition and dissociative symptoms; however, negative symptoms have been understudied and findings reported inconsistent. Subsequently, this paper aimed to examine this area further in order to help add to previous literature, positioning the focus solely on negative symptoms in psychosis. Furthermore, this paper also sought to investigate whether negative symptoms were significantly influenced by experiencing CA and if so, did it differ between genders (Addington, Addington & Patten, 1996; Dworkin 1990; Usall et al., 2001). Consequently, this study aimed to contribute to the already growing CA-psychosis literature and to continue towards a better understanding of the impact abuse in childhood can cause.

Method

Design

The study consisted of a cross-sectional design comprised of two sections. The first section consisted of interviewer-rated questions, followed by the second part involving several self-report measures. Participants were recruited from the Early Intervention Service (EIS) in the Birmingham and Solihull Mental Health NHS Foundation Trust. Ethical approval was granted from the NRES Committee West Midlands – The Black Country on the 29th June 2013 (REC reference: 13/WM/0213).

Participants

The EIS offer a clinical service for young people (aged 16-35 years) presenting with first-episode psychosis. For this study, 69 young people presenting with psychotic disorders were recruited. Predominantly, participants had received a diagnosis of psychosis (63.8%), followed by schizophrenia (21.7%: including schizoaffective disorder) and bipolar disorder (10.1%). Of this sample, 50 participants were male, with ages ranging from 17-36 years old (Mean: 25.40 years; SD: 4.77). Over half of the sample was of a white British ethnicity (59.4%). Additionally, the participants often lived at home (55.1%), were not currently in a relationship (76.8%) or in education or employment (60.9%). Forty percent of the sample had completed their GCSE/NVQ Level 1 or 2 (41.2%); followed by a further 25% who received A-Level/GNVQ/BTEC/NVQ Level 3 qualifications. Cannabis use was disclosed by 73.9% of the sample.

Young people were excluded from the study if they were unable to provide informed consent or lacked the English capacity to understand and participate in the assessment.

Materials

Data used for this investigation were taken from a larger study, aimed at exploring the psychological and neurobiological overlap between psychosis and autism. Results focusing on this will be reported elsewhere. Subsequently, measures which focused on unrelated areas were excluded for this study.

Demographics:

Basic questions were asked including: cannabis use and age of first use, highest level of education and current work status, accommodation status, history of childhood mental health problems.

Psychotic Symptoms:

The Positive and Negative Syndrome Scale (PANSS; Kay, Fisbein & Opler, 1987) aims to provide a comprehensive measure of the severity of psychotic symptoms. The scale consists of 18 items gathered from the Brief Psychiatric Rating Scale (Overall & Gorham, 1962) and a further 12 items from the Psychopathology Rating Scale (Singh & Kay, 1975). Items measured positive and negative symptoms, in addition to general psychopathology. Each symptom was rated from 1 (absent) to 7 (extreme). Scores were collected to produce a total score for each subscale (positive, negative and general psychopathology), as well as the overall PANSS total score (ranging from 30 to 210). A higher score indicates greater symptom severity. This scale has received high levels of inter-rater reliability, with good levels of internal consistency reported in the positive (global $\alpha = 0.62$), negative (global $\alpha = 0.92$) and general psychopathology scale (global $\alpha = 0.55$) (Peralta & Cuesta, 1994). Additionally, the scales showed strong concurrent validity when assessed with two clinically valid scales currently used to assess schizophrenia (Peralta & Cuesta, 1994).

Childhood Trauma:

The Brief Childhood Trauma Questionnaire (CTQ: Bernstein et al., 2003; Bernstein & Fink, 1994) was administered to examine the presence of CA and neglect. The scale consists of 28 self-report questions, tapping into five domains: childhood physical, sexual and emotional abuse and both physical and emotional neglect. Furthermore, an additional three questions were included within the CTQ in order to screen for false-negative trauma reports. Respondents, whether from a clinical or non-clinical sample, score each item on a 5-point scale from 1 ("Never true") to 5 ("very often true). Scores are then added up to give an overall total, as well as individual breakdowns for each subgroup of CA. From this, scoring is classified into levels of severity according to the manuals cut-off points, ranging from: 'absent', 'low', 'medium' and 'high'. The CTQ has received high levels of internal consistency (α= 0.95), alongside strong levels of construct and discriminant validity (Bernstein & Fink, 1998; Fink, Bernstein, Handelsman, Foote & Lovejoy, 1995).

