MOTIVATION-RELATED PREDICTORS OF PHYSIOLOGICAL STRESS REACTIVITY

by

AIDEN JAMES CHAUNTRY

A thesis submitted to the University of Birmingham

for the degree of

MASTER OF SCIENCE BY RESEARCH

School of Sport, Exercise and Rehabilitation Sciences

College of Life and Environmental Sciences

The University of Birmingham

September 2018

ABSTRACT

This thesis used laboratory studies to examine the relationship between physiological reactivity to acute stress and motivation-related behavioural manifestations. Chapter 2 reported that lower blood pressure reactivity was associated with dysfunctional behavioural perseverance. This chapter also revealed that self-report and behavioural perseverance measures, in general, do not correlate. Chapter 3 demonstrated that poor self-reported resilience was related to blunted heart rate reactivity. Chapter 4 is slightly different in that it is a methodological chapter, it outlines the approach for a future study which will examine the relationship between physiological stress reactivity and fatigue in Anti-Neutrophil Cytoplastic Antibodies (ANCA)-associated vasculitis patients. Overall, the empirical research reported in this thesis adds further support that blunted stress response patterns are maladaptive and relate to adverse behavioural outcomes that appear to reflect motivational dysregulation. This thesis also extends the literature by providing direct evidence that attenuated reactivity can predict both self-reported and objectively measured motivation-related behavioural outcomes.

DEDICATION

To my Nan, Peggy. It would be impossible to ever thank you enough for the ways in which you have helped and supported me, right from day one. Without you I would not be where I am today that is for sure. I will never forget everything you have done for me, nor the great times we shared. As a small token of my appreciation, this thesis is dedicated in your memory.

ACKNOWLEDGEMENTS

There are, of course, many people I must thank and acknowledge for their help and support during my MSc by research degree. First and foremost, my primary supervisor Professor Anna Whittaker. I really could not have asked for a better supervisor. You introduced to the world of cardiovascular reactivity and inspired me to peruse a research career in this area. Without your help, support and advice, producing this thesis would not have been possible, not without a mental breakdown anyway! I consider myself very lucky to have been under your supervision for the past 2 years and look forward to hopefully working with you at some point again in the future. Next, my secondary supervisor, Dr Sarah Williams, thank you for providing feedback on my work and for your comments and guidance throughout this past year. I would also like to thank Professor Joan Duda, the employment opportunity that you provided for me has allowed me to become a more well-rounded researcher and has given me important skills to take forward into the next step of my career.

I must also acknowledge the many friends I have made throughout my time at the University of Birmingham. The past four years really have been the best years of my life. The list is endless, but a special mention must go to the “SportEx lads”, to the guys of Block 7 Maple Bank (and honorary members), to the “Hubert Estate” (including the extended family), to the BEDsoc FC lads, and the boys of “Big John”.

Finally, to my family, thank you for always being there for me and supporting me in everything I do (I promise I will get a proper job one day!). Special recognition must however go to my mum Sheena; for the sacrifices you have made, the love you have given and the support you have provided I shall be eternally grateful. It is not an overstatement that I owe everything to you. Similarly, my step dad Jon; you have been there for me every step of the way providing help, guidance, and the occasional food package; things I will never forget.

TABLE OF CONTENTS

Chapter 5 General discussion

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

ANCA	Anti-neutrophil Cytoplasmic Antibodies
ANOVA	Analysis of Variance
AUCg	Area Under the Curve
BMI	Body Mass Index
BP	Blood Pressure
BPM	Beats Per Minute
CD	Compact Disc
CD-RISC	Connor-Davison Resilience Scale
CP	Cold Pressor
CRAVE	Cardiovascular Reactivity And Vasculitis Experience
DBP	Diastolic Blood Pressure
ELISA	Enzyme-Linked Immunosorbent Assay
fMRI	functional Magnetic Resonance Imaging
Grit-s	Short Grit Scale
HADS	Hospital Anxiety and Depression Scale
HPA	Hypothalamic-Pituitary-Adrenal
HR	Heart Rate
ICC	Intraclass Correlation Coefficient
MFI-20	20-Item Multidimensional Fatigue Inventory
mmHg	Millimetres of Mercury
NHS	National Health Service
PASAT	Paced Auditory Serial Addition Test
RPE	Rated Perceived Exertion
SAM	Sympathetic-Adrenal-Medullary
SBP	Systolic Blood Pressure
SD	Standard Deviation
SE	Standard Error
SES	Socio-Economic Status
SF-36	36-Item Medical Outcomes Survey, Short-Form

CHAPTER ONE

GENERAL INTRODUCTION

Background

Early research concluded that stress is a non-specific response that drastically perturbs homeostasis (Selye, 1956), a phenomenon that has long been viewed as fundamental to health and human survival (Cannon, 1915). For this reason, stress was, and still is, viewed with negative connotations. However, as Selye argued, the stress response is adaptive *per se*, and without one humans would cease to exist. Additionally, he also put forth the suggestion that severe or prolonged responses pose a threat to health and well-being (Selye, 1956). This early work into stress has fuelled many years of research, with the literature now supporting Selye's claims. Those with blunted and exaggerated stress responses appear to be at greater risk of developing adverse health and behavioural outcomes (Phillips, 2011). This forms the basis of this thesis.

Stress exposure can be broken down into chronic (long-term) stress, for example, as a caregiver, and acute (short-term) stress, for example, during laboratory mental arithmetic tasks. Although both have received research attention, this thesis will focus on the latter. To cope with stress, the human body has two main stress response systems; the sympathetic-adrenal-medullary (SAM) axis, whose activation governs changes in blood pressure and heart rate (Lovallo, 2005) and the hypothalamic-pituitary-adrenal (HPA) axis, which alters circulating cortisol concentrations (Kudielka & Wüst, 2010). During episodes of stress, specific neural structures assess the threat and adjust patterns of autonomic and endocrine outflow accordingly (Lovallo, 2016). However, like many biological systems, there are large individual differences; SAM and HPA output during stress is hugely heterogenous (Carroll, 1992) which appears to be a result of genetic (Wu, Snieder, & de Geus, 2010) and environmental (Lovallo, Farag, Sorocco, Cohoon, & Vincent, 2012) interactions (Lovallo et al., 2016). Nevertheless, despite this biological variability, at the individual level the

magnitude of physiological responses demonstrate high levels of temporal stability (Ginty, Gianaros, Derbyshire, Phillips, & Carroll, 2013; Manuck & Schaefer, 1978). Thus, individuals can broadly be categorised as either low, moderate or high physiological responders to stress, which is significant because each pattern of response has its own associated health and behavioural correlates (Phillips, 2011).

Exaggerated reactivity and health

Research into exaggerated reactivity and health is underpinned almost entirely by "the reactivity hypothesis", or the postulation that consistently exaggerated cardiovascular responses to acute stress are implicated in the aetiology of cardiovascular pathologies, primarily hypertension (Obrist, 1981). There is a large and compelling literature comprising both cross-sectional and prospective studies that support the hypothesis (Carroll et al., 2001; Carroll et al., 1996; Carroll, Ginty, Painter, et al., 2012; Carroll, Phillips, Der, Hunt, & Benzeval, 2011; Carroll, Ring, Hunt, Ford, & MacIntyre, 2003; Markovitz, Raczynski, Wallace, Chettur, & Chesney, 1998; Matthews et al., 2004; Treiber et al., 2003), using data from large epidemiological projects, including the West-of-Scotland Twenty-07 study, the Dutch Famine Birth Cohort, the Whitehall II study, the CARDIA study, and the Caerphilly study. Importantly, this evidence shows that the positive relationship between reactivity and hypertension has remained intact over many years of research, across different methodologies and in diverse populations. In addition, meta-analyses and reviews also attest to this association (Chida & Steptoe, 2010; Schwartz et al., 2003; Treiber et al., 2003) and confirm the robustness and validity of the reactivity hypothesis. Further, this stress response pattern is not exclusively associated with hypertension but is also related to poor neuronal efficiency (Wawrzyniak, Hamer, Steptoe, & Endrighi, 2016), atherosclerosis (Barnett, Spence, Manuck, & Jennings, 1997; Everson et al., 1997; Kamarck et al., 1997), left ventricular hypertrophy

(Allen, Matthews, & Sherman, 1997; Georgiades, Lemne, De Faire, Lindvall, & Fredrikson, 1997) and even cardiovascular disease mortality (Carroll, Ginty, Der, et al., 2012). Evidently, this physiological response pattern is highly maladaptive.

Possible mechanisms underpinning the effects of exaggerated reactivity on health

Several potential mechanisms can explain the link between exaggerated reactivity to acute psychological stress and cardiovascular pathology. First, during exercise there is a need for sharp increases in heart rate (HR) and blood pressure (BP) to match the augmented metabolic demand for oxygen induced by physical activity and increased muscle activity (Astrand, Cuddy, Saltin, & Stenberg, 1964). However, during psychological stress there is only a slight metabolic demand, if any (Balanos et al., 2010). Therefore, exaggerated physiological responses to this type of stress appear to be metabolically unjustified (Balanos et al., 2010; Carroll, Phillips, & Balanos, 2009; Turner & Carroll, 1985). It has been suggested that this this cardiovascular-metabolic disengagement leads to vulnerability by placing the cardiovascular system under superfluous amounts of stress, which over time can lead to wear and tear and increased susceptibility to cardiovascular disease (Carroll, Turner, & Prasad, 1986; Carroll, Phillips, et al., 2009). In addition to cardiovascular-metabolic explanations, there also mechanisms put forth which centre around exaggerated reactivity being associated with: maladaptive lipoprotein profiles (Howes, Abbott, & Straznicky, 1997), greater insulin resistance (Waldstein & Burns, 2003) and increased inflammatory response patterns (Danesh et al., 2004). Further, although exaggerated cortisol reactivity has received less attention, it too is associated with cardiovascular disease (Girod & Brotman, 2004) and this can possibly be explained by increased coronary artery calcification (Hamer, O'Donnell, Lahiri, & Steptoe, 2010) and associated elevations in blood pressure (Hamer & Steptoe, 2012).

Blunted reactivity

At the other extreme of the cardiovascular reactivity continuum is blunted or low reactivity. Given that this cardiovascular response pattern is coupled more closely with the lower metabolic demands associated with psychological stress, i.e., is more metabolically justified (Carroll, Phillips, et al., 2009; Turner & Carroll, 1985), it is perhaps easy to see why this response pattern was assumed to be benign or even protective (Carroll, Lovallo, & Phillips, 2009). However, even many years ago in the very early stages of stress research, Selye argued that stress responses are adaptive and thus, by implication, it could be taken that he also believed that not having a stress response i.e., blunted reactivity, would be maladaptive. Importantly, there is now a convincing body of literature which supports this (Carroll, Lovallo, et al., 2009; Phillips, 2011). With closer examination of the physiology, it is not surprising that this response pattern is potentially damaging; the stress response activates the cardiovascular system and adrenal medulla in preparation for the fight-or-flight response and increases cortisol output into the circulation to assist in liberating stored energy (Carroll, Ginty, Whittaker, Lovallo, & de Rooij, 2017). Therefore, from an evolutionary perspective without these two biological responses in the face of danger or stress, it is easy to see why non-responding would not be adaptive and might put such individuals at greater risk of poor health.

Blunted reactivity and health

The same epidemiological studies that link exaggerated reactivity with negative health outcomes, as well as separate laboratory studies, also implicate blunted reactivity in the development of negative health outcomes: depression (Phillips et al., 2011; Salomon, Clift, Karlsdóttir, & Rottenberg, 2009; York et al., 2007), anxiety (de Rooij, Schene, Phillips, & Roseboom, 2010), obesity (Carroll, Phillips, & Der, 2008; Phillips, Roseboom, Carroll, & De

Rooij, 2012) and poor self-reported health (de Rooij & Roseboom, 2010; Phillips, Der, & Carroll, 2009). Interestingly, these correlates, like an exaggerated response pattern, are associated with cardiovascular pathology (Guh et al., 2009; Stewart et al., 2017; Van der Kooy et al., 2007).

Blunted reactivity and addictions

In addition to adverse health outcomes, blunted reactivity is also associated with negative health behaviours, in the form of addictions. For example, an attenuated stress response pattern is consistently evidenced in smokers (Al'Absi, 2006; Al'Absi, Wittmers, Erickson, Hatsukami, & Crouse, 2003; Girdler, Jamner, Jarvik, Soles, & Shapiro, 1997) including those wearing nicotine patches (Girdler et al., 1997) and can predict relapse in those who have recently quit (Al'Absi, 2006). This latter study is important as it shows that physiological blunting is associated with addiction *per se*, rather than a direct result of temporary abstinence during cessation. In addition to cigarette addiction, alcohol dependent individuals show blunted cardiovascular responses to acute stress when compared to those without the dependency (Lovallo, Dickensheets, Myers, Thomas, & Nixon, 2000; Panknin, Dickensheets, Nixon, & Lovallo, 2002). Interestingly, attenuated reactivity is also observed in the descendants of alcoholic parents without an alcohol addiction themselves (Moss, Vanyukov, Yao, & Kirillova, 1999; Sorocco, Lovallo, Vincent, & Collins, 2006). This demonstrates that blunted reactivity as a phenomenon manifests prior to addictive behaviour rather than being a cause of it, and, again, contests the assumption that blunted reactivity is a biological outcome from substance abuse or abstinence from such substances. Further, to confirm this, blunted reactivity is also characteristic of those with certain non-substance dependencies: exercise (Heaney, Ginty, Carroll, & Phillips, 2011), disordered eating (Ginty, Phillips, Higgs, Heaney,

& Carroll, 2012; Koo-Loeb, Pedersen, & Girdler, 1998) and gambling (Paris, Franco, Sodano, Frye, & Wulfert, 2010).

Blunted reactivity as a marker of motivational dysregulation

Although initially appearing diverse, it has been hypothesised that the correlates of blunted physiological reactivity are similar in that they reflect motivational dysregulation or a dysfunction in the fronto-limbic brain regions associated with motivation and goal-directed behaviours (Carroll, Ginty, Whittaker, Lovallo, & de Rooij, 2017; Carroll, Lovallo, et al., 2009; Phillips, 2011). This extends to suggest that blunted reactivity may actually manifest as a peripheral marker for central motivational dysfunction (Carroll, Lovallo, et al., 2009; Lovallo, 2006). There is evidence from functional Magnetic Resonance Imaging (fMRI) studies which attests to this hypothesis; motivation-related brain regions, for example, the anterior and posterior cingulate cortex and amygdala (Bush, Luu, & Posner, 2000; Hagemann, Waldstein, & Thayer, 2003; Lovallo, 2005a) are hypo-activated or deactivated in blunted responders during exposure to acute bouts of stress (Gianaros, May, Siegle, & Jennings, 2005; Ginty et al., 2013). In addition, those with depression and obesity, which have already been outlined as correlates of blunted reactivity, show blunted frontal and subcortical limbic activity in response to anticipatory and consummatory food reward (Stice, Spoor, Bohon, & Small, 2008) and when observing negative arousal images (Holsen et al., 2011), respectively. Interestingly, alongside motivational processes, frontal and subcortical brain regions also support: cardiovascular control, physiological stress responses, autonomic regulation and behavioural processes (Bush et al., 2000; Carroll, Lovallo, et al., 2009; Hagemann et al., 2003; Lovallo, 2005a). This therefore suggests a link between the brain, cardiovascular reactivity and general/motivation-contingent behaviours.

Blunted reactivity and behaviour

As research suggests that blunted reactivity can predict behavioural outcomes in the form of dependencies, it is possible that this response pattern can also signal general manifestations of poor behavioural regulation. Although in the early stages, there is now emerging evidence to support this contention; individuals with high impulsivity/impaired response inhibition (Allen, Hogan, & Laird, 2009; Bennett, Blissett, Carroll, & Ginty, 2014; Bibbey, Ginty, Brindle, Phillips, & Carroll, 2016; Muñoz & Anastassiou-Hadjicharalambous, 2011) and externalising psychopathology i.e., behavioural disorders typified by disinhibition (Heleniak, McLaughlin, Ormel, & Riese, 2016) exhibit diminished physiological reactivity to acute stress.

Blunted reactivity and motivation-related behaviours

Aligned with the motivational dysregulation hypothesis, there is now preliminary evidence which implicates hypoactive stress response patterns with negative motivation-related outcomes. For example, blunted responders perform more poorly during lung function spirometry assessments (Carroll et al., 2013; Carroll, Bibbey, Roseboom, et al., 2012) which require motivation and effort to register a high reading (Crim et al., 2011). However, interestingly, these individuals are not consciously aware of any differences in motivation/effort (Brindle, Whittaker, Bibbey, Carroll, & Ginty, 2017) and do not self-report differences in task engagement (Bibbey et al., 2016; Ginty, Phillips, Higgs, et al., 2012). Thus, it appears that those with blunted reactivity may be unconsciously less motivated than their exaggerated counterparts, and, if this is the case, blunted reactivity could be a useful marker in predicting deficiencies in motivation-governed behaviours. However, as yet, only a limited number of motivation-related behavioural manifestations have been explored in parallel with physiological reactivity.

Overview of the present thesis

Thus, the present thesis explored how physiological reactivity to acute stress is associated with motivation-related behaviours. The second chapter examined the relationship between cardiovascular reactivity to acute stress and self-reported and behavioural perseverance. It also investigated whether self-reported and behavioural perseverance correlated. Using the same dataset and methodological approach as the second chapter, the third chapter explored whether resilience and cardiovascular reactivity are related. The fourth is a methodological chapter which outlines the approach for the planned study "CRAVE" (Cardiovascular Reactivity And Vasculitis Experience). This research will examine whether cardiovascular and cortisol reactivity is related to fatigue, and related symptoms, in vasculitis patients. The sections below briefly outline the justification for each of the studies that constitute this thesis, however, each is discussed in more depth within the individual chapters. The exception to this is the fourth chapter, as a methodical chapter there is no comprehensive introduction and thus there is a more exhaustive justification presented below.

Cardiovascular reactivity and perseverance (Study 1, Chapter 2)

Perseverance is an adaptive behaviour with research highlighting its importance during academic/career progression (Andersson & Bergman, 2011) and for general health and well-being (Abrantes et al., 2008; Murphy, Stojek, & MacKillop, 2014; Quinn, Brandon, & Copeland, 1996; Steinberg et al., 2012). As blunted reactivity has been associated with poor behavioural (Bibbey et al., 2016) and motivational (Carroll et al., 2013) regulation, there is reason to believe it might also be related with poor perseverance. Indeed, those with blunted reactivity are less likely to complete the entirety of studies i.e., shun follow up tasks (Ginty, Brindle, & Carroll, 2015) and are more likely to relapse during substance cessation (Al'Absi,

2006; Back et al., 2010; Junghanns et al., 2003; Lovallo, 2006). Although these are not direct perseverance measures, this research, on the whole, suggests that blunted reactivity may be characteristic of those with lower perseverance. If this finding is consistent in the present study, a simple stress test could have prognostic value in identifying those who unconsciously have low perseverance and hence may need extensive support during situations which typically require high levels of perseverance, for example, substance cessation (Abrantes et al., 2008; Steinberg et al., 2012).

Cardiovascular reactivity and resilience (Study 2, Chapter 3)

Similarly, resilience or "personal qualities that enable one to thrive in the face of adversity" (Connor & Davidson, 2003, *P*.76) may also be related to cardiovascular reactivity. Resilience is a key stress protection mechanism (Bonanno, 2004) important in a variety of settings such as elite sport (Sarkar & Fletcher, 2014) and in health and well-being (Min, Lee, Lee, Lee, & Chae, 2012; Min, Lee, & Chae, 2015; O'Rourke, 2004). The literature surrounding the reactivity-resilience relationship is highly contradictory; positive relationships have been evidenced (Galatzer-Levy et al., 2014), alongside negative (Ruiz-Robledillo, Romero-Martínez, & Moya-Albiol, 2017) and null (Black, Balanos, & Whittaker, 2017) associations. This seems partly attributable to small sample sizes and the lack of statistical adjustment for potential confounding variables, which, overall, limits the ability to draw any firm conclusions with respect to this association. Therefore, Study 3 will address these limitations. In line with the model of motivational dysregulation, if a consistent positive relationship manifests, enhancing resilience might lead to a more adaptive pattern of cardiovascular reactivity in the face of stress.

Physiological reactivity and fatigue in patients (Methodological approach, Chapter 4)

Fatigue is a negative phenomenon associated with motivation (Boksem, Meijman, & Lorist, 2006) with physical, cognitive, emotional and functional components (Dittner, Wessely, & Brown, 2004). Fatigue manifests in a wide range of medical disorders (Donovan, Jacobsen, Small, Munster, & Andrykowski, 2008; Stone, Richards, & Hardy, 1998), hinders functional ability (Ream & Richardson, 1996) and negatively impacts quality of life (Basu et al., 2014). In vasculitis patients, fatigue is identified as the greatest burden of the disease, more so than physical symptoms (Herlyn, Hellmich, Seo, & Merkel, 2010) and is also the primary origin of poor quality of life (Basu et al., 2014). Therefore, it would be easy to believe that fatigue is an important marker of disease activity in those with ANCA-associated vasculitis. However, evidence suggests that fatigue does not always correlate with disease severity/activity (Basu et al., 2013; Hajj-Ali et al., 2011). Thus, fatigue may be a manifestation of something other than the disease itself, such as motivational processes. Further, research suggests that fatigue in ANCA-associated vasculitis patients is centrally rather than peripherally governed. For example, patients report an increased rating of perceived exertion (RPE), yet record reduced voluntary activation of muscle during contractions and give-up sooner on endurance tasks compared to controls, which, cannot explained by physiological differences (McClean et al., 2016). These tasks also require motivation for success (McCormick, Meijen, & Marcora, 2015; McNair, 1996). Interestingly, increased RPE was also found to be associated with reduced motivation measured via the 36-item Medical Outcomes Short-Form survey (SF-36; Ware & Sherbourne, 1992), a questionnaire which will be used in Study 3. Thus, although fatigued individuals have an increased perception of effort they actually perform more poorly during motivation-contingent tasks, which aligns with previous research (Carroll, Bibbey, Roseboom, et al., 2012; Carroll et al., 2013), and report lower self-reported motivation. In

addition, mental fatigue is also associated with a lack of motivation in other studies (Boksem et al., 2006; Chaudhuri & Behan, 2000) to the extent where improving motivation can help to ease the effect of mental fatigue (Boksem et al., 2006). Overall, this highlights the possibility that fatigue, as a centrally governed mechanism, is associated with central motivational dysregulation; fatigue could be yet another correlate of blunted physiological reactivity which manifests as a result of central dysfunction.

As previously presented, blunted physiological reactivity is associated with depression (Phillips et al., 2011; Salomon, Clift, Karlsdóttir, & Rottenberg, 2009; York et al., 2007), anxiety (de Rooij et al., 2010) and poor self-reported health (de Rooij & Roseboom, 2010; Phillips, Der, & Carroll, 2009). Given the association between these outcomes and fatigue (Brown & Kroenke, 2009; Demyttenaere, De Fruyt, & Stahl, 2005; Dolan & Kudrna, 2015), it is possible that individuals with or at risk of developing fatigue will also exhibit attenuated physiological responses to acute stress. There is some prior evidence to support this, for example, those reporting high exhaustion/burnout showed blunted cortisol responses to stress (Jönsson et al., 2015; Kudielka et al., 2006). But not all of literature supports this contention, for example, null relationships have also reported between exhaustion and HR and cortisol reactivity (Nicolson & Van Diest, 2000). However, it is important to note that these studies examined vital exhaustion as opposed to fatigue *per se*, and although there is great similarity (Keltikangas-Järvinen & Heponiemi, 2004), there are also differences. For example, vital exhaustion also considers increased irritability and demoralization whereas fatigue does not (Nicolson & Van Diest, 2000). Further, individuals with blunted HR reactivity also show a worsening of physical disability over time (Phillips, Der, Shipton, & Benzeval, 2011), which, demonstrates that blunted reactivity is also associated with physical symptomology. Overall,

there is reason to believe that blunted reactivity might be associated with fatigue and thus there is a need to directly examine this relationship. A simple stress test could have clinical applications in identifying ANCA-associated vasculitis patients at greater risk of developing fatigue. As fatigue is a key marker of quality of life, this could indicate those who may need more through support and require frequent medical attention over the course of their treatment plan.

Hypotheses informing the three studies

In Study 1, it was hypothesised that self-reported and behavioural perseverance would be positively associated with cardiovascular reactivity to acute active and passive psychological stress. In relation to the secondary aim of Study 1, the hypothesis was that self-report and behavioural perseverance would be weakly correlated. With regard to Study 2, it was hypothesised that individuals with lower resilience would show blunted cardiovascular reactivity. Finally, the hypothesis that guided Study 3 methodology is that blunted cardiovascular and cortisol responses to acute psychological stress would predict greater fatigue in ANCA-associated vasculitis patients.

My contribution to the studies included within the thesis

The present thesis encompasses two experimental studies (Chapters 2 and 3, Studies 1 and 2) and a methodological chapter that outlines the approach for a future study for which data collection will begin shortly (Chapter 4, Study 3). Chapter 2 (Study 1) will be adapted slightly to submit as an article for scientific publication with support from Professor Anna Whittaker (AW) and Dr Sarah Williams (SW). It is also hoped that the eventual study associated with Chapter 4 (Study 3) will also be published with corroboration from AW, Professor Lorraine

Harper (LH) and an independent clinical research fellow. The idea for Studies 1 and 2 was put forth by AW with support from myself and the idea behind study 3 was generated by AW and LH. All data was collected by myself and team of six third-year undergraduate students. I completed the statistical analyses for all studies with the support from AW and AW provided feedback on the initial drafts of each chapter. With regard to Study 3, I was responsible for data collection. However, an extraordinary long research governance and National Health Service (NHS) ethical approval procedure meant that this research was no longer possible to conduct within the time constrains of a one-year masters by research course, although the methodology was piloted. In addition, the eventual data analysis for Study 3 would have also been my responsibility under the supervision of AW. Nevertheless, I will still be assisting with the eventual publication write-up, alongside AW and LH (data permitting).

References

Abrantes, A. M., Strong, D. R., Lejuez, C. W., Kahler, C. W., Carpenter, L. L., Price, L. H., … Brown, R. A. (2008). The role of negative affect in risk for early lapse among low distress tolerance smokers. *Addictive Behaviors*, *33*(11), 1394–1401.

Al'Absi, M. (2006). Hypothalamic-pituitary-adrenocortical responses to psychological stress and risk for smoking relapse. *International Journal of Psychophysiology*, *59*(3), 218–227.

Al'Absi, M., Wittmers, L. E., Erickson, J., Hatsukami, D., & Crouse, B. (2003). Attenuated adrenocortical and blood pressure responses to psychological stress in ad libitum and abstinent smokers. *Pharmacology Biochemistry and Behavior*, *74*(2), 401–410.

Allen, M. T., Hogan, A. M., & Laird, L. K. (2009). The relationships of impulsivity and cardiovascular responses: The role of gender and task type. *International Journal of Psychophysiology*, *73*, 369–376.

Allen, M. T., Matthews, K. A., & Sherman, F. S. (1997). Cardiovascular reactivity to stress and left ventricular mass in youth. *Hypertension*, *30*(4), 782–787.

Andersson, H., & Bergman, L. R. (2011). The role of task persistence in young adolescence for successful educational and occupational attainment in middle adulthood. *Developmental Psychology*, *47*(4), 950–960.

Astrand, P.-O., Cuddy, T. E., Saltin, B., & Stenberg, J. (1964). Cardiac output during submaximal and maximal work. *Journal of Applied Physiology*, *19*(1), 268–274.

Back, S. E., Hartwell, K., DeSantis, S. M., Saladin, M., McRae-Clark, A. L., Price, K. L., … Brady, K. T. (2010). Reactivity to laboratory stress provocation predicts relapse to

cocaine. *Drug and Alcohol Dependence*, *106*(1), 21–27.

Balanos, G. M., Phillips, A. C., Frenneaux, M. P., McIntyre, D., Lykidis, C., Griffin, H. S., & Carroll, D. (2010). Metabolically exaggerated cardiac reactions to acute psychological stress: The effects of resting blood pressure status and possible underlying mechanisms. *Biological Psychology*, *85*(1), 104–111.

Barnett, P. a, Spence, J. D., Manuck, S. B., & Jennings, J. R. (1997). Psychological stress and the progression of carotid artery disease. *Journal of Hypertension*, *15*(1), 49–55.

Basu, N., Mcclean, A., Harper, L., Amft, E. N., Dhaun, N., Luqmani, R. A., … Jones, G. T. (2013). Explaining fatigue in ANCA-associated vasculitis. *Rheumatology*, *52*(9), 1680–1685.

Basu, N., McClean, A., Harper, L., Amft, E. N., Dhaun, N., Luqmani, R. A., … Macfarlane, G. J. (2014). The characterisation and determinants of quality of life in ANCA associated vasculitis. *Annals of the Rheumatic Diseases*, *73*(1), 207–211.

Bennett, C., Blissett, J., Carroll, D., & Ginty, A. T. (2014). Rated and measured impulsivity in children is associated with diminished cardiac reactions to acute psychological stress. *Biological Psychology*, *102*, 68–72.

Bibbey, A., Ginty, A. T., Brindle, R. C., Phillips, A. C., & Carroll, D. (2016). Blunted cardiac stress reactors exhibit relatively high levels of behavioural impulsivity. *Physiology and Behavior*, *159*(1), 40–44.

Black, J. K., Balanos, G. M., & Whittaker, A. C. (2017). Resilience, work engagement and stress reactivity in a middle-aged manual worker population. *International Journal of Psychophysiology*, *116*(1), 9–15.

Boksem, M. A. S., Meijman, T. F., & Lorist, M. M. (2006). Mental fatigue, motivation and action monitoring. *Biological Psychology*, *72*, 123–132.

Bonanno, G. A. (2004). Loss, Trauma, and Human Resilience: Have We Underestimated the Human Capacity to Thrive after Extremely Aversive Events? *American Psychologist*, *59*(1), 20–28.

Brindle, R. C., Whittaker, A. C., Bibbey, A., Carroll, D., & Ginty, A. T. (2017). Exploring the possible mechanisms of blunted cardiac reactivity to acute psychological stress. *International Journal of Psychophysiology*, *113*, 1–7.

Brown, L. F., & Kroenke, K. (2009). Cancer-related fatigue and its associations with depression and anxiety: A systematic review. *Psychosomatics*.

Bush, G., Luu, P., & Posner, M. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Sciences*, *4*(1), 215–222.

Cannon, W. B. (1915). *Bodily changes in pain, hunger, fear and rage*. New York, US: D Appleton & Company.

Carroll, D. (1992). *Health psychology: Stress, behaviour and disease*. London: The Falmer Press.

Carroll, D., Bibbey, A., Roseboom, T. J., Phillips, A. C., Ginty, A. T., & De Rooij, S. R. (2012). Forced expiratory volume is associated with cardiovascular and cortisol reactions to acute psychological stress. *Psychophysiology*, *49*(6), 866–872.

Carroll, D., Davey Smith, G., Sheffield, D., Willemsen, G., Sweetnam, P. M., Gallacher, J. E., & Elwood, P. C. (1996). Blood pressure reactions to the cold pressor test and the prediction of future blood pressure status: data from the Caerphilly study. *Journal of*

Epidemiology and Community Health, *52*(8), 528–529.

Carroll, D., Davey Smith, G., Shipley, M. J., Steptoe, A., Brunner, E. J., & Marmot, M. G. (2001). Blood pressure reactions to acute psychological stress and future blood pressure status: A 10-year follow-up of men in the whitehall II study. *Psychosomatic Medicine*, *63*(5), 737–743.

Carroll, D., Ginty, A. T., Der, G., Hunt, K., Benzeval, M., & Phillips, A. C. (2012). Increased blood pressure reactions to acute mental stress are associated with 16-year cardiovascular disease mortality. *Psychophysiology*, *49*(10), 1444–1448.

Carroll, D., Ginty, A. T., Painter, R. C., Roseboom, T. J., Phillips, A. C., & de Rooij, S. R. (2012). Systolic blood pressure reactions to acute stress are associated with future hypertension status in the Dutch Famine Birth Cohort Study. *International Journal of Psychophysiology*, *85*(2), 270–273.

Carroll, D., Ginty, A. T., Whittaker, A. C., Lovallo, W. R., & de Rooij, S. R. (2017). The behavioural, cognitive, and neural corollaries of blunted cardiovascular and cortisol reactions to acute psychological stress. *Neuroscience and Biobehavioral Reviews*, *77*(1), 74–86.

Carroll, D., Lovallo, W. R., & Phillips, A. C. (2009). Are large physiological reactions to acute psychological stress always bad for health? *Social and Personality Psychology Compass*, *3*, 725–743.

Carroll, D., Phillips, A. C., & Balanos, G. M. (2009). Metabolically exaggerated cardiac reactions to acute psychological stress revisited. *Psychophysiology*, *46*(2), 270–275.

Carroll, D., Phillips, A. C., & Der, G. (2008). Body mass index, abdominal adiposity, obesity,

and cardiovascular reactions to psychological stress in a large community sample. *Psychosomatic Medicine*, *70*(6), 653–660.

Carroll, D., Phillips, A. C., Der, G., Hunt, K., & Benzeval, M. (2011). Blood pressure reactions to acute mental stress and future blood pressure status: Data from the 12-year follow-up of the West of Scotland Study. *Psychosomatic Medicine*, *73*(9), 737–743.

Carroll, D., Phillips, A. C., Der, G., Hunt, K., Bibbey, A., Benzeval, M., & Ginty, A. T. (2013). Low forced expiratory volume is associated with blunted cardiac reactions to acute psychological stress in a community sample of middle-aged men and women. *International Journal of Psychophysiology*, *90*(1), 17–20.

Carroll, D., Ring, C., Hunt, K., Ford, G., & MacIntyre, S. (2003). Blood pressure reactions to stress and the prediction of future blood pressure: Effects of sex, age, and socioeconomic Position. *Psychosomatic Medicine*, *65*(6), 1058–1064.

Carroll, D., Turner, J. R., & Prasad, R. (1986). The effects of level of difficulty of mental arithmetic challenge on heart rate and oxygen consumption. *International Journal of Psychophysiology*, *4*, 167–173.

Chaudhuri, A., & Behan, P. O. (2000). Fatigue and basal ganglia. *Journal of the Neurological Sciences*, *179*, 34–42.

Chida, Y., & Steptoe, A. (2010). Greater cardiovascular responses to laboratory mental stress are associated with poor subsequent cardiovascular risk status: A meta-analysis of prospective evidence. *Hypertension*, *55*(4), 1026–1032.

Connor, K. M., & Davidson, J. R. T. (2003). Development of a new Resilience scale: The Connor-Davidson Resilience scale (CD-RISC). *Depression and Anxiety*, *18*(2), 76–82.

Crim, C., Celli, B., Edwards, L. D., Wouters, E., Coxson, H. O., Tal-Singer, R., & Calverley, P. M. A. (2011). Respiratory system impedance with impulse oscillometry in healthy and COPD subjects: ECLIPSE baseline results. *Respiratory Medicine*, *105*, 1069–1078.

Danesh, J., Wheeler, J. G., Hirschfield, G. M., Eda, S., Eiriksdottir, G., Rumley, A., … Gudnason, V. (2004). C-reactive protein and other circulating markers of inflammation in the prediction of coronary heart disease. *The New England Journal of Medicine*.

de Rooij, S. R., & Roseboom, T. J. (2010). Further evidence for an association between self-reported health and cardiovascular as well as cortisol reactions to acute psychological stress. *Psychophysiology*, *47*(1), 1172–1175.

de Rooij, S. R., Schene, A. H., Phillips, D. I., & Roseboom, T. J. (2010). Depression and anxiety: Associations with biological and perceived stress reactivity to a psychological stress protocol in a middle-aged population. *Psychoneuroendocrinology*, *35*(6), 866–877.

Demyttenaere, K., De Fruyt, J., & Stahl, S. M. (2005). The many faces of fatigue in major depressive disorder. *International Journal of Neuropsychopharmacology*, *8*, 93–105.

Dittner, A. J., Wessely, S. C., & Brown, R. G. (2004). The assessment of fatigue: A practical guide for clinicians and researchers. *Journal of Psychosomatic Research*, *56*(2), 157–170.

Dolan, P., & Kudrna, L. (2015). More years, less yawns: Fresh evidence on tiredness by age and other factors. *Journals of Gerontology - Series B Psychological Sciences and Social Sciences*, *70*, 576–580.

