Investigating neurocognitive mechanisms of adolescent vulnerability to emotional disorder via experimental methods and cognitive training in typically developing adolescents

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Patricia Beloe

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Birkbeck University of London

Declaration.

I, Patricia Beloe, confirm the work presented in this thesis is my own

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Abstract

The aim of this thesis was to examine mechanisms involved in cognitive vulnerability to emotional disorder in adolescence through the lens of Attentional Control Theory (ACT; Eysenck et al., 2007) integrated with the Strength Model of Control (Baumeister et al., 1998; 2018), and investigate the use of attentional control training to reduce vulnerability to emotional disorder in typically developing adolescents. Study 1 used behavioral and ERP methods to investigate the differential age effects of resource depletion on negative thought proliferations, examining the association between the Error Related Negativity (ERN), an electrophysiological measure of compensatory control during depletion, and subsequent emotional reactivity. Findings indicated no effect of cognitive depletion on emotional reactivity, however an elevated ERN predicted higher emotional reactivity in adults contrasted with a converse association in adolescents. Moreover, a larger ERN also predicted burnout and worry increases in adolescents 18 months later. Study 2 explored the efficacy of computerized working memory training to boost processing efficiency and adolescent emotional resilience. Study 2's findings showed training improved working memory performance and was instrumental in immediate and sustained reductions in self-reported anxiety and depression symptoms in the training group relative to active controls. Study 3 aimed to replicate study 2's finding in adolescent worriers, exploring more extensive behavioral and emotional vulnerability measures. It also explored neural correlates of training transfer, with the ERN as the primary neural outcome, plus several other ERP markers of cognitive control relevant to emotion processing. Although working memory performance improved, there were no significant group effects of training transfer to internalizing symptoms, emotional regulation, inhibitory control, behavioral interference or neural outcomes post-training or 3-months later. Nevertheless, the rate of training improvement was associated with declining anxiety

symptoms from pre-training to follow-up and decreased P(e) amplitudes, an ERP involved in performance monitoring and associated with the motivational significance of errors. P(e) reductions were in turn associated with lower worry, rumination and depression at follow-up. Findings suggested it was possible to reduce anxiety and depression symptoms in typically developing adolescents using a low cost computerized training intervention targeting attentional control. However, the efficacy of training in reducing emotional vulnerability may not be consistent, with training transfer to emotional and neurocognitive processing subject to individual differences in training responsivity. The findings also provide novel insight into a potential neurocognitive mechanism underlying vulnerability to the onset and maintenance of emotional disorder which may modulate susceptibility to negative thought proliferation and is subject to developmental differences. These findings have implications for developing interventions to reduce the burden of mental health problems in adolescence, in addition to general relevance for cognitive models of psychopathology.

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Abbreviations

AC	Attentional Control
ACC	Anterior Cingulate Cortex
ACS	Attentional Control Scale
ACT	Attentional Control Theory
ADHD	Attention Deficit and Hyperactivity Disorder
ANOVA	Analysis of Variance
CBT	Cognitive Behavioural Therapy
CEMH	Compensatory Error Monitoring Hypothesis
CRN	Correct Related Negativity
CNV	Contingent Negative Variation
DSM	Diagnostic and Statistical Manual of Mental Disorders
EEG	Electro Encephalography
DLPFC	Dorsolateral Prefrontal Cortex
EF	Executive Function
ERN	Error Negativity
ERP	Event Related Potential
ESRC	Economic and Social Research Council
FMRI	Functional Magnetic Resonance Imaging
MEG	Magnetoencephalography
GAD	Generalised Anxiety Disorder
GCSE	General Certificate of Secondary Education

Hz	Hertz
IC	Inhibitory Control
IFG	Inferior Frontal Gyrus
LPP	Late Positive Potential
MDD	Major Depressive Disorder
ms	Milliseconds
μV	Microvolts
OCD	Obsessive Compulsive Disorder
OECD	Organization for Economic Co-operation and Development
P(e)	Error Positivity
PCC	Posterior Cingulate Cortex
PSWQ	Penn State worry questionnaire
PTSD	Post-Traumatic Stress Disorder
RCT	Randomised Control Trial
RT	Reaction Time
SAD	Social Anxiety Disorder
SBI	School Burnout Inventory
SDQ	Strengths and Difficulties Questionnaire

SSRI	Selective Serotonin Reuptake Inhibitors
STAI	Stait Trait Anxiety Inventory
tDCS	Transcranial Direct Current stimulation
UN	United Nations
VLPFC	Ventrolateral Prefrontal Cortex
WM	Working Memory
WMC	Working Memory Capacity
WML	Working Memory Load

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CHAPTER 1

1 General introduction

We rely on a complex cognitive apparatus to pursue successful goal-directed action. A central tool in this apparatus is attentional control, the ability to flexibly manage what we pay attention to at any given moment to support goal directed action. The quality of this ability is crucial for many aspects of our behaviour and cognition. In psychologically healthy individuals these abilities predict academic success and life outcomes (McTeague et al., 2016) and this association is evident in early development (Blair & Razza, 2007). It is also intrinsically involved in our ability to manage our emotions, playing an important part in our affective experience (Zelazo & Cunningham, 2007). Attentional control is correlated with psychopathology and variations in it are a trans-diagnostic characteristic of several psychological disorders (Hsu et al., 2015; McTeague et al., 2016; Snyder et al., 2015). Although much is known about the interconnectedness of cognition and emotion and concomitant implications for psychopathology, many gaps remain (Dolcos et al., 2020; Okon-Singer et al., 2015; Pessoa, 2008).

Of interest in the current thesis is the question of how we apply this understanding to develop interventions that can reduce disorder vulnerability via improving central cognition. Evidence in the case of depression for instance indicates that repeated depression episodes are elicited by 'progressively milder stressors' (De Raedt & Koster 2010, pp. 50) thus early intervention should be paramount in addressing lifelong disease burden. This is especially important in the context of adolescents and young people, when the risk of first onset of disorder is high (Solmi et al., 2021; Vizard et al., 2020). Cognitive training procedures that target specific control functions such as working memory (WM), attentional and inhibitory control represent a highly theoretically driven and evidence-based intervention approach. In addition to exploring its potential to reduce incidence, interventions can also contribute to better causal models of psychopathology.

Adolescents have been curiously neglected relative to other age groups in much of the research on cognitive training over the past 20 years, although that has begun to change (Mewton et al., 2020). The aim of this thesis was to address two interrelated research questions. The first is to extend extant research on cognitive training methods aimed at promoting well-being and optimizing emotional functioning. Specifically, it explores the validity and potential of WM training (WMT) as a candidate intervention to boost attentional control and promote emotional resilience in typically developing adolescents. The second focuses on the elaboration of a mechanism to understand how processing inefficiency may interact with elevated executive control demands during adolescence to exacerbate vulnerability to emotional disorder, with an extended aim of targeting this mechanism through WMT.

1.1 Chapter overview.

This introductory chapter begins by defining adolescence and outlines epidemiological research on the breadth and prevalence of psychological problems in adolescence to contextualise the research motivation. The chapter proceeds to present literature on prominent theoretical models that have been used to understand the etiology and maintenance of anxiety and depression. These are integrated with literature from developmental cognitive neuroscience to develop a theory-driven approach to cognitive training interventions for adolescents. This approach is adopted in the studies outlined in Chapters 4 and 5 and provide a rationale for the investigation of mechanism linking cognitive processing efficiency and emotional vulnerability outlined in Chapter 3. Finally, a review of current literature on cognitive training for targeting affective processes will be discussed, with a focus on identifying lacunae in the adolescent research.

1.2 Adolescence

1.2.1 Characterising adolescence

Adolescence refers to the period of development between childhood and adulthood, starting with the onset of puberty and, though less well-defined, ending when individuals reach physical and sexual maturity and meet culturally-defined milestones that mark them out as adults. The UN currently delineates adolescence as ranging from 10-19 years, although there is increasing motivation to extend this age-range up to 24 years to reflect current knowledge and understanding of adolescent development (Sawyer et al., 2018).

Adolescence is characterised by significant growth and change in multiple aspects of an individual's life. Dramatic changes to the body, the mind and the brain occur alongside a transformation in the complexity of adolescents' social context and society's expectations of them (Blakemore, 2019). Adolescents also experience dramatic changes in motivation, novelty and sensation-seeking accompanied by the increased desire for the fellowship and approbation of peers, alongside an aversion to the converse (Blakemore & Mills, 2014). For many adolescents, this is a period of emotional highs and lows, tussles for independence from parents and the acceptance of peers, and a striving towards the expression, recognition and acceptance of an emerging autonomous adult self. Most young people weather 'the storm and the stress' of adolescence (Blakemore, 2019; Casey et al., 2010; Hall, 1904). Nevertheless experiences vary, and adolescence can herald a deterioration in mental health for a significant number of young people, frequently marking the beginning of a chronic and lifetime struggle with mental ill-health (Kessler et al., 2005).

1.1.1 Prevalence of mental health disorders in adolescence

For many adults suffering from chronic and long-term anxiety, depression, or psychosis, the age of first onset was adolescence. Large scale epidemiological research indicates between 35 to 50% of disorders emerge by the age of 14, and 62-75% by age 25 (Kessler et al., 2005; Solmi et al., 2021). This leads many authors to regard adolescence as a period of elevated risk for broad psychopathology (Paus et al., 2008; Powers & Casey, 2015). Others however suggest risk may be more circumscribed and specific to social and emotional disorders, namely conditions characterised by anxiety, negative affect and socially motivated distress and which are likely triggered and exacerbated by the social and developmental vicissitudes of adolescence (Rapee et al., 2019).

There is also evidence that incidences of childhood and adolescent emotional disorders are increasing, particularly in adolescent girls (Blomqvist et al., 2019; Bor et al., 2014; Collishaw, 2015; Collishaw & Sellers, 2021; Mishina et al., 2018; Patalay & Gage, 2019; Thorisdottir et al., 2017; Twenge et al., 2020). The most recent UK data suggests that in 2020, 16% of 5 - 16 year olds had a likely mental disorder compared with 10.8% in 2017 (Vizard et al., 2020). In the 2020 data, incidence rates increased considerably with age and there was a pronounced gender disparity in older adolescents: Amongst 17-22 year-olds, 27% of girls versus 13.3% boys had a probable mental disorder. Some recent work indicates gender disparities may be due to earlier pubertal onset in girls (Mendle et al., 2010), whilst others suggest girls' response to academic stress contributes to this disparity (Giota & Gustafsson, 2017; Högberg et al., 2020). In terms of increasing prevalence, the recent UK data was not disorder-specific and increases may be partly attributed to the coronavirus pandemic (Vizard et al., 2020). Other recent pre-pandemic sources indicate that increases in prevalence over recent years are specific to emotional disorders (Deighton et al., 2019; Rapee et al., 2019; Sadler et al., 2018), consistent with international findings (Collishaw & Sellers, 2020). These increases are likely due to numerous factors including increased awareness, symptom disclosure and diagnoses of psychological disorders, austerity, poverty, academic stress (Davey, 2018; OECD, 2017; Putwain, 2021), deterioration of peer relationships (The Children's Society, 2020) and of life satisfaction (Orben, Lucas et al., 2020), and increased social media use (Twenge, 2018; Twenge & Martin, 2020), although evidence for the latter is contested (Orben & Przybylski, 2019; Vuorre et al., 2021). Despite popular concern about deleterious effects of social media, adolescents themselves report their biggest stressor is school and academic pressure (Anniko et al., 2019), with data from the Organization for Economic Co-operation and Development (OECD) indicating that more than half of school children report worrying about exam performance (OECD, 2017; Putwain, 2021).

1.1.2 Vulnerability and intervention approaches

Our understanding of adolescence has changed dramatically this century (Patton et al., 2018), thanks in part to neuroscientific research which has transformed our understanding of the adolescent brain and how this influences cognitive, emotional and social development (Blakemore & Mills, 2014; Patton et al., 2018). Several leading scholars and advocates have formulated hypotheses that the patterns of mental health deterioration witnessed during adolescence may arise from the peculiarities of adolescent brain development (Paus et al., 2008). This refers to changes in brain structure and function necessary to facilitate the cognitive development from which arises exploration, learning and flexible adaptation to changing social environments needed to acquire adult-level autonomy (Cohen-Kadosh et al., 2014). This adaptiveness is associated with protracted development of prefrontal circuits crucial for higher level cognition and emotional regulation (Giedd et al., 1999; Gogtay et al., 2004; Somerville et al., 2011; Somerville, 2013; Tottenham & Galván, 2016). A biological trade-off for a prolonged period of neuroplasticity may be the emergence of perturbations in those prefrontal cortical networks while the attentional control system remain in flux (Paus et al., 2008). One outcome of these disturbances may be emotional regulation difficulties which can contribute to risk for psychological disorders because of the central role of attentional control in emotional and self-regulation (Cohen-Kadosh et al., 2014). Evidence to support this hypothesis will be discussed later in this thesis.

Policy makers recognise that social, emotional and physical health during adolescence has a major bearing on lifetime health and well-being outcomes (Patton et al., 2018). Development of novel interventions based on increased understanding of adolescent brain and cognitive development has been highlighted as a research priority (Mei et al., 2020). Budgetary considerations – mental health provision is under-resourced worldwide (Signorini et al., 2017) – create the imperative for developing scalable evidenced-based interventions with potential for online delivery.

Some promising research has emerged from work with clinically and sub-clinically vulnerable adults indicating that neurocognitive vulnerabilities to emotional disorders could be targeted with simple computerized cognitive training exercises (reviewed in Derakshan, 2020; see also Dolcos et al., 2020; Koster et al., 2017; Shani et al., 2021). This indicates potential for translation to adolescents. Despite recognising adolescence as a period of significant cognitive and emotional developmental sensitivity, adolescents have been largely ignored in WMT research, one the biggest areas of cognitive enhancement research in the past 20 years. Hence, this thesis attempts to bridge some of this gap, by focusing on exploring the effects of training on a variety of neurocognitive, behavioural and disorder-relevant self-report outcomes in adolescents. Moreover, the research also investigates how a neurocognitive vulnerability mechanism identified in adults may have different implications for adolescents and its viability as a target for cognitive training.

1.2 Neurocognitive mechanisms in vulnerability to emotional disorder

In this section I will outline research on the role of neurocognitive mechanisms in the aetiology and maintenance of emotional disorders, as these mechanisms form a key target in the application of cognitive training for anxiety and depression in adults. Before outlining theory and findings, I first define attentional control, as the construct is central to this thesis, outlining where it sits in relation to other cognitive control constructs central to cognitive, clinical neuropsychological and developmental research.

1.2.1 Attentional control as key cognitive control process

1.2.1.1 Defining attentional control

Attentional control refers to the ability to regulate attention, awareness and concentration (Helzer et al., 2009; Rothbart & Bates, 2006) and is regarded a central construct underlying executive control resources generally (Miyake et al., 2000). It can also be described as the ability to flexibly manage what we pay attention to at any given moment in the service of goal directed action. It is closely linked to the inhibition of prepotent responses and the management of task-irrelevant, distracting information, as well as involving the filtering efficiency and updating functions of WM systems. Attentional control resources are also engaged with maintaining task goals online in WM (Berggren & Derakshan, 2013). As a result, individual differences in attentional control abilities are linked to the overall efficiency of WM, and specifically to individual differences in WM capacity (Kane et al., 2001; Shipstead et al., 2015).

The concept of attentional control is closely aligned with a range of other constructs widely used in the literature, including executive control and executive function (EF), the central executive of WM, cognitive control, top-down control, emotional regulation, and self-regulation. There is an extensive literature dealing with self-regulatory processes in relation to cognitive development and mental health. One of the challenges when integrating findings across these studies is inconsistency in terminology and overlapping constructs (Nigg, 2021). These constructs share several key characteristics in the sense that they deal with both intentional and deliberate, as well as automatic, allocation of attention and cognitive resources. They are also characterised by the quality of the balance between deliberate and automatic processing in achieving task goals. To this end, whist this thesis deals primarily with attentional control, many of these related and overlapping constructs are referred to throughout the thesis in reference to integrating the work of others researchers but are essentially capturing similar processeses.

Attentional control is measured in a variety of ways usually determined by research discipline. Self-report scales such as the Attentional Control Scale (ACS; Derryberry & Read, 2002) or Attentional Control Scale for children (Muris et al., 2004) are most commonly used in clinical and developmental studies. In contrast, in cognitive and affective, and neuroscience research attentional control is measured using a range of laboratory tasks also used to measure executive functions (Gagne et al., 2017). As there is mixed evidence on the relationship between behavioural and self-report measures of attentional control, caution is warranted in interpreting self-reported attentional control as a direct proxy for cognitive abilities (Williams et al., 2017).

1.2.1.2 Development of attentional control

Attentional control abilities undergo protracted improvements across development (Cohen-Kadosh et al., 2014; Davidson et al., 2006). Research on the development of attentional control, particularly in the context of associated brain development, tends to fit within in the framework of the tripartite model of executive functions (Miyake & Friedman, 2012; Miyake et al., 2000). According to this model, higher order control of thought, behaviour and emotion is supported by three core abilities, 'inhibition' (the ability to inhibit prepotent responses), 'shifting' (the ability to flexibly guide switches between mental sets or tasks) and 'updating', (refers to updating and monitoring in WM). Whilst these form distinct abilities measured by different tasks, a central executive ability - attentional control - underlies the coherent and unified orchestration of all three abilities (Miyake et al., 2012; Spruijt et al., 2020).