Procedure:

Participants were provided with information regarding the study, detailing what it involved and its confidential nature. The consent form was then completed before beginning the semi-structured interview (See Chapter 2: Meeting Participants for materials). The interview was split into three sections, with breaks offered throughout. On average, the interview stage lasted approximately one hour and thirty minutes. After the interview, the participant then completed the self-report questionnaire. Once finished, the participant was thanked for their participation and reimbursed £15 for their time.

Analysis:

Factor analysis was used to reduce the PANSS dataset into homogeneous sets allowing for the production, for this particular study, of the 'negative symptom' factor. From this, the relationship between previous childhood abuse and the incidence of negative symptoms could be investigated. The analysis revealed eight factors, contrasting significantly from previous literature which often cited the presence of five factors (one being the 'negative symptom' factor). Through inspection of the data, it was clear that negative symptoms were being clustered together.

The core assumptions of factor analysis were examined to ensure they were met. The sample size was found to be adequate (Kaiser-Meyer-Olkin =0.618), alongside a significant result for the Bartletts test of sphericity (p=.001). However, the determinant result was below the recommended value of 0.00001 (N=2.819 E-010). Additionally, the correlation matrix was explored as variables correlating too highly or lowly with one another can cause problems (Field, 2009). In this case, a large number of correlations within the matrix were below 0.3, subsequently indicating that the variables did not measure the same underlying constructs (Tabachnick & Fidell, 2001). Thus, although initially the clustering of negative symptoms was noticeable, the core assumptions were not met. Therefore, the eight factor model found was disregarded due to the possible production of erroneous results.

In order to resolve this, the adoption of a similar previous model of the PANSS was sought. The PANSS factor structure has been heavily studied and seems to be unaffected by age, severity of symptoms and chronicity of illness (White, Harvey, Opler & Lindenmayer, 1997). To ensure maximum generalizability, a closely-matched sample was required, sharing similar characteristics with participants in the current study. Emsley et al (2003) met these qualities

and consequently, their factor structure was used. Their study consisted of a larger sample, comprised of 535 patients with early psychosis (Males: 380). The mean age of the participants was 26.0 years (SD: 6.9), similar to that of the current study sample (Mean: 25.4 years; SD: 4.77). The PANSS five factor model produced by this study was felt appropriate due to the similarities in the sample group. Patients recruited for Emsley's study had all received a diagnosis of a schizophrenic disorder in the past 12 months and had a maximum of two lifetime psychiatric hospitalisations. Thus, this matched the current studies sample, which again, looked towards patients who had suffered a psychotic experience with few psychiatric hospitalisations and who had also recently come into contact with Early Intervention Services.

To obtain the five factor structure, Emsley et al. (2003) conducted a principal components factor analysis using equamax rotation. This specific rotation was chosen due to its consistency across studies examining the PANSS scale. The five factors found matched those previously found throughout the PANSS literature (Bell, Lysaker, Beam-Goulet, Milstein & Lindenmayer, 1994; Lançon, Aghababian, Llorca & Auguier, 1998; Lançon, Auquier, Nayt & Reine, 2000; Lépine, Piron & Chapatot, 1989; Mass, Schoemig, Hitschfeld, Wall & Haasen, 2000). Following this, the factors were named: 'Negative', 'Positive', 'Disorganised' (or cognitive), 'Excited' and 'Anxiety/depression'. Cumulatively, the factors explained a total of 54.7% of the variance, with the 'negative' factor accounting for 15.4% of the variance.

The aim of this study was to examine the relationship between CA and negative symptomatology in FEP and therefore, only the negative factor from the structure was used. This factor was made up of eight sections from the PANSS, gathered from the negative and the general psychopathology section. Thus, this consisted of: 'Blunted Affect', 'Emotional

Withdrawal', 'Poor Rapport', 'Passive/Apathetic Withdrawal', 'Spontaneity', 'Motor Retardation', 'Volition' and 'Social Avoidance'.