Donovan, K. A., Jacobsen, P. B., Small, B. J., Munster, P. N., & Andrykowski, M. A. (2008). Identifying clinically meaningful fatigue with the Fatigue Symptom Inventory. *Journal*

of Pain and Symptom Management, *36*(5), 480–487.

Everson, S. a, Lynch, J. W., Chesney, M. a, Kaplan, G. a, Goldberg, D. E., Shade, S. B., … Salonen, J. T. (1997). Interaction of workplace demands and cardiovascular reactivity in progression of carotid atherosclerosis: population based study. *British Medical Journal*, *314*(7080), 553–558.

Galatzer-Levy, I. R., Steenkamp, M. M., Brown, A. D., Qian, M., Inslicht, S., Henn-Haase, C., … Marmar, C. R. (2014). Cortisol response to an experimental stress paradigm prospectively predicts long-term distress and resilience trajectories in response to active police service. *Journal of Psychiatric Research*, *56*(1), 36–42.

Georgiades, A., Lemne, C., De Faire, U., Lindvall, K., & Fredrikson, M. (1997). Stress-induced blood pressure measurements predict left ventricular mass over three years among borderline hypertensive men. *European Journal of Clinical Investigation*, *27*(9), 733–739.

Gianaros, P. J., May, J. C., Siegle, G. J., & Jennings, J. R. (2005). Is there a functional neural correlate of individual differences in cardiovascular reactivity? *Psychosomatic Medicine*, *67*(1), 31–39.

Ginty, A. T., Brindle, R. C., & Carroll, D. (2015). Cardiac stress reactions and perseverance: Diminished reactivity is associated with study non-completion. *Biological Psychology*, *109*, 200–205.

Ginty, A. T., Gianaros, P. J., Derbyshire, S. W. G., Phillips, A. C., & Carroll, D. (2013). Blunted cardiac stress reactivity relates to neural hypoactivation. *Psychophysiology*, *50*(3), 219–229.

Ginty, A. T., Phillips, A. C., Higgs, S., Heaney, J. L. J., & Carroll, D. (2012). Disordered eating behaviour is associated with blunted cortisol and cardiovascular reactions to acute psychological stress. *Psychoneuroendocrinology*, *37*(5), 715–724.

Girdler, S. S., Jamner, L. D., Jarvik, M., Soles, J. R., & Shapiro, D. (1997). Smoking status and nicotine administration differentially modify hemodynamic stress reactivity in men and women. *Psychosomatic Medicine*, *59*(3), 294–306.

Girod, J. P., & Brotman, D. J. (2004). Does altered glucocorticoid homeostasis increase cardiovascular risk? *Cardiovascular Research*, *64*, 217–226.

Guh, D. P., Zhang, W., Bansback, N., Amarsi, Z., Birmingham, C. L., & Anis, A. H. (2009). The incidence of co-morbidities related to obesity and overweight: A systematic review and meta-analysis. *BMC Public Health*, *9*(88), 1–20.

Hagemann, D., Waldstein, S. R., & Thayer, J. F. (2003). Central and autonomic nervous system integration in emotion. *Brain and Cognition*, *52*(1), 79–87.

Hajj-Ali, R. A., Wilke, W. S., Calabrese, L. H., Hoffman, G. S., Liu, X., Bena, J., … Langford, C. A. (2011). Pilot study to assess the frequency of fibromyalgia, depression, and sleep disorders in patients with granulomatosis with polyangiitis (Wegener's). *Arthritis Care & Research*, *63*, 827–833.

Hamer, M., O'Donnell, K., Lahiri, A., & Steptoe, A. (2010). Salivary cortisol responses to mental stress are associated with coronary artery calcification in healthy men and women. *European Heart Journal*, *31*, 424–429.

Hamer, M., & Steptoe, A. (2012). Cortisol responses to mental stress and incident hypertension in healthy men and women. *The Journal of Clinical Endocrinology and*

Metabolism, *97*(1), 29–34.

Heaney, J. L. J., Ginty, A. T., Carroll, D., & Phillips, A. C. (2011). Preliminary evidence that exercise dependence is associated with blunted cardiac and cortisol reactions to acute psychological stress. *International Journal of Psychophysiology*, *79*(2), 323–329.

Heleniak, C., McLaughlin, K. A., Ormel, J., & Riese, H. (2016). Cardiovascular reactivity as a mechanism linking child trauma to adolescent psychopathology. *Biological Psychology*, *120*, 108–119.

Herlyn, K., Hellmich, B., Seo, P., & Merkel, P. A. (2010). Patient-reported outcome assessment in vasculitis may provide important data and a unique perspective. *Arthritis Care & Research*, *62*(1), 1639–1645.

Holsen, L. M., Spaeth, S. B., Lee, J. H., Ogden, L. A., Klibanski, A., Whitfield-Gabrieli, S., & Goldstein, J. M. (2011). Stress response circuitry hypoactivation related to hormonal dysfunction in women with major depression. *Journal of Affective Disorders*, *131*(1), 379–387.

Howes, L. G., Abbott, D., & Straznicky, N. E. (1997). Lipoproteins and cardiovascular reactivity. *British Journal of Clinical Pharmacology*, *44*(1), 319–324.

Jönsson, P., Österberg, K., Wallergård, M., Hansen, Å. M., Garde, A. H., Johansson, G., & Karlson, B. (2015). Exhaustion-related changes in cardiovascular and cortisol reactivity to acute psychosocial stress. *Physiology and Behavior*, *151*(1), 327–337.

Junghanns, K., Backhaus, J., Tietz, U., Lange, W., Bernzen, J., Wetterling, T., … Driessen, M. (2003). Impaired serum cortisol stress response is a predictor of early relapse. *Alcohol and Alcoholism*, *38*(2), 189–193.

Kamarck, T. W., Everson, S. A., Kaplan, G. A., Manuck, S. B., Jennings, J. R., Salonen, R., & Salonen, J. T. (1997). Exaggerated blood pressure responses during mental stress are associated with enhanced carotid atherosclerosis in middle-aged finnish men: Findings from the Kuopio Ischemic Heart Disease Study. *Circulation*, *96*(11), 3842–3848.

Keltikangas-Järvinen, L., & Heponiemi, T. (2004). Vital exhaustion, temperament, and cardiac reactivity in task-induced stress. *Biological Psychology*, *65*(2), 121–135.

Koo-Loeb, J. H., Pedersen, C., & Girdler, S. S. (1998). Blunted cardiovascular and catecholamine stress reactivity in women with bulimia nervosa. *Psychiatry Research*, *80*(1), 13–27.

Kudielka, B. M., Von Känel, R., Preckel, D., Zgraggen, L., Mischler, K., & Fischer, J. E. (2006). Exhaustion is associated with reduced habituation of free cortisol responses to repeated acute psychosocial stress. *Biological Psychology*, *72*(2), 2006.

Kudielka, B. M., & Wüst, S. (2010). Human models in acute and chronic stress: assessing determinants of individual hypothalamus-pituitary-adrenal axis activity and reactivity. *Stress*, *13*, 1–14.

Lovallo, W. R. (2005a). Cardiovascular reactivity: Mechanisms and pathways to cardiovascular disease. *International Journal of Psychophysiology*, *58*(1), 119–132.

Lovallo, W. R. (2005b). *Stress & health: Biological and psychological interactions*. *Stress and Health: Biological and Psychological Interactions*.

Lovallo, W. R. (2006). Cortisol secretion patterns in addiction and addiction risk. *International Journal of Psychophysiology*, *59*(3), 195–202.

Lovallo, W. R., Dickensheets, S. L., Myers, D. A., Thomas, T. L., & Nixon, S. J. (2000).

Blunted stress cortisol response in abstinent alcoholic and polysubstance-abusing men. *Alcoholism: Clinical and Experimental Research*, *24*(5), 651–658.

Lovallo, W. R., Enoch, M. A., Acheson, A., Cohoon, A. J., Sorocco, K. H., Hodgkinson, C. A., … Goldman, D. (2016). Early-life adversity interacts with FKBP5 genotypes: Altered working memory and cardiac stress reactivity in the Oklahoma Family Health Patterns Project. *Neuropsychopharmacology*, *41*(7), 1724–1732.

Lovallo, W. R., Farag, N. H., Sorocco, K. H., Cohoon, A. J., & Vincent, A. S. (2012). Lifetime adversity leads to blunted stress axis reactivity: Studies from the Oklahoma Family Health Patterns Project. *Biological Psychiatry*, *71*(4), 344–349.

Manuck, S. B., & Schaefer, D. C. (1978). Stability of individual differences in cardiovascular reactivity. *Physiology and Behavior*, *21*(4), 675–678.

Markovitz, J. H., Raczynski, J. M., Wallace, D., Chettur, V., & Chesney, M. a. (1998). Cardiovascular reactivity to video game predicts subsequent blood pressure increases in young men: The CARDIA study. *Psychosomatic Medicine*, *60*(2), 186–191.

Matthews, K. A., Katholi, C. R., McCreath, H., Whooley, M. A., Williams, D. R., Zhu, S., & Markovitz, J. H. (2004). Blood pressure reactivity to psychological stress predicts hypertension in the CARDIA study. *Circulation*, *110*, 74–78.

McClean, A., Morgan, M. D., Basu, N., Bosch, J. A., Nightingale, P., Jones, D., & Harper, L. (2016). Physical fatigue, fitness, and muscle function in patients with Antineutrophil Cytoplasmic Antibody-Associated Vasculitis. *Arthritis Care & Research*, *68*(9), 1332–1339.

Min, J. A., Lee, N. Bin, Lee, C. U., Lee, C., & Chae, J. H. (2012). Low trait anxiety, high

resilience, and their interaction as possible predictors for treatment response in patients with depression. *Journal of Affective Disorders*, *137*, 61–69.

Min, J. A., Lee, C. U., & Chae, J. H. (2015). Resilience moderates the risk of depression and anxiety symptoms on suicidal ideation in patients with depression and/or anxiety disorders. *Comprehensive Psychiatry*, *56*(2), 103–111.

Moss, H. B., Vanyukov, M., Yao, J. K., & Kirillova, G. P. (1999). Salivary cortisol responses in prepubertal boys: The effects of parental substance abuse and association with drug use behavior during adolescence. *Biological Psychiatry*, *45*(10), 1293–1299.

Muñoz, L. C., & Anastassiou-Hadjicharalambous, X. (2011). Disinhibited behaviors in young children: Relations with impulsivity and autonomic psychophysiology. *Biological Psychology*, *86*, 349–359.

Murphy, C. M., Stojek, M. K., & MacKillop, J. (2014). Interrelationships among impulsive personality traits, food addiction, and Body Mass Index. *Appetite*, *73*(1), 45–50.

Nicolson, N. A., & Van Diest, R. (2000). Salivary cortisol patterns in vital exhaustion. *Journal of Psychosomatic Research*, *49*(5), 335–342.

Obrist, P. (1981) *Cardiovascular psychophysiology: A perspective*. New York: Plenum Press.

O'Rourke, N. (2004). Psychological resilience and the well-being of widowed women. *Ageing International*, *29*(3), 267–280.

Panknin, T. L., Dickensheets, S. L., Nixon, S. J., & Lovallo, W. R. (2002). Attenuated heart rate responses to public speaking in individuals with alcohol dependence. *Alcoholism: Clinical and Experimental Research*, *26*(6), 841–847.

Paris, J. J., Franco, C., Sodano, R., Frye, C. A., & Wulfert, E. (2010). Gambling pathology is

associated with dampened cortisol response among men and women. *Physiology and Behavior*, *99*(1), 230–233.

Phillips, A. C. (2011). Blunted as well as exaggerated cardiovascular reactivity to stress is associated with negative health outcomes. *Japanese Psychological Research*, *53*(2), 177–192.

Phillips, A. C., Der, G., & Carroll, D. (2009). Self-reported health and cardiovascular reactions to psychological stress in a large community sample: Cross-sectional and prospective associations. *Psychophysiology*, *46*(1), 1020–1027.

Phillips, A. C., Der, G., Shipton, D., & Benzeval, M. (2011). Prospective associations between cardiovascular reactions to acute psychological stress and change in physical disability in a large community sample. *International Journal of Psychophysiology*, *81*(3), 332–337.

Phillips, A. C., Hunt, K., Der, G., & Carroll, D. (2011). Blunted cardiac reactions to acute psychological stress predict symptoms of depression five years later: Evidence from a large community study. *Psychophysiology*, *48*(1), 142–148.

Phillips, A. C., Roseboom, T. J., Carroll, D., & De Rooij, S. R. (2012). Cardiovascular and cortisol reactions to acute psychological stress and adiposity: Cross-sectional and prospective associations in the dutch famine birth cohort study. *Psychosomatic Medicine*, *70*(4), 699–710.

Quinn, E. P., Brandon, T. H., & Copeland, A. L. (1996). Is task persistence related to smoking and substance abuse? The application of learned industriousness theory to addictive behaviors. *Experimental and Clinical Psychopharmacology*, *4*(1), 186–190.

Ream, E., & Richardson, A. (1996). Fatigue: A concept analysis. *International Journal of Nursing Studies*, *33*(5), 519–529.

Ruiz-Robledillo, N., Romero-Martínez, A., & Moya-Albiol, L. (2017). Lower cortisol response in high-resilient caregivers of people with autism: the role of anger. *Stress and Health*, *33*(4), 370–377.

Salomon, K., Clift, A., Karlsdóttir, M., & Rottenberg, J. (2009). Major depressive disorder is associated with attenuated cardiovascular reactivity and impaired recovery among those free of cardiovascular disease. *Health Psychology*, *28*(2), 157-.

Sarkar, M., & Fletcher, D. (2014). Psychological resilience in sport performers: a review of stressors and protective factors. *Journal of Sports Sciences*, *32*(15), 1419–1434.

Schwartz, A. R., Gerin, W., Davidson, K. W., Pickering, T. G., Brosschot, J. F., Thayer, J. F., … Linden, W. (2003). Toward a causal model of cardiovascular responses to stress and the development of cardiovascular disease. *Psychosomatic Medicine*, *65*, 22–35.

Selye, H. (1956). *The stress of life*. New York, US: McGraw-Hill

Sorocco, K. H., Lovallo, W. R., Vincent, A. S., & Collins, F. L. (2006). Blunted hypothalamic-pituitary-adrenocortical axis responsivity to stress in persons with a family history of alcoholism. *International Journal of Psychophysiology*, *59*(1), 210–217.

Steinberg, M. L., Williams, J. M., Gandhi, K. K., Foulds, J., Epstein, E. E., & Brandon, T. H. (2012). Task persistence predicts smoking cessation in smokers with and without schizophrenia. *Psychology of Addictive Behaviors*, *26*(1), 850–858.

Stewart, R. A. H., Hagström, E., Held, C., Wang, T. K. M., Armstrong, P. W., Aylward, P. E., … Wallentin, L. (2017). Self-reported health and outcomes in patients with stable

coronary heart disease. *Journal of the American Heart Association*, *6*(8), 60–67.

Stice, E., Spoor, S., Bohon, C., & Small, D. M. (2008). Relation between obesity and blunted striatal response to food is moderated by TaqIA A1 allele. *Science*, *17*(1), 449–452.

Stone, P., Richards, M., & Hardy, J. (1998). Fatigue in patients with cancer. *European Journal of Cancer*, *34*(11), 1670–1676.

Treiber, F. A., Kamarck, T., Schneiderman, N., Sheffield, D., Kapuku, G., & Taylor, T. (2003). Cardiovascular reactivity and development of preclinical and clinical disease states. *Psychosomatic Medicine*, *65*(1), 46–62.

Turner, J. R., & Carroll, D. (1985). Heart rate and oxygen consumption during mental arithmetic, a video game, and graded exercise: Further evidence of metabolically-exaggerated cardiac adjustments? *Psychophysiology*, *22*, 261–267.

Van der Kooy, K., van Hout, H., Marwijk, H., Marten, H., Stehouwer, C., & Beekman, A. (2007). Depression and the risk for cardiovascular diseases: Systematic review and meta analysis. *International Journal of Geriatric Psychiatry*, *22*(7), 613–626.

Waldstein, S. R., & Burns, H. O. (2003). Interactive relation of insulin and gender to cardiovascular reactivity in healthy young adults. *Annals of Behavioural Medicine*, *25*(3), 163–171.

Ware, J. E., & Sherbourne, C. D. (1992). The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Medical Care*, *30*(6), 473–483.

Wawrzyniak, A. J., Hamer, M., Steptoe, A., & Endrighi, R. (2016). Decreased reaction time variability is associated with greater cardiovascular responses to acute stress. *Psychophysiology*, *53*(5), 739–748.

Wu, T., Snieder, H., & de Geus, E. (2010). Genetic influences on cardiovascular stress reactivity. *Neuroscience and Biobehavioral Reviews*, *35*, 58–68.

York, K. M., Hassan, M., Li, Q., Li, H. H., Fillingim, R. B., & Sheps, D. S. (2007). Coronary artery disease and depression: Patients with more depressive symptoms have lower cardiovascular reactivity during laboratory-induced mental stress. *Psychosomatic Medicine*, *69*, 521–528.

CHAPTER TWO

CARDIOVASCULAR REACTIVITY AND PERSEVERANCE: BLUNTED BLOOD PRESSURE RESPONSES TO ACUTE STRESS ARE A MARKER OF POOR BEHAVIOURAL PERSEVERANCE

Abstract

Exaggerated cardiovascular responses to acute stress are implicated in the development of cardiovascular pathologies. It is now clear that blunted reactivity also reflects a maladaptive response pattern. Emerging evidence suggests that attenuated physiological stress reactions are associated with general manifestations of poor behavioural regulation. However, as yet, only a small number of behaviours, such as impulsivity, have been explored in detail. The aim of this present study was to examine the relationship between cardiovascular reactivity to acute stress and self-reported and behavioural perseverance. It also explored whether self-reported and behavioural perseverance measurements correlated. Participants (N=115) completed a validated perseverance questionnaire before heart rate and blood pressure measurements were taken at rest and during exposure to 4-minute mental arithmetic and cold pressor stress tasks. Participants then endeavoured to complete an impossible puzzle tracing task; the length of time expended, and number of attempts, were recorded and conceptualised as behavioural perseverance. After splitting the sample by stress task order (due to a large order effect) blunted blood pressure reactivity was associated with low behavioural perseverance, and this relationship withstood adjustment for significant confounders (gender and CP time). Self-reported perseverance and cardiovascular reactivity did not correlate, nor did self-reported and behavioural perseverance. The significant findings add to a growing body of evidence that implicates blunted reactivity as a marker for poor behavioural regulation. They also show that attenuated reactivity can predict motivation-related behavioural outcomes. Measuring physiological responses to acute stress could have prognostic implications for identifying those with deficiencies in perseverance, who may need more support during situations that typically require high perseverance, such as smoking cessation (Abrantes et al., 2008; Steinberg et al., 2012)

Introduction

It is now widely accepted that there are large individual differences in cardiovascular stress reactions exhibited during acute exposure to stress (Carroll, 1992), the magnitude of which are relatively consistent and stable over time (Ginty et al., 2013; Manuck & Schaefer, 1978). It is also clear that these differences can have an impact on health and behaviour (Carroll, Phillips, & Balanos, 2009; Chida & Steptoe, 2010; Phillips, Hunt, Der, & Carroll, 2011) dependent on whether one exhibits exaggerated or blunted responses (Carroll, Lovallo, & Phillips, 2009).

Dominating the early research into the relationship between physiological stress responses and health was the reactivity hypothesis, which postulated that consistently exaggerated cardiovascular reactions to acute stress are implicated in the aetiology of cardiovascular pathologies, specifically hypertension (Obrist, 1981). This hypothesis is now supported via a plethora of compelling evidence from robust research (Carroll et al., 2001; Carroll et al., 1996; Carroll, Ginty, Painter, et al., 2012; Carroll, Phillips, Der, Hunt, & Benzeval, 2011; Carroll, Ring, Hunt, Ford, & MacIntyre, 2003; Markovitz, Raczynski, Wallace, Chettur, & Chesney, 1998; Matthews et al., 2004; Treiber et al., 2003), using data from large epidemiological studies, including the West-of-Scotland Twenty-07 study, the Dutch Famine Birth Cohort, the Whitehall II study, the CARDIA study and the Caerphilly study. Collectively, these findings emphasise the reliability of this association across samples in different countries/cultures, using different protocols and various stress tasks. In addition, large magnitude physiological stress responses are also evident in those with: poor neuronal efficiency (Wawrzyniak et al., 2016), atherosclerosis (Barnett et al., 1997; Everson et al., 1997; Kamarck et al., 1997) and left ventricular hypertrophy (Allen, Matthews, & Sherman, 1997; Georgiades, Lemne, De Faire, Lindvall, & Fredrikson, 1997). This response pattern is

also predictive of cardiovascular disease mortality (Carroll, Ginty, Der, et al., 2012). Overall, meta-analyses and reviews confirm the reactivity hypothesis and show that exaggerated cardiovascular reactions in response to acute stress are detrimental to health (Chida & Steptoe, 2010; Schwartz et al., 2003; Treiber et al., 2003).

It has been proposed that exaggerated cardiovascular responses to acute psychological stress are detrimental to health because they are metabolically unjustified, i.e., occur without an associated augmented metabolic demand for oxygen (Carroll, Phillips, et al., 2009; Turner & Carroll, 1985). Researchers have suggested that this perturbs homeostasis and places the cardiovascular system under unnecessary stress which can have damaging effects on the cardiovascular system and beyond (Carroll, Turner, & Prasad, 1986; Carroll, Phillips, et al., 2009). Therefore, on this basis, one might expect low cardiovascular reactivity to be an adaptive response pattern.

For this reason, small magnitude or blunted acute stress responses were once viewed as benign or even protective (Carroll, Lovallo, & Phillips, 2009). However, more recent evidence has challenged this misconception, showing that blunted reactivity is also harmful to health (Carroll, Lovallo, et al., 2009; Lovallo, 2011; Phillips, Ginty, & Hughes, 2013). This includes evidence from the same large datasets that implicated exaggerated reactivity in aetiology of cardiovascular disease, as well as independent studies. The research shows that blunted reactivity is associated with a range of adverse health outcomes including: depression (Phillips et al., 2011; Salomon, Clift, Karlsdóttir, & Rottenberg, 2009; York et al., 2007), anxiety (de Rooij et al., 2010) and obesity (Carroll, Phillips, & Der, 2008; Phillips, Roseboom, Carroll, & De Rooij, 2012), as well as being related to poorer self-reported health (de Rooij & Roseboom, 2010; Phillips, Der, & Carroll, 2009). These health outcomes, like

exaggerated reactivity, are also implicated in the development of a range of cardiovascular pathologies (Guh et al., 2009; Stewart et al., 2017; Van der Kooy et al., 2007).

Further, blunted reactivity also appears to relate to negative behavioural patterns that are detrimental to health. Research has shown that attenuated cardiac stress responses are characteristic of smokers (Al'Absi, 2006; Al'Absi et al., 2003; Girdler et al., 1997) and predict relapse in those who have recently quit (Al'Absi, 2006). It is important to note that this blunting effect cannot be attributed to temporary abstinence during the research process, as smokers who used nicotine patches throughout still exhibited diminished physiological stress reactivity (Girdler et al., 1997). Likewise, in comparison to those without an alcohol dependency, alcohol dependent individuals show blunted cardiovascular responses to acute stressors (Lovallo et al., 2000; Panknin et al., 2002), as do the offspring of alcoholic parents who have not yet developed an addiction themselves (Moss et al., 1999; Sorocco et al., 2006). This suggests that blunted reactivity may precede addictive behaviour. It also insinuates that blunting is not a direct result of chemical alteration from the substances or abstinence from substance abuse. This is further supported by the fact that blunted reactivity is also evident in those with a range of non-substance based dependencies: exercise (Heaney et al., 2011), disordered eating (Ginty, Phillips, Higgs, et al., 2012; Koo-Loeb et al., 1998) and gambling (Paris et al., 2010). In sum, it appears that both blunted and exaggerated cardiovascular reactions to acute stress reflect maladaptive response patterns. Therefore, responses that are harmful to cardiovascular and general health reside at both extremes of the reactivity continuum (Carroll, Lovallo, et al., 2009; Phillips, 2011).

Researchers have put forth the suggestion that the common feature shared between the correlates of blunted cardiovascular reactivity is a dysfunction in the fronto-limbic brain regions associated with motivation and goal-directed behaviours (Carroll, Ginty, Whittaker,

Lovallo, & de Rooij, 2017; Carroll, Lovallo, et al., 2009; Phillips, 2011), such that, blunted reactivity may be a peripheral marker for central motivational dysregulation (Carroll, Lovallo, et al., 2009; Lovallo, 2006). Functional Magnetic Resonance Imaging (fMRI) studies have provided evidence in favour of this, demonstrating amygdala and anterior/posterior cingulate cortex deactivation in those with blunted reactivity when exposed to stressful stimuli (Gianaros et al., 2005; Ginty et al., 2013). Interestingly, it is these brain areas which support cardiovascular control/responses to stress (Carroll, Lovallo and Phillips, 2009), co-ordinate motivational/behavioural processes, and modulate autonomic regulation (Bush et al., 2000; Hagemann et al., 2003; Lovallo, 2005a). In further support, those displaying certain attenuated reactivity-related correlates, such as depression or obesity, have also been shown to exhibit blunted frontal and subcortical responses (Holsen et al., 2011; Stice, Spoor, Bohon, & Small, 2008) during exposure to negative arousal images and in the anticipation period prior to the consumption of a milkshake, respectively. Overall, it seems that exaggerated cardiovascular responses are detrimental to health because they are metabolically unjustified, but it may be that blunted reactivity exerts its maladaptive influence through being a marker of motivational dysregulation.

If blunted reactivity is truly a marker of central dysfunction, one might assume that it would be associated with general manifestations of poor behavioural regulation. Although limited, there is now available evidence to support this contention; high impulsivity and impaired response inhibition has been found to be associated with diminished cardiovascular reactivity (Allen, Hogan, & Laird, 2009; Bennett, Blissett, Carroll, & Ginty, 2014; Bibbey, Ginty, Brindle, Phillips, & Carroll, 2016; Muñoz & Anastassiou-Hadjicharalambous, 2011). Further, those with blunted cardiac stress responses are more likely to develop externalising psychopathology i.e., psychiatric disorders typified by disinhibition (Heleniak et al., 2016),

and perform more poorly during lung function spirometry examinations (Carroll et al., 2013; Carroll, Bibbey, Roseboom, et al., 2012),which, are motivation-contingent and reflect effort (Crim et al., 2011). However, it is important to note that blunted reactors are not consciously aware of any differences in motivation/effort (Brindle et al., 2017) and do not self-report differences in task engagement (Bibbey et al., 2016; Ginty, Phillips, Higgs, et al., 2012). In sum, these findings demonstrate that blunted reactivity is reflected in actual behavioural manifestations.

Consequently, there is reason to believe that cardiovascular reactivity might also be associated with perseverance. Perseverance is an adaptive behaviour and key contributing factor in leading a successful and healthy life (Andersson & Bergman, 2011). Research has emphasised its importance during academic/career progression (Andersson & Bergman, 2011) and when attempting to refrain from adopting poor health behaviours (Quinn et al., 1996). In parallel with blunted reactivity, low perseverance is also implicated in relapse during cigarette and other substance cessation (Abrantes et al., 2008; Steinberg et al., 2012) and has been shown to contribute to obesity (Murphy et al., 2014). Given the associations between smoking/obesity and cardiovascular disease (Ambrose & Barua, 2004; Van Gaal, Mertens, & De Block, 2006), diabetes (Patja et al., 2005) and cancer (Le Marchand, Wilkens, Kolonel, Hankin, & Lyu, 1997), and the fact that perseverance is predictive of future cardiovascular disease (Cramer, Benedict, Muszbek, Keskinaslan, & Khan, 2008), it is therefore an important behaviour to examine. Thus, it seems prudent to identify early indicators of low perseverance, so that specific interventions can be developed to support individuals most likely to adopt negative health behaviours, such as substance addictions, and relapse following cessation. One such marker could be diminished physiological reactivity to acute stress.

When compared to the physiological assessment of cardiovascular reactivity i.e., blood pressure and heart rate assessment to a standardised psychological stressor, the measurement of behavioural and motivational constructs like perseverance is far more complex (Touré-Tillery & Fishbach, 2014). There is some evidence to suggest that individuals can accurately self-report behaviour in a manner which adequately reflects their actual behaviour (Corral-Verdugo & Figueredo, 1999), however, other studies have completely rejected this contention (Fuj, Hennessy, & Mak, 1985). From a meta-analytical perspective, it seems self-reports do have some value and provide a key insight, but do not always accurately predict true behaviour (Kormos & Gifford, 2014; Prince et al., 2008). Examples of this lack of correlation between self-report and objective behavioural measurements occurs in studies assessing physical activity levels (Prince et al., 2008) and diet (Freedman, Kipnis, Schatzkin, Tasevska, & Potischman, 2010). It seems that this can be partly attributed to response and recall bias (Hebert, Clemow, Pbert, Ockene, & Ockene, 1995; Prince et al., 2008); many individuals are often drawn into providing "socially desirable" or unreliable answers (Bazelais, Lemay, & Doleck, 2016; Duckworth, Peterson, Matthews, & Kelly, 2007). Overall, utilising a combination of both self-report and objective measurement techniques could help towards addressing these issues (Freedman et al., 2010). However, as yet, no studies have employed both self-report and objective measures of perseverance in cardiovascular reactivity research.

Although limited, there is some prior evidence to suggest that perseverance may be associated with blunted reactivity. As previously mentioned, those with diminished physiological stress responses are more likely to relapse during alcohol (Junghanns et al., 2003; Lovallo, 2006) and smoking (Al'Absi, 2006) cessation, as well as during treatment for cocaine addiction (Back et al., 2010). One may infer this behaviour as an index of reduced perseverance. However, it is possible that these findings actually reflected relapse as opposed to

perseverance *per se*. Thus, perhaps more compelling evidence is available when looking at study non-completion as an index of perseverance. Research showed that diminished cardiovascular reactivity patterns to acute stress predicted the failure to complete a simple online-based one year follow-up assessment, despite repeated promptings and the offering of a financial incentive (Ginty et al., 2015). However, although more persuasive, study non-completion might still be considered an indirect and weak measure of perseverance. Overall, although there is some preliminary evidence to suggest that blunted reactivity might be associated with perseverance, the relationship between direct perseverance and reactivity has, of yet, received sparse attention.

Consequently, the aim of this present study was to directly examine the relationship between cardiovascular reactivity and self-reported and behavioural perseverance. A secondary objective was also to investigate whether self-report and behavioural perseverance measurements correlated. It was hypothesised that blunted reactors would score lower on a self-reported perseverance questionnaire and demonstrate poorer behavioural perseverance compared with individuals with high or exaggerated reactivity. In relation to the second hypothesis, it was expected that self-report and behavioural perseverance would be weakly correlated.

Methods

Participants

Participants were 115 University of Birmingham students enrolled via verbal, email and social media-based recruitment strategies. The mean (SD) age of the sample was 19.8 (1.81) years and there was a total of 86 females (75%).

Study design

This laboratory study utilised a cross-sectional design to examine whether cardiovascular reactivity to acute stress was associated with self-reported and behavioural perseverance. Participants provided written informed consent and the project was approved by the University of Birmingham's STEM Ethics Committee (ERN_14-0089A).

Measures

Questionnaires

Grit

The Short Grit Scale (grit-S; Duckworth & Quinn, 2009) was administered to measure grit, defined by Duckworth and Quinn, (2009) as "perseverance and passion for long-term goals" (*P*. 1087). When completing this eight-item instrument, participants used a five-point Likert scale, from "very much like me" to "not at all like me", to indicate their agreement with four statements which examined the consistency of their interests/passions, for example, "I often set a goal but later choose to pursue a different one" and four which focused on their tendency to maintain effort, for example, "I am a hard worker". When participants had finished answering the questions, the experimenter averaged the data and divided this score by eight; higher scores (nearer to five) reflect greater grit. When compared to the full Grit Scale (Duckworth, Peterson, Matthews, & Kelly, 2007), the grit-s boasts improved psychometric properties, with Cronbach's alpha's ranging from .73 to .83 and a test-retest reliability of .68 (Duckworth & Quinn, 2009). Evidence of high internal consistency ($\alpha = .79$) was also demonstrated in recent research using a similar sample to the present study (Gilchrist, Fong, Herbison & Sabiston, 2018). In this present research the internal reliability of the grit-s was

.74. Finally, the grit-s boasts good convergent and discriminant validity (Schmidt, Fleckenstein, Retelsdorf, Eskreis-Winkler, & Möller, 2017).

Resilience

The well-validated Connor-Davison Resilience Scale (CD-RISC; Connor & Davidson, 2003) uses 25 items to investigate psychological resilience or "personal qualities that enable one to thrive in the face of adversity" (Connor & Davidson, 2003, *P*.76). Example items include: "I can deal with whatever comes my way", "I tend to bounce back after illness or hardship" and "I am not easily discouraged by failure". When completing the CD-RISC, participants responded using a five-point Likert scale where 0 = ("not true at all") and 4 = ("true all the time"); larger scores indicate greater resilience. Evidence of high test-retest reliability (.87) and internal consistency (α = .89) of the CD-RISC has been reported in the literature (Connor & Davidson, 2003) and the Cronbach's alpha of the questionnaire in the present study was .84. Research has also demonstrated the instrument to have acceptable convergent and discriminant validity (Connor & Davidson, 2003) and supported its capacity to distinguish between those with greater and lesser resilience (Connor & Davidson, 2003).

Socio-demographic information

Participants completed a set of standardised questions which collected basic socio-demographic information, including age, sex, and ethnicity. There was also a requirement for female participants to circle yes or no to taking the contraceptive pill and record the date of their last menstrual period. Further, participants were asked to choose from a selection of occupation categories, for example, managerial or skilled-manual, which best indicates their head of household's occupation, or most recent occupation. This data was used to the classify

socioeconomic position (manual or non-manual) using the Registrar General's (1980) Classification of Occupations.

Evaluation of stress tasks

Participants completed six questions measuring how: stressful, difficult, arousing, confusing, embarrassing and engaging they found the active mental stress task. Further, participants also indicated how successful they perceived their performance to be. In relation to the passive stress task, participants completed two questions to assess subjective perceptions of task stressfulness and difficulty. For all questions, participants responded on a 7-point Likert scale, where 0 = ("not at all stressful/difficult etc.") and 6 = ("extremely stressful/difficult etc."). The results obtained using these two instruments supported analyses into whether there were reactivity-related differences in stress task appraisals or *vice versa*.

Cardiovascular measures

Systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) were discontinuously measured from the left arm using a standard brachial artery cuff and Omron (model M5-I) semi-automatic sphygmomanometer (Omron Healthcare UK Ltd., West Sussex, United Kingdom). These cardiovascular measurements were obtained during minutes two, four, six and eight of the first baseline period and the second and fourth minutes of the stress periods and secondary baseline phase. Additionally, cardiovascular measurements were also taken during minute six of the ten-minute adaptation period for familiarity purposes and to ensure the equipment was functioning correctly, however, these were not recorded.

Laboratory tasks

Acute psychological stress tasks

The Paced Auditory Serial Addition Test (PASAT; Gronwall, 1977), is an acute psychological stressor that reliably perturbs cardiovascular activity (Phillips, Carroll, Burns, & Drayson, 2005; Phillips, Carroll, Hunt, & Der, 2006; Phillips, Der, Hunt, & Carroll, 2009) with good test-retest reliability (Willemsen et al., 1998). During a four-minute version of this active mental stress task, participants were presented, via a compact disc (CD) player, with a series of single digit numbers and were instructed to add consecutive integers whilst remembering the most recent number in memory to add to the next number read out by the CD. For example, if they heard one and then seven, they had to add those two numbers together and verbally report the answer "eight". They then had to remember the second number of that pair i.e. seven and then add this to the next number that was presented to them. Thus, the task involved both mental arithmetic and working memory. In addition, the rate at which the numbers were presented increased throughout; the time intervals between two numbers began at two seconds for the first two minutes but decreased to one second during the final two minutes. An experimenter wearing a white laboratory coat sat close to the participant and obtrusively marked their performance; any missed or incorrect answers resulted in a 5-point deduction from the 1000-point total all participants started with. This final points total (out of 1000) was operationalised as objective PASAT performance. The experimenter, using a buzzer, delivered a single aversive noise burst to the participants during any of the last five numbers in every block of ten. If possible, this was made to coincide with errors made by the participant, but if no error occurred then randomly. However, it was emphasised to the participants before the test commenced that this noise would directly signify a negative aspect of their performance, i.e. incorrect answers, hesitation, mumbling

etc. The PASAT also induced competition and social evaluative tendencies. A leaderboard was in clear view of the participants so they could attempt to better the score of others/avoid performing worse than their peers. In addition, participants were also informed that they would be videotaped throughout the task and were instructed to watch themselves live on a television screen; they were notified that their tape would be assessed by "independent body language experts", but, in reality, no such recording/assessment occurred.