Extensive literature shows qualitative and quantitative increases in these abilities from childhood throughout adolescence and early adulthood, and which are supported by protracted change in the structure and function of the prefrontal cortex (Crone & Steinbeis, 2017; Huizinga et al., 2006; Malagoli & Ussai, 2018; Satterthwaite et al., 2013; Velanova et al., 2008, 2009). For instance, adolescents display adult-like inhibitory control but differ to adults in performance consistency (Padmanabhan et al., 2011), whereas WM performance continues to improve well into the early twenties (Darki & Klingberg, 2015; Satterthwaite et al., 2013). WM improvements are supported by a gradual increase in blood oxygen level dependent (BOLD) activations in the dorsolateral prefrontal cortex (DLPFC), ventrolateral prefrontal cortex (VLPFC) and parietal cortex, which continues into adulthood (Crone & Steinbeis, 2017; Darki & Klingberg, 2015; Jolles et al., 2011, Satterthwaite et al., 2013), whilst inhibitory control development is supported by increased or more differentiated prefrontal cortical recruitment (Chevalier et al., 2019; Velanova et al., 2008). Another marker of attentional control development is progressive specialisation of fronto-parietal circuits evidenced by a transition from diffuse to increasingly focal patterns of cortical task activity (Durston et al., 2006). Furthermore, there is increased modulation of network activations, meaning a progression from indiscriminate prefrontal cortical activations regardless of task demands in children and younger adolescents, to more titrated load-matched activations as development progresses (Chevalier et al., 2019; Durston et al., 2006; Velanova et al., 2008). In summary, development of attentional control is constrained by protracted brain development, particularly of the lateral prefrontal cortical circuits; consequently executive function abilities continue to develop in efficiency and effectiveness throughout adolescence.

1.2.1.3 Attentional control and trans-diagnostic vulnerability to emotional disorder

A large body of research shows evidence of an influential role for attentional control in vulnerability to anxiety and depression (Berggren & Derakshan, 2013; Derakshan, 2020; Koster et al., 2017). There is evidence of associations between anxiety and negative emotionality and individual differences in the capacity to exercise voluntary control over attention in adults (Derryberry & Reed, 2002; Moran, 2016; Snyder et al., 2015), but also in children (Eisenberg et al., 2001; Muris, 2006; Muris et al., 2004) and adolescents (Muris et al., 2007; Sportel et al., 2011). Furthermore, findings from genetics research indicate that poorer attentional control may represent a phenotypic and genetic risk factor for a range of anxiety disorders during adolescence (Gagne et al., 2017). Attentional control deficits and perturbations are also observed in post-traumatic stress disorder (PTSD) (Bardeen & Orcutt, 2011; Polak et al., 2012), schizophrenia (Arkin et al., 2020), substance abuse (Abdullaev et al., 2010; Salo et al., 2007) and suicidality (Thompson & Ong, 2018).

Attentional control impairment is also associated with depression in adults (Fossati, et al., 2002; Hammar & Årdal, 2009; Snyder, 2013; Wagner et al., 2012) and youth (Kertz et al., 2016, 2019). Evidence is less conclusive in developmental studies however. A 2015 meta-analysis found that children and adolescents with a diagnosis of major depression performed worse than controls on a variety of executive function measures, with largest effects on inhibitory control tasks (Wagner et al., 2015). However a review published the same year came to a different conclusion suggesting there was no reliable relationship (Vilgis et al., 2015). There may be several reasons for this inconsistency. Wagner et al. (2015) only included studies featuring participants with an acute MDD diagnosis, whereas Vilgis et al. (2015) also included participants with a diagnosis of dysthymia, therefore symptom severity and diagnostic status may have influenced outcomes. In addition, age may have been a factor. Almost all 17 studies in the Wagner meta-analysis had exclusively adolescent samples. In contrast, the Vilgis review included a majority of studies with highly heterogeneous samples with regard to age. Many of these studies had participants whose ages ranged from 6 to 18 years within a single study, which is problematic when taking into account the development of executive function. Finally, where Vilgis et al. (2015) assessed studies on whether there were significant differences between clinical groups and controls, Wagner et al.'s (2015) meta-analytic results provide effect sizes which arguably provide a more reliable assessment of the effects (Kertz et al., 2019). These studies focussed on individuals with a clinical diagnosis of depression, so do not provide insight on children and youth at risk of depression or depressive symptomology in typically developing young people. Although several studies suggest that poor EF co-occurs with higher depressive symptomology (Mullins et al., 2020; Waszczuk et al., 2015) others do not (Wagner, Alloy et al., 2015). So again findings are inconsistent and meta-analytic studies of the relationship between EFs and depression symptoms in these non-clinical groups is lacking.

While the majority of evidence linking attentional control to disorders is correlational (Moran, 2016), influences are likely to be bidirectional and to also involve developmental cascades (Koster et al., 2017; Morea & Calvete, 2021). Support for the causal influence of attentional control on the emergence or persistence of psychopathologies is evident from several longitudinal studies showing it predicted the onset and course of child and adolescent psychopathology (Bufferd et al., 2014; Hankin, 2015; Kertz et al., 2016; Mills et al., 2016; Sportel et al., 2013) or risk factors for psychopathology, such as sleep disturbance (Lovato & Gradisar, 2014; Nelson et al., 2018; Tomaso et al., 2020). However, a recent cross-lagged longitudinal study found that internalising and externalising problems in early adolescence predicted WM capacity and inhibitory control in later adolescence rather than the reverse (Donati et al., 2021). This study also echoed a similar finding on the direction of effects which was reported by Briant et al. (2020). Taken together, there is evidence of robust links between attentional control deficits and emotional disorder, however more research is needed to elaborate bidirectional influences.

1.2.2 Theoretical frameworks for understanding how attentional control influences emotion processing

Two inter-related mechanisms explain how attentional control abilities influence vulnerability to the onset and maintenance of depression and anxiety disorders. The first involves the modulation of automatic threat and negativity biases by attentional control, and the second relates to the role of attentional control and executive function in the development and execution of adaptive emotional regulation strategies.

1.2.2.1 Dual processing models

Neuroscience research has generated models of emotion processing based on reciprocal interactions between two brain systems. The first is a fast-acting system responsible for rapid bottom-up stimulus appraisal and response generation and is concentrated in the limbic structures, with a preeminent role for the amygdala (Dolan & Vuilleumier, 2003; Pessoa & Adolphs, 2010). The second is the slower, more effortful dorsal regulatory system, modulated by structures in the frontal cortex, especially the DLPFC (Corbetta & Shulman, 2002). Elaborate stimulus processing is regulated by top-down attentional control and higher order cognition; emotional experiences are modulated via associative cortex areas, including the ventromedial and DLPFC (Ochsner et al., 2012). More elaborate models also highlight a strategic role for the anterior cingulate cortex (ACC) which sits at the confluence between the dorsal and ventral circuits, with extensive neuronal projections linking it to lateral prefrontal cortex, parietal cortex, amygdala and basal ganglia (Moser et al., 2013; Shackman et al., 2011), playing a central role in evaluating and regulating emotional salience (Etkin et al., 2011). The nature and quality of these mutual and reciprocal interactions between bottom-up and top-down attention control has a significant bearing on our behaviour, influencing how we set and maintain goals, and the extent to which we are able to determine what to ignore and what to attend to from the myriad stimuli we encounter.

1.2.2.2 Attentional control and automatic processing

Interrelations between top-down and bottom-up attentional systems are central to some neurocognitive models of psychopathology, where pathology is thought to emerge from imbalances between them (Bishop 2009; Comte et al., 2015; Powers & Casey, 2015; Shanmugan et al., 2016). According to the Attentional Control Theory (ACT; Eysenck et al., 2007) for instance, cognitive impairments in anxiety are associated with impaired central executive processes involved in goal-directed action, resulting from an excess of negative or worrisome information in WM which consumes limited central executive resources. Implicated in this is increased primacy of the stimulus-driven attentional system and a simultaneous downgrading of volitional attention control, resulting in broad cognitive impairments. This is supported by extensive evidence that trait anxiety, associated with broad vulnerability to emotional disorders, is linked to preferential processing of threat stimuli (Bar-Haim et al., 2007; Bishop, 2004, 2009; Eysenck & Derakshan, 2009; Mogg & Bradley, 2018; Veerapa et al., 2020). Numerous studies also report general anxiety-related decrements in attentional control even with neutral and non-emotional distractors, pointing to general cognitive impairments in anxious people (Moran & Moser, 2015). It is proposed that attentional control modulates attentional biases to negative or alarming information via the inhibition of attentional capture by irrelevant stimuli (Eysenck et al., 2007) and that anxiety-related impairments in the inhibition of attention to distractors encourage a bias towards negative content (Basanovic et al., 2021). Support for the role of attentional control in predicting attentional bias to threat comes from a study by Chen et al. (2017). These researchers applied transcranial direct current stimulation (tDCS) to the DLPFC to enhance attentional control, resulting in decreased attentional bias to threat compared to a sham condition. In addition Basanovic et al. (2017) found that the extent to which healthy volunteers acquired and eliminated attentional biases in an attention bias modification procedure was governed by variation in attentional control capacity reflected in antisaccade task performance. Better anti-saccade performance mediated greater flexibility and ability to modify attentional biases. Taken together, these studies show that differences in attentional control are instrumental in influencing the individual's exposure to negative or threatening content.

There is evidence of anxiety-related impairments in all three core executive functions as defined by Miyake and colleagues (Miyake et al., 2000), but in particular inhibition and shifting (see Berggren & Derakshan, 2013 and Moran, 2016, for reviews). For instance, several studies show anxiety-related differences in the ability to inhibit a dominant response driven by bottom-up attention (Derakshan et al., 2009; Hallion et al., 2016; Moran & Moser, 2015). In one study Derakshan et al. (2009) showed that compared to typical controls anxious participants were significantly slower to make an anti-saccade but were just as fast to make pro-saccades when presented with a peripheral stimulus. Studies examining task switching indicate that anxiety is associated with longer reaction times in switch trials (Ansari et al., 2008; Derakshan et al., 2009), and less efficient task-set reconfiguration, a process that requires attentional control (Hartanto & Yang, 2016). Studies focussed on WM monitoring and updating are less common, and Berggren and Derakshan's (2013) review contended that anxiety-related impairments in updating may be limited to high stress situations. This is supported by a recent study that found individuals with maths anxiety had greater difficulty in a WM updating task with numerical stimuli which purportedly increased situational stress in this group (Pelegrina et al., 2020). According to

Gustavson and Miyake (2016) when analysis focuses on trait worry rather than anxiety, there is evidence that high trait worriers take longer to respond to relevant and irrelevant probes on a WM updating task using a neutral word list. Their findings suggested that trait worry, which is highly predictive of anxiety, was systematically involved in disrupted WM updating even in the absence of stress.

Developmental findings

A natural attentional bias towards threatening stimuli is already present in infancy, increases with age, and the strength of this bias can distinguish between anxious children and healthy controls (Dudeney et al., 2015, Thompson & Steinbeis, 2020). Studies amongst children and adolescents examining attentional control as a temperamental construct find attentional control moderates the association between attentional bias to threat and negative affect (Lonigan & Vasey, 2009) and anxiety symptoms (Susa et al., 2012). For instance, Lonigan & Vasey had 10-17 year olds do a dot probe task assessing negative attentional biases. Only participants who were high in negative affect and low in attentional control demonstrated an attentional bias towards threat. In another study, Susa et al. (2012) examined the predictive power of the dot probe threat response for predicting anxiety scores in 9-14 year olds. Attentional bias did not independently predict anxiety, however when exploring the interaction between attentional bias and attentional control, they found that bias to threat predicted anxiety symptoms only in children with low attentional control. Only a limited number of studies examined the predictions of ACT in relation to children and adolescents using experimental measures of attentional control. These largely support the findings from adult studies indicating that anxious children and adolescents also have difficulty inhibiting the processing of task irrelevant distractors (Hadwin et al., 2009; Jazbec et al., 2005; Waszczuk et al., 2015) and less efficient WM (Visu-Petra et al., 2011). Moreover, several studies indicate that the effects of anxiety on cognitive performance are most profound for children and adolescents with low WM capacity (Owens et al., 2012, 2014). However not all findings support ACT predictions. A recent study with 10-15-year-olds reported that trait anxiety was associated with higher scores on several tasks measuring set shifting and WM, and that WM capacity mediated the relationship between trait anxiety and academic achievement, indicating that anxious adolescents with higher WM were more likely to perform well academically (Alfonso & Lonigan, 2021). The researchers in this study emphasised accuracy over speed and did not gather data on reaction times, so accuracy gains may have arisen from compensatory effort at the expense of performance efficiency (see section 1.3.1 for discussion of compensatory effort and processing efficiency in anxiety). In another study, there was some evidence that anxiety severity only interfered with attentional control at high cognitive load in adolescents (Smith et al., 2021). Although this study featured clinically anxious adolescents with high heterogeneity and comorbidity, so is difficult to compare with other findings. Taken together evidence broadly supports the existence of links between anxiety and attentional control deficits in non-clinical child and adolescent samples, although further research is needed to examine trade-offs between accuracy and efficiency.

Depression

Diminished control over the contents of WM is also regarded as a core process linking attentional control impairments to depression (Joorman & Vanderlind, 2014) with interpretation biases prejudicing the contents of WM towards negative and against positive information (Everaert et al., 2017). Several areas of research show that adults and adolescents with depression diagnoses selectively attend to negative stimuli and have difficultly disengaging from or inhibiting the processing of negative information (Colich et al., 2016; Gotlib & Joorman, 2010, Ladouceur et al., 2005, 2006; see also Lemoult & Gotlib, 2019, for a review) or have difficulty attending to neutral information (Tavitian et al., 2014). Studies also show that both experimental and self-report measures of attentional control moderate the association between negative self-referential biases (the tendency to privilege stimuli if they endorse negative schemas about the self) and depression severity (Colich et al., 2016; Lemoult & Gotlib, 2019).

These findings collectively demonstrate that impaired attentional control can lead to prolonged engagement with threatening, negative or distressing content, instigating a cascade of cognitive events that can result in full blown worry or rumination episodes, both of which contribute to the development and maintenance of anxiety and depression disorders (Bardeen, 2020; Goodwin et al., 2017; Gotlib & Joorman, 2010; Koster et al., 2017).

1.2.2.3 Emotional regulation and attentional control

Attentional control also influences vulnerability to emotional disorder in its role as 'gatekeeper' of emotional regulation (Bardeen, Fergus et al., 2015; Bardeen, Tull et al., 2015; Gross, 1998, 2015). Gross (1998) has referred to emotional regulation as the "processes by which individuals influence which emotions they have, when they have them and how they experience and express these emotions" (Gross, 1998, p. 275). Individual differences and deficits in emotional regulation are associated with many forms of psychopathology in adults and adolescents (Wante et al., 2018) and can predict symptoms longitudinally (Garnefski et al., 2001; McLaughlin, et al., 2011). Emotional regulation supports the down-regulation of negative affect and up-regulation of positive affect. Evidence for this has been extended to ecologically valid real-life adolescent experience, as well as laboratory-based proxies (Silk et al., 2003; Wante et al., 2018).

There are areas of overlap between dual process models of psychopathology and information processing models for understanding emotional regulation (Gross, 2015), and research in both traditions indicate a clear role for top-down control over attention (Rapee et al., 2019). For instance, rumination and worry are conceptualised as maladaptive forms of emotional regulation (Aldao & Nolen-Hoeksema, 2012) and as previously highlighted are significantly influenced by poorer inhibition and WM updating (Gustavson & Miyake, 2016; Joorman & Gotlib, 2010; Moran, 2016). Numerous studies indicate that better executive functions and attentional control abilities support more consistent implementation of adaptive regulation strategies such as cognitive reappraisal, a cognitive strategy where an event's meaning is re-interpreted in a less self-destructive light, serving to down-regulate the emotional response (Ahmed et al., 2015; Gross, 2015, Lantrip et al., 2016; Rapee, 2019; Zelazo & Cunningham, 2007; Zimmer-Gembeck & Skinner, 2011). In a related finding, Schmeichel et al. (2008) found that participants with high relative to low WM capacity were more effective in an emotional down-regulation task and exhibited fewer emotional responses. Pe et al. (2013) also found evidence that higher WM capacity supported the use of reappraisal. Adaptive emotional regulation strategies are associated with reduced anxiety and depression in adults and adolescents, whereas the converse is found for maladaptive strategies like suppression, avoidance and rumination (Aldao et al., 2010; Compass et al., 2017; Rood et al., 2009; Schäfer et al., 2017). Some work on reappraisal indicates that it only protects against disorder in those who already engage in frequent worry and rumination (Aldao & Nolen-Hoeksema, 2012; Arditte Hall et al., 2018) suggesting protective utility in reducing maladaptive strategies. Studies also demonstrate that the extent to which treatments for depression are based on adaptive emotional regulation strategies can predict recovery (Arditte & Joorman, 2011; Radkovsky et al., 2014). Similarly, instructing healthy adolescents to engage in adaptive strategies such as cognitive reappraisal (Rood et al., 2012) or adopting a neutrally-observant attitude to thoughts (Hilt & Pollak, 2012) can increase positive and decrease negative affect and rumination (Schäffer et al., 2017), although this may be only temporary (Volkaert et al., 2019). Taken together these studies indicate adaptive emotional regulation sustains good mental health and recovery from disorder in adults and adolescents, but may be dependent on strong executive functional abilities to support it.

1.2.2.4 Attentional control and the development of emotional regulation

The role of attention in emotional regulation is already evident in infants who learn the rudiments of self-soothing by engaging attention away from negative stimuli or when soothing is scaffolded by caregiver distraction towards positive stimuli (Harman et al., 1997). Meanwhile temperament research has indicated that advances in the voluntary control of behaviours emerges at around 5 years, driven by emerging executive functions, which in turn support improved emotional regulation (Zelazo & Cunningham, 2007). Adolescent emotional development involves acquiring and honing skills and strategies to cope adaptively with negative emotional events without parental scaffolding (Wante et al., 2018). There are two broad developmental trends in ER development: an increase in the capacity to implement a more extensive range of volitional regulation skills, and improvements in the ability to apply the right strategy in the right context (Zimmer-Gembeck & Skinner, 2011).