Results

The presence of CA was found in a subsection of the patients who participated, determined by the CTQ cut-off points for each subscale (Bernstein & Fink, 1998). Out of all the different subsets of abuse types, childhood physical neglect was shown to be the most frequent, with a disclosure from 33 participants. Although the highest reported, only 13 participants (18.8%) experienced severity levels of medium and above. In contrast, 21.7% of participants experienced high levels of childhood emotional neglect and therefore, this subcategory presented with a higher severity level. This was followed by emotional abuse (15.9%), physical abuse (13%) and sexual abuse (5.8%). These findings were based on participants who had experienced medium levels of abuse or higher, as defined by the cut-off points. A visual representation of this can be seen in Table 1. 'Medium' and 'High' levels of abuse are depicted, as well as the overall total of the sample who disclosed abuse (Low to high levels of severity).

Table 1: Visual representation of childhood abuse within the sample

	Physical abuse	Sexual abuse	Emotional abuse	Physical neglect	Emotional neglect
Overall Total	14	10	16	33	23
Medium	1	0	3	4	0
High	8	4	8	9	15

A chi-squared test was then performed to test whether childhood abuse and neglect differed between genders. To conduct the test, childhood physical, sexual and emotional abuse were grouped together, as well as emotional and physical neglect. The results of the

chi-square test revealed the absence of a relationship between gender and CA (X^2(df =1, N=69) = .008, p = .929) and gender and childhood neglect (X^2(df =1. N=69) = .118, p=.731).

The relationship between childhood abuse (sexual, physical, emotional and neglect) and negative psychotic symptoms was then assessed. To test and assess this, a series of correlations were carried out between the negative symptom factor (Mean: 13.60; SD: 5.84; Range: 8-29) and the five groups of CA. Through analysing these findings, it was evident that the CA subgroups did not correlate significantly with the negative symptoms of psychosis. This was also apparent when males and females were viewed separately. Females who had experienced physical neglect appeared to have the strongest correlation coefficient, although this was non-significant (R= 0.346; p= .160). Correlation coefficients and their respective significance levels can be found in Table 2.

Table 2: Pearson's Correlation Coefficients for Childhood Abuse and Negative Symptomatology

	Physical abuse: Total Score	Emotional abuse: Total Score	Sexual abuse: Total Score	Emotional neglect: Total Score	Physical neglect: Total Score
Negative symptoms Correlation Coefficient: Sig.	 .065 .607	 .161 .195	 .189 .129	 .064 .604	 .190 .124
Males Correlation Coefficient: Sig.	 .044 .767	 .176 .232	 .188 .200	 .008 .957	 .117 .423
Females Correlation Coefficient: Sig.	 .134 .596	 .199 .429	 .218 .386	 .176 .485	 .346 .160

Data were further explored visually, through observing the scatterplots. This confirmed the absence of a correlation for all variables (see Appendices at the end of chapter). Subsequently, exploration of the data revealed that CA did not increase or decrease the presence of negative symptoms in psychosis. Therefore, no further statistical analysis was needed.

Discussion

Through analysing the data, it was apparent that variants of CA did not correlate with negative symptoms, neither increasing nor decreasing their presence. Thus, this suggests the absence of a specific type of CA or neglect which leads to higher levels of negative symptoms. Finally, results concluded no relationship between the presence of negative symptoms in FEP and the past exposure to CA, regardless of type. When reviewing previous literature, the study's findings provide additional support for the existence of negative symptoms in those individuals with an abusive childhood. This was especially true for those who reported emotional abuse and neglect. Hence, this confirms documented findings from previous studies who noted this occurrence (Kim et al., 2006; Read et al., 2005; Schenkel et al., 2005). When analysing significant relationships between abuse and negative symptoms though, findings did not emulate those found in Vogel et al. (2011). However, this is the second study of note to have sought to identify the existence of this relationship. Thus, this study contributes to existing research by offering additional insight into the relationship between CA and symptomatology.

There are many justifiable reasons to explain the differences in the results produced between these studies (e.g. Vogel et al., 2011). The current study used the PANSS to measure psychotic symptoms in FEP patients, followed by adopting the negative symptoms factor produced by Emsley et al. (2003). In comparison, the symptoms defined as negative in Vogel's study were gathered from administering the Scale for the Assessment of Negative Symptoms (SANS: Andreasen, 1983). Consequently, the symptoms analysed in each study differed due to the assessment scales used. Thus, the significant findings reported in Vogel's (2011) study may be due to the inclusion of symptoms absent in the current research.