The cold pressor (CP; Barnett, Hines, Schirger, & Gage, 1963) stress task was also administered and involved each participant keeping the right hand, up to the wrist fold, submerged in cold water of between 0 - 4°C for as long as possible. However, during this passive stress task it was made clear to each participant that they were free to withdraw their hand at any time. Further, there was a maximum time limit of four minutes; after which the participants were asked to remove their hand from the water if it was still submerged. When the hand was withdrawn, participants were given tissues so that they could thoroughly dry themselves and the length of time the hand remained in the water was recorded; this was conceptualised as a behavioural measure of perseverance. Research has demonstrated the reliability of the CP task in provoking a cardiovascular response (Allen, Sherwood, Obrist, Crowell, & Grange, 1987).

Perseverance puzzle task

To directly measure behavioural perseverance, participants were asked to complete four Euler puzzles (Szetho, n.d.), a paradigm used by previous authors (e.g. Bibbey et al., 2016). During this task, participants had to trace along all of the lines on a piece of paper without lifting the highlighter from the page and tracing along each line once only. If they made a mistake they

were instructed to use another piece of paper and this was continued until they successfully completed the puzzle. The puzzles involved more lines as the participants progressed, however, the final puzzle was impossible. The time taken to complete each puzzle was recorded, as were the number of attempts and were used as measures of perseverance. The time taken and number of attempts were particularly important during the final impossible puzzle, as this differentiated the perseverers and non-perseverers.

Procedure

University of Birmingham students were informed about the study via email, social media, and verbal recruitment strategies in lectures and seminars. Before taking part in the study, all participants were asked to read an information sheet and signed a written informed consent form which signified their consent for participation. All participants were also asked to refrain from eating (one hour), smoking or consuming caffeine (two hours), exercising vigorously (four hours) and consuming alcohol (12 hours) prior to their involvement. Further, participants were asked if they were currently ill/infectious and were not able to participate if this was the case, or if they were on any medication (other than the contraceptive pill). Every testing session was conducted in the same laboratory within the School of Sport, Exercise and Rehabilitation Sciences at the University of Birmingham with sessions starting at either 0900h, 1100, 1300h or 1500h. The experiment consisted of six main periods: a 10-minute adaptation, 10-minute baseline, four-minute stress task (active or passive), four-minute recovery period, four-minute stress task (active or passive) and finally, the Euler puzzle task; the two stress tasks were presented in a randomised counterbalanced order using an online random number generator. All testing sessions began with the signing of the informed consent document and each participant confirmed that they met the inclusion criteria outlined above

i.e., were not currently ill/infectious, had not exercised vigorously in the past four hours etc. Then, height, using the Leicester Height Measure Stadiometer (Seca, Birmingham, United Kingdom) and weight, using portable mechanical scales (Salter, Kent, United Kingdom) measurements were taken and body mass index (BMI) was subsequently calculated (weight/height^2). A brachial artery cuff was then attached to the participant's left arm before they reclined quietly during a 10-minute adaptation period; cardiovascular measurements (SBP, DBP, and HR) were taken during the sixth minute for familiarity purposes and to ensure the equipment was functioning correctly. During the adaptation period, participants were asked to complete the three questionnaires detailed above i.e., the socio-demographic questionnaire, the grit-s and the CD-RISC. Following this, participants entered a formal 10-minute baseline period where SBP, DBP and HR measurements were taken at minutes two, four six and eight. Depending on the outcome of the randomised counterbalancing, the participants then completed either the PASAT or the CP task. Using protocol A, i.e., the PASAT first protocol as an example, wearing a white laboratory coat, the experimenter read aloud a set of standardised PASAT instructions and participants undertook a short practice test to confirm that they understood what was required of them. The experimenter then turned on the television allowing participants to visibly see themselves and the 4-minute PASAT commenced; cardiovascular measurements were taken at minutes two and four. To conclude, the PASAT score was calculated and participants completed the post-PASAT rating scales before entering a four-minute recovery period where cardiovascular measurements were again taken at minutes two and four. If the PASAT was completed first, the CP task came next. Individuals were instructed by the experimenter still wearing a white laboratory coat, to try and keep their hands submerged in the cold water for as long as possible. However, it was made clear that participants were free to withdraw their hand at any time. If the hand was still

immersed in the water after the fourth minute the experimenter announced that the task was over, and the participants were asked to remove their hand. During the CP task, again, cardiovascular measurements were taken at minutes two and four. The participants then dried their hand, completed the post-CP rating scales and sat down at a nearby desk in preparation for the Euler puzzle task. The experimenter read aloud the Euler puzzle instructions making certain that participants understood the requirements of the task. The stopwatch was then started, and a researcher recorded the time and number of attempts it took each participant to complete the puzzles, or in the case of the impossible puzzle, endeavoured to complete the puzzle. Finally, the participants were thanked, awarded research credits as necessary, and informed that they were free to leave.

Data analysis

Data analysis was conducted using IBM SPSS software, version 23. Firstly, ethnicity and socio-economic status were statistically converted into binary variables; white/non-white and manual/non-manual, respectively. Then, cardiovascular data was averaged across each period (baseline 1, PASAT, baseline 2 and CP). Because the PASAT and CP stress tasks were presented using a counterbalanced approach, an order variable was used to identify the baseline data associated with each task; this led to the formation of PASAT baseline and CP baseline variables. Cardiovascular reactivity to the PASAT and CP task was then calculated by subtracting average PASAT/CP stress values from average PASAT/CP baseline values, respectively. Descriptive and frequency statistics were conducted for all variables (socio-demographic, self-report and average cardiovascular). One-way ANOVAs were used to investigate the effect of order and previous PASAT experience on reactivity and resting cardiovascular activity. Univariate ANOVAs for categorical variables and correlations for continuous variables were used to examine the impact of socio-demographic factors on

cardiovascular data, questionnaire scores/ratings and performance variables (PASAT score, CP time and puzzle time/attempts). This revealed two major potential confounding variables that required statistically adjusting for during the main analyses: task order and gender. Additionally, these confounders have also been associated with perseverance and/or cardiovascular reactivity in previous research (Carroll, Phillips & Lovallo, 2011; Von Culin, Tsukayama & Duckworth, 2014). To confirm that the PASAT and CP task perturbed cardiovascular activity, repeated measures ANOVAs were conducted (with time as four points: baseline 1, stress 1, baseline 2, stress 2). Pearson's correlations were used to examine the relationships between questionnaire-based perseverance scores, behavioural perseverance, and cardiovascular reactivity. Any significant relationships were then re-examined using multiple linear regressions, adjusting for any appropriate confounding variables as covariates in the model. Partial eta-squared (η^2) and change in R-squared (ΔR^2) were used as indices of effect size. Additionally, slight variations in degrees of freedom reflect occasional missing data.

Results

One hundred and fifteen University of Birmingham students were recruited by means of verbal, email and social media-based advertisements. The mean (SD) age of the sample was 19.8 (1.81) years with a total of 86 females (75%). In terms of ethnicity, 94 (82%) described themselves as "white", 15 (13%) as "Asian", three (3%) as "black" and three (3%) as "other". Based on parental occupation, 98 (85%) were deemed to be of a non-manual socio-economic background, and five (4%) attested to taking medication (inhaled corticosteroids). The overall socio-demographic, anthropometric and previous PASAT experience characteristics of the sample are summarised in Table 2.1.

Table 2.1. Socio-demographic, anthropometric and previous Paced Auditory Serial Addition Test experience characteristics of the sample (N=115)

	Mean (SD)	N (%)
Age (years)	19.8 (1.81)	
Sex (female)		86 (75)
Ethnicity (white)		94 (82)
Body mass index (kg/m^2)	23.1 (3.08)	
Parental occupation (non-manual)		98 (85)
Completed PASAT before (no)		105 (92)
Stress task order (PASAT first)		64 (56)

Order and socio-demographic influence on cardiovascular activity and stress task ratings

One-way ANOVAs revealed that stress task order significantly influenced CP baseline HR, $F(1,113) = 4.32$, $p = .04$, such that, participants in the PASAT first group had a lower baseline HR prior to the CP task compared with those who completed the CP first. Consequently, order was also significantly associated with CP HR reactivity; when the PASAT was completed first, CP HR reactivity was higher, $F(1,113) = 11.21$, $p = .001$, than when the CP was the first task. Additionally, cardiovascular activity differed by gender; males exhibited more exaggerated SBP and DBP reactions to the CP task, $F(1,113) = 12.23$, $p = .001$, and $F(1,113) = 4.53$, $p = .04$, respectively.

Further, the participants who had previously completed the PASAT achieved a greater PASAT score (actual performance), $F(1,113) = 5.07$, $p = .03$, rated their performance as better

(subjective perception of performance), $F(1,113) = 4.40$, $p = .04$, and reported the task to be less embarrassing, $F(1,113) = 4.55$, $p = .04$, when compared to those who had not previously completed it. Additionally, there was a gender influence on self-reported ratings of PASAT performance, $F(1, 113) = 4.85$, $p = .03$, PASAT engagement, $F(1, 113) = 5.75$, $p = .02$, and CP stressfulness, $F(1, 113) = 4.30$, $p = .04$. Males gave higher ratings than females for all three variables. The mean (SD) stress task appraisal ratings for both the PASAT and CP task are summarised in Table 2.2. Overall, any significant variables were noted and adjusted for as potential confounders, as appropriate, during the main analyses.

Table 2.2. Subjective appraisals of the Paced Auditory Serial Addition Test and cold pressor task.

	Mean	SD
PASAT difficulty	5.0	0.79
PASAT stressfulness	4.5	1.04
PASAT arousing	3.4	1.46
PASAT performance	1.8	1.29
PASAT confusing	4.0	1.62
PASAT engaging	4.3	1.27
PASAT embarrassing	4.1	1.48
Cold pressor difficulty	3.2	1.60
Cold pressor stressfulness	2.3	1.44

Cardiovascular reactions to the PASAT and CP task.

A repeated measures ANOVA revealed that both the PASAT and CP task significantly perturbed cardiovascular activity. There were significant main effects of time for: SBP, $F(3, 112) = 137.92$, $p < .001$, $\eta^2 = .787$, DBP, $F(3, 112) = 169.93$, $p < .001$, $\eta^2 = .820$) and HR, $F(3, 112) = 58.25$, $p < .001$, $\eta^2 = .609$. As illustrated in Figures 2.1-2.3, all cardiovascular variables significantly increased in response to the stress tasks. The mean (SD) cardiovascular baseline and reactivity data is shown in Table 2.3.

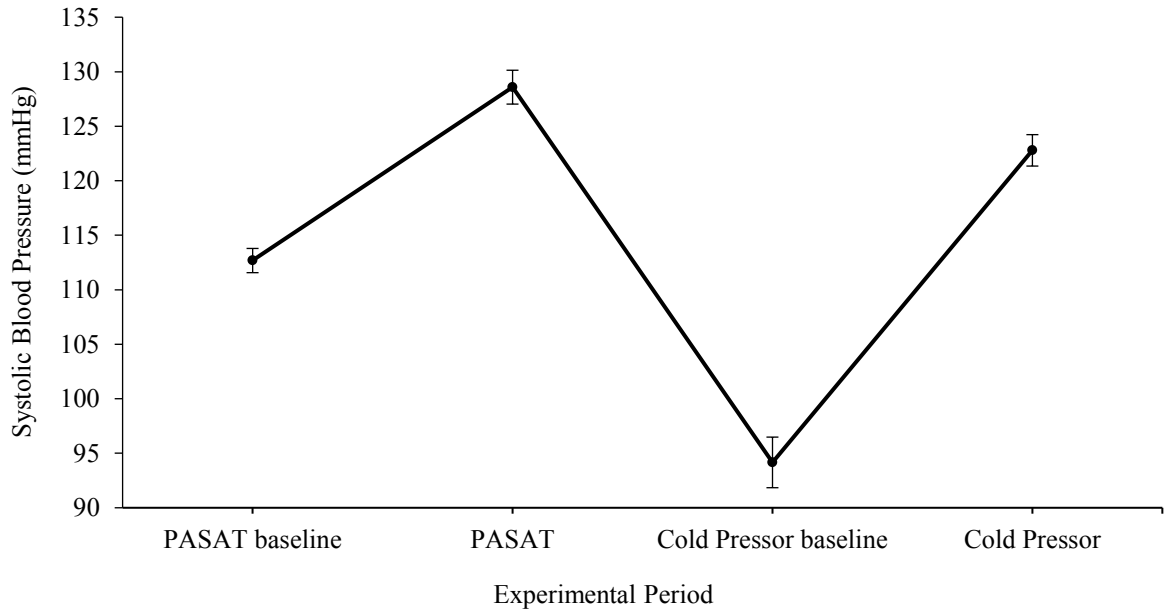

Figure 2.1. Mean (SE) systolic blood pressure during PASAT baseline, the PASAT, CP baseline and the CP task. N.B. The order of stress tasks represents protocol 1 (PASAT first) but data was averaged for all participants at all time points.

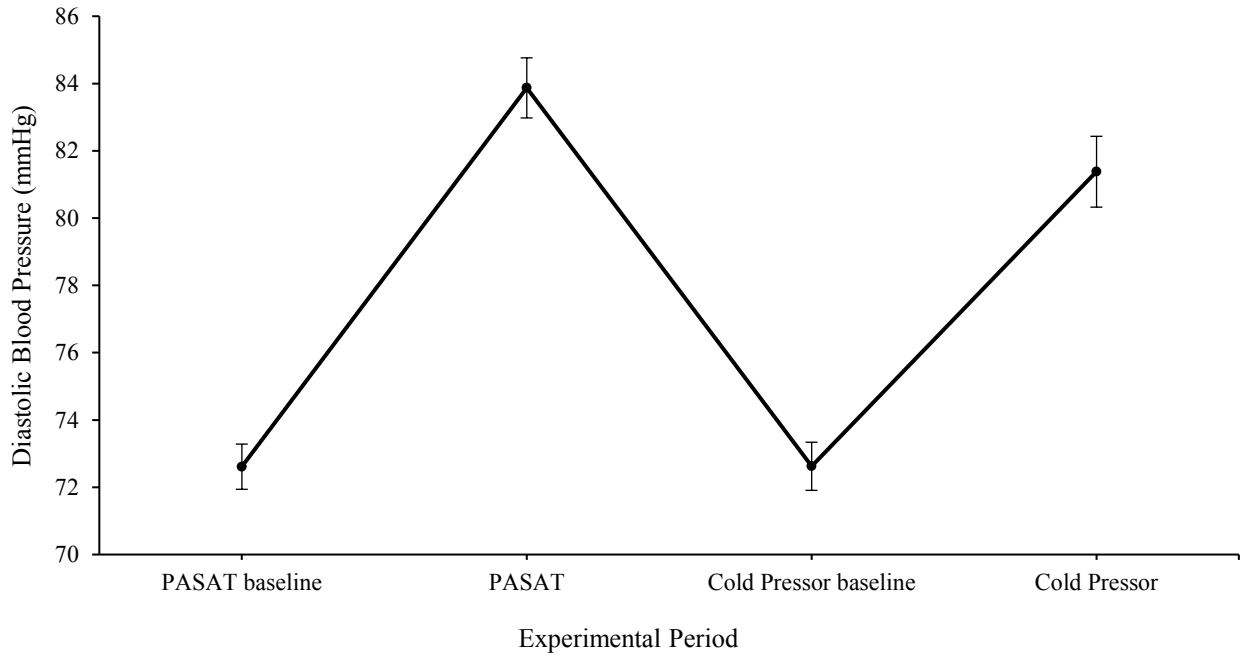

Figure 2.2. Mean (SE) diastolic blood pressure during PASAT baseline, the PASAT, CP baseline and the CP task. N.B. The order of stress tasks represents protocol 1 (PASAT first) but data was averaged for all participants at all time points.

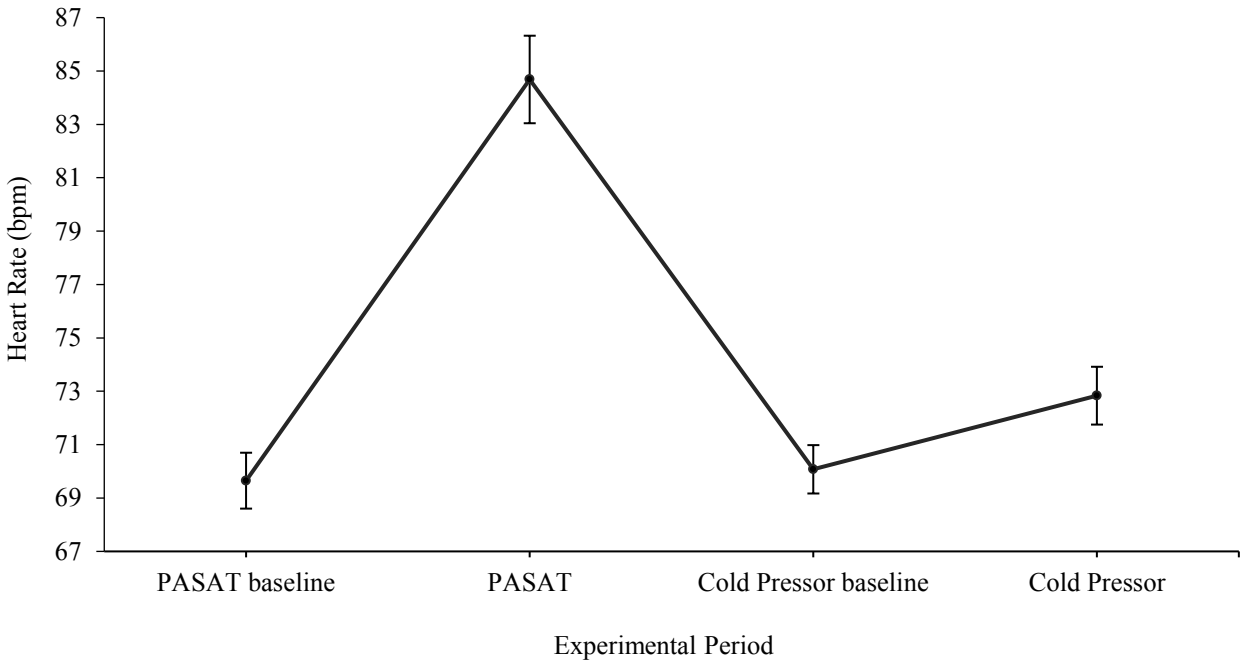

Figure 2.3. Mean (SE) heart rate during PASAT baseline, the PASAT, CP baseline and the CP task. N.B. The order of stress tasks represents protocol 1 (PASAT first) but data was averaged for all participants at all time points.

Table 2.3. Mean (SD) baseline cardiovascular activity and cardiovascular reactivity data associated with the Paced Auditory Serial Addition Test and cold pressor task.

	Mean	SD
PASAT SBP baseline (mmHg)	112.7	11.91
PASAT DBP baseline (mmHg)	72.6	7.21
PASAT HR baseline (bpm)	69.7	11.23
PASAT SBP reactivity (mmHg)	15.9	10.38
PASAT DBP reactivity (mmHg)	11.3	6.38
PASAT HR reactivity (bpm)	15.0	12.12
Cold pressor SBP baseline (mmHg)	112.94	11.31
Cold pressor DBP baseline (mmHg)	72.6	7.67
Cold pressor HR baseline (bpm)	70.7	11.57
Cold pressor SBP reactivity (mmHg)	9.84	10.15
Cold pressor DBP reactivity (mmHg)	8.75	8.92
Cold pressor HR reactivity (bpm)	2.18	7.26

Cardiovascular stress reactions to the PASAT and CP task with adjustment for order

Due to the large stress task order effect on cardiovascular activity, as previously described, the repeated measures ANOVAs above were repeated entering task order as a between-subjects variable. There were still significant main effects of time for SBP, $F(3,111) = 136.17$, $p < .001$, $\eta^2 = .786$, DBP, $F(3, 111) = 165.90$, $p < .001$, $\eta^2 = .818$, and HR, $F(3, 111) = 56.57$, $p < .001$, $\eta^2 = .605$, as well as time by order interaction effects for DBP, $F(3, 111) = 4.59$, $p = .005$, $\eta^2 = .111$, and HR, $F(3, 111) = 23.68$, $p < .001$, $\eta^2 = .390$. These effects are shown in Figures 2.4 - 2.6.

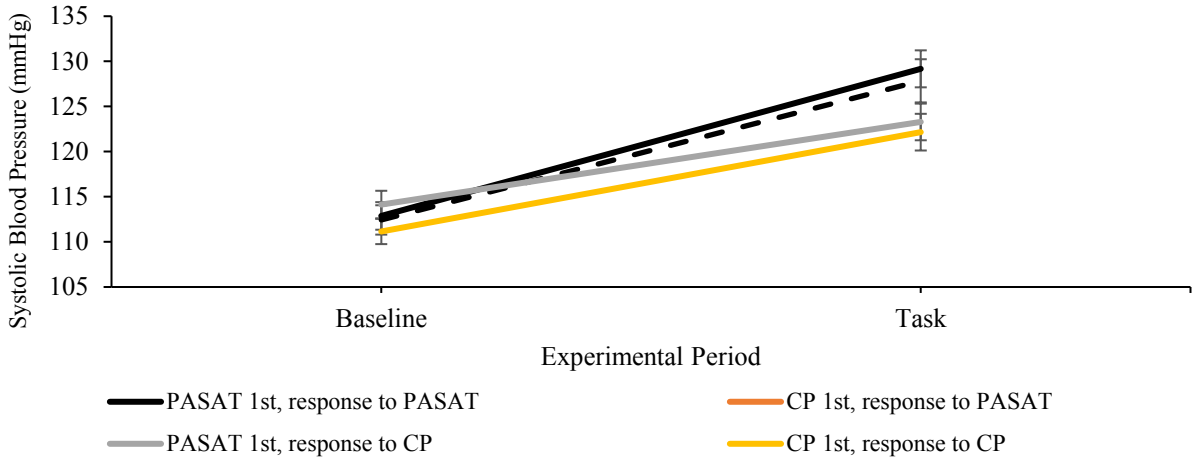

Figure 2.4. Mean (SE) systolic blood pressure reactivity to the PASAT and CP split by task order

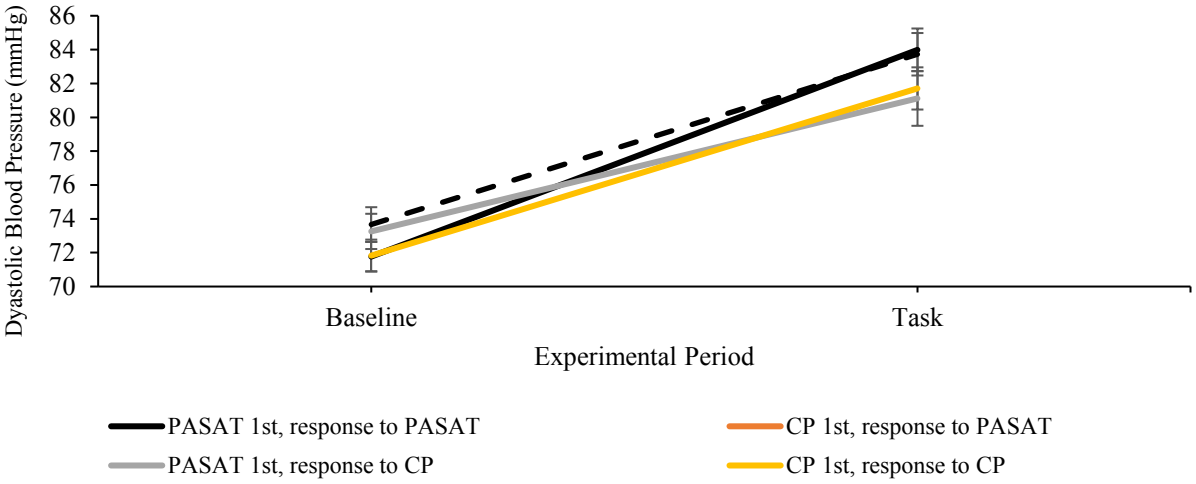

Figure 2.5. Mean (SE) diastolic blood pressure reactivity to the PASAT and CP split by task order

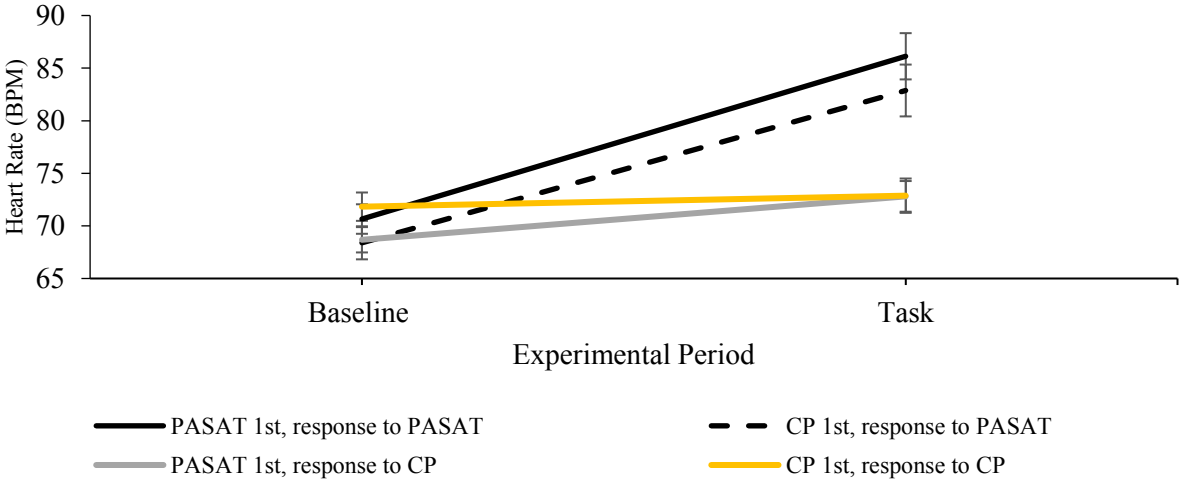

Figure 2.6. Mean (SE) heart rate reactivity to the PASAT and CP split by task order

Correlational analyses between self-reported grit and resilience

Table 2.4 shows the mean (SD) total scores for the Grit-s and the CD-RISC. Pearson's correlations revealed that grit was positively associated with resilience, $r(113) = .511$, $p < .001$, and self-reported ratings of how confusing the participants found the PASAT, $r(113) = .185$, $p = 0.48$. Gritter individuals reported having greater resilience and found the PASAT less confusing.

Table 2.4. Mean (SD) responses to the Short Grit Scale (grit-s) and Connor Davidson Resilience Scale (CD-RISC) and scores for behavioural measures of perseverance.

	Mean	**SD**
Questionnaires		
Grit-s total	3.4	0.54
CD-RISC total	68.7	8.95
Behavioural measures	*Mean*	*SD*
CP time spent in water (seconds)	161.2	88.37
PASAT Score (out of 1000)	722.5	108.49
Number of sheets of attempts at puzzle 4	23.8	17.49
Time taken on puzzle 4 (seconds)	1046.5	623.67

Self-reported perseverance and behavioural perseverance

Pearson's correlations also revealed that self-reported perseverance (grit-s total score) was significantly and positively associated with participant PASAT score, $r(113) = .198$, $p = .03$); grittier individuals scored more highly on the PASAT (performed better). However, self-

reported grit was not associated with any other behavioural perseverance measure: time spent in the cold water (CP), number of attempts at puzzle 4, or time taken on puzzle 4. The mean (SD) values for the behavioral measures of perseverance are summarised in Table 2.4.

Self-reported and behavioural perseverance and cardiovascular reactivity to acute stress

Correlation analyses demonstrated that self-reported perseverance was not associated with PASAT or CP cardiovascular reactivity. However, puzzle 4 attempts and puzzle 4 time were significantly positively correlated with CP reactivity. As shown in Table 2.5, those who persevered had greater reactivity. Further, a positive relationship was found between CP time, and SBP, $r(113) = .59$, $p < .001$, DBP, $r(113) = .66$, $p < .001$, and HR, $r(113) = .45$, $p < .001$, reactivity to the CP task. Unsurprisingly, those who persevered with sustained hand submersion during the task exhibited greater cardiovascular responses. It is highly likely that this is because they had longer to physiologically react. Finally, there were no significant associations between perseverance measures and PASAT reactivity.

Table 2.5. Correlations between attempts at puzzle 4, time taken on puzzle 4 and cold pressor cardiovascular reactivity

	Attempts at puzzle 4	Time taken on puzzle 4
Time taken on Puzzle 4	.629***	
CP SBP reactivity	.285**	.273**
CP DBP reactivity	.303**	.234*
CP HR reactivity	.253**	.240**

*** $p < .001$, ** $p < .01$, * $p < .05$

Perseverance and cardiovascular reactivity with adjustment for confounders

Due to the identification of potential confounding variables (gender, task order, and CP time), the relationships between self-reported and behavioural perseverance, and reactivity, were re-examined using linear regressions adjusting for these confounders. Following this, there were still significant positive relationships between CP time and CP SBP ($\beta = .236$, $p < .001$) and HR reactivity ($\beta = .216$, $p < .001$). In addition, post-adjustment, number of attempts at puzzle 4 remained significantly related to CP SBP ($\beta = .16$, $p = .03$) and DBP ($\beta = .17$, $p = .02$) reactivity and marginally predicted HR reactivity to the CP task ($\beta = .14$, $p = .09$). Those who recorded fewer attempts at the unsolvable puzzle showed a general pattern of lower CP reactivity. However, puzzle 4 time was no longer significantly associated with CP reactivity.

Secondary analysis: Perseverance and cardiovascular reactivity split by task order

Given the order effect, the sample was split to create two groups: those who completed the PASAT first and those who completed the CP task first. The correlations above were then repeated. The relationship between self-reported perseverance and cardiovascular reactivity remained non-significant. However, when examining the association between behavioural perseverance and reactivity, several significant associations now emerged. When the PASAT was completed first, number of attempts at puzzle 4 was significantly related to CP SBP, $r(60) = .304$, $p = 016$), CP DBP, $r(60) = .343$, $p = .006$, CP HR, $r(60) = .277$, $p = .029$, PASAT SBP, $r(60) = .283$, $p = .026$) and PASAT DBP reactivity, $r(60) = .352$, $p = .005$. The participants who used more sheets attempting to complete puzzle 4 had a higher PASAT SBP and DBP reactivity and produced a larger overall cardiovascular response to the CP task. Similarly, when the PASAT was first, time taken on puzzle 4 was significantly related to CP SBP, $r(62) = .366$, $p = .003$, CP DBP, $r(62) = .253$, $p = .044$, CP HR reactivity $r(62) = .323$, p

= .009 and to PASAT DBP reactivity $r(62) = .247$, $p = .049$. Participants who spent longer attempting to complete puzzle 4 had a higher DBP reactivity to the PASAT and exhibited more exaggerated overall CP cardiovascular (SBP, DBP and HR) reactions. When the CP task was completed first, there were still no significant associations.

Behavioural perseverance and cardiovascular reactivity, by group, with adjustment for confounders

Regression analyses were then conducted on significant relationships, adjusting for potential confounding variables as appropriate (gender for CP SBP and DBP reactivity; CP time for all CP reactivity). When the PASAT was completed first, adjusted models revealed that attempts at puzzle 4 still marginally predicted CP SBP, $\beta = .19$, $p = .06$, $\Delta R^2 = .035$, and HR reactivity, $\beta = .19$, $p = .08$, $\Delta R^2 = .034$, and significantly predicted CP DBP reactivity, $\beta = .24$, $p = .02$, $\Delta R^2 = .055$. Still, no significant effects emerged in the group that completed the CP task first. Analogous analyses for PASAT reactivity (where no confounders needed to be adjusted for) revealed that number of attempts at puzzle 4 was significantly related to PASAT SBP, $\beta = .28$, $p = .03$, $\Delta R^2 = .080$,) and PASAT DBP reactivity, $\beta = .35$, $p = .005$, $\Delta R^2 = .053$, but not to PASAT HR reactivity. In relation to puzzle 4 time, when the PASAT was completed first, associations with reactivity were no longer significant in adjusted analyses. The analogous statistics for the relationships between PASAT reactivity and time taken on puzzle 4 are exclusive for PASAT DBP reactivity, $\beta = .25$, $p = .049$, $\Delta R^2 = .052$. All in all, when the PASAT was first, number of attempts and time taken on puzzle 4 were significantly positively associated with PASAT reactivity, but most consistently for DBP reactivity.

Sensitivity analyses: taking time in the CP into account in calculating CP reactivity

Given that not all participants remained with their hand in the CP and CP time was strongly related to CP reactivity, new reactivity variables were formulated using minute 2 (i.e. the first cardiovascular reading) from the CP task minus baseline. The mean (SD) values for SBP, DBP, and HR reactivity to the CP were now 12.6 (11.61) mmHg, 10.9 (10.92) mmHg, and 3.1 (8.76) bpm, respectively. As before, CP time was still significantly correlated with CP reactivity, and number of attempts on puzzle 4 and time spent on puzzle 4 still remained significantly associated with CP SBP, DBP and HR reactivity. These values are shown in Table 2.6.

Table 2.6. Correlations between cold pressor time, attempts at puzzle 4, time taken on puzzle 4 and cold pressor cardiovascular reactivity

	Attempts at puzzle 4	CP time	Time taken on puzzle 4
CP time	.219**		.281**
Time taken on puzzle 4	.629**	.281**	
CP SBP reactivity	.219*	.500***	.250**
CP DBP reactivity	.316**	.560***	.205*
CP HR reactivity	.251**	.383***	.284**

*** $p < .001$, ** $p < .01$, * $p < .05$

Taking CP time into account in calculating CP reactivity and regressions with adjustment for confounders.

As above, regressions were repeated with adjustment for significant confounders (order, CP time, gender). Puzzle 4 attempts remained significantly associated with CP SBP, $\beta = .21$, $p = .009$, $\Delta R^2 = .044$, and DBP reactivity, $\beta = .18$, $p = .03$, $\Delta R^2 = .029$, but now only marginally predicted HR reactivity, $\beta = .15$, $p = .07$, $\Delta R^2 = .022$. Associations between puzzle 4 time and reactivity were abolished except for CP HR reactivity, $\beta = .18$, $p = .03$, $\Delta R^2 = .030$; individuals who demonstrated less perseverance at the puzzles showed a pattern of lower CP reactivity. When the PASAT was first and the file was split by task order, as before, and again significant confounders were adjusted for (gender, CP time), puzzle 4 attempts remained significantly associated with CP SBP, $\beta = .26$, $p = .02$, $\Delta R^2 = .066$, and DBP reactivity, $\beta = .32$, $p = .008$, $\Delta R^2 = .106$, but not with HR reactivity. Associations between puzzle 4 time and reactivity were abolished.

Analysis only with those who kept their hand in the CP water for the initial 2 minutes

A further manipulation check was investigated to ensure that time in the CP was not overly affecting the results; the analyses above were repeated with only those who persevered in the CP for 2 minutes (i.e., allowing time for the initial cardiovascular reading) included (N = 70). CP time was now only significantly (negatively) associated with CP SBP reactivity, $p = .04$. As before, adjusting for significant covariates where relevant (gender, order, CP time), puzzle 4 attempts remained significantly associated with CP SBP, $\beta = .32$, $p = .005$, $\Delta R^2 = .099$, DBP, $\beta = .38$, $p = .001$, $\Delta R^2 = .141$, and HR reactivity, $\beta = .27$, $p = .01$, $\Delta R^2 = .071$. Associations between puzzle 4 time and reactivity were abolished except for CP HR reactivity, $\beta = .27$, $p = .01$, $\Delta R^2 = .073$. Overall, individuals who demonstrated less perseverance on the puzzles showed a pattern of lower CP reactivity.