These improvements are supported by the development of inhibitory control and the brain areas that support it (Hare et al., 2008; Larsen & Luna, 2018; Rapee et al., 2019; Steinberg et al., 2008; Tottenham et al., 2011). For instance, Cohen et al., (2016) compared cognitive control under emotionally aversive conditions in early-to–mid-adolescence, late adolescence and adulthood using an emotional go/no-go task and functional neuroimaging. Older adolescents had poorer inhibitory control than adults, but better inhibitory control than younger adolescents although under emotionally aversive conditions only, whereas no differences emerged for positive or neutral conditions. Moreover performance decrements in adolescents relative to adults were accompanied by attenuated fronto-parietal activations in circuits implicated in mature cognitive control when faced with fearful cues and increased activity in the ventromedial prefrontal cortex, characteristic of immature emotional processing (Casey et al., 2019). Brain maturation enables a transition from relying on 'basic external emotional regulation strategies, such as support seeking, to relying on internal strategies, such as distraction and cognitive reappraisal' (Wante et al., 2018, pp 998), with the transition facilitated by the emergence of higher cognitive control capacities (Ahmed et al., 2015; Wante et al., 2018).

In summary, attentional control impairments are highly implicated in broad vulnerability to anxiety and depression via increased or prolonged exposure to negative content in WM, or through its influence on the adoption of maladaptive emotional regulation strategies. Similar to adults, anxious adolescents and children appear to experience significant difficulty with inhibiting task-irrelevant distractors and updating the content of WM, but this has only been examined in a small number of studies. None of these studies compared adults to children/adolescents or examined age-related or developmental differences, so we do not know if developmental sensitivities exist. In the context of emotional regulation, studies indicate a central role for attentional control in the execution and development of adaptive and psychologically healthy emotional regulation strategies.

1.2.3 Brain development and adolescent neurocognitive vulnerability to emotional disorder

A recent review has highlighted that the well-documented reports of a peak onset in psychological disorders in adolescence reflects a subset of socio-emotional disorders; including generalised and social anxiety disorders, eating disorders and depression rather than psychological disorder generally (Rapee et al., 2019). These disorders share common characteristics; principally negative affect, mood issues, emotional dysregulation, distress around interpersonal issues and fears of negative evaluations of the self by others (Rapee et al. 2019), which are linked to very specific changes in emotional functioning that emerge with the onset of puberty during typical development (Blakemore, 2019). For instance, during adolescence there is an increase in the instability and frequency of emotions relative to other periods of life (Rapee et al., 2019). Adolescents experience more frequent and higher intensity negative emotions than adults, and the experience of negative emotion increases alongside decreasing positive emotional episodes in older relative to younger teens, a pattern which is more pronounced in girls relative to boys (see Bailen et al., 2019 for a review) which presages higher prevalence of emotional disorders in girls (Sadler et al., 2018; Vizard et al., 2020). This indicates high emotional reactivity may be an important risk factor during adolescence.

1.2.3.1 <u>Imbalance model of neurocognitive developmental risk for vulnerability</u>

Neurocognitive accounts of development attribute adolescent increases in emotional reactivity to be partly due to an imbalance between earlier maturation of limbic system structures implicated in emotion, reward and social information processing, including the amygdala, insula, and nucleus accumbens (Blakemore, 2008; Casey et al., 2008, 2019), in contrast to protracted development of the prefrontal, parietal and temporal cortices which underpin mature cognitive control and which support the regulation of emotional activations originating in the limbic system (Casey et al., 2019; Heller et al., 2016). For instance, Heller et al. (2016) reported that functional connectivity between the amygdala and ventral striatum was inversely correlated with age in a sample of 5-32 year-olds and predicted cognitive control following emotional cues. Conversely connectivity between the medial prefrontal cortex and amygdala was associated with better inhibitory control to emotional cues and mediated the association between amygdala-ventral-striatal connectivity and control over affective cues. This demonstrated a hierarchical progression of increasing down-regulation of limbic areas by the prefrontal cortex over the course of development (Casey et al., 2019).

Adolescents frequently demonstrate impressive and adult-like cognitive control capabilities (Conklin et al., 2007; Crone & van der Molen, 2004; Luciana & Collins, 2012; Steinberg et al., 2009), however prefrontal control weaknesses are more likely to emerge in emotional or socially salient contexts (Schweizer et al., 2020), as greater impulsivity and reactivity to emotional and social stimuli are observed in adolescents compared to adults (Foulkes & Blakemore, 2016). Whilst adolescence may be an emotionally challenging period, only a minority of young people will experience clinically significant symptoms of psychological disorder (Blakemore, 2019). Amongst those who do develop a disorder, evidence indicates impairments in different dimensions of cognitive control in affective contexts is highly prevalent (Schweizer et al., 2020). Studies reviewed in Schweizer et al. (2020) reported that adolescents diagnosed with or vulnerable to emotional disorders have cognitive control deficits under emotional and not neutral conditions in comparison to typically developing or low risk adolescents (Kilford et al., 2015; Ladouceur et al., 2013; Mărcuş et al., 2016). Moreover, evidence exploring cross-lagged relationships find deficits in affective control predict subsequent development of clinically significant mental health difficulties rather than the reverse (Kilford et al., 2015). This is also supported by neural evidence indicating adolescents at risk for, or diagnosed with, a socio-emotional disorder can be distinguished from healthy controls by differences in brain structure (Adleman et al., 2012; Dobson et al., 2021; Gold et al., 2016), functional activation (Jalbrzikowski et al., 2017; Roy et al., 2013) and resting state connectivity across fronto-parietal executive and salience networks involving the ACC and amygdala-PFC connectivity (Geng et al., 2016). Note that the salience network refers to a network of interconnections in a set of limbic, para-limbic and frontal structures that are central to detecting the salience and significance of stimuli and triggering the engagement of cognitive control (Seeley et al., 2019).

1.2.3.2 Executive load increases during adolescence

The brain maturation reviewed above takes place alongside significant additional exogenous and endogenous changes which place high executive load on the emotional and regulatory system (Luciana & Collins, 2013). This includes the onset of sexual maturation and overt physiological changes that impact not only how adolescents views themselves, but also how they are perceived and responded to by others (Blakemore, 2019). Adolescents also become highly socially motivated with a significant expansion in the size, complexity (Blakemore & Choudhury, 2006) and instability of social networks (Chan & Poulin, 2009), and although social relationships are rewarding, evidence suggests that social interactions form one of the most challenging aspects of their everyday life (Pyhältö et al., 2010). These increasingly complex social situations require the processing of larger amounts of information and necessitate combined thinking about one's own and others' mental states. This is demonstrated nicely in a study which combined perspective

-taking under high and low cognitive load and compared performance between adults and adolescents (Mills et al., 2015). In this study participants used social cues to guide their decisions in a task that sometimes required taking another's perspective. Cognitive load was also manipulated by memorising digit sets of different size during the main task. Overall, adolescents were less accurate than adults on high cognitive load trials and under high social load (i.e. when perspective taking was needed). Moreover adolescents were especially subject to the deleterious effects of cognitive load when social load was higher and they needed to adopt another's perspective (Mills et al., 2015). In addition to increased social load in adolescence, other stressors include, but are not limited to, increased negative life events (Larson & Ham, 1993), academic pressure (Anniko et al., 2019), and increased exposure to sexual harassment and assault (Brown et al., 2020). Therefore the reconfiguration of the executive control network and the reduced executive capacity relative to adults, is taking place alongside dramatic increases in executive load (Luciana & Collins, 2013).

1.2.3.3 Sensitive periods - opportunity and risk

Larsen and Luna (2018) have characterised adolescence as a critical period for the development of higher order cognitive control. By critical period they refer to time-specific and brain structure-specific development that coincides with the maturation of cognitive abilities. Evidence for this includes enhanced neural plasticity and reconfiguration of brain networks involved in executive control during adolescence. Increased neuroplasticity in the prefrontal cortex means structural and functional connectivity in these regions can be particularly sensitive to what the adolescent is experiencing, thinking and doing (Larsen & Luna, 2018). This is highly adaptive and supports extensive learning during this period, however may also increase the sensitivity of brain structure and function to negative life events and high stress, with longer lasting consequences than at other times (Blakemore, 2019; Crone & Dahl, 2012; Larsen & Luna, 2018; Paus et al., 2008). Evidence for effects of stress on prefrontal development and subsequent risk or disorder during adolescence is reported in human and non-human animals (see Larsen & Luna, 2018 for a review). Equally, impoverished inputs may also have long term consequences. For instance, seminal research on critical periods in early development showed absence of input to the mammalian visual system in an early developmental window resulted in functional blindness despite no impairments or damage to the eye (Wiesel & Hubel, 1963). Evidence from rodent studies indicate impoverished social interactions during adolescence result in extensive alterations in PFC circuitry including neuronal signalling, myelination and dendritic density, which persist into adulthood and are associated with cognitive impairment (Larsen & Luna, 2019). These models lend support to the idea that developmental perturbations during human adolescence can impact fine tuning of cognitive control networks, which could have cascading effects on emotion processing where there is a causal link between cognitive control and emotion processing. These hypotheses have not been directly tested in humans because of the obvious ethical considerations. However, research emerging in the post-Covid period may elucidate possible impacts of social isolation on human brain development as a result of the enforced isolation of lockdown measures (Orben, Tomova et al., 2020).

In summary, the imbalance model of adolescent cognitive and emotion development highlights that underlying characteristics of the reconfiguration of subcortical and regulatory brain circuits implicated in cognitive control and socio emotional processing may increase individual's exposure to emotional dysregulation during adolescence. Inefficient or inconsistent attentional control mechanisms may be unable to meet situational demands if the context is highly emotive.

Finally, adolescent cognitive development takes place in the context of experiences that place high demands on developing attentional control systems. Enhanced neural plasticity during this period means environmental inputs could be more likely to result in long term alterations in executive and regulatory circuity, presenting both risk and opportunity.

1.3 Is there a cost for trying too hard? Integrating ACT and the strength model of control

1.3.1 Attentional Control Theory and processing inefficiency

Attentional Control Theory (ACT) has been a fruitful theory for investigating links between attention control and anxiety. As highlighted earlier, impairments in attentional control can arise from the competing effects of worry on limited working capacity (Berggren & Derakshan, 2013). Accordingly, extensive findings have shown poorer performance on tasks measuring attentional control (e.g. anti-saccade, go/no go) amongst high relative to low anxious people (Pacheco-Unguetti et al., 2010, for reviews see Berggren & Derakshan, 2013; Shi et al., 2019). ACT also provides a mechanism for how anxiety impairs performance during exams (Beilock, 2008; Putwain & Symes, 2018) or leads to 'choking' under pressure (Bertrams et al., 2013). Although less studied in youth, these findings also extend to children (Cheie & Visu-Petra, 2012; Ng & Lee, 2015; Ursache & Raver, 2014; Waszczuk et al., 2015) and teenagers (Owens et al., 2012; Smith et al., 2021) indicating ACT predictions should also hold during development.

A key prediction of ACT is that anxiety may necessitate compensatory neural processing to maintain good performance. Evidence has shown that the distracting effects of worry are greater for performance efficiency than for effectiveness (Ansari, et al., 2008; Ansari & Derakshan, 2011), evidenced for instance by relatively slower reaction times and higher self-reported effort (Berggren & Derakshan, 2013; Shi et al., 2019) and reduced performance efficiency (Edwards,et al., 2015, 2017). Neuroimaging findings also provide evidence of greater neural activations during cognitive task performance in anxious relative to low anxious individuals (Basten et al., 2011, 2012; Fales et al., 2008). For example, Basten et al. (2011) recorded fMRI during a Stroop task featuring neutral task stimuli. Across all participants there was an increase in activation on incongruent relative to congruent trials in several areas of lateral prefrontal, medial frontal, parietal and occipito-temporal cortices, reflecting additional attention deployment to inhibit distractor information. However, the magnitude of this difference was greater in anxious people. Compared to the low anxious groups, high trait anxious participants exhibited increased DLPFC task activations and reduced coupling with posterior lateral frontal regions and dorsal ACC, reflecting disrupted connectivity in the cortical networks supporting inhibitory control during the Stroop task. Moreover, trait anxiety explained differences in activation strength which could not be explained by Stroop performance differences (Basten et al., 2011).

In a subsequent study Basten et al. (2012) compared activation differences between WM manipulation (high load) and maintenance (low load) in a region of the DLPFC associated with attentional control processes, and examined differential effects of trait anxiety on the contrast between these activations. There were more pronounced increases in brain activation during manipulation relative to maintenance in the high trait anxiety participants compared to low anxiety group. Moreover trait anxiety explained activation strength variance over and above that which was due to behavioural performance. Fales et al. (2008) were also interested in the effects of trait anxiety on WM processing efficiency. They employed a mixed block fMRI design to compare differences in temporal dynamics of WM task activations between groups of high and low anxious individuals. Behavioural performance on the WM nback task did not differ significantly between high and low anxious groups, however there was evidence of greater transient activation of DLPFC and VLPFC regions associated with attentional control in the high anxious group, where contrasts were WM trial activation compared to fixation trials. In addition, increased transient activity in the anxious group was accompanied by reduced sustained activity in DLPFC across blocks when compared to low anxious participants, where sustained activation was the average activity across entire nback blocks compared to fixation or at rest blocks. This provides further evidence that the increases in transient activation reflects compensatory processing in the high anxious participants to mitigate poorer sustained activation involved in top-down control. There is also evidence of compensatory processing from ERP research (Ansari & Derakshan, 2011; Owens et al., 2015). Ansari & Derakshan (2011) showed high anxiety was associated with stronger frontal activations of the contingent negative variation (CNV), an ERP indexing intense cognitive effort. Together these findings support the proposition that anxiety is associated with processing inefficiency and that compensatory processing mitigate the debilitating effects of worry or thought intrusions on top-down goal maintenance.

1.3.2 The Error Related Negativity (ERN)

The neural mechanisms through which we monitor and respond to errors can provide insight into how compensatory cognitive control and effort are instantiated in the brain. The ERN, an event related potential peaking within 0-100ms after an erroneous response, is one of the most widely studied neural indices of error processing. It is thought to signal a reactive control response to errors and a marshalling of behavioural adaption to compensate for mistakes and adjust future performance (Falkenstein et al., 1999, 2000; Gehring et al., 1993). Analysis of the ERN shows that its amplitudes are increased when accuracy is emphasised over speed (Falkenstein et al., 2000; Gehring et al., 1993) which reflects greater attention to errors and reactive control to adjust future performance, evidencing the ERN's sensitivity to contextual manipulation. The dual mechanism of control model of cognitive control (DMC; Braver, 2012) further emphasises the compensatory function of the ERN. This model differentiates between reactive and proactive processes which emerge along a distinct temporal continuum. Proactive control processes involve engagement of active goal maintenance via the DLPFC. It is pre-emptive, rule-based and resource demanding (Braver, 2012). Conversely, reactive control drives attentional engagement towards task goals via activations in the ACC and stimulus-sensitive salience networks on a case-by-case and just-in-time basis and modulated in response to the effectiveness of proactive control (Moser et al., 2013).

Of particular relevance to this thesis is the widespread evidence that anxiety, worry and negative affect are associated with larger ERN amplitudes (Hajcak et al., 2003, 2004; Olvet & Hajcak, 2008), and preliminary evidence of an exaggerated ERN in adults with burnout (Golonka et al., 2017). One explanation for the elevated ERN in anxiety is that it reflects compensatory effort to mitigate the effects of worry on WMC and top-down control (Moser et al., 2013) and mirrors the observed processing inefficiencies in anxiety (Berggren & Derakshan, 2013; Fales et al., 2008). Consistent with attentional control and processing efficiency theory, larger ERNs in anxiety are not associated with better performance, indicating anxious individuals can match non anxious' performance through increased compensatory effort (Moser et al., 2013). In a study in which anxious and non-anxious participants performed a task where they were incentivised to improve performance, incentives led to increased ERN amplitudes in the non-anxious participants, but were unchanged for anxious participants, suggesting those individuals were already maximising available compensatory processes (Endrass et al., 2010). Taken together, this research suggests the ERN can represent compensatory effort in anxiety and its amplitudes may represent a valid distal measure of neural processing efficiency.

1.3.3 Ego depletion and the hidden cost of compensatory processing

On the surface, compensatory control mechanisms appear adaptive. They improve performance by engaging additional resources where needed (Sylvester et al., 2012). However, processing inefficiency implies relatively greater cognitive effort to achieve comparable performance accuracy and it is not currently clear if a predisposition towards compensatory effort is without a cost elsewhere. A cost-benefit approach to neurocognition would deem it not only plausible, but likely, that compensatory processing will incur a cost in some other domain (Kurzban et al., 2013).

The strength model of self-regulation characterises all acts of executive functioning, self-control and self-regulation as derived from a limited central resource which is prone to depletion (André et al., 2019; Baumeister et al., 1998, 2018). The model proposes that 'after exerting self-control, subsequent acts of self-control, even in different contexts, would suffer' (Baumeister et al., 2018, pp. 141), referring to this phenomenon as 'ego depletion'. For example, this proposes to explain why the willpower to abstain from alcohol might be undermined by particularly demanding day. Findings support the existence of ego depletion and a deleterious effect on self-regulation and effortful cognition (Dang, 2018; Dang et al., 2021; Maranges & Baumeister, 2016), although evidence for this effect is inconclusive (Friese et al., 2019; Hagger et al., 2016).

Although the exact nature of this central resource is not well defined (Heatherton & Wagner, 2011), and the mechanism debated (Dang, 2021; Inzlicht & Schmeichel, 2012) the model offers a useful framework in which to consider that one possible consequence or cost to compensatory effort will be subsequent failures in self-regulation. This is borne out by evidence that prolonged periods of cognitive exertion can deplete subsequent cognitive control (Boksem & Topps, 2008) and emotional regulation (Grillon et al., 2015). Lorist et al. (2005) found cognitive depletion was associated with impaired performance monitoring and error adjustment, whilst others reported impaired focused attention, planning and cognitive flexibility after cognitive effort (Boksem & Tops, 2008; Garrison et al., 2019; Schmeichel, 2007; Van der Linden et al., 2003). Depletion effects have not been widely studied in developmental samples, however one recent study found depleting effects of cognitive effort were associated with subsequent decline in cognitive task performance, processing speed and sustained attention in adolescents (Josev et al., 2019). Depletion effects were also shown for 6-9 year olds, where taxing behavioural control before prosocial decision-making resulted in children displaying less generosity and altruism. Although prior behavioural control did not impact subsequent emotional response, taxing emotional regulation increased later angry responses to injustice (Steinbeis, 2018). Together these studies present some tentative evidence that children and adolescents may also be vulnerable to depletion effects on regulatory processes.