Additionally, the sample size was contrastingly different. A total of 25 psychotic patients and 35 non-psychotic clinical patients were used in Vogel's study, whereas this study used a larger sample of 69 patients with psychosis. Therefore, participants may have generally presented with more negative symptoms (regardless of CA) and therefore, are not representative of the wider population.

One of the key variables thought to influence the relationship between CA and psychosis was gender. Interestingly, although a greater incidence rate of CA was found amongst females, males were found to be more psychologically affected (Maric et al., 2003; Preston et al., 2002; Thorup et al., 2007). Findings were believed to emulate previous research; however when males and females were analysed individually, results proved non-significant. Therefore, findings were not able to support males' increased proneness to higher levels of negative symptoms. This was similarly found in females, where the presence of negative symptoms were not influenced by a traumatic childhood. However, this too, may be due to the size of the sample (N=69; Males: 50; Females: 19). Consequently, replicating these findings on a larger scale will add clarity to whether males are more prone to negative symptoms.

Patients with psychosis experience a variety of positive (e.g. hallucinations), negative (e.g. affective blunting) and secondary symptoms (e.g. anxiety). Various psychological, biological and social factors can influence the symptoms which may present. Subsequently, the experience of childhood abuse and neglect may have a greater influence on positive symptoms, for example auditory hallucinations (Kennedy et al., 2002; Read et al., 2005) and disorganised/cognitive deficits (Lysaker et al., 2005). The exposure to trauma may shield the patients from experiencing high levels of negative symptoms. This concept was raised by

Vogel et al. (2011) who found that childhood trauma and dissociation could act as protective barriers against negative symptoms. Hence, participants in this study may have benefited from this unique factor.

Limitations

Data were collected using both interviewer-rated questions and self-report measures and consequently, has several limitations. During the interview, a relaxed atmosphere ensured the participants felt comfortable disclosing their thoughts and personal information. Although all interviewers were trained on the measures, different styles and techniques may have caused the research to be biased. Unconscious cues may have been used, unknowingly guiding the participants' response. Additionally, respondents may have consciously or unconsciously misrepresented the truth. For example, participants may have felt unable to describe certain behaviours or events that may have occurred due to fear of how the interviewer may perceive them. Imperfect recall may also occur, whereby the participants remember little about an event occurring previously and therefore, may slightly misrepresent the truth.

Within this study, the CTQ involves sensitive questions about events that occurred in their childhood. Therefore, respondents may minimise, exaggerate or distort the existence of childhood abuse. Similarly, the use of self-report questions may lead the respondent to either over- or under-exaggerate the answer to a specific question. For example, this may be due to wanting to be perceived in a favourable light. In addition, the reliability of recalling traumatic events that occurred several years prior to a psychotic episode has been brought into question (Roemer, Litz, Orsillo, Ehlich & Friedman, 1998; Wessely et al., 2003). Although this may be a serious limitation, reports have surprisingly revealed that psychiatric

patients tend to underreport abuse experienced (Briere & Zaidi, 1989; Dill, Chu, Grob & Eisen, 1991; Read, 1997). Moreover, high levels of corroborating evidence were documented in cases of childhood sexual abuse by psychiatric patients (Goodman et al., 1999; Herman & Schatzow, 1987; Meyer, Muenzenmaier, Cancienne & Struening, 1996; Read et al., 2003). However, the possibility of recall bias should be considered.

A common problem shared amongst researchers is the lack of control held over extraneous variables. When working with patients who are experiencing FEP, there are many obstacles which may present. An example of this is the participants' mood which may fluctuate (as in the case of those with bipolar disorder) and therefore may not be representative of their true self. Alongside this, when examining the presence of symptoms, the PANSS only takes into consideration how the participant has been in the last seven days. Thus, clinical reports made on the day of the interview may not accurately portray their normal behaviour. Various cognitive models have argued that individuals' current moods can influence recall of traumatic events (e.g., Gilligan & Bower, 1984). Subsequently, the mood the respondent may be in on the day of the interview may impact the symptoms they report as well as their responses to the CTQ.