Finally, these analyses were repeated once more with the sample split by task order. In the PASAT first group, puzzle 4 attempts remained significantly associated with CP SBP, $\beta = .39$, $p = .02$, $\Delta R^2 = .146$, DBP, $\beta = .57$, $p < .001$, $\Delta R^2 = .316$, and HR reactivity, $\beta = .34$, $p = .049$, $\Delta R^2 = .112$. Associations between puzzle 4 time and BP reactivity remained non-significant, and the relationship between puzzle 4 time and CP HR reactivity withstood this adjustment, $\beta = .46$, $p = .005$, $\Delta R^2 = .211$.

Discussion

The present study examined, in a mixed-sex student sample, the relationship between cardiovascular reactivity to acute stress and self-reported and behavioural perseverance. It also explored whether self-reported and behavioural perseverance correlated. Self-reported perseverance was not related to cardiovascular reactivity. Following adjustment for potential confounders (gender and CP time), low behavioural perseverance, conceptualised as recording fewer impossible puzzle attempts, marginally predicted blunted CP SBP and HR reactivity and significantly predicted blunted CP DBP reactivity. In analogous analyses, number of puzzle 4 attempts was also positively associated with PASAT BP (SBP and DBP) reactivity and time taken on puzzle 4 was significantly and positively correlated with PASAT DBP reactivity. On average, blunted BP responders recorded less overall time and attempts endeavouring to complete an impossible puzzle. This provides preliminary evidence to show that low behavioural perseverance is predictive of blunted cardiovascular reactivity, with DBP reactivity emerging as the strongest and most consistent correlate. However, it is important to note that in these analyses the sample was split by task order, and all significant findings were unique to group that completed the PASAT first; potential reasons for this will be discussed. It is also important to highlight the fact that findings were not consistent across cardiovascular responses (HR and BP) or stress tasks (active and passive). In relation to the secondary

objective, self-reported perseverance was positively associated with PASAT performance, which could be construed as a weak measure of behavioural perseverance. However, it was not related to any other behavioural measure. Therefore, it appears on the whole that self-report and behavioural perseverance measurement techniques do not correlate.

To the knowledge of the author, this present study is the first to examine the relationship between self-reported perseverance and cardiovascular reactivity to acute stress. Despite the null findings, this current study, alongside previous research, has shown that blunted cardiovascular reactivity is associated with low behavioural perseverance (Ginty et al., 2015). As self-reported and objective measurements of the same construct are often found to be at least low-to-moderately correlated (Prince et al., 2008), it was perhaps surprising to find that no significant associations emerged for self-reported perseverance. Nevertheless, this finding is in agreement with a previous study that reported significant associations between perseverance and negative affect only for behavioural and not self-reported perseverance (Steinberg & Williams, 2013).

It is possible that the null findings in relation to self-reported perseverance can be partly explained in terms of social desirability bias. As perseverance is such an overtly adaptive trait, it not difficult to believe that participants would attempt to manipulate their questionnaire responses in a bid to portray themselves as more perseverant. In doing so, this will have had decreased data variability, increased measurement error (Cote & Buckley, 1988) and overall, limited the ability to find significant relationships between variables (Zerbe & Paulhus, 1987). In support, researchers have suggested that the grit-s is highly susceptible to the influence of social desirability bias (Bazelais, Lemay, & Doleck, 2016; Duckworth, Peterson, Matthews,

& Kelly, 2007) due to its transparency (Duckworth, Peterson, Matthews, & Kelly, 2007).

The null findings that initially emerged in the present study when examining the relationship between behavioural perseverance and cardiovascular reactivity mirror that of previous research (Bibbey et al., 2016). Bibbey and colleagues and the present study both used a similar sample, the same stress task (PASAT) and the same behavioural perseverance paradigm (impossible Euler puzzle). This could go some way in explaining the similar null findings; it is possible that one or more of these factors were thwarting the emergent of significance. However, the PASAT has been reliably shown to perturb cardiovascular activity (Phillips, Carroll, Burns, & Drayson, 2005; Phillips, Carroll, Hunt, & Der, 2006; Phillips, Der, Hunt, & Carroll, 2009) and impossible puzzle tasks have been used to measure behavioural perseverance with success in previous research, including in student samples (Wallace, Ready, & Weitenhagen, 2009).

As previously mentioned, due to a large order effect the sample was split to create two orthogonal groups: those who completed the PASAT first and those who completed the CP task first. In addition, appropriate confounding variables for CP reactivity were statistically adjusted for. Following this, the results from the present study supported the original hypothesis that blunted reactivity would be associated with low perseverance. These updated findings differ from results gathered by Bibbey and colleagues who found no significance when examining the reactivity-perseverance relationship whatsoever. This can perhaps be attributed to disparities in study design; Bibbey et al. (2016) initially screened participants and selected extreme groups of modest size on the basis of HR reactivity, who then completed the behavioural perseverance measure. In the present cross-sectional study, participants only

attended one laboratory session, during which the relationship between blunted PASAT reactivity and low perseverance manifested only in BP reactivity. Thus, there is a parsimonious explanation that if Bibbey and colleagues had selected extreme groups on the basis of BP reactivity, or used a similar design to the present study, comparable findings may have emerged.

The significant findings were in agreement with the remainder of the existing literature; blunted physiological reactivity to stress has been associated with low perseverance, both in terms of study non-completion (Ginty et al., 2015) and quicker relapse times during alcohol (Junghanns et al., 2003; Lovallo, 2006) and smoking (Al'Absi, 2006) cessation. However, in the present study, blunted BP reactivity emerged as the most robust correlate of low perseverance, whereas previous research suggests that attenuated heart rate (and cardiac output) reactivity are more strongly predictive (Ginty et al., 2015). This finding from the present study is perhaps surprising, as most negative behavioural correlates associated with blunted reactivity appear to be more strongly and reliably predicted by blunted HR, not BP reactivity (Bennett et al., 2014; Ginty, Phillips, Higgs, et al., 2012). One plausible explanation for this centres around the different techniques used to assess perseverance, such that, different measures of perseverance may relate to different types of reactivity through different mechanisms. Perhaps in the present study, which offers a more direct measurement, poor perseverance is reflected through BP reactivity, whereas deficiencies in perseverance examined through the opportunistic technique used by Ginty et al. (2015) manifest in attenuated HR reactivity. Another explanation is that Ginty and colleagues used a beat-to-beat HR measurement technique whereas HR was measured discontinuously in the present study. It could be that the latter technique offers a weaker and less sensitive measurement of HR

reactivity which would limit the ability to find significance for this variable. However, this is unlikely given the many previous studies that showed associations between variables and blunted HR reactivity measured discontinuously (e.g. Phillips, Der, Hunt, et al., 2009).

The studies above which implicate blunted physiological reactivity in faster relapse times during alcohol (Junghanns et al., 2003; Lovallo, 2006) and smoking (Al'Absi, 2006) cessation have focused entirely on the hypothalamic-pituitary-adrenal (HPA) axis i.e., participants exhibited blunted cortisol responses. This therefore differs to the present study, which examined the cardiovascular system in isolation. However, cardiovascular and cortisol stress responses are often strongly correlated (Cacioppo, 1994). Thus, it is highly conceivable that if these cessation-based studies also measured cardiovascular activity, blunted BP reactions would have been reported. This is corroborated by studies showing associations between smoking behaviour *per se* and blunted HR reactivity (e.g., Phillips, Der, Hunt, et al., 2009). Regardless of these differences, the results from the present study help to build a stronger argument overall that perseverance is associated with general physiological blunting. This is because dysfunctional behavioural perseverance has now been associated with a variety of blunted physiological responses to acute stress: heart rate, blood pressure, cardiac output and cortisol.

The present study extends the literature by demonstrating the perseverance-reactivity relationship in response to multiple stress tasks, including a passive stressor (i.e., the CP task). Previous research has relied exclusively on active psychological stressors such as the PASAT to perturb the stress response system (Ginty et al., 2015; Bibbey et al., 2016), as these are often shown to be more effective in altering cardiovascular reactivity compared to passive stressors (Brown, Szabo, & Seraganian, 1988; Zakowski, Cohen, Hall, Wollman, & Baum,

1994). However, as low behavioural perseverance is now shown to be related to blunted physiological reactivity in response in to both types of stress, this strengthens the contention that attenuated physiological stress responses are, in fact, associated with low perseverance. However, in opposition to previous research, perseverance was not related to HR reactivity in the present study and significant associations were not found to be consistent for both behavioural perseverance measures (time taken on the impossible puzzle and number of attempts at the puzzle). Therefore, this line of reasoning should be viewed with caution. Nevertheless, much of the previous reactivity-perseverance research has relied exclusively on cessation, and the ability of individuals to persevere in refraining from unhealthy behaviour choices to measure perseverance. However, this present study has demonstrated the same positive relationship when examining whether individuals would actively persevere with a somewhat unpleasant task. In terms of real-world generalisability, this could be likened to persevering with a new diet plan. Thus, again, this extends this area of research further, as it shows that blunted reactivity is not exclusively a marker of cessation but is also predictive of different domains of behavioural perseverance. However, as mentioned previously, it should be noted that effects were not consistent for both direct behavioural perseverance measures (time taken on the impossible puzzle and attempts at the impossible puzzle).

Although self-report and objective measures of a particular construct are often found to be at least low-to-moderately correlated (Prince et al., 2008), in this present study, self-report and objective perseverance were not related. As previously mentioned, this is in agreement with another perseverance-based study, which reported significant associations for the behavioural measure alone (Steinberg & Williams, 2013). Further, this finding also concurs with the results from other studies conducted in a variety of different domains which report a lack of

association between self-reported and behavioural measurement techniques (Fuj et al., 1985). For example, when assessing physical activity levels (Prince et al., 2008) or dietary intake (Freedman et al., 2010). In the present study, one plausible explanation for why the two measures may not have correlated is that they were measuring different manifestations of perseverance. It has been suggested that behavioural perseverance assessments often examine "state perseverance" whereas self-reported questionnaires assess "trait perseverance" (Steinberg & Williams, 2013). Participants may be predisposed to be more or less perseverant (i.e., trait perseverance) but may transiently display different levels of perseverance on a day-to-day basis, dependent on the situational environment at the time (i.e., state perseverance). If this is true, this is a likely explanation for the lack of cross-measure significance. Perhaps the stressful nature of the laboratory tasks and setting impacted perseverance in the state situation, making it different from their trait perseverance measured prior to the tasks. This can be explained in terms of the strength model of self-control (Baumeister, Bratslavsky, Muraven, & Tice, 1998; Baumeister, Vohs, & Tice, 2007) which stipulates that we have limited capacity to undertake behaviours involving self-control and perseverance. This model argues that this capacity can be temporarily depleted after an initial self-control involving behaviour, which impairs future self-control behaviours. For example, choosing to persevere for longer with the two stress tasks may have reduced some participants' inner resources, meaning they were less likely to persevere with the impossible puzzle task previously used as a psychological stressor (Habhab, Sheldon, & Loeb, 2009). However, this is unlikely given that perseverers on the CP task also persevered for longer with the puzzles. Nevertheless, this model could also help explain why the relationship between perseverance and reactivity was only evident for behavioural perseverance. It is possible that the stress tasks depleted resources differently due to extensive variability in how individuals appraise and respond to

laboratory stressors (Carroll et al., 2000). However, there is also evidence that rejects these overall explanations grounded in the strength model of self-control; subjective ratings of CP and PASAT stressfulness were not related to Euler puzzle attempts or time in this present study. Nonetheless, given the issues surrounding self-reported data that have been previously discussed, this is perhaps not surprising. However, there is also more objective conflicting evidence; those who persevered for longer on the CP task also spent longer and recoded more attempts on puzzle 4. If the strength model of self-control was correct, one might have expected these relationships to be in the opposite direction. This is because a longer CP time would have depleted inner resources by a more extreme margin, therefore leaving less remaining resources to persevere with the puzzle task. Overall, it is unclear why self-report and behavioural measures did not correlate, which suggests further, and direct research is required.

As mentioned throughout, despite counterbalancing the order in which the stress tasks were presented to the participants, there was still a large order effect; participants who completed the CP task first had a higher baseline HR prior to the CP task, when compared to those who undertook the PASAT first. Accordingly, the order effect also influenced HR reactivity; when the CP task was completed first participants exhibited a lower CP HR reactivity than when the PASAT was completed first. This cannot be attributed to simple explanations such as a lack of recovery time, as the order effect was particularly apparent when participants completed the CP task first and thus had nothing to actually recover from i.e., they had higher baseline cardiovascular activity before undertaking any of the tasks. Second, it cannot be that the physical nature of cold stress *per se* was physiologically impacting the baseline for the next task, as the order effect directly impacted the specific baseline for the CP task itself, only

when the CP task was first. Or simply put, the initial baseline HR prior to the CP was higher than the next baseline value following the CP when the CP was first, and, therefore, could not have been impacted by the CP task. The authors cannot think of any physiological explanation for why recovery values from the PASAT would be lower than baseline values prior to the PASAT when the PASAT was first, which would potentially be another reason for the lower baseline prior to the CP if the CP was second. Third, it is not possible that the CP task instructions contributed to an anticipatory stress response during the baseline period before the CP task commenced, as this information was concealed until after baseline measurements concluded. Although there is no clear explanation for this order effect, it has implications for future studies that use the CP as one of a number of stress tasks. It would seem appropriate that future studies administer the CP task last (Willemsen et al., 1998), and, as in the present protocol, incorporate adequate baseline periods to account for any overshoot of recovery following the PASAT. However, there is so specific explanation for this and similar effects have not been observed in previous studies which included recovery (Whittaker, unpublished personal communication).

The present study is not without limitations. First, although the overall total sample size was originally reasonable (Allen et al., 1997), after splitting the sample the respective sizes of the two groups were relatively small. However, they were still of comparable size to sub-groups within other studies (Kristen Salomon, Bylsma, White, Panaite, & Rottenberg, 2013). Second, the order effect *per se* was a major weakness and negatively impacted the cardiovascular profile of the participants who completed the CP task first; it appeared that these participants were not responding and/or recovering to the stress tasks as expected. However, the stress tasks were presented in a counterbalanced manner, a technique used with success in previous

research, even when the CP task was included (Ring et al., 2000). In future studies, administering the PASAT first seems a more sound methodological choice and previous research supports this (Willemsen et al., 1998). Third, the sample included disproportionally more females then males. Research has demonstrated that there are sex differences in cardiovascular responses to stress (Stone, Dembroski, Costa Jr., & MacDougall, 1990) and in perseverance (Christensen & Knezek, 2014; Kiefer & Shih, 2006). However, gender was statistically adjusted for in all necessary analyses and there were no gender differences in self-reported or behavioural perseverance in the current study. Fourth, as the present study was observational it is not possible to determine causality. There is a potential that an uncontrolled variable was confounding the results and mediated the relationship between cardiovascular reactivity and perseverance (Christenfeld, Sloan, Carroll, & Greenland, 2004). However, the present study adjusted for all necessary confounding variables which is a major strength. Fifth, the Euler puzzle perseverance task lacks ecological validity, and thus just because participants persevered/did not persevere on this task does not make it generalisable to real life situations, for example, persevering with long-term exercise programs. However, at present, there is no direct gold standard behavioral measure of perseverance, nor an ecologically valid one, and the Euler puzzle task has been used to examine perseverance in previous research (Bibbey et al., 2016). Further, it is possible that demand characteristics had a significant impact on the internal validity of the study; participants may have quickly realised that the puzzle was not possible and just continued to persevere as an attempt to appear as a "good participant". However, participants completed three possible puzzles in a bid to disguise the fact that the final puzzle was impossible and were assured that it was possible if they asked. Similarly, the behaviour or mere presence of the investigator recording the puzzle time and attempts may have impacted the participants in such a way that it led to

atypical perseverance being measured. However, the experimenter read a set of standardized instructions and although they observed the task, this was done out of the participants' range of vision. Another limitation is the possibility of large individual differences in the personalities and demeanor of the participants. It is possible that those with greater confidence, and other similar traits, may have been the ones who asked to stop and therefore appeared as non-perseverers, possibly independent of actual perseverance. In future studies, it may be advantageous for the experimenter to leave the room during the Euler puzzle task and observe covertly, as this should hopefully encourage participants to exhibit more typical perseverance. However, this could also encourage cheating and contribute to non-engagement with the task. Overall, it would seem advantageous for future research to statistically adjust for a wide range of personality and behavioural traits. Next, it is possible that the self-report and behavioural techniques used to examine perseverance explored different constructs; with behavioural examining state perseverance and self-report assessing trait perseverance (Steinberg & Williams, 2013). However, the fact that both self-report and objective measures of perseverance were administered concurrently is novel within the cardiovascular reactivity literature and is a major strength of this present study. Nonetheless, future studies may benefit from modifying self-report measures in a manner which allows them to also examine state perseverance i.e., rephrase some questions to focus on how perseverant participants feel at "the current moment in time". It would also be interesting to explore how state perseverance is impacted by previous engagement in laboratory stress tasks, in line with the strength model of self-control (Baumeister, Bratslavsky, Muraven, & Tice, 1998; Baumeister, Vohs, & Tice, 2007).

Future research might choose to repeat and extend this study and directly examine the relationship between perseverance and physiological reactivity by comprehensively exploring the cardiovascular system and HPA axis in parallel. Authors should follow the PASAT first protocol, incorporate long recovery periods and include multiple measures of both self-report; for example, the Two Item Self-Report Persistence Measure (Steinberg et al., 2007) and behavioural; for example, mirror tracing (Quinn et al., 1996), breath holding (Hajek, Belcher, & Stapleton, 1987) perseverance. This would help to generate a stronger argument that blunted reactivity is associated with low perseverance. Future studies may then consider exploring the impact of real-world factors, such as the deemed importance of the task/situation and consequences of persevering/giving up, on the reactivity-perseverance relationship. It would be interesting to see whether blunted reactors physiologically differ and/or differ in terms of perseverance, as a function of whether the task and/or consequence is deemed to be of personal importance. In addition, findings from this type of research would lead to a more thorough understanding of the undoubtedly complex reactivity-perseverance relationship, including how it may interact with real world situational variables.

In this present study, poorer behavioural perseverance, conceptualised as recording less overall time and attempts endeavouring to complete an impossible puzzle task, was predictive of blunted BP reactivity to acute stress. Although the findings were not consistent across all conditions, this current research still adds further support to a growing and already convincing body of evidence that implicates blunted reactivity as a maladaptive response pattern (Carroll, Ginty, Whittaker, Lovallo, & de Rooij, 2017; Carroll, Lovallo, et al., 2009; Phillips, 2011). It appears that blunted reactivity is a peripheral marker for central motivational dysfunction (Carroll, Lovallo, et al., 2009; Lovallo, 2006) and poor behavioural regulation (Ginty et al.,

2015) corroborated by behaviours such as impulsivity (Allen et al., 2009; Bibbey et al., 2016) and poor perseverance in this present and previous research (Ginty et al., 2015). Measuring physiological responses to acute stress has the potential to be a simple yet useful prognostic marker in identifying those who unconsciously have low perseverance, who may need more support when in situations typically requiring high perseverance, for example, adherence to rehabilitation, cessation from unhealthy behaviours, coping with stress. However, before the applications of this research can be explored, further research investigating the foundations of the perseverance-reactivity relationship is required and evidence of consistency across stress tasks and physiological responses would be important to find.

References

Abrantes, A. M., Strong, D. R., Lejuez, C. W., Kahler, C. W., Carpenter, L. L., Price, L. H., … Brown, R. A. (2008). The role of negative affect in risk for early lapse among low distress tolerance smokers. *Addictive Behaviors*, *33*(11), 1394–1401.

Al'Absi, M. (2006). Hypothalamic-pituitary-adrenocortical responses to psychological stress and risk for smoking relapse. *International Journal of Psychophysiology*, *59*(3), 218–227.

Al'Absi, M., Wittmers, L. E., Erickson, J., Hatsukami, D., & Crouse, B. (2003). Attenuated adrenocortical and blood pressure responses to psychological stress in ad libitum and abstinent smokers. *Pharmacology Biochemistry and Behavior*, *74*(2), 401–410.

Allen, M. T., Hogan, A. M., & Laird, L. K. (2009). The relationships of impulsivity and cardiovascular responses: The role of gender and task type. *International Journal of Psychophysiology*, *73*, 369–376.

Allen, M. T., Matthews, K. A., & Sherman, F. S. (1997). Cardiovascular reactivity to stress and left ventricular mass in youth. *Hypertension*, *30*(4), 782–787.

Ambrose, J. A., & Barua, R. S. (2004). The pathophysiology of cigarette smoking and cardiovascular disease: An update. *Journal of the American College of Cardiology*, *43*(10), 1731–1737.

Andersson, H., & Bergman, L. R. (2011). The role of task persistence in young adolescence for successful educational and occupational attainment in middle adulthood. *Developmental Psychology*, *47*(4), 950–960.

Back, S. E., Hartwell, K., DeSantis, S. M., Saladin, M., McRae-Clark, A. L., Price, K. L., …

Brady, K. T. (2010). Reactivity to laboratory stress provocation predicts relapse to cocaine. *Drug and Alcohol Dependence*, *106*(1), 21–27.

Barnett, P. a, Spence, J. D., Manuck, S. B., & Jennings, J. R. (1997). Psychological stress and the progression of carotid artery disease. *Journal of Hypertension*, *15*(1), 49–55.

Baumeister, R. F., Bratslavsky, E., Muraven, M., & Tice, D. M. (1998). Ego depletion: Is the active self a limited resource? *Journal of Personality and Social Psychology*, *74*(5), 1252–1265.

Baumeister, R. F., Vohs, K. D., & Tice, D. M. (2007). The strength model of self-control. *Current Directions in Psychological Science*, *16*(6), 351–355.

Bazelais, P., Lemay, D. J., & Doleck, T. (2016). How does grit impact college students' academic achievement in science? *European Journal of Science and Mathmatics Education*, *4*(1), 33–43.

Bennett, C., Blissett, J., Carroll, D., & Ginty, A. T. (2014). Rated and measured impulsivity in children is associated with diminished cardiac reactions to acute psychological stress. *Biological Psychology*, *102*, 68–72.

Bibbey, A., Ginty, A. T., Brindle, R. C., Phillips, A. C., & Carroll, D. (2016). Blunted cardiac stress reactors exhibit relatively high levels of behavioural impulsivity. *Physiology and Behavior*, *159*(1), 40–44.

Brindle, R. C., Whittaker, A. C., Bibbey, A., Carroll, D., & Ginty, A. T. (2017). Exploring the possible mechanisms of blunted cardiac reactivity to acute psychological stress. *International Journal of Psychophysiology*, *113*, 1–7.

Brown, T. G., Szabo, A., & Seraganian, P. (1988). Physical versus psychological

determinants of heart rate reactivity to mental arithmetic. *Psychophysiology*, *25*(5), 532–537.

Bush, G., Luu, P., & Posner, M. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Sciences*, *4*(1), 215–222.

Cacioppo, J. T. (1994). Social neuroscience: Autonomic, neuroendocrine, and immune responses to stress. *Psychophysiology*, *31*(2), 113–128.

Carroll, D., Bibbey, A., Roseboom, T. J., Phillips, A. C., Ginty, A. T., & De Rooij, S. R. (2012). Forced expiratory volume is associated with cardiovascular and cortisol reactions to acute psychological stress. *Psychophysiology*, *49*(6), 866–872.

Carroll, D., Davey Smith, G., Sheffield, D., Willemsen, G., Sweetnam, P. M., Gallacher, J. E., & Elwood, P. C. (1996). Blood pressure reactions to the cold pressor test and the prediction of future blood pressure status: data from the Caerphilly study. *Journal of Epidemiology and Community Health*, *52*(8), 528–529.

Carroll, D., Davey Smith, G., Shipley, M. J., Steptoe, A., Brunner, E. J., & Marmot, M. G. (2001). Blood pressure reactions to acute psychological stress and future blood pressure status: A 10-year follow-up of men in the whitehall II study. *Psychosomatic Medicine*, *63*(5), 737–743.

Carroll, D., Ginty, A. T., Der, G., Hunt, K., Benzeval, M., & Phillips, A. C. (2012). Increased blood pressure reactions to acute mental stress are associated with 16-year cardiovascular disease mortality. *Psychophysiology*, *49*(10), 1444–1448.

Carroll, D., Ginty, A. T., Painter, R. C., Roseboom, T. J., Phillips, A. C., & de Rooij, S. R. (2012). Systolic blood pressure reactions to acute stress are associated with future

hypertension status in the Dutch Famine Birth Cohort Study. *International Journal of Psychophysiology*, *85*(2), 270–273.

Carroll, D., Ginty, A. T., Whittaker, A. C., Lovallo, W. R., & de Rooij, S. R. (2017). The behavioural, cognitive, and neural corollaries of blunted cardiovascular and cortisol reactions to acute psychological stress. *Neuroscience and Biobehavioral Reviews*, *77*(1), 74–86.

Carroll, D., Harrison, L. K., Johnston, D. W., Ford, G., Hunt, K., Der, G., & West, P. (2000). Cardiovascular reactions to psychological stress: The influence of demographic variables. *Journal of Epidemiology and Community Health*, *54*(11), 876–877.

Carroll, D., Lovallo, W. R., & Phillips, A. C. (2009). Are large physiological reactions to acute psychological stress always bad for health? *Social and Personality Psychology Compass*, *3*, 725–743.

Carroll, D., Phillips, A. C., & Balanos, G. M. (2009). Metabolically exaggerated cardiac reactions to acute psychological stress revisited. *Psychophysiology*, *46*(2), 270–275.

Carroll, D., Phillips, A. C., & Der, G. (2008). Body mass index, abdominal adiposity, obesity, and cardiovascular reactions to psychological stress in a large community sample. *Psychosomatic Medicine*, *70*(6), 653–660.

Carroll, D., Phillips, A. C., Der, G., Hunt, K., & Benzeval, M. (2011). Blood pressure reactions to acute mental stress and future blood pressure status: Data from the 12-year follow-up of the West of Scotland Study. *Psychosomatic Medicine*, *73*(9), 737–743.

Carroll, D., Phillips, A. C., Der, G., Hunt, K., Bibbey, A., Benzeval, M., & Ginty, A. T. (2013). Low forced expiratory volume is associated with blunted cardiac reactions to

acute psychological stress in a community sample of middle-aged men and women. *International Journal of Psychophysiology*, *90*(1), 17–20.

Carroll, D., Ring, C., Hunt, K., Ford, G., & MacIntyre, S. (2003). Blood pressure reactions to stress and the prediction of future blood pressure: Effects of sex, age, and socioeconomic Position. *Psychosomatic Medicine*, *65*(6), 1058–1064.

Carroll, D., Turner, J. R., & Prasad, R. (1986). The effects of level of difficulty of mental arithmetic challenge on heart rate and oxygen consumption. *International Journal of Psychophysiology*, *4*, 167–173.

Chida, Y., & Steptoe, A. (2010). Greater cardiovascular responses to laboratory mental stress are associated with poor subsequent cardiovascular risk status: A meta-analysis of prospective evidence. *Hypertension*, *55*(4), 1026–1032.

Christenfeld, N. J. S., Sloan, R. P., Carroll, D., & Greenland, S. (2004). Risk factors, confounding, and the illusion of statistical control. *Psychosomatic Medicine*, *66*(1), 868–875.

Christensen, R., & Knezek, G. (2014). Comparative measures of grit , tenacity and perseverance. *International Journal of Learning, Teaching and Educational Research*, *8*(1), 16–30.

Connor, K. M., & Davidson, J. R. T. (2003). Development of a new Resilience scale: The Connor-Davidson Resilience scale (CD-RISC). *Depression and Anxiety*, *18*(2), 76–82.

Corral-Verdugo, V., & Figueredo, A. J. (1999). Convergent and divergent validity of three measures of conservation behavior. The multitrait-multimethod approach. *Environment and Behavior*, *31*(6), 805–820.

Cote, J. a., & Buckley, M. R. (1988). Measurement error and theory testing in consumer research: an illustration of the importance of construct validation. *Journal of Consumer Research*, *14*(4), 579–582.

Cramer, J. A., Benedict, A., Muszbek, N., Keskinaslan, A., & Khan, Z. M. (2008). The significance of compliance and persistence in the treatment of diabetes, hypertension and dyslipidaemia: A review. *International Journal of Clinical Practice*, *62*(1), 76–87.

Crim, C., Celli, B., Edwards, L. D., Wouters, E., Coxson, H. O., Tal-Singer, R., & Calverley, P. M. A. (2011). Respiratory system impedance with impulse oscillometry in healthy and COPD subjects: ECLIPSE baseline results. *Respiratory Medicine*, *105*, 1069–1078.

de Rooij, S. R., & Roseboom, T. J. (2010). Further evidence for an association between self-reported health and cardiovascular as well as cortisol reactions to acute psychological stress. *Psychophysiology*, *47*(1), 1172–1175.

de Rooij, S. R., Schene, A. H., Phillips, D. I., & Roseboom, T. J. (2010). Depression and anxiety: Associations with biological and perceived stress reactivity to a psychological stress protocol in a middle-aged population. *Psychoneuroendocrinology*, *35*(6), 866–877.

Duckworth, A. L., Peterson, C., Matthews, M. D., & Kelly, D. R. (2007). Grit: Perseverance and passion for long-term goals. *Journal of Personality and Social Psychology*, *92*(6), 1087–1101.

Duckworth, A. L., & Quinn, P. D. (2009). Development and validation of the short Grit Scale (Grit-S). *Journal of Personality Assessment*, *91*(2), 166–174.

Everson, S. a, Lynch, J. W., Chesney, M. a, Kaplan, G. a, Goldberg, D. E., Shade, S. B., … Salonen, J. T. (1997). Interaction of workplace demands and cardiovascular reactivity in

progression of carotid atherosclerosis: population based study. *British Medical Journal*, *314*(7080), 553–558.

Freedman, L. S., Kipnis, V., Schatzkin, A., Tasevska, N., & Potischman, N. (2010). Can we use biomarkers in combination with self-reports to strengthen the analysis of nutritional epidemiologic studies? *Epidemiologic Perspectives and Innovations*, *7*(1), 2–9.

Fuj, E. T., Hennessy, M., & Mak, J. (1985). An evaluation of the validity and reliability of survey response data on household electricity conservation. *Evaluation Review*, *9*(1), 93–104.

Georgiades, A., Lemne, C., De Faire, U., Lindvall, K., & Fredrikson, M. (1997). Stress-induced blood pressure measurements predict left ventricular mass over three years among borderline hypertensive men. *European Journal of Clinical Investigation*, *27*(9), 733–739.

Gianaros, P. J., May, J. C., Siegle, G. J., & Jennings, J. R. (2005). Is there a functional neural correlate of individual differences in cardiovascular reactivity? *Psychosomatic Medicine*, *67*(1), 31–39.

Ginty, A. T., Brindle, R. C., & Carroll, D. (2015). Cardiac stress reactions and perseverance: Diminished reactivity is associated with study non-completion. *Biological Psychology*, *109*, 200–205.

Ginty, A. T., Gianaros, P. J., Derbyshire, S. W. G., Phillips, A. C., & Carroll, D. (2013). Blunted cardiac stress reactivity relates to neural hypoactivation. *Psychophysiology*, *50*(3), 219–229.

Ginty, A. T., Phillips, A. C., Der, G., Deary, I. J., & Carroll, D. (2011a). Cognitive ability and

simple reaction time predict cardiac reactivity in the West of Scotland Twenty-07 Study. *Psychophysiology*, *48*(1), 1022–1027.

Ginty, A. T., Phillips, A. C., Der, G., Deary, I. J., & Carroll, D. (2011b). Heart rate reactivity is associated with future cognitive ability and cognitive change in a large community sample. *International Journal of Psychophysiology*, *82*(1), 167–174.

Ginty, A. T., Phillips, A. C., Higgs, S., Heaney, J. L. J., & Carroll, D. (2012). Disordered eating behaviour is associated with blunted cortisol and cardiovascular reactions to acute psychological stress. *Psychoneuroendocrinology*, *37*(5), 715–724.

Ginty, A. T., Phillips, A. C., Roseboom, T. J., Carroll, D., & DeRooij, S. R. (2012). Cardiovascular and cortisol reactions to acute psychological stress and cognitive ability in the Dutch Famine Birth Cohort Study. *Psychophysiology*, *49*(1), 391–400.

Girdler, S. S., Jamner, L. D., Jarvik, M., Soles, J. R., & Shapiro, D. (1997). Smoking status and nicotine administration differentially modify hemodynamic stress reactivity in men and women. *Psychosomatic Medicine*, *59*(3), 294–306.

Gronwall, D. M. A. (1977). Paced Auditory Serial-Addition Task: A Measure of Recovery from Concussion. *Perceptual and Motor Skills*, *44*(2), 367–373.

Guh, D. P., Zhang, W., Bansback, N., Amarsi, Z., Birmingham, C. L., & Anis, A. H. (2009). The incidence of co-morbidities related to obesity and overweight: A systematic review and meta-analysis. *BMC Public Health*, *9*(88), 1–20.

Habhab, S., Sheldon, J. P., & Loeb, R. C. (2009). The relationship between stress, dietary restraint, and food preferences in women. *Appetite*, *52*(2), 437–444.

Hagemann, D., Waldstein, S. R., & Thayer, J. F. (2003). Central and autonomic nervous

system integration in emotion. *Brain and Cognition*, *52*(1), 79–87.

Hajek, P., Belcher, M., & Stapleton, J. (1987). Breath-holding endurance as a predictor of success in smoking cessation. *Addictive Behaviors*, *12*(1), 285–288.

Heaney, J. L. J., Ginty, A. T., Carroll, D., & Phillips, A. C. (2011). Preliminary evidence that exercise dependence is associated with blunted cardiac and cortisol reactions to acute psychological stress. *International Journal of Psychophysiology*, *79*(2), 323–329.

Hebert, J. R., Clemow, L., Pbert, L., Ockene, I. S., & Ockene, J. K. (1995). Social desirability bias in dietary self-report may compromise the validity of dietary intake measures. *International Journal of Epidemiology*, *24*(2), 389–398.

Heleniak, C., McLaughlin, K. A., Ormel, J., & Riese, H. (2016). Cardiovascular reactivity as a mechanism linking child trauma to adolescent psychopathology. *Biological Psychology*, *120*, 108–119.

Holsen, L. M., Spaeth, S. B., Lee, J. H., Ogden, L. A., Klibanski, A., Whitfield-Gabrieli, S., & Goldstein, J. M. (2011). Stress response circuitry hypoactivation related to hormonal dysfunction in women with major depression. *Journal of Affective Disorders*, *131*(1), 379–387.

Junghanns, K., Backhaus, J., Tietz, U., Lange, W., Bernzen, J., Wetterling, T., … Driessen, M. (2003). Impaired serum cortisol stress response is a predictor of early relapse. *Alcohol and Alcoholism*, *38*(2), 189–193.

Kamarck, T. W., Everson, S. A., Kaplan, G. A., Manuck, S. B., Jennings, J. R., Salonen, R., & Salonen, J. T. (1997). Exaggerated blood pressure responses during mental stress are associated with enhanced carotid atherosclerosis in middle-aged finnish men: Findings

from the Kuopio Ischemic Heart Disease Study. *Circulation*, *96*(11), 3842–3848.

Kiefer, A., & Shih, M. (2006). Gender differences in persistence and attributions in stereotype relevant contexts. *Sex Roles*, *54*, 859–868.

Koo-Loeb, J. H., Pedersen, C., & Girdler, S. S. (1998). Blunted cardiovascular and catecholamine stress reactivity in women with bulimia nervosa. *Psychiatry Research*, *80*(1), 13–27.

Kormos, C., & Gifford, R. (2014). The validity of self-report measures of proenvironmental behavior: A meta-analytic review. *Journal of Environmental Psychology*, *40*(1), 359–371.

Le Marchand, L., Wilkens, L. R., Kolonel, L. N., Hankin, J. H., & Lyu, L. C. (1997). Associations of sedentary lifestyle, obesity, smoking, alcohol use, and diabetes with the risk of colorectal cancer. *Cancer Research*, *57*(21), 4787–4794.

Lovallo, W. R. (2005). Cardiovascular reactivity: Mechanisms and pathways to cardiovascular disease. *International Journal of Psychophysiology*, *58*(1), 119–132.

Lovallo, W. R. (2006). Cortisol secretion patterns in addiction and addiction risk. *International Journal of Psychophysiology*, *59*(3), 195–202.

Lovallo, W. R. (2011). Do low levels of stress reactivity signal poor states of health? *Biological Psychology*, *86*(1), 121–128.