In light of extensive findings linking attentional control to susceptibility to threat distractors and heighted emotional reactivity, the predictions from the strength model of control could add to ACT by explaining how bidirectional influences between anxiety and attentional control might occur. Indeed, Heatherton and Wagner (2011) specified that depletion sensitizes individuals to environmental cues, increasing the effects of automatic processing on cognition and behaviour, including increased interference from negative thoughts and feelings that would otherwise be suppressed (Maranges et al., 2017). This is supported by a number of studies, which found that depletion was associated with increased negative and decreased positive bias in a semantic matching task (Maranges et al., 2017), thoughts about death (Gailliot et al., 2006) and worry distractions during a test (Bertrams et al., 2013). Finally, one study tested the effect of depletion on emotional regulation, and it indeed found that, compared with the control group, a group who performed a demanding cognitive task were poorer at down-regulating emotion in a subsequent exercise (Grillon et al., 2015). It is not clear if compensatory processing consumes more of the 'central resource', but if it does, these findings imply that individuals with poorer processing efficiency may be more likely to have subsequent attentional control failures after a period of effort or regulation.

It is important to address criticism regarding the depletion effect itself, and the proposition that it represents an exhausted resource (Hagger et al., 2010). The existence of a depletion effect was called into question by a meta-analysis suggesting the effect was overestimated (Carter et al., 2015) and a large multi-lab replication attempt which failed to find a significant ego depletion effects (Hagger et al., 2016). However a subsequent meta-analysis addressed limitations in the Carter et al. (2015) study which were linked to inclusion criteria and bias correction methods (Dang et al., 2018). The updated analysis' results supported the depletion effect if an alternative bias correction (trim and fill) was used. Additionally, the latest analysis found variability in the efficacy of the different depletion tasks, including strongest effects emerging for the Stroop and emotional video tasks in contrast to limited efficacy of attention video tasks in triggering depletion effects. Based on the latter, Dang et al. (2021) went on to conduct a multi-site replication using the Stroop task as a depletion exercise. Results across 12 labs reported a medium depletion effect. Therefore whilst the existence of ego depletion effects have been challenged, more recent evidence suggests small or absent effects may be linked to the appropriateness of tasks used to induce and detect effects.

The mechanisms to explain these effects is debated. Some dismiss the resource account and posit the sensation and manifestation of fatigue on performance reflects conflict between current and competing goals in the context of naturally constrained resources (Hockey, 2011;

Simon et al., 2020). Engaging resources on one task must occur at the expensive of other goals, so a cost-benefit decision is imposed (Kurzban et al., 2013). As a consequence, depletion effects may reflect reduced motivation to exert control, alongside attention losses (Kool et al., 2013; Inzlicht & Schmeichel, 2012). This point is supported by studies showing manipulations of motivation via incentives can eliminate depletion effects (e.g. Luethi et al., 2016, see also Inzlicht & Friese, 2019). However, regardless of whether depletion effects represents a motivation loss rather than a central resource cost, it is unclear what precisely triggers motivation decrements and if, why and how much the strength of depletion effects differs between individuals. Variation in processing efficiency therefore may still influence depletion effects with real world relevance.

1.3.4 Relevance of ego depletion and vulnerability in adolescents

Adolescents may be especially vulnerable to depletion effects and these may impact academic performance, disrupt emotional regulation with potential consequences for long-term wellbeing. Luciana and Collins (2013) have highlighted that youth vulnerability to emotional disorder may be just as much influenced by a general increase in executive load during adolescence as it is on executive capacity limitations. As highlighted earlier, many studies demonstrate that adolescents can frequently perform just as well as adults in executive tasks but differ to adults in the consistency and circumstances of successful control (Conklin et al., 2007; Crone & van der Molen, 2004; Luciana & Collins, 2013; Luna et al., 2004; Steinberg et al., 2009). As also highlighted earlier, adolescence is a period of significant physiological and environmental change, increased social and relational complexity and heightened exploration and autonomy seeking. Adolescents also experience heightened emotional and reward sensitivity which increases demand for regulation. Finally, adolescents spend most of their lives in full-time education where they are expected to engage with material of increasing complexity, on which they will be tested during a gruelling set of high stakes exams. The multiple specific challenges of adolescence are demanding of executive resources and together place a high burden on a limited capacity system, which is likely to influence emotional regulation and affect (Luciana & Collins, 2013). Individual differences in processing efficiency therefore may be even more relevant to emotional vulnerability in adolescence and could represent an important target for intervention.

In summary, the previous section has highlighted the processing efficiency theory of attentional control deficits and drawn upon evidence demonstrating that attentional control impairments can be mitigated by compensatory cognitive effort. Integrating these findings with the strength model of cognitive control and findings from the ego depletion literature, I have formulated the hypothesis that individuals who rely on compensatory processing may be at increased risk for subsequent failures in regulation, which may be especially pertinent during adolescence.

1.4 Targeting emotional vulnerability with attentional control training

Findings from cognitive neuroscientific research have established that neural circuits underlying attentional control processes can be enhanced using computerised cognitive training methods (Constantinidis & Klingberg, 2016). A variety of training techniques (discussed in greater detail in Chapter 2) specifically target the attentional control and updating components of WM (Jaeggi et al., 2017). Findings from research on WMT interventions report enhanced cognition, including improved performance on WM tasks and related cognitive abilities, extending to more generalised improvements in fluid intelligence and everyday attention (Cantarella et al., 2017; Jaeggi et al., 2008, 2011; Loosli et al., 2012). There has been considerable debate around the efficacy of training interventions on general cognitive performance because of mixed findings and conflicting meta-analytic findings (Au et al., 2015; Katz et al., 2021; Soveri et al., 2017). Evidence for near transfer effects, where training results in pre to post intervention improvements on tasks that are similar to the training tasks is well supported, however far transfer, the generalisation of training effects to more distal measures is much rarer (Diamond & Ling, 2019; Smid et al., 2020). However, there is some indication that the emphasis on using standard cognitive tasks as outcome measures in training studies means important real world benefits of training may be overlooked (Jaeggi et al., 2017).

Researchers working at the intersection of cognitive and affective neuroscience have recently begun investigating the relevance of these training techniques for clinical psychological application (Keshavan, et al., 2017), applying theoretical approaches based on evidence of inter-relations between psychological disorder, emotional dysregulation and attentional control impairments and inefficiencies. For instance, it was proposed that WMT should increase the efficiency of attentional control, enabling better control of internal distractors and reducing susceptibility to worry and rumination (Cohen & Ochsner, 2008). Accumulating evidence indicates that attentional control training interventions are associated with reduced vulnerability to emotional disorders (Derakshan, 2020 and Dolcos et al., 2020), including worry reduction (Course-Choi et al., 2017; Lotfi, Ward et al., 2020) and improved adaptive and or decreased maladaptive emotional regulation in clinically diagnosed (Peckham & Johnson, 2018; Siegle et al., 2014), at risk (Hoorelbeke et al., 2016) and unselected participants (Cohen & Mor, 2018; Schweizer et al., 2011). Some findings also indicate efficacy of training to improve symptomatology directly, including reductions in trait and test anxiety symptoms (Hadwin & Richards, 2016; Sari et al., 2020), improved depressive mood (Motter et al., 2016), reduced social anhedonia (Zhang, Wang et al., 2019) and PTSD symptoms (Larsen et al., 2019; Schweizer et al., 2017). Studies also show WMT can improve cognitive functioning in individuals with clinical or subclinical symptoms of emotional disorder (Hoorelbeke et al., 2016; Owens et al., 2013). Owens et al. (2013) had dysphoric students train for 2 weeks using either an adaptive nback or control task. In the training group, training-related gains in WM were accompanied by bigger gains in WM capacity and neural filtering efficiency compared to the active controls.

Other studies show that transfer of training to emotional outcomes may not be clear-cut (Motter et al., 2018; Sari et al., 2016). In one study, Sari et al. (2016) examined the transfer effects of three weeks of WMT on anxiety, inhibitory control under conditions of high threat, and the ratio of slow to fast wave EEG, a resting state EEG correlate of attentional control. Relative to controls, nback training lead to improved attentional control evident at both a neural and behavioural level, indicating training was highly effective in reducing the ratio of slow wave to fast wave EEG, leading to improved attentional control performance. Emotional transfer was not straightforward, however. There were no significant group differences in anxiety post training, however there were significant associations between training improvement and anxiety reduction post training, indicating that differences in the efficacy of transfer to emotional outcomes may be governed by variations in individual's responsiveness to training. However participants were assessed directly after training only, with no follow up. It is possible that training transfer from attentional control to emotional vulnerability measures may require a period of post training consolidation (Berger et al., 2020; Borella et al., 2013; Swainston & Derakshan, 2018).

1.5 Emotional WM training

An alternative approach assumes that to impact emotional vulnerability, WMT should specifically target affective control, the ability to exercise top down control under affective circumstances (Schweizer et al., 2011; Cohen & Ochsner, 2018). Emotional WMT protocols are similar to standard WMT, but the training task stimuli are designed to activate emotion processing (Schweizer et al., 2011, 2013). The emotional nback task pioneered by Schweizer et al. (2011) was an adaptation to the nback task developed by Jaeggi et al. (2008) and featured emotional faces and words rather than neutral stimuli such as letters or shapes. There is evidence that emotional WMT can reduce anxiety and improve emotional regulation in typical adults (Lotfi et al., 2020; Schweizer et al., 2011, 2013) and evidence from one study has shown it can reduce adolescent PTSD symptoms in a clinical sample (Schweizer et al., 2017).

One review has suggested that emotional WMT is likely to have greater impact on emotional vulnerability outcomes than the standard training (Cohen & Ochnser, 2018), as has been suggested by findings from Schweizer et al. (2011). Howeve, Pan et al. (2020) directly compared neutral and emotional WMT in the same study, and hypothesized that both approaches could reduce emotional vulnerability, but in different ways. The study differentiated between explicit and implicit emotional regulation (Etkin et al., 2015). They suggested that WMT using neutral stimuli could improve explicit emotional regulation strategies (e.g. cognitive reappraisal), via increased WMC and executive functions but would not impact implicit emotional regulation. This is because the latter is less reliant on WMC and linked to automatic processing of the affective value of stimuli (Pan et al., 2020). The authors reasoned that repeated exposure to emotional stimuli improves implicit affective control, which is operationalized in emotional Stroop tasks similar to that used by Schweizer et al. (2011). Indeed Pan et al. found support for this hypothesis.

Both neutral and emotional variants of the nback task improved explicit emotional regulation and decreased self-reported anxiety and stress scores. However only emotional WMT improved implicit regulation in an emotional Stroop task which was further supported by a reduced attentional bias to threat manifest in a reduction of the P3 ERP threat response in the Stroop task. This study featured adults only so cannot be generalized to adolescents and requires further replication. Nevertheless it begins to clarify important distinctions in the mechanisms of action in both forms of training.

1.6 Reducing adolescent emotional vulnerability through cognitive training

Comparatively few cognitive training studies have targeted adolescent emotional vulnerability, despite a strong case for their potential as an early intervention. There is evidence of a developmental mismatch between emotional and executive brain areas, whereby the brain's limbic regions (e.g. amgydala, nucleus accumbens) which are are central to emotion, reach developmetal maturity significantly earlier than prefrontal cortical areas critical for higher level cognitive control (Mills et al., 2014). This divergence indicates the theoretical potential that training may strengthen or scaffold top-down control over emotional reactivity during that critical mismatch or imbalance period (Casey et al., 2015, 2019). There is also evidence that EF impairments frequently precede the onset of a range of disorders suggesting training may constitute a promising pathway for prevention in vulnerable adolescents (Mewton et al., 2020). Thirdly, evidence that brain circuits may be highly responsive to environmental input during sensitive periods characterised by high neuroplasticity indicate timely training interventions could protect the top-down control system from perturbations that may disrupt development with lasting impact (Galván, 2010; Larsen & Luna, 2018).

1.6.1.1 Review of existing training studies

A limited number of studies have explored cognitive training in adolescents. Most of these studies have employed WMT to target attentional deficit and hyperactivity disorder (ADHD) symptoms or cognitive enhancement in vulnerable groups (Diamond & Ling, 2019; Sala & Gobet, 2017). These studies are reviewed in more detail in Chapter 2. A small subset of these studies has however investigated the effect of WMT on adolescents at risk of or clinically diagnosed with anxiety. Findings are inconclusive. Roughan and Hadwin (2011) and Hadwin and Richards (2016) had at-risk participants do 5 weeks of WM training or a cognitive behavioural therapy (CBT) intervention (Hadwin & Richards, 2016), or no training (Roughan & Hadwin, 2011). In both studies, WMT lead to decreased anxiety and improved inhibitory control following training, although this was not sustained at follow-up in Roughan and Hadwin (2011), and both the WMT and CBT groups were comparably improved, indicating possible Hawthorne effects (Hadwin & Richards, 2016). Study limitations included low power and inadequate controls (the CBT control cannot rule out demand characteristics), although Roughan and Hadwin (2016) used robust randomisation and blinding procedures. Two larger studies explored the effects of two different neutral WMT paradigms on mental health outcome measures in preadolescent primary school children (Hitchcock & Westwell, 2017) and at risk 16-24-year-olds (Mewton et al., 2020) using robust samples, controls and randomisation and blinding measures. Neither found significantly reduced teacher (Hitchcock & Westwell, 2017) or self-reported emotional and behavioural difficulties, or alcohol consumption changes following training (Mewton et al., 2020).

Additional studies worked with unselected adolescents to determine if training would impact risky behaviour, but results were contradictory. Boendermaker et al. (2018) found that

WMT had no effect on risky alcohol consumption although pre-training drinking levels were almost at floor, so there was little room for improvement. Rosenbaum et al. (2017) on the other hand found WMT was associated with reduced lab-based risk-taking in the presence of peers post training, alongside improved WM capacity, indicating promising effects of training to support adolescent regulatory behaviour in challenging contexts. Finally, one adolescent study used an adaptive emotional WMT to examine effects of training on emotional wellbeing in unselected 11-18 year olds (De Voogd et al., 2016). Participants were assessed pre and post training with follow up assessments at 3, 6 and 12 months. Although WM capacity improved for both groups, there were no significant post-training difference between them. Similarly, some improvements in emotional functioning at short and long term follow-up were detected in both groups, which were possibly non-specific time effects or a shared active ingredient in the two tasks. A possible explanation for the lack of significant group differences could be dose-related. Training was low intensity (8 sessions distributed across 4 weeks), therefore dosage may have been insufficient for a low risk group. Moreover, the training (n = 129) and control (n= 39) group sample sizes were dramatically different, and although linear mixed effects models were used in statistical analysis, sample size effects may have influenced the results (De Voogt et al., 2016).

Three studies used cognitive training techniques in clinical settings. Sweeney et al. (2018) recruited 14-21-year-olds undergoing substance abuse treatment to train for 5 weeks. Outcome measures included self-reported emotional regulation, substance abuse and risky behaviour, in addition to several measures of higher order cognition. No measure was significantly altered by training relative to control groups in pre- to post-training comparisons. Analysis of substance traces in urine did however suggest a possible benefit from training. Drug use in the experimental group remained stable but increased in the control group, suggesting training may have supported abstinence. Schweizer et al. (2017) found clinical benefits from emotional WMT relative to controls, evidenced by improved cognitive control, reduced post-traumatic stress disorder symptoms and increased use of adaptive emotional regulation strategies post-training in teenagers awaiting treatment for PTSD. Finally, evidence from Passarotti et al. (2020) indicated that CogMed training improved digit span performance and inhibitory control in 10-16-year-olds with primary diagnoses of either ADHD or paediatric bipolar disorder (PBD), leading to reduced emotional dysregulation in the PBD group and reduced depression in the ADHD group. Although it was promising to find these effects in adolescents with severe mood dysregulation, this study was significantly limited by the lack of a control group, small sample and no self-reported adolescent symptomology.

1.6.1.2 Limitations in existing research

The mixed results from these studies may be accounted for by heterogeneity in many elements of study design, including training task paradigms, training intensity, sample characteristics and controls, as well as outcome measures. For instance, although several studies used CogMed training, a commercially available package widely used in school settings and designed to treat WM deficits and ADHD (Hadwin & Richards, 2016; Hitchcock & Westwell, 2017; Passarotti et al., 2020; Roughan & Hadwin, 2011; Sweeney et al., 2018), the remaining studies used a diverse set of training packages. Secondly, the literature indicates gender should be accounted for in adolescent mental health research because of earlier pubertal onset and a higher prevalence of internalising disorders in girls (Campbell et al., 2020; Sisk & Foster, 2004). Whilst some of the studies reported that gender was balanced between the training and the control groups (e.g. Hadwin & Richards, 2016; Hitchcock & Westwell, 2017) most studies did not. Moreover, in a majority of studies between 65-78% of participants were female so the findings may not generalise to boys. Finally, outcome measures varied widely across all studies. With the exception of the strengths and difficulties questionnaire (SDQ), which was used twice (Mewton et al., 2020; Roughan & Hadwin, 2011), no single emotional or mental health measure was common to these studies.

In order to assess the potential of WMT as a possible early intervention to reduce adolescent vulnerability to emotional disorder, more research is needed to clarify the most potent combinations of intervention elements to impact emotional regulation and mental health outcome measures in typically developing adolescents.