Future research

This study provided a much-needed insight into the relationship between CA and negative symptoms. To continue developing knowledge in this relatively new topic area, future studies should look to replicate the study with a larger sample group. The current study analysed a total of 69 participants with FEP in an inner city area. Consequently, the results collected are limited and unrepresentative of the clinical clientele group in question, reducing their generalizability. A larger database would be able to test the subgroups of CA

and neglect to see if the absence of a correlation with negative symptoms is still true. This would be valued work to add clarity to the contradictory findings of the current study and that of Vogel et al. (2011). In addition, using the SANS measure (Andreasen, 1983) alongside the PANSS should be considered as this will provide a clearer indication of whether negative psychotic symptoms are affected by CA and neglect.

A potentially interesting area to explore is whether or not negative symptoms differ between ethnic groups. Studies have highlighted the impact social marginalisation has on creating negative schemas which lead to risk of psychosis (Garety, Kuipers, Fowler, Freeman & Bebbington, 2001). Bhugra and colleagues (1997) highlighted how ethnic minority groups experience higher levels of social adversity and deprivation. Consequently, it may be of use to examine this is more detail to see whether this influences negative symptomatology (Bhugra, Leff, Mallett, Der, Corridan & Rudge, 1997).

Implications

From a research stance, this study offers an exciting new take on how CA and neglect can influence symptomatology. Findings gathered from this research can generate interest in this relatively new area, due to the difference in results compared to Vogel (2011) and the severe lack of existing studies. This study allows for the formulation of various questions regarding negative symptoms, alongside building interest in other factors which may too, be influenced by CA (e.g. disorganised, anxiety/depression, excitement symptoms).

Within the clinical world, understanding CA and neglect and how the effects of this can continue to impact later life is important. Thus, the provision of more information on whether CA can influence FEP and the symptoms they present with is very useful. This study

has been able to highlight the absence of a relationship between CA and negative symptoms. This can therefore be useful for new admissions with FEP when trying to understand their symptomatology and derive formulations to help provide suitable treatment plans.

In conclusion, this study explores a relatively untouched area, providing new evidence between CA and negative symptoms. Knowledge gained through research helps to generate suitable ways to best care for patients (Read, McGregor, Coggan & Thomas, 2006). Therefore, although this study has several limitations (e.g. sample size) the results gathered are able to widen current knowledge on the link between CA and FEP symptomatology; thus, is important for both researchers and clinicians. Nevertheless, future research into this area is needed to further clarify findings and in turn, add to the clinical world.