Lovallo, W. R., Dickensheets, S. L., Myers, D. A., Thomas, T. L., & Nixon, S. J. (2000). Blunted stress cortisol response in abstinent alcoholic and polysubstance-abusing men. *Alcoholism: Clinical and Experimental Research*, *24*(5), 651–658.

Manuck, S. B., & Schaefer, D. C. (1978). Stability of individual differences in cardiovascular

reactivity. *Physiology and Behavior*, *21*(4), 675–678.

Markovitz, J. H., Raczynski, J. M., Wallace, D., Chettur, V., & Chesney, M. a. (1998). Cardiovascular reactivity to video game predicts subsequent blood pressure increases in young men: The CARDIA study. *Psychosomatic Medicine*, *60*(2), 186–191.

Matthews, K. A., Katholi, C. R., McCreath, H., Whooley, M. A., Williams, D. R., Zhu, S., & Markovitz, J. H. (2004). Blood pressure reactivity to psychological stress predicts hypertension in the CARDIA study. *Circulation*, *110*, 74–78.

Moss, H. B., Vanyukov, M., Yao, J. K., & Kirillova, G. P. (1999). Salivary cortisol responses in prepubertal boys: The effects of parental substance abuse and association with drug use behavior during adolescence. *Biological Psychiatry*, *45*(10), 1293–1299.

Muñoz, L. C., & Anastassiou-Hadjicharalambous, X. (2011). Disinhibited behaviors in young children: Relations with impulsivity and autonomic psychophysiology. *Biological Psychology*, *86*, 349–359.

Murphy, C. M., Stojek, M. K., & MacKillop, J. (2014). Interrelationships among impulsive personality traits, food addiction, and Body Mass Index. *Appetite*, *73*(1), 45–50.

Panknin, T. L., Dickensheets, S. L., Nixon, S. J., & Lovallo, W. R. (2002). Attenuated heart rate responses to public speaking in individuals with alcohol dependence. *Alcoholism: Clinical and Experimental Research*, *26*(6), 841–847.

Paris, J. J., Franco, C., Sodano, R., Frye, C. A., & Wulfert, E. (2010). Gambling pathology is associated with dampened cortisol response among men and women. *Physiology and Behavior*, *99*(1), 230–233.

Patja, K., Jousilahti, P., Hu, G., Valle, T., Qiao, Q., & Tuomilehto, J. (2005). Effects of

smoking, obesity and physical activity on the risk of type 2 diabetes in middle-aged Finnish men and women. *Journal of Internal Medicine*, *258*(4), 356–362.

Phillips, A. C. (2011). Blunted as well as exaggerated cardiovascular reactivity to stress is associated with negative health outcomes. *Japanese Psychological Research*, *53*(2), 177–192.

Phillips, A. C., Carroll, D., Burns, V. E., & Drayson, M. (2005). Neuroticism, cortisol reactivity, and antibody response to vaccination. *Psychophysiology*, *42*(2), 232–238.

Phillips, A. C., Carroll, D., Hunt, K., & Der, G. (2006). The effects of the spontaneous presence of a spouse/partner and others on cardiovascular reactions to an acute psychological challenge. *Psychophysiology*, *43*(6), 633–640.

Phillips, A. C., Der, G., & Carroll, D. (2009). Self-reported health and cardiovascular reactions to psychological stress in a large community sample: Cross-sectional and prospective associations. *Psychophysiology*, *46*(1), 1020–1027.

Phillips, A. C., Der, G., Hunt, K., & Carroll, D. (2009). Haemodynamic reactions to acute psychological stress and smoking status in a large community sample. *International Journal of Psychophysiology*, *73*(3), 273–278.

Phillips, A. C., Ginty, A. T., & Hughes, B. M. (2013). The other side of the coin: Blunted cardiovascular and cortisol reactivity are associated with negative health outcomes. *International Journal of Psychophysiology*, *90*(1), 1–7.

Phillips, A. C., Hunt, K., Der, G., & Carroll, D. (2011). Blunted cardiac reactions to acute psychological stress predict symptoms of depression five years later: Evidence from a large community study. *Psychophysiology*, *48*(1), 142–148.

Phillips, A. C., Roseboom, T. J., Carroll, D., & De Rooij, S. R. (2012). Cardiovascular and cortisol reactions to acute psychological stress and adiposity: Cross-sectional and prospective associations in the dutch famine birth cohort study. *Psychosomatic Medicine*, *70*(4), 699–710.

Prince, S., Adamo, K., Hamel, M., Hardt, J., Gorber, S., & Tremblay, M. (2008). A comparison of direct versus self-report measures for assessing physical activity in adults: a systematic review. *International Journal of Behavioral Nutrition and Physical Activity*, *1*(5), 56–80.

Quinn, E. P., Brandon, T. H., & Copeland, A. L. (1996). Is task persistence related to smoking and substance abuse? The application of learned industriousness theory to addictive behaviors. *Experimental and Clinical Psychopharmacology*, *4*(1), 186–190.

Register General's *Classification of occupations* (1980). London: HMSO.

Ring, C., Harrison, L. K., Winzer, A., Carroll, D., Drayson, M., & Kendall, M. (2000). Secretory immunoglobulin A and cardiovascular reactions to mental arithmetic, cold pressor, and exercise: Effects of alpha-adrenergic blockade. *Psychophysiology*, *37*(1), 634–643.

Salomon, K., Bylsma, L. M., White, K. E., Panaite, V., & Rottenberg, J. (2013). Is blunted cardiovascular reactivity in depression mood-state dependent? A comparison of major depressive disorder remitted depression and healthy controls. *International Journal of Psychophysiology*, *90*(1), 50–57.

Salomon, K., Clift, A., Karlsdóttir, M., & Rottenberg, J. (2009). Major depressive disorder is associated with attenuated cardiovascular reactivity and impaired recovery among those free of cardiovascular disease. *Health Psychology*, *28*(2), 157-.

Schmidt, F. T. C., Fleckenstein, J., Retelsdorf, J., Eskreis-Winkler, L., & Möller, J. (2017). Measuring Grit: A German validation and a domain-specific approach to grit. *European Journal of Psychological Assessment*, *32*(2), 111–118.

Schwartz, A. R., Gerin, W., Davidson, K. W., Pickering, T. G., Brosschot, J. F., Thayer, J. F., … Linden, W. (2003). Toward a causal model of cardiovascular responses to stress and the development of cardiovascular disease. *Psychosomatic Medicine*, *65*, 22–35.

Szetho. (n.d.). Euler Puzzles. Retrieved from http://www.szetho.com

Sorocco, K. H., Lovallo, W. R., Vincent, A. S., & Collins, F. L. (2006). Blunted hypothalamic-pituitary-adrenocortical axis responsivity to stress in persons with a family history of alcoholism. *International Journal of Psychophysiology*, *59*(1), 210–217.

Steinberg, M. L., Krejci, J. A., Collett, K., Brandon, T. H., Ziedonis, D. M., & Chen, K. (2007). Relationship between self-reported task persistence and history of quitting smoking, plans for quitting smoking, and current smoking status in adolescents. *Addictive Behaviors*, *32*, 1451–1460.

Steinberg, M. L., & Williams, J. M. (2013). State, but not trait, measures of persistence are related to aegative affect. *Journal of Studies on Alcohol and Drugs*, *74*(4), 584–588.

Steinberg, M. L., Williams, J. M., Gandhi, K. K., Foulds, J., Epstein, E. E., & Brandon, T. H. (2012). Task persistence predicts smoking cessation in smokers with and without schizophrenia. *Psychology of Addictive Behaviors*, *26*(1), 850–858.

Stewart, R. A. H., Hagström, E., Held, C., Wang, T. K. M., Armstrong, P. W., Aylward, P. E., … Wallentin, L. (2017). Self-reported health and outcomes in patients with stable coronary heart disease. *Journal of the American Heart Association*, *6*(8), 60–67.

Stice, E., Spoor, S., Bohon, C., & Small, D. M. (2008). Relation between obesity and blunted striatal response to food is moderated by TaqIA A1 allele. *Science*, *17*(1), 449–452.

Stone, S. V, Dembroski, T. M., Costa Jr., P. T., & MacDougall, J. M. (1990). Gender differences in cardiovascular reactivity. *Journal of Behavioral Medicine*, *90*(1), 50–57.

Touré-Tillery, M., & Fishbach, A. (2014). How to measure motivation: A guide for the experimental social psychologist. *Social and Personality Psychology Compass*, *8*(7), 328–341.

Treiber, F. A., Kamarck, T., Schneiderman, N., Sheffield, D., Kapuku, G., & Taylor, T. (2003). Cardiovascular reactivity and development of preclinical and clinical disease states. *Psychosomatic Medicine*, *65*(1), 46–62.

Turner, J. R., & Carroll, D. (1985). Heart rate and oxygen consumption during mental arithmetic, a video game, and graded exercise: Further evidence of metabolically-exaggerated cardiac adjustments? *Psychophysiology*, *22*, 261–267.

Van der Kooy, K., van Hout, H., Marwijk, H., Marten, H., Stehouwer, C., & Beekman, A. (2007). Depression and the risk for cardiovascular diseases: Systematic review and meta analysis. *International Journal of Geriatric Psychiatry*, *22*(7), 613–626.

Van Gaal, L. F., Mertens, I. L., & De Block, C. E. (2006). Mechanisms linking obesity with cardiovascular disease. *Nature*, *444*(7121), 875–880.

Von Culin, K. R., Tsukayama, E., & Duckworth, A. L. (2014). Unpacking grit: Motivational correlates of perseverance and passion for long-term goals. *Journal of Positive Psychology*, *9*(4), 306–312.

Wallace, H. M., Ready, C. B., & Weitenhagen, E. (2009). Narcissism and task persistence.

Self and Identity, *8*(1), 78–93.

Wawrzyniak, A. J., Hamer, M., Steptoe, A., & Endrighi, R. (2016). Decreased reaction time variability is associated with greater cardiovascular responses to acute stress. *Psychophysiology*, *53*(5), 739–748.

Willemsen, G., Ring, C., Carroll, D., Evans, P., Clow, A., & Hucklebridge, F. (1998). Secretory immunoglobulin A and cardiovascular reactions to mental arithmetic and cold pressor. *Psychophysiology*, *35*(3), 252–259.

York, K. M., Hassan, M., Li, Q., Li, H. H., Fillingim, R. B., & Sheps, D. S. (2007). Coronary artery disease and depression: Patients with more depressive symptoms have lower cardiovascular reactivity during laboratory-induced mental stress. *Psychosomatic Medicine*, *69*, 521–528.

Zakowski, S. G., Cohen, L., Hall, M. H., Wollman, K., & Baum, A. (1994). Differential effects of active and passive laboratory stressors on immune function in healthy men. *International Journal of Behavioral Medicine*, *1*(2), 163–184.

Zerbe, W. J., & Paulhus, D. L. (1987). Socially desirable responding in organizational behavior: A reconception. *Academy of Management Review*, *12*(2), 250–264.

CHAPTER THREE

BLUNTED HEART RATE REACTIVITY TO ACUTE PASSIVE STRESS IS CHARACTERISTIC OF THOSE WITH LOWER RESILIENCE

Abstract

Exaggerated and blunted cardiovascular reactions to acute stress are both maladaptive response patterns associated with a range of adverse health and behavioural outcomes. Recent evidence suggests that blunted reactivity, as a marker of poor behavioural regulation, manifests in everyday behaviours, however, the evidence is limited. The present study explored whether low resilience was predictive of attenuated cardiovascular reactivity using the same dataset and methodological approach as the previous chapter. Participants (N=115) completed a validated resilience questionnaire before their cardiovascular activity (heart rate and blood pressure) was measured prior, and during exposure to active (mental arithmetic) and passive (cold pressor) psychological stress. After the sample was split by stress task order (due to a large order effect) lower self-reported resilience was associated with attenuated HR reactivity to passive stress. This relationship survived statistical adjustment for time spent with hand submerged in the cold pressor, and gender, as potential confounding variables. This study adds further evidence to show that negative motivation-related behavioural outcomes manifest in those with blunted reactivity. Further, improving resilience may lead to a more adaptive pattern of stress responding.

Introduction

Cardiovascular reactions in response to acute stress differ substantially between individuals (Carroll, 1992). In support of the reactivity hypothesis (Obrist, 1981), there is a large and compelling literature that implicates exaggerated cardiovascular reactivity in the pathophysiology of cardiovascular disease development: hypertension (Carroll, Ginty, Painter, et al., 2012; Carroll et al., 2011; Matthews et al., 2004), atherosclerosis (Barnett et al., 1997; Kamarck et al., 1997) and left ventricular hypertrophy (Allen, Matthews, & Sherman, 1997; Georgiades, Lemne, De Faire, Lindvall, & Fredrikson, 1997). Exaggerated reactivity even extends to predict cardiovascular disease mortality (Carroll et al., 2012). Overall, the sheer support for the reactivity hypothesis is demonstrated both meta-analytically and in a range of reviews (Chida & Steptoe, 2010; Schwartz et al., 2003; Treiber et al., 2003)

By implication, it was assumed that low or blunted reactivity was benign or even protective (Carroll et al., 2009). However, more recent evidence has demonstrated that attenuated responses, like exaggerated, are associated with adverse health outcomes: depression (Phillips, Hunt, Der, & Carroll, 2011; Salomon, Clift, Karlsdóttir, & Rottenberg, 2009; York et al., 2007), anxiety (de Rooij et al., 2010), obesity (Carroll, Phillips, & Der, 2008; Phillips, Roseboom, Carroll, & De Rooij, 2012) and poor self-reported health (de Rooij & Roseboom, 2010; Phillips, Der, & Carroll, 2009). This highlights the need for a revision of the original reactivity hypothesis, to account for maladaptive correlates at both extremes of the cardiovascular reactivity continuum (Carroll et al., 2009; Phillips, 2011).

Attenuated physiological reactivity is not just associated with negative health but also negative behavioural outcomes. Blunted responses are characteristic of those with an

addiction to smoking cigarettes (Al'Absi et al., 2003; Girdler et al., 1997) and can even predict relapse during smoking cessation (Al'Absi, 2006) independent of the physiological impact that abstinence may have (Girdler et al., 1997). Blunted reactivity also manifests in alcohol dependent individuals (Lovallo et al., 2000; Panknin et al., 2002) and the offspring of alcoholic parents who have no known alcohol addiction (Moss et al., 1999; Sorocco et al., 2006). This suggests that blunted reactivity may actually predate and be a marker of addiction, as opposed to being a result of physiological alteration caused by the chemical nature of the substances. In further support of this, attenuated reactivity is also related to a number of non-substance dependencies (Ginty, Phillips, Higgs, et al., 2012; Heaney et al., 2011; Koo-Loeb et al., 1998; Paris et al., 2010).

It has been suggested that the correlates of blunted reactivity share a singular commonality in that they reflect motivational dysregulation (Carroll, Lovallo, et al., 2009; Lovallo, 2006) in the fronto-limbic brain regions which control motivated and goal-directed behaviours (Carroll, Ginty, Whittaker, Lovallo, & de Rooij, 2017; Carroll et al., 2009; Phillips, 2011). In support of this, fMRI studies have demonstrated fronto-limbic deactivation in blunters during exposure to stressful stimuli (Gianaros et al., 2005; Ginty et al., 2013). Further, fronto-limbic brain regions also control cardiovascular responses to stress (Carroll et al., 2009), coordinate motivational/behavioural processes and modulate autonomic regulation (Bush et al., 2000; Hagemann et al., 2003; Lovallo, 2005a). In sum, it is clear that the evidence surrounding the motivational dysregulation hypothesis is convincing. However, if blunted reactivity is truly a marker of central dysfunction, one would assume that attenuated physiological responses would be associated with general manifestations of poor behavioural regulation.

There is now emerging evidence which demonstrates this; blunted reactivity is associated with high impulsivity/impaired response inhibition (Allen, Hogan, & Laird, 2009; Bennett, Blissett, Carroll, & Ginty, 2014; Bibbey, Ginty, Brindle, Phillips, & Carroll, 2016; Muñoz & Anastassiou-Hadjicharalambous, 2011) and externalising psychopathology (Heleniak et al., 2016). Similarly, those with blunted reactivity have been shown to perform poorly during motivation and effort-contingent behavioural tasks, for example, lung function spirometry assessments (Carroll et al., 2012; Carroll et al., 2013). However, interestingly, this must be unconsciously regulated, as blunted responders are unaware of any motivational (Brindle et al., 2017) and/or task engagement/performance differences (Bibbey et al., 2016; Ginty, Phillips, Higgs, et al., 2012) in their behaviour, compared to non-blunted responders.

Therefore, if blunted reactivity is reflected in actual motivation-related behaviours, in line with the model of motivational dysregulation, there is reason to believe that blunted reactivity will be associated with poor resilience. Although there is no standardised definition of resilience, most are formed using the foundations of two fundamental concepts: adversity and positive adaption (Fletcher & Sarkar, 2013). As the Connor-Davison Resilience Scale (CD-RISC; Connor & Davidson, 2003) has been used as the primary resilience measure in this present study, the definition offered by Connor & Davison has been selected for use i.e., "personal qualities that enable one to thrive in the face of adversity" (Connor & Davidson, 2003, *P*.76).

Resilience is highly adaptive and a protective mechanism against the impact of negative stressors (Bonanno, 2004). Research has demonstrated its wide-ranging importance, for example: for athletes in elite sport (Sarkar & Fletcher, 2014), for general health and well-

being (O'Rourke, 2004), in depression (Min et al., 2012), in anxiety (Min et al., 2015) and in disordered eating behaviours (Calvete, las Hayas, & Gómez del Barrio, 2018).

Resilience is clearly an important construct, and, at its core, shares many similarities with perseverance. For example, both are powerful attributes that can help individuals overcome obstacles and/or meet a particular goal. Further, resilience can be considered a key component of perseverance (Perkins-Gough et al., 2018), and as the previous chapter, and other research (Martin, Byrd, Watts, & Dent, 2015) has demonstrated there is a positive association between grit and resilience. However, it is important to emphasise that despite their similarities, they are still separate entities, with a major difference being that perseverance directly involves goal setting whereas resilience does not (Stoffel & Cain, 2018). Overall, it is important to understand how resilience, as a motivation-related construct, is associated with cardiovascular reactivity and to compare how this relationship is similar or dissimilar to the perseverance-reactivity relationship investigated in the previous chapter.

The existing literature surrounding resilience and physiological reactivity is both limited and contradictory. Research has demonstrated that poor resilience is associated with attenuated cortisol (Galatzer-Levy et al., 2014) but not BP (Black et al., 2017; Corina & Adriana, 2013) or HR (Black et al., 2017) reactivity to acute stress. Similarly, others have reported that attenuated cortisol reactivity is linked to high resilience (Ruiz-Robledillo et al., 2017) or not with resilience at all (Black et al., 2017). Thus, it is impossible to draw any firm conclusions with regard to whether physiological reactivity is associated with resilience. It seems that these studies are limited by small sample sizes and a lack of statistical adjustment for potential

confounding variables; this could go some way in explaining the inconsistent findings. Therefore, there is a need for more robust research which takes into account these limitations.

Thus, the present study aims to examine the relationship between self-reported resilience and cardiovascular reactivity to active and passive psychological stress, after adjusting for a range of potential confounders. Despite the inconsistencies within the literature, as blunted reactivity has previously been associated with manifestations of poor behavioural regulation, it was hypothesised that those with lower resilience would show a pattern of hypoactive cardiovascular responding to stress.

Methods

The same dataset used in the previous chapter to examine the perseverance-reactivity relationship was also used to investigate any potential associations between resilience and cardiovascular reactivity in this present chapter. Thus, the sample, questionnaire scores, cardiovascular activity data and general methodological approach remains the same, and for this reason is not repeated below. The novel feature of this chapter is the focus on the Connor Davidson Resilience Scale and examining its association with cardiovascular reactivity to acute stress.

Measures

Questionnaires

Resilience

The well-validated Connor-Davison Resilience Scale (CD-RISC; Connor & Davidson, 2003) uses 25 items to investigate psychological resilience. Example items include: “I can deal with

whatever comes my way", "I tend to bounce back after illness or hardship" and "I am not easily discouraged by failure". When completing the CD-RISC, participants respond using a five-point Likert scale where 0 = ("not true at all") and 4 = ("true all the time"); larger scores indicate greater resilience. Evidence of high test-retest reliability (r = .87) and internal consistency (α = .89) of the CD-RISC have been reported in the literature (Connor & Davidson, 2003) and the Cronbach's alpha for the questionnaire in the present study was .84. Research has also demonstrated that the instrument has acceptable convergent and discriminant validity (Connor & Davidson, 2003) and supported its capacity to distinguish between those with greater and lesser resilience (Connor & Davidson, 2003).

Results

As per the previous chapter, the sample consisted of 115 University of Birmingham students who enrolled via verbal, email and social media-based recruitment strategies. The mean (SD) age of the sample was 19.8 (1.81) years with a total of 86 females (75%). The socio-demographic, anthropometric and previous PASAT experience characteristics of the sample are again summarised in Table 3.1.

Table 3.1. Socio-demographic, anthropometric and previous Paced Auditory Serial Addition Test experience characteristics of the sample (N=115)

	Mean (SD)	N (%)
Age (years)	19.8 (1.81)	
Sex (female)		86 (75)
Ethnicity (white)		94 (82)
Body mass index (kg/m^2)	23.1 (3.08)	
Parental occupation (non-manual)		98 (85)
Completed PASAT before (no)		105 (92)
Stress task order (PASAT first)		64 (56)

Order and socio-demographic influence on cardiovascular activity and stress task ratings

One-way ANOVAs revealed that the order in which the stress tasks were undertaken significantly influenced CP baseline HR, $F(1,113) = 4.32$, $p = .04$, such that, compared with the individuals who completed the PASAT first, participants in the CP first group had a higher baseline HR prior to the CP task. Consequently, order was also significantly associated with CP HR reactivity; when the CP was completed first, CP HR reactivity was lower, $F(1,113) = 11.21$, $p = .001$, than when the PASAT was the first task. Additionally, cardiovascular activity differed by gender; males exhibited more exaggerated SBP and DBP reactions to the CP task, $F(1,113) = 12.23$, $p = .001$, and $F(1,113) = 4.53$, $p = .04$, respectively.

Further, participants who had previously completed the PASAT achieved a greater PASAT score (actual performance), $F(1,113) = 5.07$, $p = .03$, rated their performance as better

(subjective perception of performance), $F(1,113) = 4.40$, $p = .04$, and the task as less embarrassing, $F(1,113) = 4.55$, $p = .04$, than those who had not previously completed it did. Additionally, there was a gender influence on self-reported ratings of PASAT performance, $F(1, 113) = 4.85$, $p = .03$, PASAT engagement, $F(1, 113) = 5.75$, $p = .02$, and CP stressfulness, $F(1, 113) = 4.30$, $p = .04$. Males gave higher ratings than females for all three variables. Overall, any significant variables were noted and adjusted for as potential confounding variables, as appropriate, during the main analyses.

Cardiovascular reactions to the PASAT and CP task.

Repeated measure ANOVAs revealed that both the PASAT and CP task significantly perturbed cardiovascular (SBP, DBP & HR) activity. There were significant main effects of time for: SBP, $F(3, 112) = 137.92$, $p < .001$, $\eta^2 = .787$, DBP, $F(3, 112) = 169.93$, $p < .001$, $\eta^2 = .820$) and HR, $F(3, 112) = 58.25$, $p < .001$, $\eta^2 = .609$. As illustrated in Figures 2.1-2.3 in the previous chapter, all cardiovascular variables significantly increased in response to the PASAT and CP stress tasks.

Cardiovascular stress reactions to the PASAT and CP task with adjustment for order.

Due to the large order effect on baseline cardiovascular activity and reactivity, as previously described, the repeated measures ANOVAs above were reexamined entering order as a between-subjects variable. There were still significant main effects of time for SBP, $F(3,111) = 136.17$, $p < .001$, $\eta^2 = .786$, DBP, $F(3, 111) = 165.90$, $p < .001$, $\eta^2 = .818$, and HR, $F(3, 111) = 56.57$, $p < .001$, $\eta^2 = .605$, as well as time by order interaction effects for DBP, $F(3, 111) = 4.59$, $p = .005$, $\eta^2 = .111$, and HR, $F(3, 111) = 23.68$, $p < .001$, $\eta^2 = .390$. These effects are shown in Figures 3.1–3.3 below.

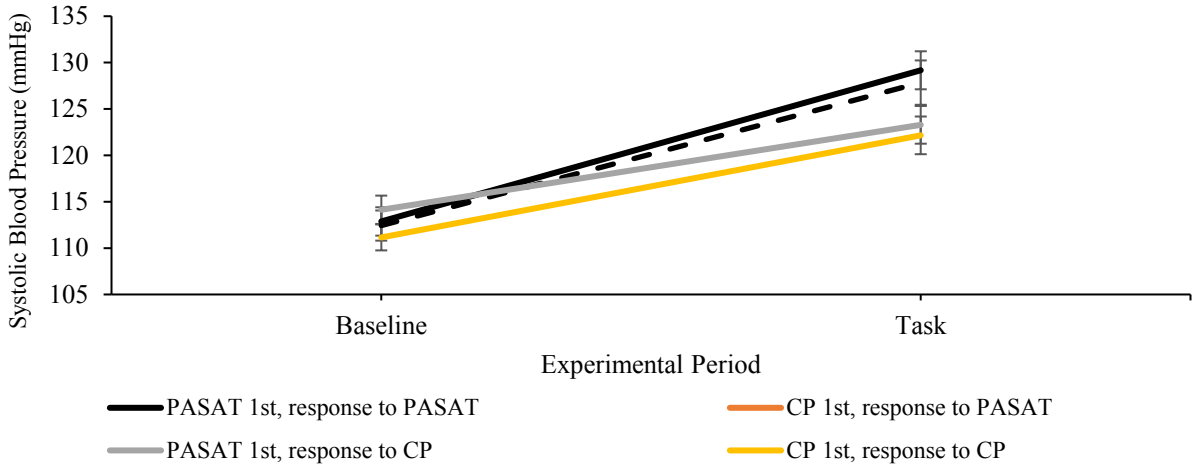

Figure 3.1. Mean (SE) systolic blood pressure reactivity to the PASAT and CP split by task order

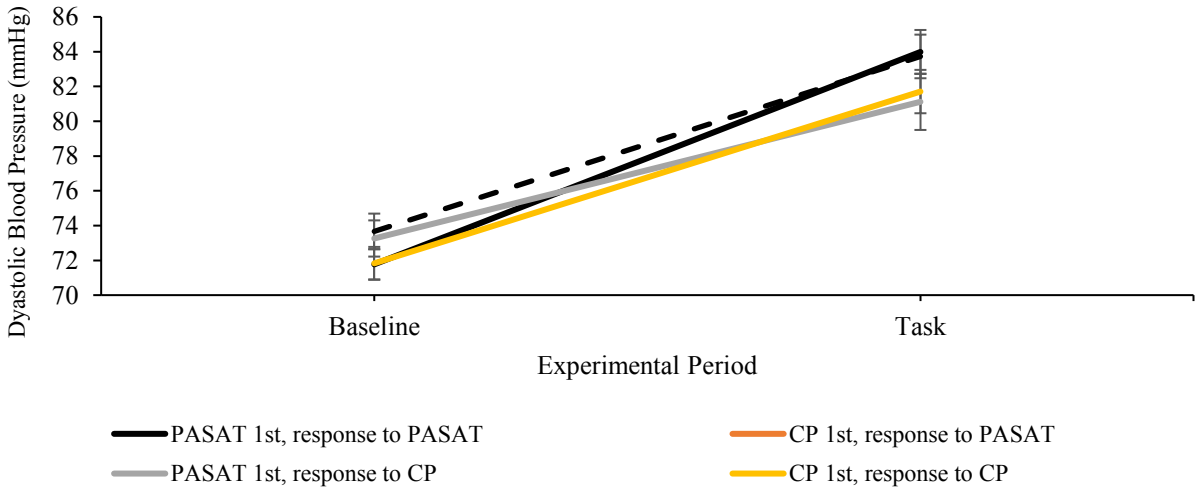

Figure 3.2. Mean (SE) diastolic blood pressure reactivity to the PASAT and CP split by task order

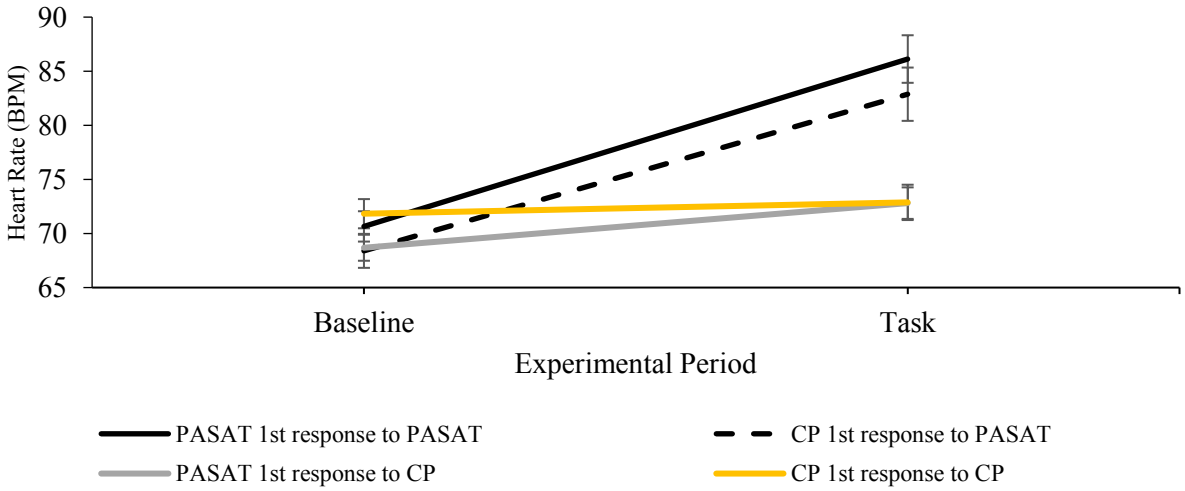

Figure 3.3. Mean (SE) heart rate reactivity to the PASAT and CP split by task order

Further, as reported in the previous chapter, the length of time the hand was submerged in the CP was unsurprisingly associated with CP reactivity: SBP, $r(113) = .59$, $p < .001$, DBP, $r(113) = .66$, $p < .001$, and HR, $r(113) = .45$, $p < .001$. As expected, those who persevered with sustained hand submersion during the task exhibited greater cardiovascular reactions. Therefore, this also needed to be controlled for, as a potential confounding variable, in future CP reactivity analyses.

Correlational analyses between resilience, self-reported grit and stress task appraisals

Table 3.2 shows the mean (SD) total scores for the Grit-s, and the CD-RISC. Pearson's correlations revealed that resilience was positively associated with grit, $r(113) = .511$, $p < .001$, and self-reported ratings of PASAT stressfulness , $r(113) = .253$, $p = 0.4$, such that, those who recorded greater resilience on the CD-RISC reported higher grit and found the PASAT more stressful.

Table 3.2. Mean (SD) responses to the Short Grit Scale (grit-s) and Connor Davidson Resilience Scale (CD-RISC).

Questionnaire scores	Mean	SD
Grit-s total	3.4	0.54
CD-RISC total	68.7	8.95

Self-reported resilience and cardiovascular reactivity to acute stress

Correlational analyses revealed that self-reported resilience (CD-RISC score) was not associated with SBP, DBP or HR reactivity, either to the PASAT or to the CP task. This was also the case when the relationships were re-examined in linear regressions adjusting for

potential confounding variables (gender, order, and CP time); the relationships between resilience and reactivity remained non-significant.

Secondary analysis: Resilience and cardiovascular reactivity split by task order

Due to the large order effect, the sample was again split to create two groups: those who completed the PASAT first and those who completed the CP task first. Following this, correlations between self-reported resilience and cardiovascular reactivity were repeated, but again, all associations remained non-significant. Regressions were then conducted and the relationships between resilience and reactivity were revisited with adjustment for the potential confounders previously identified (gender for CP SBP and DBP reactivity; CP time for all CP reactivity variables). Adjusted models revealed that in the PASAT first group, self-reported resilience (CD-RISC score) was positively associated with HR reactivity to the CP task (β = .27, p = .01, ΔR^2 = .073), such that, those who completed the PASAT first and exhibited more exaggerated HR reactions during the CP task also reported having greater resilience. However, no significant effects emerged in the CP first group, for PASAT cardiovascular reactivity or when examining CP SBP and DBP reactivity.

Finally, the significant relationship above was re-examined using CP reactivity derived from the first value during CP stress and including only those individuals who kept their hand in the CP for at least two minutes (N = 70). As before, CP time and gender were also statistically adjusted for. This regression analysis revealed that lower resilience was still predictive of blunted HR reactivity (β = .36, p = .03, ΔR^2 = .127). Thus, it is highly likely that this relationship manifested independent of the time participants persevered in the CP task.

Discussion

This present study examined the relationship between cardiovascular reactivity to acute stress and self-reported resilience. As per the previous chapter, due to a large order effect the sample was split in two. In the group that completed the PASAT first, lower resilience was associated with blunted HR reactivity to the CP task. This remained statistically significant after adjusting for gender and CP time as potential confounding variables. CP SBP and DBP reactivity were not associated with resilience, nor was PASAT cardiovascular (SBP, DBP, HR) reactivity in general.

In the current study, greater resilience was associated with exaggerated HR reactivity. Accordingly, this provides preliminary evidence that poor resilience is a potential predictor of blunted HR reactivity. However, it should be noted that this effect was only apparent in the group that completed the PASAT first and in response to passive stress only, so replication would be necessary to establish these findings. Nevertheless, this finding aligns with previous research which relates blunted reactivity, particularly blunted HR reactivity, to adverse behavioural outcomes (Bibbey et al., 2016; Ginty et al., 2015). It is not clear why individuals with low resilience would show a blunted response, but given that resilience is a key stress protection mechanism (Bonanno, 2004) it is possible that blunting initially emerges to protect against the development of exaggerated and harmful cardiovascular patterns (Crump, Sundquist, Winkleby, & Sundquist, 2016). However, due to the negative correlates associated with blunted responding, which reflect less flexibility within the stress response system (Ginty et al., 2012; Heaney et al., 2011; Phillips et al., 2011), it is likely that this response pattern is in fact not particularly adaptive, although it may protect against cardiovascular disease risk initially. Eventually, blunted responses may lead to alterations in the brain

associated with central motivational dysregulation (Carroll, Ginty, Whittaker, Lovallo, & de Rooij, 2017; Carroll et al., 2009), which would put such individuals at risk of developing other negative health outcome like depression (Phillips et al., 2011; Salomon, Clift, Karlsdóttir, & Rottenberg, 2009; York et al., 2007) and obesity (Carroll, Phillips, & Der, 2008; Phillips, Roseboom, Carroll, & De Rooij, 2012). On the other hand, it also plausible that low resilience is simply another manifestation of motivational dysregulation, rather than a mechanism developed as an initially adaptive response.

The present findings do not align with the explanation offered by Ruiz-Robledillo and colleagues into the reactivity-resilience relationship. These authors argue that resilience is key to maintaining homeostatic reactivity, as it encourages stress to be appraised as less threatening (Ruiz-Robledillo, De Andrés-García, Pérez-Blasco, González-Bono, & Moya-Albiol, 2014). Thus, this explanation is grounded in classic appraisal theory (Lazarus & Folkman, 1984). However, in the present study, those with greater resilience self-reported the PASAT as more rather than less stressful which contests their explanation. Further, if the explanation presented by Ruiz-Robledillo and colleagues was correct, one would expect reactivity to remain relatively moderate during stress exposure in those with high resilience. However, in the present study, reactivity was substantially higher in resilient individuals. All in all, it is obvious that more direct research is needed to understand the underlying mechanisms which may explain why resilience seems to influence physiological reactivity.

When comparing the present results to a similar study that also examined the HR reactivity-resilience relationship, the findings are not supportive; Corina and Adriana (2013) reported no significant relationship. Their sample was of smaller size than the current study and was

comprised entirely of older male participants. This could go some way in explaining the null results, particularly as no significant relationships emerged during sub-analyses in the current study when examining males alone. Further, the stress tasks utilised by both studies were dissimilar; in the present study, the relationship between blunted reactivity and low resilience was found only in response to the CP task, a passive psychological stressor, whereas Corina and Adriana (2013) used a unique active psychological stressor (simulated train collision). In the present study, no significant relationships emerged between resilience and reactivity in response to active stress. Therefore, there is reason to believe that if Corina and Adriana (2013) induced passive stress, their findings may have aligned with the results of the present study. Further, it could be that their active stressor was inadequate for reactivity research, as it has received little validation in the literature. However, their analyses still demonstrated its efficacy in perturbing cardiovascular activity to suggest otherwise. Taken together, one possibility is that the resilience-HR reactivity relationship exclusively emerges during exposure to passive but not active psychological stress. However, as before, more research is needed to explore this contention.