1.6.1.3 Research gaps

A notable limitation in the studies reviewed above is that only three of these studies used a self-report measure of anxiety or depression symptoms (De Voogt et al., 2016; Hadwin & Richards, 2016; Mewton et al., 2020). None measured worry or rumination, two important indicators of anxiety and depression risk and no study has assessed symptoms in typically developing secondary school adolescents. Note, the average age of participants in Mewton et al. (2020) was 18 years. Whilst emotional regulation measures provide essential insight to mechanisms of change that should lead to reductions in distress and negative affect, it is important to assess the impact of training on symptom prevalence. Parent and teacher report, whilst effective for younger children, may be less reliable than self-report for assessing adolescents' symptoms (Youngstrom et al., 2000). It is clear that a deeper understanding of the efficacy of cognitive enhancement training on adolescent mental health and well-being needs to directly capture the young person’s own experience of symptoms.

One of the most frequently used paradigms in the adult cognitive training literature is the nback task, a continuous performance updating task commonly used to assess WM (Diamond & Ling, 2019; Jaeggi et al., 2003; Kirchner, 1958). A substantial proportion of adult studies investigating the effects of WMT on emotional vulnerability have used interventions based on this task, and many of these studies have reported training-related improvements of emotional regulation or disorder symptoms (e.g. Sari et al., 2016, 2020; Schweizer et al, 2013; Swainston & Derakshan, 2018; Zhao et al., 2020). No study to date has investigated the effects of nback training on emotional vulnerability in adolescents, despite evidence that it may have clinically potent characteristics. CogMed is the most common training package used by researchers examining emotional outcome measures in developmental populations, which is consistent with a general preference for CogMed training in childhood studies of WMT for cognitive enhancement (Diamond & Ling, 2019). There is therefore a clear research gap regarding the possible effects of nback training in adolescent populations.

1.6.1.4 Neuroplastic effects of attentional control training

Adults

Findings from fMRI and electrophysiological research using electro-encephalography (EEG) support the theoretical proposition that attentional control training can impact the neural circuity that underlies emotion processing in typical participants. In one study, training on an emotional nback task led to enhanced adaptive emotional regulation, which was mediated by increased post training activity in the fronto-parietal regions associated with top-down regulation and WM when contrasted with pre training activations (Schweizer et al., 2013). Two recent studies examined the effects of WMT using emotional and/or neutral training stimuli on the late positive potential (LPP) (Pan et al., 2020; Xiu et al., 2018), an electrophysiological marker sensitive to emotional intensity with a source reported to be in the subcortical and cortical areas associated with emotion processing, including the amygdala, insula and ventrolateral prefrontal cortex (Dennis & Hajcak, 2009; Liu et al., 2012). Both studies showed that nback training led to pre to post training reductions in LPP amplitudes during emotional reappraisal, compared to no changes amongst the controls (Pan et al., 2020; Xiu et al., 2018).

No studies have examined effects of WMT on downregulation of the amygdala response, however this was examined in one cognitive training study targeting pure interference control. Cohen et al. (2016) had participants complete 18 sessions of training on either a high or low interference inhibitory control task, where emotional interference was measured before and after training using fMRI. The high interference inhibitory control training led to reduced activation in the right amygdala in pre to post training comparisons of reactivity to aversive pictures, as well as a trend increase in functional connectivity between the amygdala and an area of the interior frontal gyrus. There were no changes amongst controls. Moreover, neural changes in these limbic and prefrontal cortical circuits were accompanied by post-training reductions in behavioural interference from aversive images. Taken together these findings indicate that improvements in emotional regulation and or improved symptoms resulting from attentional control training may emerge from neuroplastic changes in the limbic and fronto-parietal systems that subserve emotion processing.

Neural correlates of attentional control training in children and adolescents

We know very little about the neural mechanisms through which attentional control training might influence emotional functioning or vulnerability to psychological disorders in adolescents. Initial findings from the adult literature suggest potential neural mechanisms, however developmental differences may exist. A very limited set of neuroimaging studies with children and adolescent samples have examined the neural correlates of attentional control training and focused on cognitive performance as the outcome of interest rather the emotional vulnerability. These studies are informative regarding training-related changes in brain activation and functional connectivity during WM and EF task performance. They indicate that WMT can result in changes to brain activation (Everts et al., 2017; Jolles et al. 2012, 2013; Stevens et al., 2016), functional connectivity (Astle et al., 2015; Barnes et al., 2016; Tseng et al., 2019; Yoncheva et al., 2017) and structure (Lee et al., 2019; Schiller et al., 2019) in fronto-parietal areas involved in WM (see Jones, 2016 for a review). This includes training-related remediation of neural activation differences between adolescents with ADHD and neurotypical peers which was accompanied by ADHD symptom alleviation (Stevens et al., 2016), and evidence that training may instigate more adult-like fronto-parietal activations in neurotypical children (Jolles et al., 2012), supporting the assertion that neuroplastic effects of WMT may mimic developmental change (Klingberg, 2010).

Only two studies assessed WMT effects on brain structure (Lee et al., 2019; Schiller et al., 2019). One found that child and early-adolescent survivors of extreme early birth had post-training increases in fractional anisotropy and decreased diffusivity, indicators of greater myelination, axonal diameter or axonal packing, in the left superior longitudinal fasciculus, a white matter tract linking frontal and parietal cortices, which was only observed in participants with improved verbal WM following training (Schiller et al., 2019). Another brain imaging study assessed structural brain changes following cognitive control training in typically developing adolescents. 11-14 year olds undertook 6 weeks of daily multicomponent cognitive training targeting numerous EF components (Lee et al., 2019). Compared to controls, the training group showed marginal improvement on a visuospatial fluid intelligence test. They also experienced a relative increase in grey matter volume in the right inferior frontal cortex, which was positively associated with Stroop improvement, suggesting this training may have impacted brain structures involved in inhibitory control. Finally, two studies found no effects of training on brain structure or function in neurotypical 12-year-olds (Jolles et al. 2013) and children who were born preterm or with low birthweight (Kelly et al., 2020). Taken together these studies show cognitive training has the potential to influence neural structures and functions that underlie performance of neutral WM and inhibitory control tasks in younger children (Astle et al., 2015; Barnes et al., 2016; Tseng et al., 2019), or mixed samples featuring both young children and early adolescents (Yoncheva et al., 2017; Schiller et al., 2019), and some very modest preliminary support that training may alter structure or function in adolescents, (Jolles et al., 2012; Lee et al., 2019; Stevens et al., 2016). Further research is needed to determine if training-related structural or functional changes in the fronto-parietal networks may influence processing in a wider brain network supporting emotional processing in children or adolescents. For instance, investigations exploring the effects of training on amygdala - prefrontal connectivity or interactions would provide important insight (Bauer et al., 2019).

1.7 Parallel traditions in clinical and cognitive research

The emphasis in the research in this thesis is on emotional vulnerability in typically developing adolescents and the assumption of a broad spectrum of symptomatology or vulnerability in all individuals, which may or may not reach clinically significant thresholds. Before outlining the aims of this thesis, it is important to clarify a distinction between research traditions featuring clinical versus non clinical groups in understanding the links between attentional control and psychological disorder. The research on ACT and neuroscientific models of anxiety vulnerability reviewed earlier in this chapter is mainly comprised of studies that feature non-patient samples, although with some exceptions (e.g. Jazbec et al., 2012, Smith et al., 2021). In this respect, emotional vulnerability is typically operationalised in measures of trait anxiety, worry, rumination and self-report responses to questionnaires assessing symptomatology. These findings are relevant to clinical populations as they highlight possible mechanisms behind clinical disorder and inform approaches for prevention or reduction of risk in emotional disorders. Trait anxiety is highly predictive of clinical disorder diagnosis for both anxiety and depression (Chambers et al., 2004; Sandi & Richter-Levin, 2010). The fact that ACT predictions have not been widely tested in clinical populations is largely a reflection of distinct research traditions - clinical versus cognitive psychological - that have historically operated independently of one another in the pursuit of understanding links between executive functions and psychopathology, although researchers have advocated greater integration between the two traditions (Keshavan et al., 2014; Koster et al., 2011; Snyder et al., 2015).

1.8 Thesis aims

In summary, adolescence is a period of vulnerability to emotional disorder. Neurocognitive models of psychopathology highlight the crucial role of top-down attentional control in emotional regulation and suggest the involvement of impairment or aberrations in executive function processes in the onset and maintenance of emotional disorders and in variation across a spectrum of symptom experience in non-clinical samples. Extensive research on adolescent development highlights that protracted brain development in the regions underlying the maturation of critical components of cognitive control creates specific vulnerabilities to emotional disorder in this age group. There is a need for theory-driven hypotheses to drive research on interventions to target neurocognitive vulnerability in adolescents to reduce risk and improve the current and prospective mental health of adolescents. ACT highlights the central role of efficient attentional control processes in the regulation of emotion. Translational research grounded within ACT has used cognitive training methods to target attentional control functions to alleviate cognitive impairments and improve emotional functioning in clinically vulnerable adult populations with some promising results. In contrast, research on cognitive training for adolescents is in its relative infancy and more research is needed to understand if and how attentional control training can be extended to support the development of emotional regulation in typically developing adolescents. To progress this endeavour, research is needed that builds on existing findings whilst recognising that adolescent needs and response to training may differ to adults.

To bridge current research gaps, this thesis addressed two interrelated research questions. The first builds on previous work in ACT (Derakshan & Eysenck, 2009; 2011; Eysenck et al., 2007) and the Resource Model of Control (Baumeister, 1998; Muraven & Baumeister, 2000) to explore if compensatory cognitive processing during attentionally demanding tasks might have hidden emotional costs, which are more pronounced in adolescents relative to adults. Numerous studies indicate processing inefficiency during attentional control tasks is linked to mental health vulnerabilities in adults and adolescents (Berggren & Derakshan, 2013; Shi et al., 2019). Moreover, developmental studies have also indicated less efficient inhibitory control and WM in adolescents relative to adults (Spronk et al., 2014; Velanova et al., 2009). No studies have attempted to investigate possible consequences of persistent compensation and how that might impact affective control generally, although previous authors have speculated that a persistent reliance on compensatory effort to meet performance goals may exhaust resources creating real-world difficulties and impairment (Moser et al., 2013).

Addressing this question directly may also aid elaboration of a mechanism through which cognitive training interventions might improve emotional well-being. This was addressed in a longitudinal study using behavioural and EEG methods which is outlined in Chapter 3. This study compared the effects of cognitive depletion on emotional reactivity triggered by a worry induction in adolescents relative to adults, using the ERN as a measure of compensatory neural processing. In addition to exploring developmental differences in depletion effects on emotional reactivity, the study also examined cross-sectional associations between the magnitude of the ERN during the depletion exercise and emotional reactivity, as well was prospective associations between this ERP and emotional vulnerability some 18 months later.

The second aim of the thesis was to extend previous training research using cognitive methods to improve well-being and optimize adolescent emotional functioning. Specifically, to explore the validity and efficacy of nback WMT as a universal intervention to boost processing efficiency and promote emotional resilience in typically developing adolescents. A notable gap in the literature has been a dearth of studies examining the effects of training on neural outcomes in this age group. The efficacy of cognitive training has been widely debated (Redick, 2019), however an emphasis on behavioural measures limits understanding of training efficacy. Studies have predominantly relied on performance outcomes such as accuracy and reaction time in computerised cognitive tasks to assess gains in attentional control, however these measures may only reveal surface level changes in AC performance. This is highlighted by studies that have found neural differences during the execution of attentional control despite similar levels on behavioural performance (Basten et al., 2012; Hogan et al., 2005). Investigating neural outcome measures relevant to emotion processing would permit better understanding of the neural impacts of training on emotional regulation and symptoms. Even in the absence of direct transfer to task performance, there may be evidence of a modulation in neural activations pointing to changes in efficiency or strategy. In addition to assessing training transfer to behavioural and self-report measures, a further aim of the thesis was therefore to broaden the levels of outcome analysis to include neural outcomes measures. These questions were addressed in two intervention studies which are outlined in Chapters 4 and 5. Specifically, Chapter 4 describes a WMT study undertaken amongst adolescents at a London school to assess primary outcome effects of nback working training on self-reported anxiety and depression, permitting an assessment of efficacy of this training intervention in reducing internalising symptoms and serving as a proof of principle. Chapter 5 outlines the second training intervention study. The aims of this study were firstly to replicate the findings from study 2 and secondly to examine effects of training on ERP measures of cognitive control recorded during attention control and emotional regulation tasks respectively, before and after a two week training intervention. The study focused in particular on the ERN, the processing efficiency measure that was investigated in study 1, as a primary neural outcome measure.

CHAPTER 2

2 Methods

2.1 Chapter overview

The aim of this chapter is to both contextualize and describe the WMT and ERP methods that were used in the three studies undertaken in this doctoral research. Although Chapter 1 introduced the principle of using attentional control training to target emotional vulnerability via WM, the chapter did not discuss specific methods of WMT in any detail, and only cursorily addressed the large body of research examining the effect of WMT on cognitive outcomes that laid the foundation for the techniques. Before describing the precise nback WMT methodology that was used in my studies, the chapter presents a more general background to computerized WMT, including a brief review of the dominant training methods, before covering nback training in more detail. It also reviews the limited research on WMT in adolescents, which serves as an important context for the current research and informed the selection of the training method applied in these studies. Finally, the first section concludes with a description of the nback training paradigm that was adopted in studies 2 and 3, including a description of the training and control tasks and their administration.

The second section of this chapter focuses on the ERP method used in studies 2 and 3. Before describing the specific methodology for EEG recording and preprocessing that was used to extract the ERPs, the section begins with a brief general introduction to the ERP method, alongside an overview for each of the 4 ERPs that were measured. This overview outlines the ERPs' key characteristics, purported neural sources, and discusses their functional significance, development and relevance to the research questions in this thesis. Lastly, the studies in this thesis used a selection of self-report scales to measure emotional vulnerability, several of which were administered in more than one study. The third and final section of this chapter is dedicated to describing these scales, what they purport to measure and their psychometric properties.

2.2 Working memory training

1.2.2 The principles of cognitive training studies

The purpose of cognitive training is to boost the efficiency and effectiveness of domain general cognitive processes through systematic repetition of mentally-demanding tasks. Its relative success should be mediated by plasticity in the underlying neurocognitive systems (Aksayli et al., 2019; Von Bastian & Oberauer, 2014; Constantinidis & Klingberg, 2016; Karbach & Shubert, 2013). In principle, this means non-trained tasks or skills should also improve as a result of training if they share the same underlying neurocognitive mechanisms as those exercised by the training task (Aksayli et al., 2019; Green et al., 2014; Jaeggi, et al., 2008). Studies distinguish between 'near' and 'far' transfer of training effects to characterize and assess training outcomes. Near transfer refers to improvements on untrained tasks that are similar to the training task, whereas far transfer refers to improvement on tasks that do not share surface features with the training task (Barnett & Ceci, 2002; Taatgen, 2021). To demonstrate a boost to domain general processes rather than mere practice effects or strategy development, a training intervention must show evidence of far transfer to tasks that theoretically rely on domain general core cognitive competences but do not share surface features (Melby-Lervåg et al., 2016).

1.2.3 Computerised WMT

The burgeoning of computerized WMT interventions started at the beginning of this century (Klingberg, 2012; Klingberg et al., 2002, 2005). Earlier attempts to train WM used explicit learning strategies, but memory improvements were limited to the trained tasks and the acquired strategies were either ineffective or not applied in other tasks or domains (Butterfield et al., 1973; Ericsson, 1980). In the Klingberg et al. (2002, 2005) studies, instead of explicit or conscious strategies to boost short-term memory, participants practiced simple computerised WM span tasks designed to target WM implicitly (Klingberg, 2010). Training was predicated on the repetition of tasks with feedback on performance and personalised adaptation of task difficulty (volume of information held in WM) on a trial by trial or block by block basis (Klingberg, 2012). Compared to control groups that trained on a non-adaptive version of the task, after 5-6 weeks of adaptive WMT participants had improved performance on verbal and nonverbal reasoning, WM span task, inhibition and ADHD symptoms (Klingberg et al., 2002, 2005).

The training protocol developed by Klingberg et al. is now marketed as CogMed (Pearson), a commercial package of 12 training tasks to improve WM in children and adults. CogMed is one of the most ubiquitous WMT protocols in the training literature, particularly in studies researching effects of training in younger children, older adults and children and adults with ADHD, although most study participants were in young to middle childhood (Diamond & Ling, 2019). The substantial body of evidence on CogMed training suggests that it significantly increases performance relative to non-adaptive control training on near transfer WM tasks (Diamond & Ling, 2019). However, despite some evidence of far transfer to untrained measures, including teacher-rated EF improvements, reduced ADHD symptoms and improved functional impairments (Bigorra et al., 2016), improved maths (Bergman-Nutley & Klingberg, 2014) and improved inattention in daily life (Green et al., 2012; Gropper et al., 2014; Spencer- Smith & Klingberg, 2015), several meta-analyses and reviews argue that once robust controls and randomisation are introduced there is limited evidence that impressive WM task training gains generalise to other measures of EF such as inhibitory control, academic ability or everyday attention (Aksayli et al., 2019; Diamond & Ling, 2019; Simons et al., 2016).

1.2.4 Nback training

The training protocol that is used in the studies reported in Chapters 4 and 5 in this thesis is based on the nback paradigm (Kirchner, 1958) and is the most commonly used form of WMT after CogMed (Jaeggi et al., 2008, Diamond & Ling, 2019). The training involves regular practice of the nback, a task widely used for assessing WM (Miller et al., 2009). Nback tasks can be either single or dual, where the single nback task features one stimulus type and the dual task features two stimuli, each from a separate domain (e.g. visuospatial or auditory). Participants observe a stream of changing stimuli, comparing each new item (single version) or items (dual version) with the stimulus information 'n' steps prior to it and responding to indicate if the compared stimuli match. For example, in a 2-back task, on any one trial participants retain information about three trials in WM – the current and the last trial, and the trial 2 steps earlier. The same principle applies for the 3-, 4-, 5- back tasks, and so forth. In summary, to be successful, participants must hold in WM the features of the current stimulus and all stimuli, up to at least n steps prior to current.