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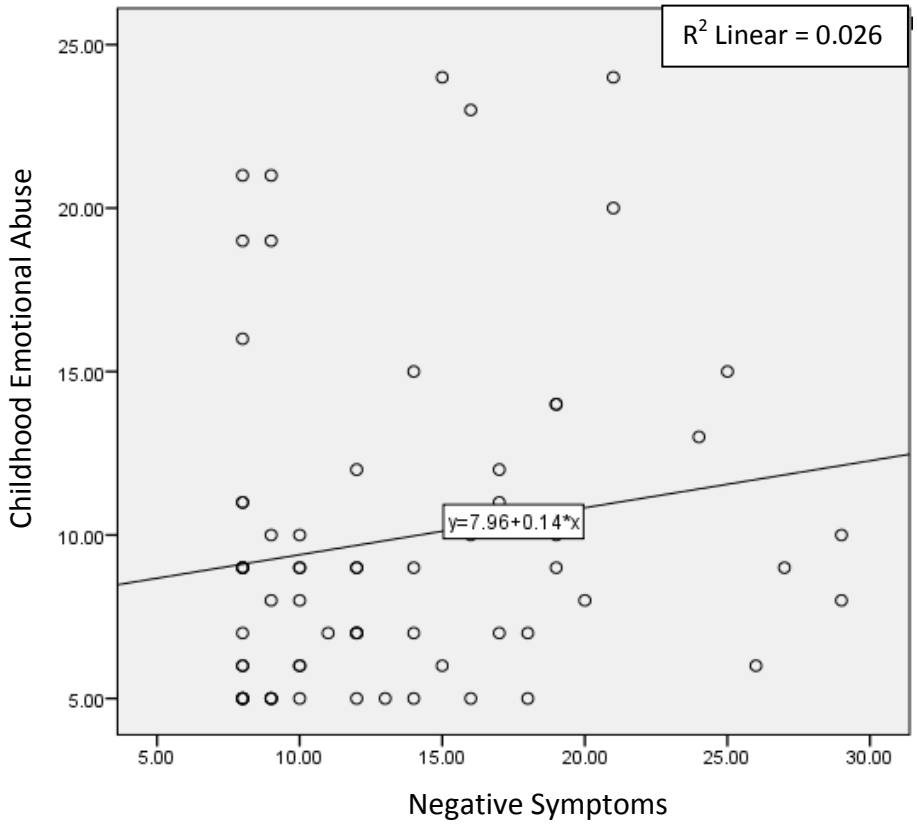
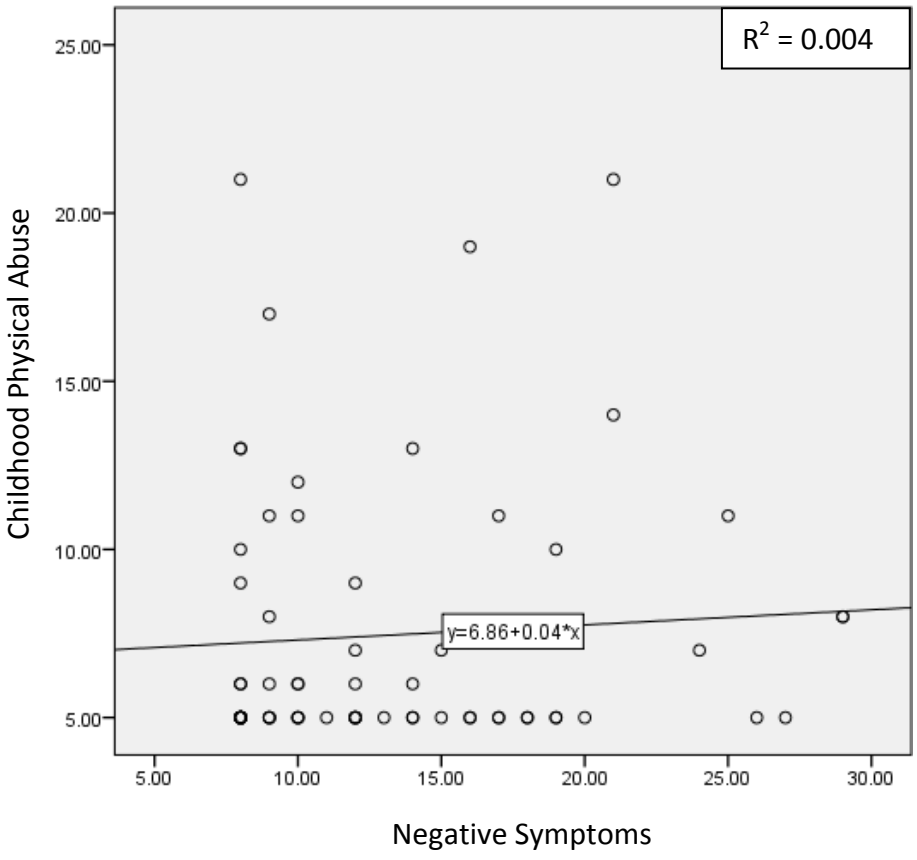
Appendices: Scatterplot diagrams illustrating childhood abuse and negative symptoms.