The null relationships which emerged between BP reactivity and resilience in this present student sample are in accordance with similar research in young policemen (Corina & Adriana, 2013) and middle-aged manual workers (Black et al., 2017). As this relationship has remained non-significant when examining a range of different population groups, this implies that it is not the demographic characteristics of samples that are inhibiting significant findings from materialising. Further, associations between resilience and other variables, for example, emotional granularity and recovery from stress have been evidenced in mixed-sex student (Tugade, Fredrickson, & Barrett, 2004) and older populations (Ong, Bergeman, Bisconti, &

Wallace, 2006) alike. One possible reason that may explain why no significant BP findings have been found relates to the resilience measurement techniques; Corina and Adriana used the Resilience Scale for Adults (Hjemdal, Friborg, Martinussen, & Rosenvinge, 2001), Black and colleagues utilised The Brief Resilience Scale (Smith et al., 2008) and the present study administered The Connor-Davison Resilience Scale. However, each measure is well validated, possesses good psychometric properties and has been used with success in previous research (Windle, Bennett, & Noyes, 2011). Therefore, this is an unlikely explanation for the lack of significance. In addition, a variety of laboratory stress tasks have been used across these studies: the PASAT, the CP task and a simulated train collision task. Analyses show that each respective stressor significantly perturbed BP, and previous research provides further evidence of this (Allen, Sherwood, Obrist, Crowell, & Grange, 1987; Phillips, Carroll, Hunt, & Der, 2006). Thus, the stress tasks themselves are an unlikely reason for the resilience-BP reactivity relationship being non-significant. Meta-analytically, resilience has been shown to be significantly associated with a diverse range of variables, in many research domains, across many samples, using many measurement techniques (Hu, Zhang, & Wang, 2015). Therefore, perhaps the association between blunted reactivity and low resilience is just simply not reflected in BP responses. However, evidence from direct and larger scale research is required to confirm this.

Although previous and current research demonstrates that resilience is not associated with BP reactivity, a study has demonstrated an association between poor resilience and attenuated cortisol responses (Galatzer-Levy et al., 2014). As cardiovascular and cortisol stress responses are often strongly correlated (Cacioppo, 1994), this could be considered surprising. However, other cardiovascular reactivity-based studies have suggested that it may be cortisol and HR

reactivity which are more consistently associated, not BP and cortisol reactivity (Ginty, Phillips, Higgs, et al., 2012; Heaney et al., 2011). Therefore, there is reason to believe that if Galatzer-Levy and colleagues also measured HR reactivity, or the present study examined cortisol, attenuated reactivity would have been reflected in both the SAM and HPA axes. Conversely, other research has found highly conflicting evidence to Galatzer-Levy and colleagues; in a sample of caregivers, lower cortisol reactivity was associated with high resilience (Ruiz-Robledillo et al., 2017). This finding is seemingly paradoxical, given that attenuated reactivity typically reflects poor behavioural regulation (Ginty et al., 2015). One possible explanation for this finding is that the stress of caregiving encouraged the development of resilience as a coping mechanism (Corina & Adriana, 2013). This is supported by the fact that caregivers often exhibit greater resilience (Bayat, 2007; Dias et al., 2015). Alongside this, the continual chronic stress of caregiving might have eventually led to an attenuated HPA response pattern, independent of resilience, given the wear and tear on the system from frequent stress exposure (McEwen, 1998). There is partial support for this from studies showing that blunted reactivity is characteristic of those who have experienced other forms of long-term adversity, for example, childhood aversity (Carpenter et al., 2007; Carpenter, Shattuck, Tyrka, Geracioti, & Price, 2011; Lovallo et al., 2012). In sum, there is reason to believe that blunted cortisol reactivity and high resilience develop independently in caregivers, in response to chronic stress. If true, this could explain why these two variables appeared negatively related when measured in parallel by Ruiz-Robledillo and colleagues.

Alternatively, this paradoxical finding can possibly be explained in terms of resilience being a mechanism which protects against exaggerated reactivity as an outcome of chronic stress (Bonanno, 2004; Gallagher-Thompson et al., 2006). Those with high resilience have been

shown to appraise stress as less threatening (Ruiz-Robledillo et al., 2014) and this has the potential to attenuate physiological reactivity over a period of time (Lazarus & Folkman, 1984). Consequently, resilience may help to maintain cortisol responses in an adaptive range in the face of stress (Ozbay, Fitterling, Charney, & Southwick, 2008). Thus, although those with high resilience exhibited lower stress responses, it could be that these were not true blunted responses. Instead it is possible that these lower responses reflected an adaptive function of resilience attempting to secure homeostasis by thwarting the development of exaggerated reactivity. By delving deeper into the results of Ruiz-Robledillo and colleagues there is some evidence to support this assumption. The authors showed that caregivers with high resilience still exhibited an increase in cortisol reactivity to acute stress, just a less extreme augmentation compared to those with low resilience, i.e., had less exaggerated and, therefore, healthier responses. In contrast, studies that implicate blunted reactivity with maladaptive outcomes often show negative cortisol reactivity, i.e., decreases in cortisol from baseline to post-stress (Ginty, Phillips, Higgs, et al., 2012; Heaney et al., 2011) i.e., true blunted reactivity. Thus, it is possible that lower reactivity reflects a more adaptive response pattern in caregivers and relates to a range of positive outcomes, such as resilience. However, even in this population, attenuated reactivity is still associated with adverse health consequences, such as depression (Romero-Martínez & Moya-Albiol, 2017). Perhaps the negative correlates of blunted reactivity still manifest in caregivers, but there are also certain coping mechanisms unique to this, and other high chronic stress populations which appear as adaptive outcomes associated with lower reactivity. There is an obvious demand for further research to explore this possibility in detail and better understand differences in reactivity trajectories across populations.

It should be acknowledged that this present study has limitations beyond those highlighted in the previous chapter i.e., modest sample size, stress task order effect, observational study design so not able to determine causality. First, resilience was exclusively assessed using one self-report measure alone. Thus, no cross-questionnaire comparisons could be conducted or validation of the self-report data through objective behavioural resilience assessment. However, the same methodological approach and dataset was used to examine how reactivity relates to a number of different motivation-related variables, with perseverance as the main focus. Therefore, it would have been inappropriate to administer a large number questionnaires or incorporate further objective measures due to respondent burden and participant fatigue (Egleston, Miller, & Meropol, 2011). Second, it has been suggested that the CD-RISC examines resilience at the individual level as opposed to the dynamic process many consider it to be (Ahern, Kiehl, Lou Sole, & Byers, 2006; Arias González, Crespo Sierra, Arias Martínez, Martínez-Molina, & Ponce, 2015; Windle et al., 2011). Further, the CD-RISC lacks evidence to justify the inclusion of some items, is limited by a ceiling effect and includes some questions which may examine coping as opposed to resilience *per se* (Ahern et al., 2006; Arias González et al., 2015; Pangallo, Zibarras, Lewis, & Flaxman, 2015; Sarkar & Fletcher, 2013; Windle et al., 2011). However, there is no gold standard resilience measure (Windle et al., 2011) and overall the CD-RISC is well validated, sound psychometrically and has been used with success in previous studies (Windle et al., 2011). Third, previous research has suggested that cortisol reactivity may be associated with resilience, yet this was unexplored in the present study. However, this would have been unsuitable due to the multiple stress task design that was employed. As cortisol is slow to respond to stress (De Vente, Olff, Van Amsterdam, Kamphuis, & Emmelkamp, 2003) there would have been a need for long baseline/recovery periods between stress exposures and thus,

the laboratory session would have had to have been extraordinarily long. Fourth, the relationship between reactivity and resilience was exclusively evident in HR reactivity to the CP task, and was therefore not consistent across all cardiovascular measures and stress tasks. However, this is similar to other research in the literature (e.g. Ginty et al., 2011b) and in the present study, significant relationships withstood the adjustment of all appropriate confounders, including CP time. Consequently, one of the many strengths of this study was the statistical control for appropriate confounding variables, such as CP time, as above, and gender, which impacts upon both cardiovascular reactivity (Stone et al., 1990) and resilience (Erdogan, Ozdogan, & Erdogan, 2015).

Future studies should extend the present research by directly and comprehensively examining the relationship between resilience and physiological reactivity within the SAM and HPA axes concurrently. There is a need to administer multiple self-report measures alongside the CD-RISC, for example, the Resilience Scale for Adults (Hjemdal et al., 2001) and the Brief Resilience Scale (Smith et al., 2008). It would also be advantageous to include behavioural measures of resilience. Although there are limited options within the literature, one potential example could be a two-task competitive paradigm, in which participants are experimentally induced to lose the first task, to examine how this impacts their recovery and performance on a second task. There have been similar paradigms used throughout the sport psychology literature (e.g. Reinboth & Duda, 2016) which may assist authors in creating suitable measures.

In conclusion, poor self-reported resilience measured via a well-validated questionnaire was associated with blunted HR reactivity to a passive stress task. This aligns with some, but not all of a literature riddled with inconsistencies. This present study does, however, show that

blunted reactivity is associated with adverse behavioural outcomes that seem to reflect motivation and motivational dysregulation. However, it must be emphasised that this finding for resilience was not consistently demonstrated across all conditions but was instead unique for HR reactivity to passive stress in the group that completed the PASAT first. Therefore, additional evidence is required to confirm and further explore this reactivity-resilience relationship, which, may benefit from following the recommendations above.

References

Ahern, N. R., Kiehl, E. M., Lou Sole, M., & Byers, J. (2006). A review of instruments measuring resilience. *Issues in Comprehensive Pediatric Nursing*, *29*, 103–125.

Al'Absi, M. (2006). Hypothalamic-pituitary-adrenocortical responses to psychological stress and risk for smoking relapse. *International Journal of Psychophysiology*, *59*(3), 218–227.

Al'Absi, M., Wittmers, L. E., Erickson, J., Hatsukami, D., & Crouse, B. (2003). Attenuated adrenocortical and blood pressure responses to psychological stress in ad libitum and abstinent smokers. *Pharmacology Biochemistry and Behavior*, *74*(2), 401–410.

Allen, M. T., Hogan, A. M., & Laird, L. K. (2009). The relationships of impulsivity and cardiovascular responses: The role of gender and task type. *International Journal of Psychophysiology*, *73*, 369–376.

Allen, M. T., Matthews, K. A., & Sherman, F. S. (1997). Cardiovascular reactivity to stress and left ventricular mass in youth. *Hypertension*, *30*(4), 782–787.

Allen, M. T., Sherwood, A., Obrist, P. A., Crowell, M. D., & Grange, L. A. (1987). Stability of cardiovascular reactivity to laboratory stressors: A 2 1 2 yr follow-up. *Journal of Psychosomatic Research*, *31*(5), 639–645.

Arias González, V. B., Crespo Sierra, M. T., Arias Martínez, B., Martínez-Molina, A., & Ponce, F. P. (2015). An in-depth psychometric analysis of the Connor-Davidson Resilience Scale: Calibration with Rasch-Andrich model. *Health and Quality of Life Outcomes*, *13*(1), 154–166.

Barnett, P. a, Spence, J. D., Manuck, S. B., & Jennings, J. R. (1997). Psychological stress and

the progression of carotid artery disease. *Journal of Hypertension*, *15*(1), 49–55.

Bayat, M. (2007). Evidence of resilience in families of children with autism. *Journal of Intellectual Disability Research*, *51*(2), 702–714.

Bennett, C., Blissett, J., Carroll, D., & Ginty, A. T. (2014). Rated and measured impulsivity in children is associated with diminished cardiac reactions to acute psychological stress. *Biological Psychology*, *102*, 68–72.

Bibbey, A., Ginty, A. T., Brindle, R. C., Phillips, A. C., & Carroll, D. (2016). Blunted cardiac stress reactors exhibit relatively high levels of behavioural impulsivity. *Physiology and Behavior*, *159*(1), 40–44.

Black, J. K., Balanos, G. M., & Whittaker, A. C. (2017). Resilience, work engagement and stress reactivity in a middle-aged manual worker population. *International Journal of Psychophysiology*, *116*(1), 9–15.

Bonanno, G. A. (2004). Loss, Trauma, and Human Resilience: Have We Underestimated the Human Capacity to Thrive after Extremely Aversive Events? *American Psychologist*, *59*(1), 20–28.

Brindle, R. C., Whittaker, A. C., Bibbey, A., Carroll, D., & Ginty, A. T. (2017). Exploring the possible mechanisms of blunted cardiac reactivity to acute psychological stress. *International Journal of Psychophysiology*, *113*, 1–7.

Bush, G., Luu, P., & Posner, M. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Sciences*, *4*(1), 215–222.

Cacioppo, J. T. (1994). Social neuroscience: Autonomic, neuroendocrine, and immune responses to stress. *Psychophysiology*, *31*(2), 113–128.

Calvete, E., las Hayas, C., & Gómez del Barrio, A. (2018). Longitudinal associations between resilience and quality of life in eating disorders. *Psychiatry Research*, *259*, 470–475.

Carpenter, L. L., Carvalho, J. P., Tyrka, A. R., Wier, L. M., Mello, A. F., Mello, M. F., … Price, L. H. (2007). Decreased adrenocorticotropic hormone and cortisol responses to stress in healthy adults reporting significant childhood maltreatment. *Biological Psychiatry*, *62*(10), 1080–1087.

Carpenter, L. L., Shattuck, T. T., Tyrka, A. R., Geracioti, T. D., & Price, L. H. (2011). Effect of childhood physical abuse on cortisol stress response. *Psychopharmacology*, *214*(1), 367–375.

Carroll, D., Bibbey, A., Roseboom, T. J., Phillips, A. C., Ginty, A. T., & De Rooij, S. R. (2012). Forced expiratory volume is associated with cardiovascular and cortisol reactions to acute psychological stress. *Psychophysiology*, *49*(6), 866–872.

Carroll, D., Ginty, A. T., Der, G., Hunt, K., Benzeval, M., & Phillips, A. C. (2012). Increased blood pressure reactions to acute mental stress are associated with 16-year cardiovascular disease mortality. *Psychophysiology*, *49*(10), 1444–1448.

Carroll, D., Ginty, A. T., Painter, R. C., Roseboom, T. J., Phillips, A. C., & de Rooij, S. R. (2012). Systolic blood pressure reactions to acute stress are associated with future hypertension status in the Dutch Famine Birth Cohort Study. *International Journal of Psychophysiology*, *85*(2), 270–273.

Carroll, D., Ginty, A. T., Whittaker, A. C., Lovallo, W. R., & de Rooij, S. R. (2017). The behavioural, cognitive, and neural corollaries of blunted cardiovascular and cortisol reactions to acute psychological stress. *Neuroscience and Biobehavioral Reviews*, *77*(1), 74–86.

Carroll, D., Lovallo, W. R., & Phillips, A. C. (2009). Are large physiological reactions to acute psychological stress always bad for health? *Social and Personality Psychology Compass*, *3*, 725–743.

Carroll, D., Phillips, A. C., & Der, G. (2008). Body mass index, abdominal adiposity, obesity, and cardiovascular reactions to psychological stress in a large community sample. *Psychosomatic Medicine*, *70*(6), 653–660.

Carroll, D., Phillips, A. C., Der, G., Hunt, K., & Benzeval, M. (2011). Blood pressure reactions to acute mental stress and future blood pressure status: Data from the 12-year follow-up of the West of Scotland Study. *Psychosomatic Medicine*, *73*(9), 737–743.

Carroll, D., Phillips, A. C., Der, G., Hunt, K., Bibbey, A., Benzeval, M., & Ginty, A. T. (2013). Low forced expiratory volume is associated with blunted cardiac reactions to acute psychological stress in a community sample of middle-aged men and women. *International Journal of Psychophysiology*, *90*(1), 17–20.

Chida, Y., & Steptoe, A. (2010). Greater cardiovascular responses to laboratory mental stress are associated with poor subsequent cardiovascular risk status: A meta-analysis of prospective evidence. *Hypertension*, *55*(4), 1026–1032.

Connor, K. M., & Davidson, J. R. T. (2003). Development of a new Resilience scale: The Connor-Davidson Resilience scale (CD-RISC). *Depression and Anxiety*, *18*(2), 76–82.

Corina, D., & Adriana, B. (2013). Impact of work related trauma on acute stress response in train drivers. *Procedia - Social and Behavioral Sciences*, *84*(1), 190–195.

Crump, C., Sundquist, J., Winkleby, M. A., & Sundquist, K. (2016). Low stress resilience in late adolescence and risk of hypertension in adulthood. *Heart*, *102*(7), 541–547.

de Rooij, S. R., & Roseboom, T. J. (2010). Further evidence for an association between self-reported health and cardiovascular as well as cortisol reactions to acute psychological stress. *Psychophysiology*, *47*(1), 1172–1175.

de Rooij, S. R., Schene, A. H., Phillips, D. I., & Roseboom, T. J. (2010). Depression and anxiety: Associations with biological and perceived stress reactivity to a psychological stress protocol in a middle-aged population. *Psychoneuroendocrinology*, *35*(6), 866–877.

De Vente, W., Olff, M., Van Amsterdam, J. G. C., Kamphuis, J. H., & Emmelkamp, P. M. G. (2003). Physiological differences between burnout patients and healthy controls: blood pressure, heart rate, and cortisol responses. *Occupational and Environmental Medicine*, *60*(1), 54–61.

Dias, R., Santos, R. L., Sousa, M. F. B. de, Nogueira, M. M. L., Torres, B., Belfort, T., & Dourado, M. C. N. (2015). Resilience of caregivers of people with dementia: a systematic review of biological and psychosocial determinants. *Trends in Psychiatry and Psychotherapy*, *37*(1), 12–19.

Egleston, B. L., Miller, S. M., & Meropol, N. J. (2011). The impact of misclassification due to survey response fatigue on estimation and identifiability of treatment effects. *Statistics in Medicine*, *30*(30), 3560–3572.

Erdogan, E., Ozdogan, O., & Erdogan, M. (2015). University students' resilience level: The effect of gender and faculty. *Procedia - Social and Behavioral Sciences*, *186*, 1262–1267.

Fletcher, D., & Sarkar, M. (2013). Psychological resilience: A review and critique of definitions, concepts, and theory. *European Psychologist*, *18*(1), 12–23.

Galatzer-Levy, I. R., Steenkamp, M. M., Brown, A. D., Qian, M., Inslicht, S., Henn-Haase, C., … Marmar, C. R. (2014). Cortisol response to an experimental stress paradigm prospectively predicts long-term distress and resilience trajectories in response to active police service. *Journal of Psychiatric Research*, *56*(1), 36–42.

Gallagher-Thompson, D., Shurgot, G. R., Rider, K., Gray, H. L., McKibbin, C. L., Kraemer, H. C., … Thompson, L. W. (2006). Ethnicity, stress, and cortisol function in Hispanic and non-Hispanic white women: A preliminary study of family dementia caregivers and noncaregivers. *The American Journal of Geriatric Psychiatry*, *14*(4), 334–342.

Georgiades, A., Lemne, C., De Faire, U., Lindvall, K., & Fredrikson, M. (1997). Stress-induced blood pressure measurements predict left ventricular mass over three years among borderline hypertensive men. *European Journal of Clinical Investigation*, *27*(9), 733–739.

Gianaros, P. J., May, J. C., Siegle, G. J., & Jennings, J. R. (2005). Is there a functional neural correlate of individual differences in cardiovascular reactivity? *Psychosomatic Medicine*, *67*(1), 31–39.

Ginty, A. T., Brindle, R. C., & Carroll, D. (2015). Cardiac stress reactions and perseverance: Diminished reactivity is associated with study non-completion. *Biological Psychology*, *109*, 200–205.

Ginty, A. T., Gianaros, P. J., Derbyshire, S. W. G., Phillips, A. C., & Carroll, D. (2013). Blunted cardiac stress reactivity relates to neural hypoactivation. *Psychophysiology*, *50*(3), 219–229.

Ginty, A. T., Phillips, A. C., Der, G., Deary, I. J., & Carroll, D. (2011). Heart rate reactivity is associated with future cognitive ability and cognitive change in a large community

sample. *International Journal of Psychophysiology*, *82*(1), 167–174.

Ginty, A. T., Phillips, A. C., Higgs, S., Heaney, J. L. J., & Carroll, D. (2012). Disordered eating behaviour is associated with blunted cortisol and cardiovascular reactions to acute psychological stress. *Psychoneuroendocrinology*, *37*(5), 715–724.

Girdler, S. S., Jamner, L. D., Jarvik, M., Soles, J. R., & Shapiro, D. (1997). Smoking status and nicotine administration differentially modify hemodynamic stress reactivity in men and women. *Psychosomatic Medicine*, *59*(3), 294–306.

Hagemann, D., Waldstein, S. R., & Thayer, J. F. (2003). Central and autonomic nervous system integration in emotion. *Brain and Cognition*, *52*(1), 79–87.

Heaney, J. L. J., Ginty, A. T., Carroll, D., & Phillips, A. C. (2011). Preliminary evidence that exercise dependence is associated with blunted cardiac and cortisol reactions to acute psychological stress. *International Journal of Psychophysiology*, *79*(2), 323–329.

Heleniak, C., McLaughlin, K. A., Ormel, J., & Riese, H. (2016). Cardiovascular reactivity as a mechanism linking child trauma to adolescent psychopathology. *Biological Psychology*, *120*, 108–119.

Hjemdal, O., Friborg, O., Martinussen, M., & Rosenvinge, J. H. (2001). Preliminary results from the development and validation of a Norwegian scale for measuring adult resilience. *Journal of Norwegian Psychology Assessment*, *38*(1), 310–317.

Hu, T., Zhang, D., & Wang, J. (2015). A meta-analysis of the trait resilience and mental health. *Personality and Individual Differences*, *76*, 18–27.

Kamarck, T. W., Everson, S. A., Kaplan, G. A., Manuck, S. B., Jennings, J. R., Salonen, R., & Salonen, J. T. (1997). Exaggerated blood pressure responses during mental stress are

associated with enhanced carotid atherosclerosis in middle-aged finnish men: Findings from the Kuopio Ischemic Heart Disease Study. *Circulation*, *96*(11), 3842–3848.

Koo-Loeb, J. H., Pedersen, C., & Girdler, S. S. (1998). Blunted cardiovascular and catecholamine stress reactivity in women with bulimia nervosa. *Psychiatry Research*, *80*(1), 13–27.

Lazarus, R. S., & Folkman, S. (1984). *Stress, appraisal and coping*. New York: Springer.

Lovallo, W. R. (2005). Cardiovascular reactivity: Mechanisms and pathways to cardiovascular disease. *International Journal of Psychophysiology*, *58*(1), 119–132.

Lovallo, W. R. (2006). Cortisol secretion patterns in addiction and addiction risk. *International Journal of Psychophysiology*, *59*(3), 195–202.

Lovallo, W. R., Dickensheets, S. L., Myers, D. A., Thomas, T. L., & Nixon, S. J. (2000). Blunted stress cortisol response in abstinent alcoholic and polysubstance-abusing men. *Alcoholism: Clinical and Experimental Research*, *24*(5), 651–658.

Lovallo, W. R., Farag, N. H., Sorocco, K. H., Cohoon, A. J., & Vincent, A. S. (2012). Lifetime adversity leads to blunted stress axis reactivity: Studies from the Oklahoma Family Health Patterns Project. *Biological Psychiatry*, *71*(4), 344–349.

Martin, J. J., Byrd, B., Watts, M. L., & Dent, M. (2015). Gritty, hardy, and resilient: Predictors of sport engagement and life satisfaction in wheelchair basketball players. *Journal of Clinical Sport Psychology*, 9(4), 345–359.

Matthews, K. A., Katholi, C. R., McCreath, H., Whooley, M. A., Williams, D. R., Zhu, S., & Markovitz, J. H. (2004). Blood pressure reactivity to psychological stress predicts hypertension in the CARDIA study. *Circulation*, *110*, 74–78.

McEwen, B. S. (1998). Stress, adaptation, and disease: allostasis and allostatic load. *Annals of the New York Academy of Sciences*, *840*(1), 33–44.

Min, J. A., Lee, N. Bin, Lee, C. U., Lee, C., & Chae, J. H. (2012). Low trait anxiety, high resilience, and their interaction as possible predictors for treatment response in patients with depression. *Journal of Affective Disorders*, *137*, 61–69.

Min, J. A., Lee, C. U., & Chae, J. H. (2015). Resilience moderates the risk of depression and anxiety symptoms on suicidal ideation in patients with depression and/or anxiety disorders. *Comprehensive Psychiatry*, *56*(2), 103–111.

Moss, H. B., Vanyukov, M., Yao, J. K., & Kirillova, G. P. (1999). Salivary cortisol responses in prepubertal boys: The effects of parental substance abuse and association with drug use behavior during adolescence. *Biological Psychiatry*, *45*(10), 1293–1299.

Muñoz, L. C., & Anastassiou-Hadjicharalambous, X. (2011). Disinhibited behaviors in young children: Relations with impulsivity and autonomic psychophysiology. *Biological Psychology*, *86*, 349–359.

Obrist, P. (1981) *Cardiovascular psychophysiology: A perspective*. New York: Plenum Press.

O'Rourke, N. (2004). Psychological resilience and the well-being of widowed women. *Ageing International*, *29*(3), 267–280.

Ong, A. D., Bergeman, C. S., Bisconti, T. L., & Wallace, K. A. (2006). Psychological resilience, positive emotions, and successful adaptation to stress in later life. *Journal of Personality and Social Psychology*, *91*(4), 730–749.

Ozbay, F., Fitterling, H., Charney, D., & Southwick, S. (2008). Social support and resilience to stress across the life span: A neurobiologic framework. *Current Psychiatry Reports*,

10(4), 304–310.

Pangallo, A., Zibarras, L., Lewis, R., & Flaxman, P. (2015). Resilience through the lens of interactionism: A systematic review. *Psychological Assessment*, *27*(1), 1–20.

Panknin, T. L., Dickensheets, S. L., Nixon, S. J., & Lovallo, W. R. (2002). Attenuated heart rate responses to public speaking in individuals with alcohol dependence. *Alcoholism: Clinical and Experimental Research*, *26*(6), 841–847.

Paris, J. J., Franco, C., Sodano, R., Frye, C. A., & Wulfert, E. (2010). Gambling pathology is associated with dampened cortisol response among men and women. *Physiology and Behavior*, *99*(1), 230–233.

Perkins-Gough, D., Verdín, D., Godwin, A., Kirn, A., Benson, L., & Potvin, G. (2018). The significance of grit: A conversation with Angela Lee Duckworth. *Social Sciences*, 7(3), 14–20.

Phillips, A. C. (2011). Blunted as well as exaggerated cardiovascular reactivity to stress is associated with negative health outcomes. *Japanese Psychological Research*, *53*(2), 177–192.

Phillips, A. C., Carroll, D., Hunt, K., & Der, G. (2006). The effects of the spontaneous presence of a spouse/partner and others on cardiovascular reactions to an acute psychological challenge. *Psychophysiology*, *43*(6), 633–640.

Phillips, A. C., Der, G., & Carroll, D. (2009). Self-reported health and cardiovascular reactions to psychological stress in a large community sample: Cross-sectional and prospective associations. *Psychophysiology*, *46*(1), 1020–1027.

Phillips, A. C., Hunt, K., Der, G., & Carroll, D. (2011). Blunted cardiac reactions to acute

psychological stress predict symptoms of depression five years later: Evidence from a large community study. *Psychophysiology*, *48*(1), 142–148.

Phillips, A. C., Roseboom, T. J., Carroll, D., & De Rooij, S. R. (2012). Cardiovascular and cortisol reactions to acute psychological stress and adiposity: Cross-sectional and prospective associations in the dutch famine birth cohort study. *Psychosomatic Medicine*, *70*(4), 699–710.

Reinboth, M., & Duda, J. L. (2016). Effects of competitive environment and outcome on achievement behaviors and well-being while engaged in a physical task. *Sport, Exercise, and Performance Psychology*, *5*(4), 324–336.

Romero-Martínez, Á., & Moya-Albiol, L. (2017). Reduced cardiovascular activation following chronic stress in caregivers of people with anorexia nervosa. *Stress: The International Journal on the Biology of Stress*, *20*(4), 390–397.

Ruiz-Robledillo, N., De Andrés-García, S., Pérez-Blasco, J., González-Bono, E., & Moya-Albiol, L. (2014). Highly resilient coping entails better perceived health, high social support and low morning cortisol levels in parents of children with autism spectrum disorder. *Research in Developmental Disabilities*, *35*(3), 686–695.

Ruiz-Robledillo, N., Romero-Martínez, A., & Moya-Albiol, L. (2017). Lower cortisol response in high-resilient caregivers of people with autism: the role of anger. *Stress and Health*, *33*(4), 370–377.

Salomon, K., Clift, A., Karlsdóttir, M., & Rottenberg, J. (2009). Major depressive disorder is associated with attenuated cardiovascular reactivity and impaired recovery among those free of cardiovascular disease. *Health Psychology*, *28*(2), 157-.

Sarkar, M., & Fletcher, D. (2013). How should we measure psychological resilience in sport performers? *Measurement in Physical Education and Exercise Science*, *17*(2), 264–280.

Sarkar, M., & Fletcher, D. (2014). Psychological resilience in sport performers: a review of stressors and protective factors. *Journal of Sports Sciences*, *32*(15), 1419–1434.

Schwartz, A. R., Gerin, W., Davidson, K. W., Pickering, T. G., Brosschot, J. F., Thayer, J. F., … Linden, W. (2003). Toward a causal model of cardiovascular responses to stress and the development of cardiovascular disease. *Psychosomatic Medicine*, *65*, 22–35.

Smith, B. W., Dalen, J., Wiggins, K., Tooley, E., Christopher, P., & Bernard, J. (2008). The brief resilience scale: Assessing the ability to bounce back. *International Journal of Behavioral Medicine*, *15*(1), 194–200.

Sorocco, K. H., Lovallo, W. R., Vincent, A. S., & Collins, F. L. (2006). Blunted hypothalamic-pituitary-adrenocortical axis responsivity to stress in persons with a family history of alcoholism. *International Journal of Psychophysiology*, *59*(1), 210–217.

Stoffel, J. M., & Cain, J. (2018). Review of grit and resilience literature within health professions education. *American Journal of Pharmaceutical Education*, 82(2), 58–64.

Stone, S. V, Dembroski, T. M., Costa Jr., P. T., & MacDougall, J. M. (1990). Gender differences in cardiovascular reactivity. *Journal of Behavioral Medicine*, *90*(1), 50–57.

Treiber, F. A., Kamarck, T., Schneiderman, N., Sheffield, D., Kapuku, G., & Taylor, T. (2003). Cardiovascular reactivity and development of preclinical and clinical disease states. *Psychosomatic Medicine*, *65*(1), 46–62.

Tugade, M. M., Fredrickson, B. L., & Barrett, L. F. (2004). Psychological resilience and positive emotional granularity: Examining the benefits of positive emotions on coping

and health. *Journal of Personality*, *72*(6), 1161–1190.

Windle, G., Bennett, K. M., & Noyes, J. (2011). A methodological review of resilience measurement scales. *Health and Quality of Life Outcomes*, *9*(8), 1477–1486.

York, K. M., Hassan, M., Li, Q., Li, H. H., Fillingim, R. B., & Sheps, D. S. (2007). Coronary artery disease and depression: Patients with more depressive symptoms have lower cardiovascular reactivity during laboratory-induced mental stress. *Psychosomatic Medicine*, *69*, 521–528.

CHAPTER FOUR

CARDIOVASCULAR REACIVITY AND VASCULITIS EXPERICNE (CRAVE): METHODOLOGICAL APPROACH

Introduction

The following chapter outlines the methodological approach for the planned project "CRAVE" which will examine whether physiological responses to acute stress are associated with fatigue, and related symptoms such as depression and anxiety in Anti-Neutrophil Cytoplastic Antibodies (ANCA)-associated vasculitis patients. Due to an unexpectedly long research governance and NHS ethical approval procedure, there was not enough time to commence this study within the constraints of a one-year Masters by Research course. However, it is expected that data collection will begin shortly, and the protocol was developed as part of this MSc degree.

ANCA-associated vasculitis is a condition that concerns the destruction or inflammation of small blood vessels (Lazarus, John, O′Callaghan, & Ranganathan, 2016) caused by "a group of multisystem auto-immune diseases comprising Wegener's granulomatosis (WG), microscopic polyangiitis (MPA) and Churg–Strauss syndrome (CSS)" (Basu et al., 2010, *P*.1383). In vasculitis patients, fatigue is highlighted as the most burdensome aspect (Herlyn et al., 2010) and most commonly reported symptom (Basu et al., 2010), as well as the main origin of poor quality of life (Basu et al., 2014). However, fatigue does not always correlate with disease severity/activity (Basu et al., 2013; Hajj-Ali et al., 2011) suggesting that it may be a manifestation of something other than the disease itself, such as motivational processes.

As with perseverance and resilience, fatigue is associated with motivation as a motivation-related behavioural manifestation (Boksem et al., 2006). For example, studies have shown a negative association between motivation and fatigue (Boksem et al., 2006; Chaudhuri & Behan, 2000) and have even demonstrated that improvements in motivation can partially alleviate mental fatigue symptoms (Boksem et al., 2006). Therefore, an obvious link between

perseverance, resilience and fatigue is the reflection of motivation or motivational processes (Boksem et al., 2006; Resnick, 2011; Von Culin et al., 2014). Further, as there is an association between perseverance and resilience, it would seem plausible that fatigued individuals would also show dysfunctional perseverance and resilience. Interestingly, there is some preliminary but indirect evidence in favour of this, for example, burnout, which integrates fatigue (Leone, Huibers, Knottnerus, & Kant, 2009), is negatively related to perseverance (Salles, Cohen, & Mueller, 2014) and resilience (Taku, 2014).

To date, no studies have examined cardiovascular responses to acute psychological stress in patients with ANCA-associated vasculitis. In addition, there has been limited investigation into how stress reactivity might relate to fatigue. If a robust relationship is found between reactivity and fatigue in vasculitis patients, a simple stress test could have clinical applications in identifying those who are at greater risk of fatigue, who may require additional medical support during their treatment process. It would also demonstrate that reactivity relates to motivation-related behavioural manifestations in clinical and not just healthy populations.

Methods

Participants

The study aims to recruit approximately 100 ANCA-associated vasculitis patients from the renal out-patient clinic at University Hospitals Birmingham. Inclusion criteria are: diagnosis of ANCA-associated vasculitis, aged 18 or above, no history of myocardial infarction in the past three months, not taking corticosteroid medications, not pregnant, can understand verbal and written instructions in English and able to conduct simple mathematic addition. Eligible participants will be posted information about the study before discussing their involvement

with the clinician during their next routine clinic visit. They will then decide whether they would like to participate or not. A maximum total of 100 participants was selected based on pragmatism, through observation into typical numbers of eligible patients who attend the clinic, and an estimation of likely attrition between recruitment and testing. An ideal sample size of 42 was determined using a previous cardiovascular stress reactivity study among middle-aged adults, which found significant correlations between behavioural/psychosocial factors and reactivity in a sample of 31 participants (Black et al., 2017). Using G-power and the R^2 of .248 to calculate the f2 effect size from this previous study equals f2 = 0.33, and when $\alpha = .05$ and power is set at .95, this equals a recommended sample size of 42 participants.

Study design

This laboratory-based pilot study will use a cross-sectional design to examine how cardiovascular and cortisol reactivity to acute psychological stress is associated with fatigue in ANCA-associated vasculitis patients. Participants will provide full written informed consent and the project has just received approval from the appropriate research ethics committee. The study is designed in a way which complies with UK Policy Frameworks for Health and Social Care, Research International Conference for Harmonisation of Good Clinical Practice guidelines, the Declaration of Helsinki and University of Birmingham policies.