Nback tasks tap WM updating, attentional control and cognitive flexibility (Jaeggi et al., 2010; Soveri, 2017). Participants must keep on top of a constant stream of changing information, encode each new stimulus, monitor, maintain and update the sequence simultaneously and clear WM of the no-longer relevant information (Diamond & Ling, 2019; Pergher et al., 2018).

Interference control processes also need to be activated when misleading lures appear (Soveri et al., 2017). Lures refer to occasions when the current stimulus matches another from the recently-activated stimuli, but does not match the target nback stimulus (Redick & Lindsey, 2013). To this end, the nback task does not exclusively tap WM capacity and there is evidence that where dual nback training transferred to measures of general intelligence, this was mediated by training-related increases in interference and impulse control (Jaeggi et al., 2011, 2012), indicating that attentional control mechanisms are critical targets in training programmes using nback tasks.

2.2.1.1 Adaptive properties of the training task

A feature of most WMT studies is adaptive adjustment of task difficulty in response to participant progress (von Bastian & Oberauer, 2014). Task difficulty increases when the participant performs accurately and decreases following repeated failures, thus difficulty is regulated according to participant's performance. This feature is considered essential as training can only induce neural plasticity if cognitive processes are challenged by new external demands calibrated to exceed routine functioning (Diamond & Ling, 2019; Lövden et al., 2010; Von Bastian & Eschen, 2016), whilst ensuring that task demands do not overwhelm. Nback training therefore increases the nback load according to the individual's expanding proficiency. By making gradual cumulative demands on WM, increasingly higher nback levels are sustained and WM capacity and attentional control can be increased (Jaeggi et al., 2012; Klingberg, 2010; Von Bastian & Eschen, 2016).

2.2.1.2 Dose and duration

There is no current consensus on the most effective duration for a WMT intervention. Where structured CogMed intervention packages consist of 25 sessions of 45 minutes training to be administered 5 days per week for 5 weeks (www.pearsonclinical.co.uk), there is currently no recommendation for nback training interventions. Intervention duration varies widely between nback studies (Pergher et al., 2019) ranging from as few as 3 to as many as 100 training sessions (Von Bastian & Oberauer, 2017). Neuroimaging evidence suggests training-related change in brain activation is more pronounced for longer interventions, and some studies indicate alterations in brain activity are not static, but rather increases in activation early in the intervention followed by subsequent decreases, reflecting neurocognitive efficiency gains alongside consolidation of training effects (Pergher et al., 2019). Hempel et al. (2004) report the consolidation effect did not emerge until the fourth week of training, supporting claims that longer interventions are desirable for achieving meaningful transfer (Jaeggi et al., 2008; Pergher et al., 2019; Von Bastian & Oberauer, 2014). However, researchers must be mindful about participant attrition and motivation loss in longer interventions, so striking a balance is essential, particularly in adolescent groups (Mewton et al., 2020). Pergher et al.'s (2019) review of research methods in nback training found that whilst most studies employed interventions lasting 10 or more days, far transfer effects were reported even in studies where fewer than 10 days' training had taken place (20% compared to 25% for ≥10 days). Furthermore, meta-analyses that examine the moderating effect of training duration, found no significant effect on outcomes (Peng & Miller, 2016; Sala & Gobet, 2017), suggesting that shorter interventions may be sufficient.

2.2.1.3 Efficacy of nback training for improving WM and cognitive control.

Similar to CogMed training, evidence on the efficacy of nback training on cognitive outcomes is mixed. Several studies reported that adaptive nback training can increase general or fluid intelligence (Au et al., 2015; Jaeggi et al., 2008, 2010; Stephenson & Halpern 2013) and interference control in a flanker task under high stress conditions (Sari et al., 2016), however other studies failed to find lasting far transfer of training effects (Chooi & Thompson, 2012; Pugin et al., 2014; Redick et al., 2013). A meta-analysis which included 33 studies with healthy adults reported that overall effect sizes for nback training transfer to untrained nback tasks was moderate, and there was only a very small effect of far transfer to other WM tasks, fluid intelligence or measures of cognitive control (Soveri et al., 2017). Diamond and Ling's (2019) review of effects of training on executive function improvements concluded that when compared with active controls nback training was only partially effective at increasing performance on untrained WM tasks and there was limited evidence that it led to improvements on executive functions.

Nonetheless there are robust studies using nback training that have found far transfer effects to attentional control from nback training (Sari et al., 2016) and where studies incorporate neural outcome measures there is evidence of far transfer of nback training to neural activity, which is associated with training task improvement. For example, Owens et al. (2013) reported increased neural filtering efficiency of WM in dysphoric participants. Others have found training associated with improvement in the most difficult condition of a WM task, accompanied by strengthening of task-related effective connectivity across fronto-parietal and parieto-occipital networks (Kundu et al., 2013) and neuroplasticity in white matter integrity in fronto-parietal cortices associated with WM (Takeuchi, 2010). Pergher (2019) has highlighted the vast heterogeneity in nback training study design to be a factor contributing to significant variations in outcomes and small effects.

This heterogeneity cuts across outcome measures (120 different transfer tasks in 51 studies reviewed), intervention duration, participant characteristics and training task attributes. This makes it challenging to compare studies and future work needs collaboration across research groups to identify the most desirable task attributes to determine optimum intervention designs.

2.2.2 **Working memory training in adolescence**

Although the effects of WMT on cognition, everyday attention and education-relevant outcomes has been widely investigated during childhood, comparatively few studies have examined the effects of WMT in typical adolescent populations. With the exception of some studies that primarily examine the effects of WMT on emotional vulnerability outcomes (Boendermaker et al., 2018; Hitchock et al., 2017; Rosenbaum et al., 2017) most adolescent studies featured clinical samples, including cancer survivors (Conklin et al., 2017), teenagers born with HIV (Fraser & Cockcroft, 2020), individuals with learning difficulties (Gray et al., 2012) and ADHD (Stevens et al., 2016). Evidence of training transfer is consistent with studies using child and adult samples, where most studies indicate that training resulted in near transfer to untrained WM measures, however far transfer to academic outcomes or executive function tasks was less common. These studies are reviewed in this section.

2.2.2.1 CogMed

Few CogMed training studies feature adolescent samples. For instance, in a recent meta-analysis of the cognitive and academic benefits of CogMed training, of the 50 studies included in the analysis, only five had an exclusively adolescent sample (i.e. participants were aged between

11-18 years) (Aksayli et al., 2019). An additional four studies had a mixed age sample with children ranging from aged 6 – 16 years, making it difficult to isolate effects of training from developmental differences. Study samples featured varied clinical groups, including children with ADHD, cancer survivors and epilepsy patients. In most studies, CogMed training led to increased performance on a variety of untrained near transfer measures of WM, with little evidence of far transfer to either executive function, academic or other measures (Gray et al., 2012; Hitchcock & Westwell, 2017; Hovik et al., 2013; Kerr & Blackwell, 2015; Steeger et al., 2016). Far transfer was rare and included a small improvement effect for maths performance in 7-15 year olds (Bergman-Nutley & Klingberg, 2014) and improved maths and reading performance in 10-12 year olds which was not accompanied by improvement on executive function (Egeland et al., 2013). Two studies with cancer survivors ranging in age from middle childhood to mid-teens reported improved WM, parent-reported learning improvements and increased processing speed which was sustained six months later in contrast to a failure to sustain post training improvement in attention at follow-up (Conklin et al., 2017; Hardy et al., 2013). Two additional exceptions were both studies that explored effects of training on emotional outcome measures. Roughan and Hadwin (2011) found adaptive CogMed training led to improved inhibition, decreased test anxiety and teacher-reported attention and emotional symptoms compared to a passive control group. The findings were undermined by the limited sample size and lack of active control. In a large study, Hadwin and Richards (2016) compared CogMed training to a cognitive behavioural therapy (CBT) control in a group of adolescents selected for high anxiety and low WM. WM was increased in the CogMed group only post training, whereas both groups demonstrated increased inhibitory control and reduced attentional biases to threat post intervention, which was sustained at follow up. These findings demonstrated promising effects of training on emotional outcomes however the CBT control cannot rule out Hawthorne effects (Klingberg, 2010; Shipstead, et al., 2010, Shipstead, Redick et al., 2012).

In summary, most adolescent CogMed training intervention studies were conducted in groups with attention or memory impairments, with some exceptions (e.g. Hitchcock & Westwell, 2016; Kun, 2007; Shavelson et al., 2007). Consistent with results in other age groups, these studies reported that training improved performance on untrained WM tasks, but far transfer directly post training or at a maximum of six months post intervention follow up remains elusive. Small improvement effects were reported on maths outcomes in two studies, however heterogeneous child and adolescent samples, or likelihood that the sample was mainly prepubescent, make it difficult to draw conclusions about adolescence. The only studies reporting clear far transfer effects were studies that had emotional measures as primary outcomes, however the evidence was undermined by the choice of controls and un-blinded ratings of participant emotional and behavioural difficulties.

2.2.2.2 Brain training 'apps'

Other adolescent WMT studies have used a heterogeneous mix of commercially available adaptive brain training games utilising WM tasks (Bikic et al., 2017; Mewton et al., 2020, Fraser & Cockcroft, 2020; Van der Molen et al., 2010). Working memory performance was increased relative to controls in all studies except Bikic (2017) which found no differential effect of training on any outcome measure in a group who practiced Scientific Brain Training™ compared to a control group who practiced a non-adaptive visuospatial puzzle. Van der Molen et al. (2010) compared adaptive and non-adaptive WMT using Jungle Memory™ training to a passive control. Directly post training only the adaptive group improved on a verbal short term memory task and there were no effects on far transfer. However, at six months follow-up, far transfer effects emerged on visual short term memory, arithmetic and story recall in both the adaptive and non-adaptive groups compared to the controls, suggesting consolidation of training occurred over time, and that adolescents with learning difficulties may not require adjustment of training difficulty to instigate far transfer. Frazer and Cockcroft (2020) also used Jungle Memory™ in a double blind RCT and found performance increases on a variety of executive function measures and fluid intelligence in adolescents born with HIV. Mewton et al. (2020) on the other hand found no evidence of far transfer to a variety of measures in older adolescents in double blind RCT using Lumosity ™ training. Whilst these studies suggest commercially available brain training apps have the potential to improve cognition in teenagers, only Jungle Memory™ helped improve executive functioning and academic performance. Too few studies have been conducted to be able to draw firm conclusions about the effectiveness of these methods in adolescence.

2.2.2.3 Nback

Most investigations using nback training have used adult samples (Diamond & Ling, 2019), although consistent with studies using CogMed training, there is limited evidence for how well adolescents respond to nback training. Pugin et al. (2014) found typically developing 10-14 year old boys improved on an auditory nback task after single nback training compared to a passive control. There were no significant group differences post training on Ravens matrices or Stroop task performance. However participants' ability to engage with training was an issue in this study. Only 50% of participants improved on the training task itself, moreover those who were categorised as 'improvers' were also higher performers at baseline, and indeed better baseline performance also predicted training task improvement. Unsurprisingly, only the steady performers improved on the auditory nback task. However the authors did not explore if there was an association between training improvement and transfer effects on inhibitory control. This finding was consistent with Jaeggi et al. (2011), who found many of their 8-10 year old participants struggled to improve on nback training task itself, although those who did improve reported significantly increased WM and fluid intelligence after training. Responses to the post training questionnaire indicated that poor training progress was related to difficulty in coping with frustrations and failures in the training (Jaeggi et al., 2011). Pugin et al. (2015) replicated the near transfer effects on auditory nback and also found evidence of changes in fronto-parietal brain areas associated with WM. Training led to an increase in slow wave EEG activity in fronto-parietal regions post training and these increases were associated with improvement in auditory nback task performance directly after training and at three months follow up. However there were several limitations to both of the Pugin et al. studies. Sample size was small, Pugin et al. (2014) featured a passive control and no randomisation, whilst Pugin et al. (2015) used no control. In another study, Rosenbaum et al. (2017) employed a training task that used nback as part of a suite of WMT tasks. Training led to increased performance on a near transfer WM task, but no far transfer to Stroop performance. A far transfer measure of risk-taking indicated the training group took fewer risks relative to controls who answered trivia questions during the allocated training time. It is impossible to isolate whether nback was the active ingredient in this study, but nonetheless it provides rare evidence of WMT far transfer in typically developing adolescents. To the best of my knowledge only one other study reported on nback training for adolescents. In a study by Tayeri et al. (2016), 13-14 year olds completed 12 x training sessions over three months, and reported that the nback training group improved on an untrained WM task, Ravens matrices and short term memory, directly after training and at follow-up. However, baseline nback group performance was poorer than controls' for all measures. The authors did not report follow-up comparisons to compare groups post training or at follow up, so it is likely improvements in the nback group represented regression towards the mean.

2.2.2.4 Summary

Despite remarkable neural plasticity during adolescence and evidence that it represents a sensitive period for learning (Fuhrmann et al., 2015; Knoll et al., 2016) surprisingly little research explores the effects of WMT in this age group and therefore many questions remain unanswered. In summary, few studies have employed nback training in adolescent samples and in those limited studies we find evidence that some participants find the training task challenging, however where they successfully engage with and improve on the training task, nback training can boost WM and there is some evidence that it may improve fluid intelligence. However evidence to date is undermined by a lack of randomisation and use of passive or no controls (Pugin et al.,2014; 2015). More research with larger samples is needed before we can draw further conclusions about nback training for adolescents. Intervention studies using other training tasks suggest WM is frequently increased by training, however transfer to executive functions and measures relevant to academic performance is less common. There is evidence for these effects in studies with passive controls and where participants and raters were not blind to study conditions, but also in studies with more robust designs, although authors of several reviews and meta-analyses argue that far transfer does not occur when study designs are randomised, blinded and have active controls (Diamond & Ling, 2018), although to date no meta-analyses have examined effects of training in adolescents only, therefore we may not generalise their conclusions to adolescents.

Nonetheless the evidence from the limited adolescent research available is consistent with these findings. Most studies to date feature participants vulnerable to cognitive impairments, therefore many of these results are not generalizable to typically developing adolescents. Finally, several potential influential factors have not been taken into account in any of these studies and which may impact whether far transfer effects would be detectable in these studies. Generally, training outcomes are measured immediately after training, and long term follow ups are rare. Most studies cannot account for long term consolidation of effects and therefore may not allow sufficient time for training effects to become apparent in behaviours or academic performance. A recent longitudinal study of a school-based WM intervention with 6-7 year olds reported large positive effects of training on maths, reading skills, fluid intelligence, inhibitory control and self-regulation (Berger et al., 2020, under review). Importantly, these far-transfer effects only emerged after 12-13 months. Moreover, when participants were revisited 3–4 years after the intervention, the training group were more likely to have been selected for higher academic streams on entering secondary school. Had the researchers only examined outcomes at the end of training they would have concluded WMT did not improve cognition. Taken together, it could suggest that many training designs may have been unable to detect true effects of training had they been present.

2.2.3 WMT and emotional outcome measures

Several recent adult studies have begun adopting WMT approaches to explore effects of attentional control training on emotional vulnerability with several studies reporting promising therapeutic effects of training on emotional outcomes measures. Researchers have been motivated to apply this technique in adolescents given evidence of emotional vulnerabilities inherent to adolescent brain and cognitive development (Fuhrmann et al., 2015; Paus et al., 2008). An overview of the current state of play in this research in both adults and adolescents and its theoretical rationale has already been outlined in Chapter 1. An nback task with neutral stimuli has not yet been used in a training intervention to target vulnerability to emotional disorder in either clinically vulnerable or typically developing adolescents. Given the evidence in adult groups, it is important therefore to investigate if using nback WMT to train attentional control is a viable intervention method to target emotional vulnerability in typically developing adolescents (Keshavan et al., 2014).

2.2.4 **Dual nback training methodology applied in experiments 2 and 3**

Studies 2 (Chapter 4) and 3 (Chapter 5) were training intervention studies. Participants in both studies trained using a dual nback training task and were randomly allocated to either an adaptive training group or a control group which trained on a non-adaptive 1-back version of the task. Training duration was not the same for both studies with the preliminary study's training intervention (Study 2) lasting 20 days and the second intervention study (Study 3), which explored effects of training on neural outcome measures, featured a training intervention of 12 days. The specific rationale for training duration is discussed in the methods and procedures section of the respective experimental chapters.

2.2.4.1 The training tasks

2.2.4.1.1 Adaptive dual nback training task

This task was equivalent to that used by Sari et al. (2016) and adapted from Jaeggi et al. (2008). Each training trial features a 3 X 3 grid with nine white cells, starting with a fixation cross within the central cell. A green block appears in one of the remaining 8 cells, accompanied by a female voice announcing a letter (one from several consonants - c, h, k, l, q, r, s, t and t). Stimulus duration was 500ms followed by a 2500ms inter stimulus interval. Participants must recall the location of the green square (spatial WM) and the letter's identity (verbal WM). This is followed by another trial stimulus. The location of the green block and the announced letter may be the same or different from the previous trial. Depending on the difficulty (n) level, the participant must indicate whether the current trial matches the one immediately before, or two, three or even four trials back. Hence nback; '*n'* referring to the number of trials earlier with which the current trial is compared. The maximum n level in both intervention studies was 4 back. If locations of the green square match, participants pressed 'A' on the keyboard and pressed 'L' if the letter matches. Both keys were pressed if location and letter sound match the comparison trial. If there is no match, no key is pressed. Participants were asked to respond as quickly and as accurately as possible. Figure 2.1 below shows a sample trial.