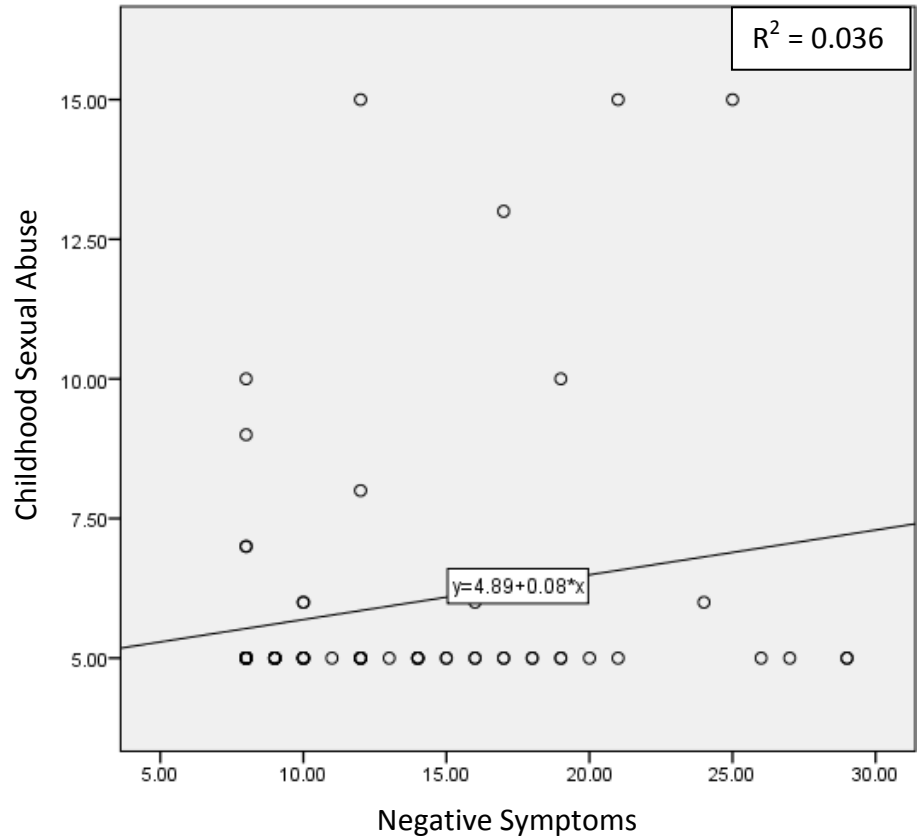
Graph 1: Childhood emotional abuse and negative symptoms



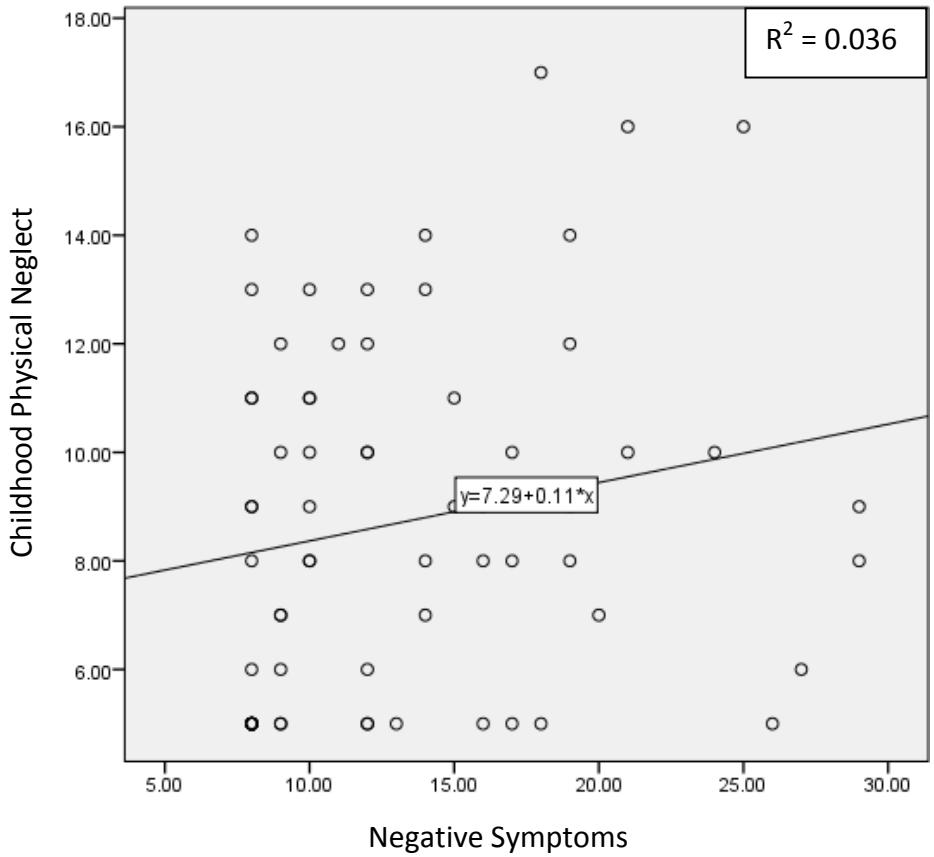
Graph 2: Childhood physical abuse and negative symptoms



Graph 3: Childhood sexual abuse and negative symptoms



Graph 4: Childhood physical neglect and negative symptoms



Graph 5: Childhood emotional neglect and negative symptoms