Measures

Questionnaires

Multidimensional Fatigue Inventory

The Multidimensional Fatigue Inventory (MFI-20; Smets, Garssen, Bonke, & De Haes, 1995) will measure the severity and nature of participants' self-reported fatigue. The MFI-20 is a commonly used 20-item questionnaire made up of five different scales, each containing four items. Participants will respond to each question using a five-point Likert Scale where 1= ("yes, that is true") and 5 = ("no, that is not true"), to indicate the extent to which each statement personally applies to them. Therefore, scores for each dimension can range between 4-20 and overall scores between 20-100. The five scales are: general fatigue (e.g. "I feel tired"), physical fatigue (e.g. "physically I feel I am in a bad condition"), reduced activities (e.g. "I get little done"), reduced motivation (e.g. "I don't feel like doing anything") and mental fatigue (e.g. "My thoughts easily wonder"). After completing the questionnaire, the experimenter will average the data and higher scores (nearer to 100) will reflect greater fatigue. The MFI-20 has been used with success to measure fatigue in patients with diverse medical conditions (Lin et al., 2009), including vasculitis (Grayson et al., 2013). It also demonstrates good psychometric properties when administered to vasculitis patients ($\alpha = .87$; Grayson et al., 2013). Adequate internal reliability has also been evidenced in terms of the five subscales of the MFI-20, with Cronbach's alpha's ranging from .74 (reduced motivation) to .88 (reduced activity) (Elbers, van Wegen, Verhoef, & Kwakkel, 2012). Further, the MFI-20 also demonstrates good test-retest reliability (ICC = .80), shows no evidence of any potential floor or ceiling effects (Elbers et al., 2012) and has acceptable discriminant and convergent validity (Lin et al., 2009).

The 36-item Medical Outcomes Short-Form survey

The 36-item Medical Outcomes Short-Form survey (SF-36; Ware & Sherbourne, 1992) is a well-used questionnaire designed to measure health and quality of life. The instrument uses one multi-item scale to assess eight health-related outcomes, four physical (physical functioning; limitations in activities due to physical problems; bodily pain; overall health perception) and four psychological (limitation in activities due to social functioning; emotional problems; general mental health; energy and vitality). The SF-36 is a valid and reliable measure when administered to a range of populations (Demiral et al., 2006; Failde & Ramos, 2000), including ANCA-associated vasculitis patients (Walsh et al., 2011). It also shows good internal consistency (Cronbach's $\alpha = .92$) in general patient samples (Elbers et al., 2012). Further, when used in large population studies (Burholt & Nash, 2011), including projects within the NHS (Garratt, Ruta, Abdalla, Buckingham, & Russell, 1993), the SF-36 still demonstrates good psychometric properties, with internal consistencies of > 0.80, both in terms of the subscales and the measure in full. In addition, the questionnaire possesses good test-reliability and construct validity (Brazier et al., 1992).

Hospital Anxiety and Depression scale

Participants will complete the Hospital Anxiety and Depression scale (HADS; Zigmond & Snaith, 1983), a well-used 14-item instrument that measures depression (7 items; mainly anhedonia rather than somatic symptomology) and anxiety (7 items). Participants respond using a 4-point scale where zero reflects low and four reflects high anxiety/depression. The HADS has been previously used in vasculitis samples with success (Koutantji et al., 2003) and has good concurrent validity (Bramley, Easton, Morley, & Snaith, 1988; Herrmann, 1997) and internal reliability; $\alpha = .90$ (depression), $\alpha = .93$ (anxiety) (Moorey et al., 1991).

There is also evidence of its effectiveness as a psychiatric screening tool (Bjelland, Dahl, Haug, & Neckelmann, 2002) together with good test-retest reliability coefficients of .85 and .84 for depression and anxiety, respectively (Herrmann, 1997).

Socio-demographic and general information questionnaire

Participants will answer a standardised set of self-report questions designed to obtain basic socio-demographic and general information, including: age, sex, ethnicity and wake-up time. In addition, female participants will state whether they are taking the contraceptive pill and note the first day of their last period (if pre-menopausal). All participants will record any immune disorders (past 12-months) and cardiovascular diseases they have suffered, as well as any current illnesses/diseases/conditions, for example, arthritis. They will also note whether they are on any continuous medication and provide details, if appropriate. These latter two variables will be also corroborated from patients' medical notes. Further, information regarding the occupation, or most recent occupation, of the household's main breadwinner will be obtained. This will be used to classify each participant's socioeconomic position (manual or non-manual) based on the Registrar General's (1980) Classification of Occupations.

Health behaviour questionnaire

A modified questionnaire (Marmot et al., 1991) from the Whitehall II study will assess participants' health behaviours in the 12-month period prior to their involvement in the present study. Participants will record, on average, the number of cigarettes they smoke (0, 1-5, 6-10, 11-20, 21+ cigarettes per day); the units of alcohol they consume (0, 1-5, 6-10, 11-20, 21-40, 40+ units per week); the number of hours they sleep (0-3, 4-5, 6-7, 8-9, 10-11, 12+

hours per night); and the frequency that use vitamin/mineral supplements (never, once a month, once a week, a few per week, every day, more than one per day). A simple categorical system will be used to score this data, for example, if a participant reports they sleep for 9 hours per night, they will be allocated a score of four for this variable (as 9 falls into the 8-9 bracket, the fourth data bracket). In addition, exercise behaviours will also be assessed; participants will note the length of time, per week, they exercise lightly, moderately and vigorously using the following scale (0, 1-2, 2-5, 6-8, 9-10, 11+ hours). A similar scoring system as above will then be used, participants will be allocated a score between 0-5 for each intensity level (e.g. one hour of exercise will lead to a score of two) and this will be multiplied by either one, two, or three depending on whether it was light, moderate or vigorous exercise, respectively. For example, one hour of vigorous exercise will equal a score of six. This technique will generate an exercise score, for each intensity, for each participant. Prior to finishing the questionnaire, participants will record their frequency of consumption of fresh fruit/vegetables and high-fat foods on a scale of 0-6, where "never" = zero, and "4 or more times a day" = six. Overall, this method of measuring health behaviour has been successfully employed in previous research projects (e.g. Burns, Carroll, Ring, Harrison, & Drayson, 2002).

Evaluation of stress tasks questionnaire

Using six self-report questions, participants will attest to how: stressful, difficult, arousing, confusing, embarrassing and engaging they find a psychological stress task. Participants will also subjectively appraise their own performance. These questions will be answered using a 7-point Likert scale, where 0 = ("not at all arousing/confusing etc.") and 6 = ("extremely arousing/confusing etc."). This instrument has been used well in many previous studies (e.g.

Black et al., 2017) and will support analyses into whether differences in reactivity magnitude impact evaluations of the stress task and/or stress task performance, or *vice versa*.

Physiological assessment

Cardiovascular measures

Systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) measurements will be obtained discontinuously from participants' non-dominant arm using a semi-automatic sphygmomanometer and standard brachial artery cuff. This cardiovascular assessment will happen every two minutes during the 10-minute baseline period, 10-minute stress task, and 20-minute recovery. Additionally, cardiovascular measurements will also be taken, but not recorded, during minute six of the adaptation period for familiarity purposes and to ensure the equipment is functioning correctly.

Salivary cortisol measures

Three saliva samples will be collected in salivettes (Sarstedt Ltd., Leicester, UK) after participants gently chew on a dental swab for one minute at three different time points: end of baseline, immediately post-stress and during the final minute of the 20-minute recovery period. Within a 24-hour period, the salivettes will be centrifuged at 3500rpm, at room temperature for five minutes, before the acellular saliva is aliquoted into Eppendorf tubes. The samples will then be labelled and frozen at -20°C, until a batch assay is conducted when all data collection has seized.

Salivary cortisol will be assayed in duplicate using an enzyme-linked immunosorbent assay (ELISA) and commercial kit (IBL International, Germany). The theory behind the ELISA assay is grounded in the competition principle and microtilerplate separation. An unknown

amount of cortisol within a sample, and standardised amount of cortisol conjugated with horseradish peroxidase will compete for identical antibody binding sites of a polyclonal cortisol antiserum coated onto the wells. After the samples are incubated for one hour the microplate will be immediately washed to stop the competition reaction and remove any unbound components. There will then be the addition of a substrate solution before a further 15-minute incubation (room temperature), and, to finish, a stop solution will be added. Finally, the optical density of the solution will be measured at 450nm, and, by using this, and a regression program (KC junior, Germany), the cortisol concentration (nmol/L) within the sample will be established (cortisol concentration is inversely proportional to optical density).

Acute psychological stress task

Participants will complete the 10-minute Paced Auditory Serial Addition Test (PASAT; Gronwall, 1977), an active psychological stress task with good test-retest reliability (Willemsen et al., 1998) that perturbs both cardiovascular physiology (Phillips, Carroll, Burns, & Drayson, 2005; Phillips, Carroll, Hunt, & Der, 2006; Phillips, Der, Hunt, & Carroll, 2009) and salivary cortisol concentrations (Phillips et al., 2005). Participants will hear a series of single digit numbers from an audio file and are required to add consecutive integers and verbally report their answer. However, they must remember the second number of the pair to add to the next number presented to them. As an example, if they hear three and then two the answer they should report is five. They then must remember the second number, in this instance, two, and add this to whatever number they hear next. As the test progresses the speed increases; the intervals between when integers are presented begin initially at 2.4 seconds (minutes one and two) but shorten by 0.4 seconds every two minutes thereafter. An experimenter wearing a white laboratory coat will be sat adjacent to the participant obtrusively scoring their performance; participants will lose five points per error from the

1000-point total that they begin with. This final score will be operationalised as objective performance. Further, all participants will hear an aversive noise burst during the last five numbers out of every block of 10, which if possible will coincide with error or hesitation. However, if there was no mistake, it will be administered randomly within this 5-number block to maintain standardisation. Nevertheless, it will be stressed to the participants that it is directly correlated with negative aspects of their behaviour and performance, i.e. incorrect answers, being hesitant etc. To induce comparability and social evaluation, a leader board will be in clear view of the participants' vision, and it will be made to appear that their performance is being visually recorded and later assessed by "independent body language experts". In reality, participants will watch their performance live on laptop screen directly in front of them, but no recording will take place.

Procedure

Any patients who attend the renal out-patient clinic at University Hospitals Birmingham and meet the inclusion criteria will be posted information about the study which will be discussed at their next clinical appointment. At this appointment, participants who wish to take part will have the chance to read the information sheet again and sign an informed consent form. They will then be called back by the researcher to arrange a follow-up testing session. All participants will be asked to refrain from eating, smoking, or consuming caffeine in the two hours preceding their testing session alongside no vigorous exercise or alcohol consumption for 12 hours. The testing session will occur in a quiet room within the NIHR-Wellcome Trust Clinical Research Facility at Queen Elizabeth Hospital Birmingham. The experiment will consist of four main periods: 10-minute adaptation (during which questionnaires will be completed), 10-minute formal baseline, 10-minute mental stress exposure and 20-minute recovery. All testing sessions will begin by ensuring that the informed consent form has been

signed and height and weight has been recorded by one of the research nurses. If not, this will be rectified before testing begins. It will then be verbally established whether participants are still eligible to participate, for example, they must confirm they have not consumed caffeine etc. in the past two hours, and, would still like to participate. In addition, participants will also be asked if they have completed the PASAT before and this will be recorded. A brachial artery cuff will then be attached to the non-dominant arm of the participant before they are seated; the adaptation period will then begin. During this, they will complete the laboratory questionnaire pack, which includes: the MFI-20, SF-36, HADS, socio-demographic assessment and health behaviour questionnaire. Cardiovascular measurements (SBP, DBP, and HR) will be taken during the sixth minute of the adaptation period for familiarity purposes and to ensure the equipment is fully functional. Next, participants complete a formal 10-minute baseline period where SBP, DBP and HR measurements are obtained at 4-time points, minutes: two, four, six and eight (questionnaire completion can continue in this period if necessary). The stress period begins with the experimenter reading out the standardised PASAT instructions, before participants undergo a short practice test to ensure they understand the requirements of the task and can adequately hear the audio track. The laptop screen in front of the participant will then be turned on, making sure they can clearly see their face live on screen via the integral video camera, and the test will begin. Again, cardiovascular measurements will be taken every two minutes (2^{nd}, 4^{th}, 6^{th} and 8^{th} minute). After the task concludes, the experimenter will calculate the participants' PASAT score and ask them to complete the post-PASAT evaluation questionnaire. Then, participants will recline quietly during a 20-minute recovery period; cardiovascular measures will be obtained every two minutes for the first ten minutes. To finish, participants will be thanked, asked if they have any questions and then informed that they are free to leave.

Data analysis

Ethnicity and socio-economic status will be statistically transformed into binary variables of white/non-white and manual/non-manual, respectively. Cardiovascular data will be averaged across each main experimental period (baseline, PASAT, recovery). This data will be used to calculate cardiovascular reactivity; participants' average baseline cardiovascular activity will be subtracted from their average cardiovascular activity during stress, for SBP, DBP and HR, respectively. The difference in cortisol concentration between final and baseline samples, as well as area under the curve (AUCg) relative to ground (which shows overall responsiveness) will be operationalised as cortisol reactivity. Descriptive and frequency statistics will be conducted for socio-demographic, self-report, cardiovascular and cortisol data. One-way ANOVAs will examine whether previous PASAT experience impacts cardiovascular and cortisol baseline/reactivity. Univariate ANOVAs (categorical variables) and correlations (continuous variables) will investigate whether there are socio-demographic influences on reactivity, questionnaire scores/ratings and PASAT performance. Overall, these statistical outputs are likely to reveal potential confounding variables that will require statistically adjusting for in any main analyses. Repeated measure ANOVAs, with time as three points (baseline, PASAT and recovery), will be undertaken to verify that the PASAT significantly perturbed cardiovascular and cortisol activity. For the main analyses, the relationship between fatigue/other questionnaires scores, and cardiovascular and cortisol reactivity will be initially investigated using Pearson's correlation. Regression analyses will then be used to re-examine any significant relationships with adjustment for appropriate confounding variables as covariates in the model. Partial eta-squared (η^2) and change in R-squared (ΔR^2) will be used as indices of effect size throughout.

References

Basu, N., Jones, G. T., Fluck, N., MacDonald, A. G., Pang, D., Dospinescu, P., … Macfarlane, G. J. (2010). Fatigue: A principal contributor to impaired quality of life in ANCA-associated vasculitis. *Rheumatology*, 49(7), 1383–1390.

Basu, N., Mcclean, A., Harper, L., Amft, E. N., Dhaun, N., Luqmani, R. A., … Jones, G. T. (2013). Explaining fatigue in ANCA-associated vasculitis. *Rheumatology*, 52(9), 1680–1685.

Basu, N., McClean, A., Harper, L., Amft, E. N., Dhaun, N., Luqmani, R. A., … Macfarlane, G. J. (2014). The characterisation and determinants of quality of life in ANCA associated vasculitis. *Annals of the Rheumatic Diseases*, 73(1), 207–211.

Bjelland, I., Dahl, A. A., Haug, T. T., & Neckelmann, D. (2002). The validity of the Hospital Anxiety and Depression Scale: An updated literature review. *Journal of Psychosomatic Research*, *52*(2), 69–77.

Black, J. K., Balanos, G. M., & Whittaker, A. C. (2017). Resilience, work engagement and stress reactivity in a middle-aged manual worker population. *International Journal of Psychophysiology*, *116*(1), 9–15.

Boksem, M. A. S., Meijman, T. F., & Lorist, M. M. (2006). Mental fatigue, motivation and action monitoring. *Biological Psychology*, 72, 123–132.

Bramley, P. N., Easton, A. M., Morley, S., & Snaith, R. P. (1988). The differentiation of anxiety and depression by rating scales. *Acta Psychiatrica Scandinavica*, *77*(2), 133–138.

Brazier, J. E., Harper, R., Jones, N. M. B., OCathain, A., Thomas, K. J., Usherwood, T., &

Westlake, L. (1992). Validating the SF-36 health survey questionnaire: New outcome measure for primary care. *British Medical Journal*, *305*(6846), 160–164.

Burholt, V., & Nash, P. (2011). Short Form 36 (SF-36) Health Survey Questionnaire: normative data for Wales. *Journal of Public Health*, *33*(4), 587–603.

Burns, V. E., Carroll, D., Ring, C., Harrison, L. K., & Drayson, M. (2002). Stress, coping, and hepatitis B antibody status. *Psychosomatic Medicine*, *64*(2), 287–293.

Chaudhuri, A., & Behan, P. O. (2000). Fatigue and basal ganglia. *Journal of the Neurological Sciences*, 179, 34–42.

Demiral, Y., Ergor, G., Unal, B., Semin, S., Akvardar, Y., Kivircik, B., & Alptekin, K. (2006). Normative data and discriminative properties of short form 36 (SF-36) in Turkish urban population. *BMC Public Health*, *6*(1), 247–254.

Elbers, R. G., van Wegen, E. E. H., Verhoef, J., & Kwakkel, G. (2012). Reliability and structural validity of the Multidimensional Fatigue Inventory (MFI) in patients with idiopathic Parkinson's disease. *Parkinsonism and Related Disorders*, *18*(5), 532–536.

Failde, I., & Ramos, I. (2000). Validity and reliability of the SF-36 Health Survey Questionnaire in patients with coronary artery disease. *Journal of Clinical Epidemiology*, *53*(4), 359–365.

Garratt, A. M., Ruta, D. A., Abdalla, M. I., Buckingham, J. K., & Russell, I. T. (1993). The SF 36 health survey questionnaire: An outcome measure suitable for routine use within the NHS? *British Medical Journal*, *306*(6890), 1440–1444.

Grayson, P. C., Amudala, N. A., McAlear, C. A., Leduc, R. L., Shereff, D., Richesson, R., … Merkel, P. A. (2013). Illness perceptions and fatigue in systemic vasculitis. *Arthritis*

Care and Research, *65*(11), 1835–1843.

Gronwall, D. M. A. (1977). Paced Auditory Serial-Addition Task: A Measure of Recovery from Concussion. *Perceptual and Motor Skills*, *44*(2), 367–373.

Hajj-Ali, R. A., Wilke, W. S., Calabrese, L. H., Hoffman, G. S., Liu, X., Bena, J., … Langford, C. A. (2011). Pilot study to assess the frequency of fibromyalgia, depression, and sleep disorders in patients with granulomatosis with polyangiitis (Wegener's). *Arthritis Care & Research*, 63(1), 827–833.

Herrmann, C. (1997). International experiences with the Hospital Anxiety and Depression Scale-A review of validation data and clinical results. *Journal of Psychosomatic Research*, *42*(1), 17–41.

Herlyn, K., Hellmich, B., Seo, P., & Merkel, P. A. (2010). Patient-reported outcome assessment in vasculitis may provide important data and a unique perspective. *Arthritis Care & Research*, 62(1), 1639–1645.

Koutantji, M., Harrold, E., Lane, S. E., Pearce, S., Watts, R. A., & Scott, D. G. I. (2003). Investigation of quality of life, mood, pain, disability, and disease status in primary systemic vasculitis. *Arthritis and Rheumatism*, *49*(6), 826–837.

Lazarus, B., John, G., O′Callaghan, C., & Ranganathan, D. (2016). Recent advances in anti-neutrophil cytoplasmic antibody-associated vasculitis. *Indian Journal of Nephrology*, 26(2), 86–96.

Leone, S. S., Huibers, M. J. H., Knottnerus, J. A., & Kant, I. (2009). The temporal relationship between burnout and prolonged fatigue: A 4-year prospective cohort study. *Stress and Health*, 25(4), 365–374.

Lin, J. M. S., Brimmer, D. J., Maloney, E. M., Nyarko, E., BeLue, R., & Reeves, W. C. (2009). Further validation of the Multidimensional Fatigue Inventory in a US adult population sample. *Population Health Metrics*, *7*(1), 7–18.

Marmot, M. G., Stansfeld, S., Patel, C., North, F., Head, J., White, I., … Smith, G. D. (1991). Health inequalities among British civil servants: the Whitehall II study. *The Lancet*, *337*(8754), 1387–1393.

Moorey, S., Greer, S., Watson, M., Gorman, C., Rowden, L., Tunmore, R., … Bliss, J. (1991). The factor structure and factor stability of the hospital anxiety and depression scale in patients with cancer. *The British Journal of Psychiatry*, *158*(2), 255–259.

Phillips, A. C., Carroll, D., Burns, V. E., & Drayson, M. (2005). Neuroticism, cortisol reactivity, and antibody response to vaccination. *Psychophysiology*, *42*(2), 232–238.

Phillips, A. C., Carroll, D., Hunt, K., & Der, G. (2006). The effects of the spontaneous presence of a spouse/partner and others on cardiovascular reactions to an acute psychological challenge. *Psychophysiology*, *43*(6), 633–640.

Phillips, A. C., Der, G., Hunt, K., & Carroll, D. (2009). Haemodynamic reactions to acute psychological stress and smoking status in a large community sample. *International Journal of Psychophysiology*, *73*(3), 273–278.

Register General's *Classification of occupations* (1980). London: HMSO.

Resnick, B. (2011). The relationship between resilience and motivation. In *Resilience in Aging: Concepts, Research, and Outcomes* (pp. 199–215). New york: Sringer.

Salles, A., Cohen, G. L., & Mueller, C. M. (2014). The relationship between grit and resident well-being. *American Journal of Surgery*, 207(2), 251–254.

Smets, E. M. A., Garssen, B., Bonke, B., & De Haes, J. C. J. M. (1995). The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *Journal of Psychosomatic Research*, *39*(3), 315–235.

Taku, K. (2014). Relationships among perceived psychological growth, resilience and burnout in physicians. *Personality and Individual Differences*, 59(2), 120–123.

Von Culin, K. R., Tsukayama, E., & Duckworth, A. L. (2014). Unpacking grit: Motivational correlates of perseverance and passion for long-term goals. J*ournal of Positive Psychology*, 9(4), 306–312.

Walsh, M., Mukhtyar, C., Mahr, A., Herlyn, K., Luqmani, R., Merkel, P. A., & Jayne, D. R. W. (2011). Health-related quality of life in patients with wewly diagnosed antineutrophil cytoplasmic antibody-associated vasculitis. *Arthritis Care & Research*, *63*(7), 1055–1061.

Ware, J. E., & Sherbourne, C. D. (1992). The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Medical Care*, *30*(6), 473–483.

Willemsen, G., Ring, C., Carroll, D., Evans, P., Clow, A., & Hucklebridge, F. (1998). Secretory immunoglobulin A and cardiovascular reactions to mental arithmetic and cold pressor. *Psychophysiology*, *35*(3), 252–259.

Zigmond, A. S., & Snaith, R. P. (1983). The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica*, *67*(6), 361–370.

CHAPTER FIVE

GENERAL DISUCSSION

The central aim of the present thesis was to generate an improved understanding of how motivation-related behaviours are associated with physiological reactivity to acute stress. Specifically, two studies examined the relationship between cardiovascular reactivity and perseverance and resilience, respectively. The third study was a proposed pilot study, for which the associated chapter (Chapter 4) outlines the methodological approach. This research will investigate the association between cardiovascular/cortisol reactivity and fatigue in ANCA-associated vasculitis patients.

Summary of results

Perseverance and reactivity

Chapter 2 provided an examination, in a mixed-sex student sample, of whether cardiovascular reactivity to acute stress was associated with self-reported and behavioural perseverance. It also investigated whether self-reported and behavioural perseverance measurements correlated. Self-reported perseverance was not related to cardiovascular reactivity. Post-adjustment for confounding variables (gender and CP time), low behavioural perseverance, conceptualised as recording fewer impossible puzzle attempts, marginally predicted blunted CP SBP and HR reactivity and significantly predicted blunted CP DBP reactivity. In addition, analogous statistics revealed that number of impossible puzzle attempts was also positively related to PASAT BP (SBP and DBP) reactivity and time taken on the puzzle (another behavioural perseverance measure) was significantly and positively correlated with PASAT DBP reactivity. In sum, those with blunted BP reactivity, particularly DBP reactivity to two psychological stress tasks, spent less time and recorded fewer attempts endeavouring to complete an impossible puzzle, which implies dysfunctional behavioural perseverance in this population. However, it must be noted that the sample was split by task order (due to a large order effect) and all significant findings emerged only in the PASAT first group. This will be

discussed later. With regard to the secondary objective, self-reported perseverance was positively associated with PASAT performance, which could be considered a weak indirect measure of behavioural perseverance, however, it was not related to any other behavioural measure. Therefore, it appears overall that self-reported and behavioural perseverance do not correlate. In sum, blunted BP reactivity to the CP task, and to a lesser extent the PASAT, could be a useful prognostic marker in identifying those with low perseverance who do not show this in non-behavioural self-report measures. This is important as these individuals may require extensive psychological support and motivational assistance during situations that typically demand high perseverance for success, for example, addiction cessation (Abrantes et al., 2008; Steinberg et al., 2012). However, further research is still required due to the inconstancies across cardiovascular responses and behavioural measures of perseverance that were found within this study.

Resilience and reactivity

Chapter 3 explored, using the same dataset and methodological approach as Chapter 2, the relationship between cardiovascular reactivity to acute stress and self-reported resilience. In the group that completed the PASAT first, lower resilience predicted blunted HR reactivity to the CP task and this relationship survived statistical adjustment for appropriate confounding variables (gender and CP time). However, CP SBP and DBP reactivity were not related with resilience, nor was PASAT cardiovascular (SBP, DBP, HR) reactivity in general. All in all, enhancing resilience might lead to a more adaptive pattern of heart rate reactivity in the face of stress, but more extensive research and replication studies are required before this can be assumed.

General implications

In line with the reactivity hypothesis (Obrist, 1981), large cardiovascular (Allen, Matthews, & Sherman, 1997; Barnett, Spence, Manuck, & Jennings, 1997; Carroll et al., 2001; Carroll et al., 1996; Carroll, Ginty, Painter, et al., 2012; Carroll, Phillips, Der, Hunt, & Benzeval, 2011; Carroll, Ring, Hunt, Ford, & MacIntyre, 2003; Chida & Steptoe, 2010; Everson et al., 1997; Georgiades, Lemne, De Faire, Lindvall, & Fredrikson, 1997; Kamarck et al., 1997; Markovitz, Raczynski, Wallace, Chettur, & Chesney, 1998; Matthews et al., 2004; Schwartz et al., 2003; Treiber et al., 2003; Wawrzyniak, Hamer, Steptoe, & Endrighi, 2016) and cortisol (Girod & Brotman, 2004; Hamer et al., 2010; Hamer & Steptoe, 2012) responses to acute stress are implicated in the aetiology of cardiovascular disease. Exaggerated cardiovascular reactivity even extends to predict cardiovascular disease mortality (Carroll, Ginty, Der, et al., 2012).

Although a more recent line of research, blunted reactivity is also associated with a range of adverse health (Carroll, Phillips, & Der, 2008; de Rooij & Roseboom, 2010; de Rooij, Schene, Phillips, & Roseboom, 2010; Phillips, Der, & Carroll, 2009; Phillips, Hunt, Der, & Carroll, 2011; Phillips, Roseboom, Carroll, & De Rooij, 2012; Salomon, Clift, Karlsdóttir, & Rottenberg, 2009; York et al., 2007) and behavioural (Al'Absi, 2006; Al'Absi, Wittmers, Erickson, Hatsukami, & Crouse, 2003; Allen, Hogan, & Laird, 2009; Bennett, Blissett, Carroll, & Ginty, 2014; Bibbey, Ginty, Brindle, Phillips, & Carroll, 2016; Carroll, Bibbey, Roseboom, et al., 2012; Carroll et al., 2013; Ginty, Phillips, Higgs, Heaney, & Carroll, 2012; Girdler, Jamner, Jarvik, Soles, & Shapiro, 1997; Heaney, Ginty, Carroll, & Phillips, 2011; Heleniak, McLaughlin, Ormel, & Riese, 2016; Koo-Loeb, Pedersen, & Girdler, 1998; Lovallo, Dickensheets, Myers, Thomas, & Nixon, 2000; Muñoz & Anastassiou-

Hadjicharalambous, 2011; Panknin, Dickensheets, Nixon, & Lovallo, 2002; Paris, Franco, Sodano, Frye, & Wulfert, 2010) outcomes. Collectively, these correlates appear to reflect dysfunctional motivation, to the extent that blunted reactivity appears to be a peripheral marker for central motivational dysregulation (Carroll et al., 2017, 2009; Lovallo, 2006; Phillips, 2011), i.e., sub-optimal functioning of the brain areas that govern motivation processes (Carroll et al., 2017, 2009; Lovallo, 2006; Phillips, 2011). Importantly, this contention is supported by neuroimaging studies, i.e., motivation-related brain areas are shown to be hypoactivated in blunted responders experiencing stress (Gianaros et al., 2005; Ginty et al., 2013). Aligned with the motivational dysregulation hypothesis, a small number of studies have now been able to indirectly show that blunted reactivity is characteristic of those who exhibit poor motivation-related behavioural outcomes (Galatzer-Levy et al., 2014; Ginty et al., 2015). This thesis is timely in that it adds an extra dimension of support to the motivational dysregulation hypothesis by showing that this response pattern can directly predict motivational-related behavioural outcomes. It also demonstrates that the correlates of blunted reactivity can extend as far as dysfunctional perseverance and resilience.

Motivation-related outcomes and reactivity trajectories

An interesting contrast between the chapters of this thesis is the cardiovascular response associated with each motivation-related behaviour. For example, perseverance (Study 1) was associated with blunted BP but not HR reactivity and resilience (Study 2) was predicted by blunted HR but not BP reactivity. Therefore, it is possible that each motivation-related behaviour has its own associated pattern of cardiovascular activity rather than reflecting cardiovascular reactivity in general. However, as yet, there is no consistent evidence of this in the literature, for example, other research has reported null associations between perseverance

and BP reactivity (Bibbey et al., 2016) or have even found it to be related to HR reactivity (Ginty et al., 2015). As there is much contradiction, this suggests that the relationship between motivation-related behaviours and reactivity trajectories might not be so simple. Further, it may be that the pattern of both HR and BP reactivity together relative to the mean/median is important (Brindle et al., 2016) but in smaller sample sizes such as the present, analysis of profiles of overall reactivity is not possible. Further, perhaps the type of experimentally induced stress used to perturb cardiovascular activity has an important bearing. For example, in the present study, perseverance was only associated with blunted BP responses to a passive stress task, whereas in another study it was associated with HR reactivity when an active stress task was used (Ginty et al., 2015). Thus, it is possible that motivation-related constructs have their own physiological reactivity trajectories individualised to different type of stress. However, if this were the case, we would have expected to see perseverance relating to PASAT reactivity in the present study, which was not the case. Overall, large scale studies using multiple stress tests and different motivation/physiological measures are needed to explore other potential reasons why different motivation-related outcomes appear to have different reactivity trajectories.

Thematic links and implications for the motivational dysregulation hypothesis

This thesis also includes the methodology for an additional study on fatigue and reactivity in a patient population. An obvious link between perseverance, resilience and fatigue is the reflection of motivation or motivational processes (Boksem et al., 2006; Resnick, 2011; Von Culin et al., 2014). Like motivation-related behaviours, motivation in general has received only limited attention in the cardiovascular reactivity literature. Nevertheless, one study demonstrated that motivation during a performance task was positively associated with

cardiovascular reactivity (May, Sanchez-Gonzalez, Seibert, Samaan, & Fincham, 2016) and another showed that exaggerated cardiac responders perform better during tasks that require intrinsic motivation and effort for success, for example, lung function spirometry assessments (Carroll, Bibbey, Roseboom, et al., 2012; Carroll et al., 2013; Crim et al., 2011). However, interestingly, these behavioural patterns must be unconsciously regulated as exaggerated and blunted responders report no difference in effort or self-reported motivation during tasks (Brindle, Whittaker, Bibbey, Carroll, & Ginty, 2017). Thus, it is also highly likely that blunted responders are unaware that they show dysfunctional perseverance or resilience, however, this needs to be explored further. Similarly, objective evidence, by means of pupil diameter and words per minute during a speech task, also implicate reactivity as a phenomenon independent of effort or engagement (Salomon, Jin, & Webb, 2015; Salomon, Bylsma, White, Panaite, & Rottenberg, 2013). In addition, this line of evidence also rejects the contention that blunted reactivity is a simple reflection of decreased task engagement associated with dysfunctional motivation.

This thesis demonstrated that blunted physiological reactivity is associated with negative motivation-related behavioural patterns, i.e., dysfunctional perseverance and resilience, which aligns with some (Abrantes et al., 2008; Al'Absi, 2006; Galatzer-Levy et al., 2014; Ginty et al., 2015; Junghanns et al., 2003; Lovallo, 2006) but not all (Bibbey et al., 2016; Black et al., 2017; Corina & Adriana, 2013; Ruiz-Robledillo et al., 2017) of the current literature. Overall, the present findings provide further evidence that blunted reactivity is a marker of motivational dysregulation (Carroll, Ginty, Whittaker, Lovallo, & de Rooij, 2017; Carroll, Lovallo, et al., 2009; Phillips, 2011). At its core, motivational dysregulation represents sub-optimal or down-regulated functioning of the brain areas that govern motivation. However, as

yet, there is only indirect and weak evidence that blunted reactivity can predict any behavioural patterns that reflect poor motivation. Therefore, the findings from this thesis extend the motivational dysregulation hypothesis and add an extra dimension of evidence, as blunted reactivity is now shown to directly predict actual motivation-related behavioural outcomes. It is also expected that fatigue will also be associated with blunted reactivity, and consequently may also be a symptom of central motivational dysregulation. There are several strands of research which support this hypothesis. First, mental fatigue is associated with poor motivation (Boksem et al., 2006; Chaudhuri & Behan, 2000) to the extent where improving motivation can help to ease the effect of fatigue (Boksem et al., 2006). Second, constructs which run parallel to fatigue, i.e., vital exhaustion and burnout, are related with attenuated cardiovascular stress responses (Jönsson et al., 2015; Kudielka et al., 2006). Third, fatigue is associated with correlates such as depression, anxiety and poor self-reported health (Brown & Kroenke, 2009; Demyttenaere et al., 2005; Dolan & Kudrna, 2015) correlates which are also associated with blunted reactivity (de Rooij & Roseboom, 2010; de Rooij et al., 2010; Phillips et al., 2009, 2011; Salomon et al., 2009; York et al., 2007). Interestingly, depression often coexists with dysfunctional motivation (Smith, 2013) with research suggesting that this depression-motivation relationship is at least part mediated by the Val^{158}Met COMT gene (Åberg, Fandiño-Losada, Sjöholm, Forsell, & Lavebratt, 2011). However, what is particularly interesting, is that this gene is also implicated in blunted stress reactivity (Mueller et al., 2012). Thus, it would be interesting to examine whether this or other genetic variations are directly related to both fatigue processes and reactivity. Overall, there appears to be a complex interactional network that links constructs which run parallel to fatigue, for example, vital exhaustion, outcomes associated with fatigue, for example, depression, motivation

processes, and autonomic stress reactivity. Thus, in light of these indirect relationships, it is highly conceivable that fatigue will directly relate to cardiovascular reactivity.

Although fatigue is a prevalent symptom reported by ANCA-associated vasculitis patients (Basu et al., 2010) and a critical factor for quality of life (Basu et al., 2014), it is not, *per se,* directly related to the severity of the disease (Basu et al., 2013; Koutantji et al., 2003). Thus, it is possible that fatigue is a manifestation of something other than vasculitis itself, such as motivational processes (Boksem et al., 2006; Chaudhuri & Behan, 2000) which could possibly be explained by dysregulated activity within the brain (Carroll et al., 2017, 2009; Lovallo, 2006; Phillips, 2011). In support, a study demonstrated that compared to controls, fatigued vasculitis patients recorded decreased muscle activation during a voluntary contraction and gave-up sooner on an endurance task, which, could not be explained by muscle or cardiovascular physiology (McClean et al., 2016). Importantly, aside from physical attributes, i.e., muscular strength and cardiorespiratory fitness, these two tasks require motivation for success (McCormick et al., 2015; McNair, 1996). Interestingly, despite performing more poorly on the two motivation-contingent tasks, vasculitis patients self-reported increased effort and lower motivation compared to healthy participants (McClean et al., 2016). Thus, overall, it seems that fatigue is of central origin, is unconsciously governed and reflects motivational processes. As such, fatigue may be yet another correlate of blunted reactivity and motivational dysregulation.