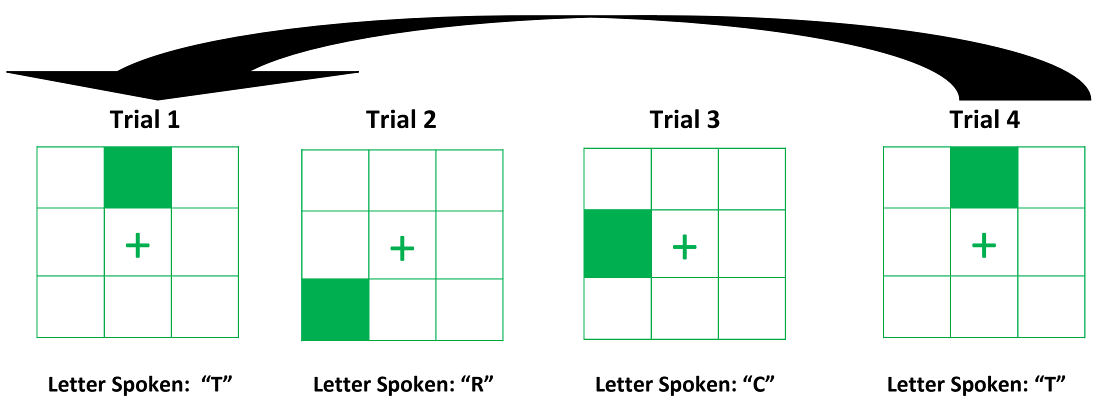


Figure 2.1 Illustration of a 3-back trial in the nback WMT task. Trial 4 is compared with trial 1. Both the location and the letter match.

Participants began each training session at the 1-back level. If 95% accuracy was attained, the participant moved to the 2-back level, where stimuli were compared with trials two trials earlier, and so forth. If 75-95% accuracy was not sustained at a new level, they reverted to the previous level in the following block. The task was adaptive because *n*-level increased or decreased in response to performance. Each training session consisted of 20 blocks, with each session lasting approximately 30 minutes. Each block featured 20 + plus n trials. For example if the block was 2-back, then there were 20 + 2 trials, if 3 back, then 20+3 trials and so forth. There were equal numbers of matches in each block, 4 verbal, 4 spatial and 2 where both were matched.

There was a 15-second pause between blocks with a countdown to the start of the next block. The upcoming *nback* level was always indicated following this pause and before trials began. Feedback on performance accuracy was provided at the end of each training session. Only one training session per day could be completed. Training was accessed remotely via internet on participants' own or school PC/laptops, but was not accessible with tablet computers or smartphones. Communications between the researcher and participants differed between the two studies because of differing school safeguarding policies and the application of experience gained in the first study. Details of the training duration and its rationale, plus monitoring procedures are reported in the respective chapters for each study.

2.2.4.1.2 Active control training task

Typically, active controls are recommended to avoid Hawthorne effects in intervention studies (Diamond & Ling, 2016; McCambridge et al., 2014; Shipstead et al., 2014). In the studies reported in Chapters 4 and 5, the intervention group was compared with an active control group which trained on a non-adaptive version of the dual nback task. In the non-adaptive control task, challenge remained at 1-back. The participant compared the current letter and location of the green square with the set of stimuli in the immediately preceding trial. All other aspects and components of the task and training procedure were identical to the adaptive dual nback described above. The demand on WM over the training period never changed and neural plasticity should not have been induced (Klingberg, 2010). Similar control groups are widely used in WMT studies (Holmes et al., 2009; Karbach et al., 2015; Klingberg, 2010). An additional rationale for a non-adaptive version of the task is that where study participants are from a cohort of young people from the same school and likely to compare notes, it is crucial that the control training appears equivalent to the active intervention, as much as is possible.

2.3 EEG recordings, data processing and ERP rationale

This section provides an introduction to the event related potential (ERP) method employed in studies 1 and 3. It also contains an overview of the specific ERPs that were measured, their relevance to cognitive control and psychopathology vulnerability, and what is known about their development. This is followed by a description of the EEG methods and the processing steps for extracting the ERPs used in the studies.

2.3.1 EEG research methods

Electroencephalography (EEG) is a non-invasive method for recording electrical brain activity from electrodes on the scalp. EEG research has several advantages over other neuroimaging methods. Its high temporal resolution provides more fine-grained information about the timing of neural events, offering insight into different stages of cognitive processing. It is non-invasive and inexpensive relative to other imaging methods, making it a highly accessible tool for research with children and young people (Downes et al., 2017). EEG data represents direct and real time brain activity in the post-synaptic electrical potential output of large numbers of cortical pyramidal neurons, all firing in synchrony (Peterson et al., 1995). The raw EEG represents the fluctuations of these voltages over time.

The Event Related Potential method (ERP) is one of the most widely used techniques to exploit the EEG for cognitive neuroscientific research. ERPs refer to small voltages or electrical signals triggered by sensory, motor or cognitive events. These are isolated from the raw EEG by marking the precise moment of events of interest (Coles & Rugg, 1995). These event-related voltage fluctuations are averaged across several trials to increase the signal to noise ratio, on the premise that any EEG activity not time-locked to the event trigger will vary non-systematically across the repeated trials, whereas the true ERP will be consistent (Coles & Rugg, 1995).

Several ERP components detected over fronto-central and parietal cortices are known electrophysiological indices of cognitive control processing (Luck & Kappenman, 2011) and also involved in emotional regulation, affect and psychopathology (Hajcak et al., 2010; Lewis et al., 2006; Megías et al., 2017; Sanger & Dorjee, 2015; Zinchenko et al., 2017). These include the Error Related Negativity (ERN) and the Error Positivity (P(e)), both of which closely follow the commission of an error, in addition to the N200 (N2) and the P300 (P3). In the nomenclature of the latter two ERPs, N refers to a negative and P a positive waveform deflection, and the number indicates approximate number of milliseconds post stimulus presentation where the peak response is typically detected. These ERPs are used to explore the development of cognitive control (Downes et al., 2017; Lo, 2018; Tamnes et al., 2013) and its association with vulnerability to psychological disorders (Lo, 2018; Moser, 2017; Righi et al., 2009; Wauthia & Rossignol, 2016; Weinberg et al., 2016).

One of the advantage of ERPs is that they can identify between group differences in cognitive processing belied by comparatively similar behavioural performance (Downes et al. 2017). For instance, a study that examined control processing in adolescent stroke patients found patients performed just as well as controls on a behavioural task. However differences emerged on the response-locked ERN indicating disruptions in patient's error monitoring, whilst processes linked to the stimulus-locked N2 and P3 were unaffected by stroke lesions (Hogan et al., 2005). The experiment reported in Chapter 3 exploits this advantage to explore hypothesised covert compensatory processing costs of mental fatigue using the ERN and P(e) from a demanding cognitive task.

ERPs are also increasingly used to examine efficacy and understand mechanisms of action in intervention studies aimed at improving cognition and behaviour or in treating psychological disorders (Bailey et al., 2019; Downes et al., 2017; Fissler et al., 2017; Hajcak et al., 2019; Ladouceur et al., 2018; Matsen et al., 2020; Zhao et al., 2020). ERPs are useful because they allow researchers to pinpoint subtle changes in control processing that might not evident in behavioural performance so provide more nuanced information on the precise control mechanisms influenced by interventions. Moreover, ERPs have the potential to be used as neurobiological markers of clinical vulnerability to psychological disorders with the ERN representing a notable example (Klawohn et al., 2020; Weinberg et al., 2015) so are highly appropriate targets when investigating impacts of interventions.

With these advantages in mind, the second training study (Chapter 5) investigated neural change following WMT using the ERN and P(e) during an attentional control task, and the N2 and P3 during an emotional regulation task (emotional Stroop) as training outcome measures. The following section contains an overview of each ERP, describing the principle characteristics of these components, their developmental profile and relevance to cognition and emotion.

2.3.2 **ERPs**

2.3.2.1 <u>ERN</u>

The ERN and the P(e) are usually elicited in response to errors where there is response conflict and are associated with the execution of cognitive control rather than early processing of the perceptual dimensions of stimuli (Falkenstein et al., 1991; Gehring et al., 1993; Overbeek et al., 2005). The ERN is a negative deflection in the EEG waveform peaking 50-100 ms after an erroneous response in speeded choice RT tasks, such as the Flanker or Go/No Go tasks and is typically detected over fronto-central electrodes (Falkenstein et al., 1991; Gehring et al., 1993; Hajcak et al., 2003). Source localisation studies indicate that the ERN is maximally generated from posterior cingulate (PCC) and ACC (Buzzell et al., 2017; Debener et al., 2005; Herrmann et al., 2004; Holroyd & Coles, 2001; Holroyd & Yeung, 2012) with several other parietal and frontal regions also implicated in error processing (Taylor et al., 2018). This is supported further by evidence that lesions to the ACC are associated with a blunted ERN (Stemmer et al., 2004). Links between the ACC and ERN remain relatively stable across age (Buzzell et al., 2017; Tamnes et al., 2013), although additional ERN generators in the insula, orbitofrontal cortex (OFC) and inferior frontal gyrus (IFG) show age-related increases in error activity (Buzzell et al., 2017). Neuroimaging indicates the ACC forms part of a central hub in the salience network (Seeley, 2019) and is instrumental in monitoring changing situational demands and orchestrating behavioural adaptations in response (Shackman et al., 2011; Shenhav et al., 2013).

2.3.2.1.1 Development and the ERN

The ERN emerges as early as aged 3 years (Grammer et al., 2014) and there are linear increases in amplitude from childhood through to maturation in early adulthood (Anokhin & Golosheykin, 2015; Buzzell et al., 2017; Davies et al., 2004; Downes et al., 2017; Ip et al., 2019; Ladouceur et al. 2004, Lo, 2015. 2018; Overbye et al., 2019; Tamnes et al., 2013). DuPuis et al. (2014) examined ERN amplitudes in 234 children aged 6 - 9 years. Amplitudes increased with age and this increase was mediated by the temporal consistency of the signal, whereas signal strength declined and was unrelated to ERN amplitudes, suggesting that development was linked to increased efficiency in recruitment of conflict monitoring resources. There are mixed views on when most significant developmental changes in the ERN occur, but reviews suggest the biggest change occurs in adolescence (Moser, 2017; Taylor et al., 2018).

The protracted development and timing of the maturation of the ERN is likely linked to functional and structural maturation in the prefrontal cortex and distributed structures involved in error processing (Downes et al., 2017). Increases in ERN amplitudes accompany performance improvements on executive control tasks (Checa et al., 2014) and tasks demanding inhibitory control under conflict (Overbye et al., 2019; Tamnes et al., 2013). fMRI research shows developmental improvements in inhibitory control performance and error processing is supported by gradual increases in the recruitment of the dorsal ACC and more widely distributed recruitment of specialised regions, in addition to task-general regions of the PFC by late adolescence and early adulthood (Tamm et al., 2002; Velanova et al., 2008). This trajectory is consistent with the development of other component processes in the cognitive control system, including WM. Increased efficiency and flexibility of the performance monitoring system therefore may underlie the maturation of the cognitive control system a whole (Luna et al., 2015).

2.3.2.1.2 Functional significance of the ERN

Several theories propose to account for the functional significance of the ERN. The ‘mismatch theory’ proposed the ERN was an error signal from detecting a mismatch between the just-executed response and the estimated correct response (Falkenstein et al., 1991). This theory was subsequently extended to include a reinforcement learning dimension, wherein the mismatch between the erroneous and correct responses would trigger a negative reinforcement signal from the basal ganglia to the ACC via the midbrain dopamine system. This produces a temporary hiatus in dopaminergic neuronal firing inhibiting ACC activity and resulting in the ERN deflection

(Inzlicht & Al Khindi, 2012) which signals behavioural modifications to improve performance (Holroyd & Coles, 2002; Holroyd & Yeung, 2012; Ladouceur et al., 2007). However, neither theory specified what cognitive control processes or mechanisms led to performance enhancements, and somewhat narrowly characterise the ERN as an error detector (Ladouceur et al., 2007; Lo, 2018).

The conflict monitoring theory of the ERN (Botvinick et al., 2004; Carter et al., 1998; Yeung et al., 2004) accounts for more of the ERN findings and extends theorizing on the functioning of the ACC (Gehring et al., 2012). This theory suggests the ERN signals high conflict rather than errors (Yeung et al., 2004). Errors activate competing response representations (correct response, the actual error response) triggering conflict, which prompts ACC signalling for increased engagement of PFC-mediated cognitive control. This is supported by fMRI evidence that ACC error activity directly predicts increased prefrontal cortical activations and performance adjustments on subsequent trials (Kerns et al., 2004; Weinberg et al., 2012). Moreover, on successful high conflict correct trials - e.g. where participants successfully negotiate the conflict in incongruent flanker trials - conflict is also evident in the stimulus-locked ERP, with a larger N2 component on incongruent relative to congruent trials, irrespective of response (Carter & van Veen 2007; Yeung et al., 2004).

2.3.2.1.3 The ERN and affective processing

The ERN is frequently associated with aspects of affective processing (See Dignath et al., 2020 for review), which is consistent with evidence of the integration of cognition and emotion in the cingulate cortex (Shackman et al., 2011). A recently introduced extension to the conflict monitoring theory, 'the affect signalling hypothesis', proposes that conflict detection stimulates a negative emotional reaction resulting in an affect-laden signal which modulates the control adaptation following errors (Dignath et al., 2020), evidenced by the association between the ERN and negative affect (Luu et al., 2000). Larger ERN amplitudes are associated with elevated anxiety, worry, feelings of helplessness, and OCD (Pfabigan et al., 2013; Ruchsow et al., 2005). Between-group comparisons featuring clinically diagnosed or highly trait anxious individuals have larger and more negative ERN amplitudes relative to healthy controls (Meyer, 2017; Meyer & Klein, 2018). The ERN also predicts elevated anxiety in individual difference studies using continuous measures of symptom severity or trait anxiety scores (Moser et al., 2013), although two recent studies did not find evidence that ERN amplitudes were associated with anxious apprehension or anxious arousal (Härpfer et al., 2020) or psychopathology dimensions (Seow et al., 2019, under review) in non-clinical adult populations.

The picture is less clear in children and adolescents because of the complicating factor of neurocognitive development and changes in normative ERN across development (Buzzell et al., 2017; Davies et al., 2004; Tamnes et al., 2013). Furthermore developmental shifts in motivational factors such as peer influence (Blakemore, 2012; Steinberg & Monahan, 2007) and the social context of errors may also fuel developmental differences in the ERN (Barker et al., 2018). Nevertheless, similar to adults, there is evidence that children and adolescents with clinically diagnosed paediatric anxiety (Ladouceur et al., 2006, 2018), social anxiety (Kujawa et al., 2016) and OCD (Hajcak et al., 2008; Santesso et al., 2006) have an elevated ERN relative to healthy controls. Notably, unlike adults, symptom severity does not correlate with ERN amplitudes in clinically anxious children (reviewed in Meyer, 2017 and Moser, 2017). Direct correlations between anxiety measures and the ERN have been found in typically developing children, however the evidence indicates the direction of the relationship between the ERN and anxiety shifts with age (Ip et al., 2019; Meyer, 2017; Moser, 2017) such that elevated anxiety is associated with a smaller ERN in early childhood (Ip et al., 2019; Lo et al., 2018; Meyer et al., 2018), whereas the relationship reverses to resemble the adult-like association in later childhood and adolescence (Ip et al., 2019; Meyer, 2017; Meyer et al., 2018; Santesso & Segalowitz, 2009). This may be because errors become more aversive as children get older triggering greater compensatory control for correction. Young children's fears tend to focus on external stimuli, such as strangers or separation, but as children get older they are also more aware of internally-derived fears such as negative evaluation by self and others and fear of failure (Moser, 2017). This may explain why errors take on a greater significance during development. Gender may also be an important moderator. Ip et al. (2019) explored the effects of age and gender in a group of 4-9 year-olds and replicated the age-related changes described above. However, anxiety was associated with the ERN in girls only, which is consistent with gender effects previously reported in adults (Moser et al., 2016; Moran et al., 2012).

A larger ERN can predict first onset of child and adolescent anxiety longitudinally using logistic regression models (Meyer et al., 2015; Meyer et al., 2018). However in some cases an enlarged ERN has been shown to be protective, with evidence that larger ERNs prospectively predicted lower anxiety and better emotional regulation in a mid-childhood community sample (Lawler et al., 2020) and fewer socioemotional behaviour problems in previously institutionalized children (McDermott et al., 2013; Troller Renfree et al., 2016). Taken together, these heterogeneous findings suggest a complex relationship between the ERN and negative affect during development.

Although the ERN has been regarded as a biomarker for anxiety in adults (Meyer, 2016) and children (Hanna et al., 2020) differential ERN activations are also evident in many other psychological disorders, including depression, schizophrenia, negative affect and substance abuse (Moran et al., 2017; Tamnes et al., 2013). Taking into account widespread comorbidity and symptom overlap in psychological disorders, it appears more likely that aberrant ERN activity represents a trans-diagnostic neurocognitive risk factor for several disorders (Riesel et al., 2019). This proposition was also supported by a recent meta-analysis which found a dissociation between internalising and externalising psychopathology factors such that internalising was associated with an enlarged ERN whilst externalising was linked to a blunted ERN (Pasion & Barbosa, 2019). Some studies however have found the ERN was unrelated to affect variables (Härpfer et al., 2020; Seow et al., 2019) and there are often indirect and more complex relationships between the ERN and clinical outcomes (Lahat et al., 2014; McDermott et al., 2009; Meyer et al., 2018; Moser, 2017).

2.3.2.1.4 Theoretical explanations for role of the ERN in anxiety

Two theories address the links between anxiety and anxious apprehension and the ERN. One proposes that the elevated ERN represents a heightened vigilance and defensive response to errors (Proudfit et al., 2013); namely anxious individuals evaluate errors as especially aversive and are experienced as a form endogenous threat (Weinberg et al., 2016). This theory proposes to explain the age effects on the ERN and anxiety in normative samples as an interaction between anxiety severity and whether anxiety is triggered by internal or external threat (Moser, 2017). As children get older and enter adolescence, changing social norms and expectations mean mistakes take on greater significance leading to increased ERNs, whereas for younger children a smaller ERN may represent poorer cognitive control over biases towards threat and greater exposure to anxiety (Weinberg et al., 2016). Theorists who support the endogenous threat theory suggest that when clinically anxious younger children display an elevated ERN, it suggests they have already acquired a heightened sensitivity to mistakes and experience them as internal threats (Weinberg, 2017).