Possible mechanisms underpinning the relationship between reactivity and motivation-related behavioural outcomes

An explanation as to why there was an association between motivation-related behaviours and blunted reactivity in the present thesis is offered by Lazarus' theory of emotion and adaption (Lazarus, 1991). This model postulates that in motivation-contingent situations, there is a

great importance placed on whether perceived personal ability can match the demands of the situation (Lazarus, 1991). This extends to suggest that individuals who believe they can be successful i.e., consider themselves to have the necessary resources, typically exhibit larger physiological responses to stress. By implication, when individuals do not believe they can successfully complete a task, or are unaware if they can meet the situational demands, this is accompanied with a more blunted physiological response pattern (Lazarus, 1991). Thus, in the present thesis, it is possible those with dysfunctional perseverance and resilience, who are arguably more used to failure, for example, those with low perseverance are more likely to fail when trying to quit smoking (Abrantes et al., 2008; Steinberg et al., 2012), did not believe they could match the situational demands imposed by the laboratory environment and/or tasks. If so, in line with Lazarus' model, this could explain their blunted stress response pattern. Research has suggested that this hypoactive physiological activity could be attributed to a decreased need for mobilization of inner resources to help cope with the situation at hand (Blascovich & Tomaka, 1996), i.e., when individuals feel that they cannot complete a task there is less demand for physiological activation. Consequently, a slightly different explanation for the effects observed in this thesis but still grounded in the Lazarus' theory, is that that those with blunted reactivity recorded poorer perseverance/resilience because the mobilization of their inner resources was less efficient. If true, this could explain why they were not able to manage the demands of the laboratory/stress tasks, and this may have been reflected as dysfunctional perseverance and resilience. A third possible mechanism is that those with blunted responses experienced early life stress/adversity, which contributed to motivational dysregulation manifested as dysfunctional perseverance and resilience, although, again, this would need to be tested.

Implications for methodology

A common theme throughout Study 2 and 3, as analyses for both studies were conducted using the same dataset, was a large stress task order effect associated primarily with HR reactivity to the CP task. This was significant despite counterbalancing the order in which the tasks were presented. Overall, participants in the CP first group had a higher baseline HR prior to the CP task compared to those who completed the PASAT first. Consequently, when the CP task was administered first, participants exhibited a lower CP HR reactivity than when the PASAT was undertaken first. Interestingly, this cannot be explained by an insufficiently long recovery period or the CP-induced stress itself, as participants had higher baseline HR activity before the CP task and their initial baseline HR prior to the CP was higher than the next baseline value following the CP when the CP was first. Similarly, the order effect cannot be attributed to a simple anticipatory cardiovascular response, as participants were unware of the CP task when CP baseline measurements were being taken. There is no obvious explanation for this order effect, but its finding does offer key methodical suggestions for future studies. It would seem advantageous to administer the PASAT before the CP task (Willemsen et al., 1998), as well as incorporate generous recovery periods to account for any recovery overshoot post-PASAT. However, PASAT cardiovascular overshoot has not been observed in any other previous studies, including in those investigating PASAT recovery (Whittaker, unpublished personal communication).

Thesis limitations

This present thesis is not without limitations. Specific limitations relating to each study have been detailed in the discussion section of each associated empirical chapter; this section outlines the general limitations of the thesis consistent across all chapters. First, although the

sample of Study 1 and 2 was of good size prior to being split in two (Allen et al., 1997), the respective size of each orthogonal sub-group were only modest. However, they were still comparable to the magnitude of other sub-groups in previous studies (e.g., Salomon et al., 2013). Second, the study was plagued by a significant order effect that negatively influenced the cardiovascular profile of the participants in the CP task first group; it appeared that these individuals were not responding and/or recovering to the stress tasks as expected. However, the tasks were counterbalanced in a bid to prevent this occurrence, a technique used with success in previous research with similar study designs and the same stress tasks as the present study (e.g., Ring et al., 2000). The author cannot articulate a reason why the order effect was apparent in this thesis, but it holds implications for future studies, as discussed above. Third, although the sample included both genders, it was overrepresented by females. This is important, as gender impacts physiological reactivity to stress (Stone et al., 1990), perseverance (Christensen & Knezek, 2014; Kiefer & Shih, 2006) and resilience (Erdogan et al., 2015). However, gender was statistically adjusted for in all necessary analyses along with any other appropriate confounding variables; deeper analysis by menstrual cycle phase (Hastrup & Light, 1984; Stoney, Matthews, McDonald, & Johnson, 1988) would also be possible but would reduce the sample further into sub-groups, and effects of menstrual cycle are not demonstrated in all studies (Shenoy, Sahana, & Shivakumar, 2014; Weidner & Helmig, 1990). Further, despite controlling for all necessary confounders, which enhanced the internal validity of the respective studies, causality still cannot be determined as the possibility that an uncontrolled confounding variable was mediating the reactivity-motivation relationships cannot be eliminated. Another limitation surrounding the empirical chapters was the lack of examination into stress response patterns reflecting the HPA axis. This prevented a comprehensive assessment into the relationship between motivation-related behaviours and

overall reactivity in the two key branches of the biological stress-response system. It would have been useful to investigate whether cardiovascular reactions correlated with cortisol responses. If so, this physiological cross-measure validation would have generated stronger evidence attest to the fact that stress reactivity and motivated-related behaviours are allied. However, as the cortisol response to stress is slow (De Vente et al., 2003) and the study used a multiple stress task design, long baseline/recovery periods in-between stress tasks would have been imperative. This would have resulted in the laboratory testing session being extremely time-consuming and may have contributed to participant fatigue (Egleston et al., 2011) or fewer participants being able to be tested in the time frame available. Nevertheless, in Study 3 where a single stress task methodology will be employed, cortisol and cardiovascular activity will be measured concurrently.

Thesis strengths

The thesis also has recognisable strengths. First, the chapters which form this thesis were novel in that used both self-report and behavioural measurement techniques when examining the relationship between motivation-related behaviours and cardiovascular reactivity (Study 1). They also incorporated both active and passive stress tests in doing so (Studies 1 and 2). In addition, Study 3 will be the first research the author is aware of to directly examine the reactivity-fatigue relationship and assess physiological reactivity in in ANCA-associated vasculitis patients. In addition, these novelties also have associated strengths which will be discussed below. For example, because both self-report and objective measurement techniques were utilised, this triangulation technique leads to a stronger overall methodological approach (Crockett, Schulenberg, & Petersen, 1987). It also supported the cross-measure objective validation of self-reported data, which, is often clouded by recall bias

(Freedman et al., 2010; Hebert et al., 1995; Prince et al., 2008), particularly in the case of behaviours such as perseverance (Bazelais, Lemay, & Doleck, 2016; Duckworth, Peterson, Matthews, & Kelly, 2007). Self-report and behavioural perseverance did not correlate in Study 2, however, this brought to attention a methodological occurrence that may have implications for future research. Behavioural measurement techniques can often reflect "state" forms of behaviour whereas self-reported measure "trait" behaviour (Steinberg & Williams, 2013). Thus, authors need to take care when selecting self-report and behavioural measures of the same phenomenon as to make sure that they are closely examining similar manifestations of the same behaviour. However, trait measures, other than multiple and repeated different tests of behaviour, would be difficult to implement, and measurement of both state and trait gives insight into which is most important in relation to reactivity. A key advantage of using different types of stress test (active and passive) in the present thesis, is that self-reported resilience, and some of the behavioural perseverance measures, only related to reactivity during exposure to passive stress. Thus, these interesting findings would have been overlooked if only one active stressor was used, which is often the case in cardiovascular reactivity-based research (Bibbey et al., 2016; Ginty et al., 2015; Heaney et al., 2011). It is also a strength that the study used a mixed-sex sample as this increases the generalisability of the results, even though only university students were included. However, it is imagined that Study 3 will attract a sample with far greater variability in terms of demographic characteristics such as age, nationality and socio-economic status. A final advantage is that studies constituting this thesis statistically controlled for any necessary confounding variables which enhanced the internal validity of the thesis as whole.

Future directions

There are several potential pathways future research can follow to build on this thesis. However, before these can be explored, there is a need to replicate the research constituting this thesis, using larger studies if possible, to confirm the relationships between cardiovascular reactivity, perseverance and resilience. It would advantageous to do this using the PASAT first protocol alone, by exploring reactivity in both the SAM and HPA axes concurrently and by administering multiple self-report and behavioural measures for each construct, in addition to what was already used in the present thesis. For example, for perseverance, additional self-report measures could include the Two Item Self-Report Persistence Measure (Steinberg et al., 2007) and for behavioural, mirror tracing (Quinn et al., 1996) or breath holding (Hajek et al., 1987) tasks could be incorporated. Post-replication, if similar findings are reported, one future pathway could be to investigate how situational factors influence the perseverance-reactivity and resilience-reactivity relationships. It would be interesting to explore how the consequence of persevering/giving up (perseverance) and the deemed importance of bouncing back from failure (resilience) affect motivation-reactivity relationships. Another pathway which could have real value is the experimental manipulation of psychological or behavioural techniques designed to improve resilience and perseverance, to examine how these might impact temporal physiological stress response patterns. For example, several factors have been highlighted to promote psychological resilience, including positive coping, positive affect and behavioural control (Meredith et al., 2011), and therefore adopting these techniques may lead to a more adaptive pattern of stress responding.

Conclusion

In conclusion, this thesis used laboratory testing to gain a deeper and more detailed understanding of the relationship between physiological reactivity to stress and motivation-

related behavioural outcomes (perseverance and resilience). It also proposed the methodological approach a future study (CRAVE) which will examine the relationship between cardiovascular/cortisol reactivity and fatigue in ANCA-associated vasculitis patients. Analyses in the empirical chapters revealed that blunted cardiovascular reactivity is associated with dysfunctional perseverance and resilience. It is also expected that the CRAVE study will reveal similar patterns of results with regard to fatigue relating to blunted stress responses. All in all, the findings from this present thesis add further support to a growing body of evidence which now confirms that blunted reactivity is maladaptive. They also extend the cardiovascular reactivity and motivational dysregulation literature as there is now direct evidence which shows that attenuated reactivity manifests in those with poor motivation-related behavioural patterns. However, it is important to note that there were inconsistencies throughout the studies within this thesis, for example, significant findings were often only evidenced for either BP or HR reactivity, or for only one of the behavioural measures of perseverance. In addition, there were also discrepancies in relation to the findings between the present and previous research, for example, perseverance was related to HR reactivity in previous research and to BP reactivity in the present study. Thus, future research and replication studies are imperative for this particular literature. Nevertheless, the current findings tentatively suggest that blunted physiological reactivity could be key marker in identifying those with motivation-related deficiencies, who may benefit from psychological support in situations that require high levels of motivation, for example, when engaging in healthy lifestyle changes. In addition, enhancing resilience and perseverance may perhaps be key interventions by which stress response patterns can be “improved”, by ensuring reactivity magnitude remains within an adaptive range in the face of stress.

References

Åberg, E., Fandiño-Losada, A., Sjöholm, L. K., Forsell, Y., & Lavebratt, C. (2011). The functional Val158Met polymorphism in catechol-O- methyltransferase (COMT) is associated with depression and motivation in men from a Swedish population-based study. *Journal of Affective Disorders*, *129*, 158–166.

Abrantes, A. M., Strong, D. R., Lejuez, C. W., Kahler, C. W., Carpenter, L. L., Price, L. H., … Brown, R. A. (2008). The role of negative affect in risk for early lapse among low distress tolerance smokers. *Addictive Behaviors*, *33*(11), 1394–1401.

Al'Absi, M. (2006). Hypothalamic-pituitary-adrenocortical responses to psychological stress and risk for smoking relapse. *International Journal of Psychophysiology*, *59*(3), 218–227.

Al'Absi, M., Wittmers, L. E., Erickson, J., Hatsukami, D., & Crouse, B. (2003). Attenuated adrenocortical and blood pressure responses to psychological stress in ad libitum and abstinent smokers. *Pharmacology Biochemistry and Behavior*, *74*(2), 401–410.

Allen, M. T., Hogan, A. M., & Laird, L. K. (2009). The relationships of impulsivity and cardiovascular responses: The role of gender and task type. *International Journal of Psychophysiology*, *73*, 369–376.

Allen, M. T., Matthews, K. A., & Sherman, F. S. (1997). Cardiovascular reactivity to stress and left ventricular mass in youth. *Hypertension*, *30*(4), 782–787.

Barnett, P. a, Spence, J. D., Manuck, S. B., & Jennings, J. R. (1997). Psychological stress and the progression of carotid artery disease. *Journal of Hypertension*, *15*(1), 49–55.

Basu, N., Jones, G. T., Fluck, N., MacDonald, A. G., Pang, D., Dospinescu, P., …

Macfarlane, G. J. (2010). Fatigue: A principal contributor to impaired quality of life in ANCA-associated vasculitis. *Rheumatology*, *49*(7), 1383–1390.

Basu, N., Mcclean, A., Harper, L., Amft, E. N., Dhaun, N., Luqmani, R. A., … Jones, G. T. (2013). Explaining fatigue in ANCA-associated vasculitis. *Rheumatology*, *52*(9), 1680–1685.

Basu, N., McClean, A., Harper, L., Amft, E. N., Dhaun, N., Luqmani, R. A., … Macfarlane, G. J. (2014). The characterisation and determinants of quality of life in ANCA associated vasculitis. *Annals of the Rheumatic Diseases*, *73*(1), 207–211.

Bazelais, P., Lemay, D. J., & Doleck, T. (2016). How does grit impact college students' academic achievement in science? *European Journal of Science and Mathmatics Education*, *4*(1), 33–43.

Bennett, C., Blissett, J., Carroll, D., & Ginty, A. T. (2014). Rated and measured impulsivity in children is associated with diminished cardiac reactions to acute psychological stress. *Biological Psychology*, *102*, 68–72.

Bibbey, A., Ginty, A. T., Brindle, R. C., Phillips, A. C., & Carroll, D. (2016). Blunted cardiac stress reactors exhibit relatively high levels of behavioural impulsivity. *Physiology and Behavior*, *159*(1), 40–44.

Black, J. K., Balanos, G. M., & Whittaker, A. C. (2017). Resilience, work engagement and stress reactivity in a middle-aged manual worker population. *International Journal of Psychophysiology*, *116*(1), 9–15.

Blascovich, J., & Tomaka, J. (1996). The biopsychosocial model of arousal regulation. *Advances in Experimental Social Psychology*, *28*(1), 1–51.

Boksem, M. A. S., Meijman, T. F., & Lorist, M. M. (2006). Mental fatigue, motivation and action monitoring. *Biological Psychology*, *72*, 123–132.

Brindle, R. C., Ginty, A. T., Jones, A., Phillips, A. C., Roseboom, T. J., Carroll, D., … De Rooij, S. R. (2016). Cardiovascular reactivity patterns and pathways to hypertension: A multivariate cluster analysis. *Journal of Human Hypertension*, *30*(12), 755–760.

Brindle, R. C., Whittaker, A. C., Bibbey, A., Carroll, D., & Ginty, A. T. (2017). Exploring the possible mechanisms of blunted cardiac reactivity to acute psychological stress. *International Journal of Psychophysiology*, *113*, 1–7.

Brown, L. F., & Kroenke, K. (2009). Cancer-related fatigue and its associations with depression and anxiety: A systematic review. *Psychosomatics*.

Carroll, D., Bibbey, A., Roseboom, T. J., Phillips, A. C., Ginty, A. T., & De Rooij, S. R. (2012). Forced expiratory volume is associated with cardiovascular and cortisol reactions to acute psychological stress. *Psychophysiology*, *49*(6), 866–872.

Carroll, D., Davey Smith, G., Sheffield, D., Willemsen, G., Sweetnam, P. M., Gallacher, J. E., & Elwood, P. C. (1996). Blood pressure reactions to the cold pressor test and the prediction of future blood pressure status: data from the Caerphilly study. *Journal of Epidemiology and Community Health*, *52*(8), 528–529.

Carroll, D., Davey Smith, G., Shipley, M. J., Steptoe, A., Brunner, E. J., & Marmot, M. G. (2001). Blood pressure reactions to acute psychological stress and future blood pressure status: A 10-year follow-up of men in the whitehall II study. *Psychosomatic Medicine*, *63*(5), 737–743.

Carroll, D., Ginty, A. T., Der, G., Hunt, K., Benzeval, M., & Phillips, A. C. (2012). Increased

blood pressure reactions to acute mental stress are associated with 16-year cardiovascular disease mortality. *Psychophysiology*, *49*(10), 1444–1448.

Carroll, D., Ginty, A. T., Painter, R. C., Roseboom, T. J., Phillips, A. C., & de Rooij, S. R. (2012). Systolic blood pressure reactions to acute stress are associated with future hypertension status in the Dutch Famine Birth Cohort Study. *International Journal of Psychophysiology*, *85*(2), 270–273.

Carroll, D., Ginty, A. T., Whittaker, A. C., Lovallo, W. R., & de Rooij, S. R. (2017). The behavioural, cognitive, and neural corollaries of blunted cardiovascular and cortisol reactions to acute psychological stress. *Neuroscience and Biobehavioral Reviews*, *77*(1), 74–86.

Carroll, D., Lovallo, W. R., & Phillips, A. C. (2009). Are large physiological reactions to acute psychological stress always bad for health? *Social and Personality Psychology Compass*, *3*, 725–743.

Carroll, D., Phillips, A. C., & Der, G. (2008). Body mass index, abdominal adiposity, obesity, and cardiovascular reactions to psychological stress in a large community sample. *Psychosomatic Medicine*, *70*(6), 653–660.

Carroll, D., Phillips, A. C., Der, G., Hunt, K., & Benzeval, M. (2011). Blood pressure reactions to acute mental stress and future blood pressure status: Data from the 12-year follow-up of the West of Scotland Study. *Psychosomatic Medicine*, *73*(9), 737–743.

Carroll, D., Phillips, A. C., Der, G., Hunt, K., Bibbey, A., Benzeval, M., & Ginty, A. T. (2013). Low forced expiratory volume is associated with blunted cardiac reactions to acute psychological stress in a community sample of middle-aged men and women. *International Journal of Psychophysiology*, *90*(1), 17–20.

Carroll, D., Ring, C., Hunt, K., Ford, G., & MacIntyre, S. (2003). Blood pressure reactions to stress and the prediction of future blood pressure: Effects of sex, age, and socioeconomic Position. *Psychosomatic Medicine*, *65*(6), 1058–1064.

Chaudhuri, A., & Behan, P. O. (2000). Fatigue and basal ganglia. *Journal of the Neurological Sciences*, *179*, 34–42.

Chida, Y., & Steptoe, A. (2010). Greater cardiovascular responses to laboratory mental stress are associated with poor subsequent cardiovascular risk status: A meta-analysis of prospective evidence. *Hypertension*, *55*(4), 1026–1032.

Christensen, R., & Knezek, G. (2014). Comparative measures of grit , tenacity and perseverance. *International Journal of Learning, Teaching and Educational Research*, *8*(1), 16–30.

Corina, D., & Adriana, B. (2013). Impact of work related trauma on acute stress response in train drivers. *Procedia - Social and Behavioral Sciences*, *84*(1), 190–195.

Crim, C., Celli, B., Edwards, L. D., Wouters, E., Coxson, H. O., Tal-Singer, R., & Calverley, P. M. A. (2011). Respiratory system impedance with impulse oscillometry in healthy and COPD subjects: ECLIPSE baseline results. *Respiratory Medicine*, *105*, 1069–1078.

Crockett, L. J., Schulenberg, J. E., & Petersen, A. C. (1987). Congruence between objective and self-report data in a sample of young adolescents. *Journal of Adolescent Research*, *2*(4), 383–392.

de Rooij, S. R., & Roseboom, T. J. (2010). Further evidence for an association between self-reported health and cardiovascular as well as cortisol reactions to acute psychological stress. *Psychophysiology*, *47*(1), 1172–1175.

de Rooij, S. R., Schene, A. H., Phillips, D. I., & Roseboom, T. J. (2010). Depression and anxiety: Associations with biological and perceived stress reactivity to a psychological stress protocol in a middle-aged population. *Psychoneuroendocrinology*, *35*(6), 866–877.

De Vente, W., Olff, M., Van Amsterdam, J. G. C., Kamphuis, J. H., & Emmelkamp, P. M. G. (2003). Physiological differences between burnout patients and healthy controls: blood pressure, heart rate, and cortisol responses. *Occupational and Environmental Medicine*, *60*(1), 54–61.

Demyttenaere, K., De Fruyt, J., & Stahl, S. M. (2005). The many faces of fatigue in major depressive disorder. *International Journal of Neuropsychopharmacology*, *8*, 93–105.

Dolan, P., & Kudrna, L. (2015). More years, less yawns: Fresh evidence on tiredness by age and other factors. *Journals of Gerontology - Series B Psychological Sciences and Social Sciences*, *70*, 576–580.

Duckworth, A. L., Peterson, C., Matthews, M. D., & Kelly, D. R. (2007). Grit: Perseverance and passion for long-term goals. *Journal of Personality and Social Psychology*, *92*(6), 1087–1101.

Egleston, B. L., Miller, S. M., & Meropol, N. J. (2011). The impact of misclassification due to survey response fatigue on estimation and identifiability of treatment effects. *Statistics in Medicine*, *30*(30), 3560–3572.

Erdogan, E., Ozdogan, O., & Erdogan, M. (2015). University students' resilience level: The effect of gender and faculty. *Procedia - Social and Behavioral Sciences*, *186*, 1262–1267.

Everson, S. a, Lynch, J. W., Chesney, M. a, Kaplan, G. a, Goldberg, D. E., Shade, S. B., …

Salonen, J. T. (1997). Interaction of workplace demands and cardiovascular reactivity in progression of carotid atherosclerosis: population based study. *British Medical Journal*, *314*(7080), 553–558.

Freedman, L. S., Kipnis, V., Schatzkin, A., Tasevska, N., & Potischman, N. (2010). Can we use biomarkers in combination with self-reports to strengthen the analysis of nutritional epidemiologic studies? *Epidemiologic Perspectives and Innovations*, *7*(1), 2–9.

Galatzer-Levy, I. R., Steenkamp, M. M., Brown, A. D., Qian, M., Inslicht, S., Henn-Haase, C., … Marmar, C. R. (2014). Cortisol response to an experimental stress paradigm prospectively predicts long-term distress and resilience trajectories in response to active police service. *Journal of Psychiatric Research*, *56*(1), 36–42.

Georgiades, A., Lemne, C., De Faire, U., Lindvall, K., & Fredrikson, M. (1997). Stress-induced blood pressure measurements predict left ventricular mass over three years among borderline hypertensive men. *European Journal of Clinical Investigation*, *27*(9), 733–739.

Gianaros, P. J., May, J. C., Siegle, G. J., & Jennings, J. R. (2005). Is there a functional neural correlate of individual differences in cardiovascular reactivity? *Psychosomatic Medicine*, *67*(1), 31–39.

Ginty, A. T., Brindle, R. C., & Carroll, D. (2015). Cardiac stress reactions and perseverance: Diminished reactivity is associated with study non-completion. *Biological Psychology*, *109*, 200–205.

Ginty, A. T., Gianaros, P. J., Derbyshire, S. W. G., Phillips, A. C., & Carroll, D. (2013). Blunted cardiac stress reactivity relates to neural hypoactivation. *Psychophysiology*, *50*(3), 219–229.

Ginty, A. T., Phillips, A. C., Higgs, S., Heaney, J. L. J., & Carroll, D. (2012). Disordered eating behaviour is associated with blunted cortisol and cardiovascular reactions to acute psychological stress. *Psychoneuroendocrinology*, *37*(5), 715–724.

Girdler, S. S., Jamner, L. D., Jarvik, M., Soles, J. R., & Shapiro, D. (1997). Smoking status and nicotine administration differentially modify hemodynamic stress reactivity in men and women. *Psychosomatic Medicine*, *59*(3), 294–306.

Girod, J. P., & Brotman, D. J. (2004). Does altered glucocorticoid homeostasis increase cardiovascular risk? *Cardiovascular Research*, *64*, 217–226.

Hajek, P., Belcher, M., & Stapleton, J. (1987). Breath-holding endurance as a predictor of success in smoking cessation. *Addictive Behaviors*, *12*(1), 285–288.

Hamer, M., O'Donnell, K., Lahiri, A., & Steptoe, A. (2010). Salivary cortisol responses to mental stress are associated with coronary artery calcification in healthy men and women. *European Heart Journal*, *31*, 424–429.

Hamer, M., & Steptoe, A. (2012). Cortisol responses to mental stress and incident hypertension in healthy men and women. *The Journal of Clinical Endocrinology and Metabolism*, *97*(1), 29–34.

Hastrup, J. L., & Light, K. C. (1984). Sex differences in cardiovascular stress responses: modulation as a function of menstrual cycle phases. *Journal of Psychosomatic Research*, *28*(3), 475–483.

Heaney, J. L. J., Ginty, A. T., Carroll, D., & Phillips, A. C. (2011). Preliminary evidence that exercise dependence is associated with blunted cardiac and cortisol reactions to acute psychological stress. *International Journal of Psychophysiology*, *79*(2), 323–329.

Hebert, J. R., Clemow, L., Pbert, L., Ockene, I. S., & Ockene, J. K. (1995). Social desirability bias in dietary self-report may compromise the validity of dietary intake measures. *International Journal of Epidemiology*, *24*(2), 389–398.

Heleniak, C., McLaughlin, K. A., Ormel, J., & Riese, H. (2016). Cardiovascular reactivity as a mechanism linking child trauma to adolescent psychopathology. *Biological Psychology*, *120*, 108–119.

Jönsson, P., Österberg, K., Wallergård, M., Hansen, Å. M., Garde, A. H., Johansson, G., & Karlson, B. (2015). Exhaustion-related changes in cardiovascular and cortisol reactivity to acute psychosocial stress. *Physiology and Behavior*, *151*(1), 327–337.

Junghanns, K., Backhaus, J., Tietz, U., Lange, W., Bernzen, J., Wetterling, T., … Driessen, M. (2003). Impaired serum cortisol stress response is a predictor of early relapse. *Alcohol and Alcoholism*, *38*(2), 189–193.

Kamarck, T. W., Everson, S. A., Kaplan, G. A., Manuck, S. B., Jennings, J. R., Salonen, R., & Salonen, J. T. (1997). Exaggerated blood pressure responses during mental stress are associated with enhanced carotid atherosclerosis in middle-aged finnish men: Findings from the Kuopio Ischemic Heart Disease Study. *Circulation*, *96*(11), 3842–3848.

Kiefer, A., & Shih, M. (2006). Gender differences in persistence and attributions in stereotype relevant contexts. *Sex Roles*, *54*, 859–868.

Koo-Loeb, J. H., Pedersen, C., & Girdler, S. S. (1998). Blunted cardiovascular and catecholamine stress reactivity in women with bulimia nervosa. *Psychiatry Research*, *80*(1), 13–27.

Koutantji, M., Harrold, E., Lane, S. E., Pearce, S., Watts, R. A., & Scott, D. G. I. (2003).

Investigation of quality of life, mood, pain, disability, and disease status in primary systemic vasculitis. *Arthritis and Rheumatism*, *49*(6), 826–837.

Kudielka, B. M., Von Känel, R., Preckel, D., Zgraggen, L., Mischler, K., & Fischer, J. E. (2006). Exhaustion is associated with reduced habituation of free cortisol responses to repeated acute psychosocial stress. *Biological Psychology*, *72*(2).

Lazarus, R. (1991). *Emotion and adaption*. *Oxford University Press*. New York: Oxford Universisty Press.

Lovallo, W. R. (2006). Cortisol secretion patterns in addiction and addiction risk. *International Journal of Psychophysiology*, *59*(3), 195–202.

Lovallo, W. R., Dickensheets, S. L., Myers, D. A., Thomas, T. L., & Nixon, S. J. (2000). Blunted stress cortisol response in abstinent alcoholic and polysubstance-abusing men. *Alcoholism: Clinical and Experimental Research*, *24*(5), 651–658.

Markovitz, J. H., Raczynski, J. M., Wallace, D., Chettur, V., & Chesney, M. a. (1998). Cardiovascular reactivity to video game predicts subsequent blood pressure increases in young men: The CARDIA study. *Psychosomatic Medicine*, *60*(2), 186–191.

Matthews, K. A., Katholi, C. R., McCreath, H., Whooley, M. A., Williams, D. R., Zhu, S., & Markovitz, J. H. (2004). Blood pressure reactivity to psychological stress predicts hypertension in the CARDIA study. *Circulation*, *110*, 74–78.

May, R. W., Sanchez-Gonzalez, M. A., Seibert, G. S., Samaan, J. S., & Fincham, F. D. (2016). Impact of a motivated performance task on autonomic and hemodynamic cardiovascular reactivity. *Stress*, *19*(3), 280–286.

McClean, A., Morgan, M. D., Basu, N., Bosch, J. A., Nightingale, P., Jones, D., & Harper, L.

(2016). Physical fatigue, fitness, and muscle function in patients with Antineutrophil Cytoplasmic Antibody-Associated Vasculitis. *Arthritis Care & Research*, *68*(9), 1332–1339.

McCormick, A., Meijen, C., & Marcora, S. (2015). Psychological determinants of whole-body endurance performance. *Sports Medicine*, *45*(7), 997–1015.

McNair, P. J. (1996). Verbal encouragement: Effects on maximum effort voluntary muscle action. *British Journal of Sports Medicine*, *30*(3), 243–245.

Meredith, L. S., Sherbourne, C. D., Gaillot, S., Hansell, L., Ritschard, H. V., Parker, A. M., & Wrenn, G. (2011). *Promoting psychological resilience in the U.S. military*. *Evaluation*.

Mueller, A., Strahler, J., Armbruster, D., Lesch, K. P., Brocke, B., & Kirschbaum, C. (2012). Genetic contributions to acute autonomic stress responsiveness in children. *International Journal of Psychophysiology*, *83*, 302–308.

Muñoz, L. C., & Anastassiou-Hadjicharalambous, X. (2011). Disinhibited behaviors in young children: Relations with impulsivity and autonomic psychophysiology. *Biological Psychology*, *86*, 349–359.

Obrist, P. (1981) *Cardiovascular psychophysiology: A perspective*. New York: Plenum Press.

Panknin, T. L., Dickensheets, S. L., Nixon, S. J., & Lovallo, W. R. (2002). Attenuated heart rate responses to public speaking in individuals with alcohol dependence. *Alcoholism: Clinical and Experimental Research*, *26*(6), 841–847.

Paris, J. J., Franco, C., Sodano, R., Frye, C. A., & Wulfert, E. (2010). Gambling pathology is associated with dampened cortisol response among men and women. *Physiology and Behavior*, *99*(1), 230–233.

Phillips, A. C. (2011). Blunted as well as exaggerated cardiovascular reactivity to stress is associated with negative health outcomes. *Japanese Psychological Research*, *53*(2), 177–192.

Phillips, A. C., Der, G., & Carroll, D. (2009). Self-reported health and cardiovascular reactions to psychological stress in a large community sample: Cross-sectional and prospective associations. *Psychophysiology*, *46*(1), 1020–1027.

Phillips, A. C., Hunt, K., Der, G., & Carroll, D. (2011). Blunted cardiac reactions to acute psychological stress predict symptoms of depression five years later: Evidence from a large community study. *Psychophysiology*, *48*(1), 142–148.

Phillips, A. C., Roseboom, T. J., Carroll, D., & De Rooij, S. R. (2012). Cardiovascular and cortisol reactions to acute psychological stress and adiposity: Cross-sectional and prospective associations in the dutch famine birth cohort study. *Psychosomatic Medicine*, *70*(4), 699–710.

Prince, S., Adamo, K., Hamel, M., Hardt, J., Gorber, S., & Tremblay, M. (2008). A comparison of direct versus self-report measures for assessing physical activity in adults: a systematic review. *International Journal of Behavioral Nutrition and Physical Activity*, *1*(5), 56–80.

Quinn, E. P., Brandon, T. H., & Copeland, A. L. (1996). Is task persistence related to smoking and substance abuse? The application of learned industriousness theory to addictive behaviors. *Experimental and Clinical Psychopharmacology*, *4*(1), 186–190.

Resnick, B. (2011). The relationship between resilience and motivation. In *Resilience in Aging: Concepts, Research, and Outcomes* (pp. 199–215).

Ring, C., Harrison, L. K., Winzer, A., Carroll, D., Drayson, M., & Kendall, M. (2000). Secretory immunoglobulin A and cardiovascular reactions to mental arithmetic, cold pressor, and exercise: Effects of alpha-adrenergic blockade. *Psychophysiology*, *37*(1), 634–643.

Ruiz-Robledillo, N., Romero-Martínez, A., & Moya-Albiol, L. (2017). Lower cortisol response in high-resilient caregivers of people with autism: the role of anger. *Stress and Health*, *33*(4), 370–377.

Salomon, K., Bylsma, L. M., White, K. E., Panaite, V., & Rottenberg, J. (2013). Is blunted cardiovascular reactivity in depression mood-state dependent? A comparison of major depressive disorder remitted depression and healthy controls. *International Journal of Psychophysiology*, *90*(1), 50–57.

Salomon, K., Clift, A., Karlsdóttir, M., & Rottenberg, J. (2009). Major depressive disorder is associated with attenuated cardiovascular reactivity and impaired recovery among those free of cardiovascular disease. *Health Psychology*, *28*(2), 157-.

Salomon, K., Jin, A. B., & Webb, A. K. (2015). Cardiovascular reactivity during a cognitive task is not related to measures of effort. *Psychosomatic Medicine*, *77*, 1–15.

Schwartz, A. R., Gerin, W., Davidson, K. W., Pickering, T. G., Brosschot, J. F., Thayer, J. F., … Linden, W. (2003). Toward a causal model of cardiovascular responses to stress and the development of cardiovascular disease. *Psychosomatic Medicine*, *65*, 22–35.

Shenoy, J. P., Sahana, P. A., & Shivakumar, J. (2014). Study of cardiovascular reactivity to mental stress in different phases of menstrual cycle. *Journal of Clinical and Diagnostic Research*, *8*(6), 1–4.

Smith, B. (2013). Depression and motivation. *Phenomenology and the Cognitive Sciences*, *12*, 615–635.

Steinberg, M. L., Krejci, J. A., Collett, K., Brandon, T. H., Ziedonis, D. M., & Chen, K. (2007). Relationship between self-reported task persistence and history of quitting smoking, plans for quitting smoking, and current smoking status in adolescents. *Addictive Behaviors*, *32*, 1451–1460.

Steinberg, M. L., & Williams, J. M. (2013). State, but not trait, measures of persistence are related to aegative affect. *Journal of Studies on Alcohol and Drugs*, *74*(4), 584–588.

Steinberg, M. L., Williams, J. M., Gandhi, K. K., Foulds, J., Epstein, E. E., & Brandon, T. H. (2012). Task persistence predicts smoking cessation in smokers with and without schizophrenia. *Psychology of Addictive Behaviors*, *26*(1), 850–858.

Stone, S. V, Dembroski, T. M., Costa Jr., P. T., & MacDougall, J. M. (1990). Gender differences in cardiovascular reactivity. *Journal of Behavioral Medicine*, *90*(1), 50–57.

Stoney, C. M., Matthews, K. a, McDonald, R. H., & Johnson, C. a. (1988). Sex differences in lipid, lipoprotein, cardiovascular, and neuroendocrine responses to acute stress. *Psychophysiology*, *25*, 645–656.

Treiber, F. A., Kamarck, T., Schneiderman, N., Sheffield, D., Kapuku, G., & Taylor, T. (2003). Cardiovascular reactivity and development of preclinical and clinical disease states. *Psychosomatic Medicine*, *65*(1), 46–62.

Von Culin, K. R., Tsukayama, E., & Duckworth, A. L. (2014). Unpacking grit: Motivational correlates of perseverance and passion for long-term goals. *Journal of Positive Psychology*, *9*(4), 306–312.

Wawrzyniak, A. J., Hamer, M., Steptoe, A., & Endrighi, R. (2016). Decreased reaction time variability is associated with greater cardiovascular responses to acute stress. *Psychophysiology*, *53*(5), 739–748.

Weidner, G., & Helmig, L. (1990). Cardiovascular stress reactivity and mood during the menstrual cycle. *Women and Health*, *16*(3), 5–21.

Willemsen, G., Ring, C., Carroll, D., Evans, P., Clow, A., & Hucklebridge, F. (1998). Secretory immunoglobulin A and cardiovascular reactions to mental arithmetic and cold pressor. *Psychophysiology*, *35*(3), 252–259.

York, K. M., Hassan, M., Li, Q., Li, H. H., Fillingim, R. B., & Sheps, D. S. (2007). Coronary artery disease and depression: Patients with more depressive symptoms have lower cardiovascular reactivity during laboratory-induced mental stress. *Psychosomatic Medicine*, *69*, 521–528.