The further elaboration of the elevated ERN in anxiety, is the compensatory error monitoring hypothesis (CEMH) which was introduced in Chapter 1 and informs the experimental hypotheses in study 1 (Chapter 3). The CEMH can still be reconciled with the ERN as a marker of conflict or error detection, and does not exclude the proposition of the elevated ERN as a reflection of error aversion in anxious individuals (Moser et al., 2013). Indeed, the more aversive an error the greater the motivation to mitigate against them. A meta-analysis of studies examining the elevated ERN in anxiety concluded that the ERN was elevated in individuals with anxious apprehension and worry-related anxiety only, but not phobia or anxious arousal (Moser et al., 2013), leading to a suggestion that an elevated ERN in anxiety represented increased compensatory control processing to counteract the distracting effects of worry on performance, as predicted by ACT. According to ACT (as discussed in Chapter 1), anxious individuals recruit compensatory cognitive control to maintain task performance, albeit with efficiency costs (Berggren & Derakshan, 2013; Shi et al., 2019). ACT predicts that worry competes for limited attentional control resources in WM increasing risk for proactive control failures. This in turn increases the need for engaging reactive control processing to maintain performance accuracy. The notion that the elevated ERN in anxiety reflects compensatory processing is supported by evidence that a larger ERN does not increase task error rates (Moser, 2017; Weinberg et al., 2018; for a review, see Weinberg et al., 2012). Furthermore, whereas performance incentives lead to increased ERNs in healthy controls, the same incentives do not impact performance or ERN amplitudes in anxious individuals, because compensatory control resources are already depleted under standard task conditions (Endrass et al., 2010; Moser, 2017).

The CEMH is primarily helpful in explaining links between the ERN and anxiety in adults (Moser, 2017; Moser et al., 2013). Evidence for changes in the relationship between anxiety and the ERN during over development mean the CEMH does not fully explain the findings (Moser, 2017). Sensitivity-to-endogenous-threat hypotheses propose errors take on greater significance in non-clinically symptomatic older children which augments the ERN alarm signal. However Moser (2017) has reasoned that the interaction between anxiety and poor cognitive control drives the acquisition of compensatory processing strategies to sustain good performance as they develop. This suggests it is possible that the interaction between anxiety and poor control gradually develops into the elevated adult-like ERN by the time they reach late childhood or early adolescence. In conclusion, it is not currently clear that any theory fully accounts for developmental findings on the relationship between the ERN and anxiety, particularly in normal populations, although we can say there is evidence for it to be present by mid adolescence in normative samples.

2.3.2.1.5 CRN

Correct responses also commonly elicit a response-locked-waveform similar in latency, scalp distribution and source localisation to the ERN, but with smaller amplitudes (Falkenstein et al., 2000; Roger et al., 2010). This is referred to as the correct related negativity (CRN) and is thought to reflect cognitive control and similar processes to the ERN. For instance, studies have found an enlarged CRN on high relative to low conflict flanker trials, and amplitude increases when an unexpected trial type is presented (Imhof & Rüsseler, 2019). This suggests that the CRN also reflects signalling from the ACC to the PFC for an increase in attention allocation (Imhof & Rüsseler, 2019; Roger et al., 2010). Some studies suggest the CRN and ERN represent the same processes which is more pronounced on error trials, whilst others indicate either entirely distinct processes or even combined processes from two different aspects of performance monitoring (Endrass et al., 2012; Imhof & Rüsseler, 2019).

2.3.2.1.6 ΔERN.

The ΔERN refers to the voltage differences between the ERN and the CRN and derived by subtracting the CRN from the ERN. This measure is frequently employed in ERN and anxiety literature (Lo, 2018; Meyer et al., 2017). The ΔERN has comparable reliability to the ERN and CRN (Riesel et al., 2013) and evidence from meta-analysis also indicates that the ΔERN is significantly associated with anxiety (Klawohn et al., 2020; Moser et al., 2013). Luck (2014) has recommended the use of subtraction-based difference waves to isolate neural outcomes of interest with greater specificity. The ΔERN is therefore a useful metric because it controls for natural variability between subjects that might be unrelated to error processing per se, enabling discrimination between error processing and general response monitoring processes common to both error and correct trials (Weinberg et al., 2016). Moreover, this may be especially useful in developmental studies because of high between-subject variability in ERP components in children and adolescents (Coch & Gullick, 2011).

2.3.2.1.7 The P(e)

The P(e) is also time-locked to the error response, but appears later than the ERN, peaking 200-400ms after an incorrect response over central parietal scalp sites (Di Gregorio et al., 2018;

Falkenstein et al., 2001; Ullsberger et al., 2010). The P(e) has received less attention than the ERN and consequently less is known about its functional significance (Overbye et al., 2019). The leading proposition is that the P(e) represents the conscious processing of errors (Overbeek et al., 2005). Whilst the ERN occurs even when participants are unaware of errors (Dehaene, 2018; Nieuwenhuis et al., 2001), the P(e) emerges only if there is conscious awareness of mistakes (Endrass et al., 2007; Shalgi et al., 2009). Another feature of the P(e) is it captures the motivational significance of the errors, and as such, the more personally salient or important the error then the larger the P(e) (Overbeek et al., 2005; Matthewson et al., 2005). Frequent errors lead to a reduced P(e) because they are less motivationally significant and indicate less 'concern' about mistakes (Falkenstein et al., 2001). Similar to the ERN, evidence suggests a generator in the ACC, although in more dorsal areas (Herrmann et al., 2004). Numerous studies report that the P(e) matures in late childhood and unlike the ERN most studies suggest there are no age related changes in the P(e) during adolescence (Davies et al., 2004; Overbye et al., 2021).

Findings on the association between the P(e) and psychopathology are varied (Moran et al., 2012). Several studies report the P(e) is not usually associated with anxiety disorders (Endrass et al., 2008; Hajcak et al., 2008; Ladouceur et al., 2006), however others have found P(e) amplitudes negatively associated with depression (Holmes & Pizzagalli, 2010), however an association in a converse direction was found for OCD behaviours in 10 year olds (Santesso et al., 2006). An exception to this found age moderated the relationship between the P(e) and parent reported anxiety, such that a smaller P(e) was associated with higher anxiety, but only in adolescents (mean age 12 years), whereas the P(e) and anxiety were unrelated in the younger group (mean age 9 years) (Meyer et al., 2012).

2.3.2.1.8 Tasks for deriving the ERN and P(e)

Studies using the ERN and P(e) derive the components using tasks where conflict can be manipulated, responses made using a single button press, and there is a clear distinction between correct and incorrect responses. The most widely used tasks are variants of the Go/NoGo, flanker and Stroop tasks (Imburgio et al., 2020; Meyer et al., 2013). Although task variation can impact ERN amplitudes, ERNs generated from each of these tasks are moderately correlated with one another (Meyer et al., 2013). Nevertheless, examinations of psychometric properties in children and adolescents using the Flanker and Go/No Go tasks indicated that whilst both tasks show good test-retest reliability across two years, internal consistency of the ERN was better for the flanker (Meyer et al., 2014) and evidence also favours the flanker task in adults (Riesel et al., 2013). Another benefit of the flanker task is that a reliable and stable signal can be derived from averaging the ERN from as few as 5 trials (Weinberg et al., 2014), although others report a minimum of 6 is preferable (Hajcak & Olvet, 2008). Finally, the strength of the association between the ERN and anxiety is also subject to task variation (Gründler et al., 2009; Meyer et al., 2013; Olvet & Hajcak, 2009) with evidence of greater reliability in the ERN-anxiety relationship reported for the flanker task (Meyer et al., 2013). Together this evidence supports the use of the flanker task for eliciting the ERN and underlies the choice of this task in the ERP experiments reported in the current thesis.

2.3.2.2 <u>N2</u>

The N2 is a negative deflection occurring fronto-centrally approximately 200-350ms after stimulus onset (Yeung et al., 2005), followed by the P3, a positive deflection at central parietal sites around 150ms later (Overbye et al., 2018). The N2 is associated with conflict detection, attention allocation to the stimulus and response inhibition (Donkers & van Boxtel, 2004;

Falkenstein et al., 1999; Ladouceur et al., 2007). It is most frequently measured during flanker, go/no go, and Stroop tasks (Lamm et al., 2012; Lo, 2018; Overbye et al., 2021). Whilst ERN amplitudes reflect effortful processing of the target or relevant-stimulus – e.g. the central arrow in the flanker task - the N2 indexes processing of the distractor stimulus, and hence N2 amplitudes capture the discrepancy between the target and distractor stimulus on correct trials (Yeung & Cohen, 2006). It is theorised therefore that the N2 reflects the degree to which attentional control must be engaged to resolve conflict and produce a correct response in the face of conflicting task stimuli. The larger the conflict or discrepancy, then the larger the N2 (Lo, 2018). It is not clear how the N2 impacts performance measures however, with evidence that a larger N2 is related to both better (Buzzell et al., 2014; Overbye et al., 2021) and poorer performance (Lamm et al., 2012). Evidence from source localisation studies and direct cortical recordings indicate the N2 is generated in the ACC in all age groups (Gratton et al., 2018; Ladouceur et al., 2007; van Veen & Carter, 2002; Yeung & Nieuwenhuis, 2007), consistent with the conflict monitoring hypothesis.

2.3.2.2.1 Development

Research on the development of the N2 is contradictory. Some studies report developmental decreases in N2 amplitudes between childhood and adolescence (Espinet et al., 2012; Lo, 2018) with decreasing N2 amplitudes indexing improved cognitive control (Lamm et al., 2014), in particular improved ability to filter task irrelevant information (Lo, 2018). However others have found a converse effect (Enoki et al., 1993; Ladouceur et al., 2004, 2007) and a recent study with 108 typically developing participants aged 8-18 reported no associations between the N2 and age, although larger N2 amplitudes were associated with better interference control independent of age (Overbye et al., 2021). Conflicting results may reflect diversity in the experimental tasks used to derive the N2 and heterogeneity in study samples. It is also not currently clear how a decrease in the N2 with age is reconciled with associations between a larger N2 and better cognitive control when the wealth of evidence on the development of cognitive control indicate improvements from childhood up until late adolescence (Larsen & Luna, 2018; Luna, 2009; Velanova et al., 2008).

2.3.2.2.2 Affective processing

Similar to the ERN, the N2 is sensitive to emotional context, which is consistent with the involvement of the ACC in processing emotionally and motivationally salient information (Kanske, 2012; Shackman et al., 2011). Inducing negative mood or presenting a threatening or emotion-laden face prior to a conflict stimulus can increase the amplitude of the N2, even under low conflict, in children (Lamm et al., 2012) adolescents (Lewis et al., 2006) and highly anxious adults (Dennis & Chen, 2009). Studies also report that anxiety is associated with increased N2 amplitudes (Hum et al., 2013; Righi et al., 2009; Ruchsow et al., 2008; Sehlmeyer et al., 2010; Wauthia & Rossignol, 2016), although some studies have found a converse effect (Kim et al., 2007). Relative increases in N2 amplitudes in anxious individuals have been interpreted as representing difficulties with inhibiting distracting information and the engagement of compensatory resources to boost performance, whereas decreased N2 amplitudes may reflect more efficient processing, especially under threatening or affective circumstances (Dennis & Chen, 2009; Lo, 2018) and is consistent with predictions of ACT of anxiety (Derakshan & Eynsenck, 2009; Eynsenck & Derakshan, 2011; Moser et al., 2013). Furthermore, Owens et al. (2015) used a modified flanker task to investigate the circumstances under which trait worry was associated with relative increases in compensatory conflict monitoring during a flanker task with emotional distractors. Behavioural performance was poorer under high load, however there were no differences between high and low worriers. Worry-prone individuals exhibited an elevated N2, but this only emerged when executing flanker trials under high cognitive load, indicating that baseline cognitive resources were insufficient and compensatory processing was needed to mitigate the effects of worry under high processing demands. Interestingly, there was no main effect of the valence of emotional distractors on N2 amplitudes, however the load costs (i.e. the increase in N2 amplitudes in high relative to low load) was significantly correlated with two measures of worry.

Interest in the role of attentional control deficits as a risk factor for psychopathology in children and adolescents has motivated research on the interaction between the N2 and temperamental risk factors, and findings are consistent with the idea that heightened N2 amplitudes indicate overactive attentional control. Henderson et al. (2010) explored links between temperamental shyness and social anxiety in 9-13 year old children and found that shyness predicted severity of social anxiety but only for children with an elevated N2 during a high flanker conflict, suggesting excessive control is implicated in mediating the associations between early temperamental risk and subsequent development of an anxiety disorder (Lamm et al., 2014; Lo, 2018; White et al., 2011).

2.3.2.3 The P3

The P3, also elicited on high conflict tasks, is a large positive deflection occurring 350-500 ms after the stimulus onset over central parietal electrodes (Polich, 2007). In contrast to the ERN and N2, it reflects processing in more distributed cortical areas and is linked to control processes involved in attention, inhibition and WM (Buzzell et al., 2014; Polich, 2004), in addition to conscious perception (Dehaene et al., 2003). The P3 captures later and more elaborate stimulus processing and reflects overlapping neural activations associated with early executive attention to the stimulus (Overbye et al., 2018; Segalowitz & Davies, 2004). It has been described as operating at the intersection of stimulus and response processing (Overbye et al., 2018). As the P3 is thought to reflect several underlying processes, some studies subdivide the P3 into two further components. The P3a, with a fronto-central topography, is associated with novelty detection and attentional orienting, whilst the parietal P3b is implicated in executive attention and WM updating (Downes et al., 2017).

2.3.2.3.1 Development

The P3 has been detected early in development and evident in children as young as 5 years, and potentially even in infancy and may reflect similar aspects of cognitive processing to adults (Riggins & Scott, 2020; van Dinteren et al., 2014). However, the developmental trajectory of the P3 remains unclear despite several reviews and meta-analyses (Downes et al., 2017; Riggins & Scott, 2020; Segalowitz et al., 2010; van Dinteren et al., 2014). Inconsistent findings may reflect differing tasks and sensory modalities (Downes et al., 2017; Segalowitz et al., 2010). A meta-analysis of 75 studies of the auditory P3 found that amplitudes increased while latencies decreased over childhood up until late adolescence and early adulthood, followed by stability until older age (van Dinteren et al., 2014). Visual domain studies of the P3 development are scarce (Riggins & Scott, 2020), however collective findings suggest that latencies decrease with age, similar to auditory tasks, whilst the amplitude of a visual P3 may decrease with age during childhood and adolescence (Riggins et al., 2020; Segalowitz et al., 2010). However, one study found divergence in the development of the sub components, which may account for some of the cross-paradigm inconsistencies (Overbye et al., 2018). Whereas a frontal P3 (analogous with the P3a) did not show age-related change, the parietal P3 increased in strength and decreased in latency with age, with increases related to improvements in task performance. Overbye et al. (2018) suggested these findings implied earlier maturation of the stimulus-driven frontal attentional processing aspects of the P3, but more protracted development of the posterior parietal P3b involved in executive attention and WM processing (Downes et al., 2017; Polich, 2007; Segalowitz et al., 2010).

2.3.2.3.2 Affective processing

Relative increases in P3 amplitudes indicate more elaborate processing and voluntary attention to stimuli (Eldar & Bar Haim, 2010; Zhang, De Beuckelaer et al., 2019), and can be sensitive to emotional and threat significance (Jiang et al., 2017; Wauthia & Rossignol, 2016). Some studies show larger P3 amplitudes in response to threat or emotional stimuli relative to neutral (Thomas et al., 2007), whereas others find no effect of valence or emotional arousal (Bechor et al., 2018, Bertsch et al., 2009; Perez Edgar & Fox, 2003). One study found an increased P3 in response to maternal anger cues in abused relative to control children and P3 amplitudes mediated the links between abuse severity and anxiety such that children who displayed larger P3 amplitudes in response to maternal anger reported more severe anxiety if they had suffered high levels of abuse (Shackman et al., 2007). This suggested more elaborate voluntary processing of mother's anger contributed to anxiety in cases of more severe abuse. Some studies find evidence of diminished P3 amplitudes in sub-clinically anxious 10-11 year olds (Éismont et al., 2009) and clinically anxious teenagers relative to controls, indicating poorer top down control of attention in anxious individuals (Bechor et al., 2018). Taken together this shows the P3 is frequently modulated by the emotional salience of the stimulus and can discriminate trait differences in attentional processing in anxious individuals.

2.3.3 **Summary**

I have provided an overview of the ERPs that will be used in the studies discussed in Chapters 3 and 5. I have described relevant properties including morphology, latency and topography and discussed what the literature indicates is the likely neural source of each ERP and the higher order cognitive and information processing in which they most likely to be involved. I have also discussed their development and how fluctuations during development can pose a challenge for how ERPs are interpreted in studies exploring their relationship to affective processing in children and adolescents.

Each of these ERPs play an important role in higher order cognitive control and offer insight into cognitive processing in clinical groups and individuals with trait vulnerability to psychopathology, but also their relevance to affective processing in typically developing and non-vulnerable populations. The ERN and P(e) were used in study 1 (Chapter 3) to explore the impact of cognitive load on conflict monitoring and the extent to which covert compensatory neural processing could predict emotional reactivity as a result of cognitive depletion. All four ERPs were used to examine the neurocognitive impact of WMT on top down cognitive control in the intervention study presented in Chapter 5.

2.3.4 **Methodology for EEG recording in experiment 1 and experiment 2.**

EEG recordings for experiments 1 and 3 followed identical procedures, although different variants of a flanker task were used in these studies. In Experiment 1, the ERN and P(e) were derived from a modified flanker task which is described in detail in the methods section of the corresponding chapter. In Experiment 3, the ERN and P(e) were derived from a standard arrow flanker task whilst the N2 and P3 were extracted from an emotional Stroop task. Tasks are also described in full in the methods sections of their respective chapters and are not discussed further here.

2.3.4.1.1 ERP data acquisition and preprocessing

Continuous EEG activity was recorded during experimental tasks using the ActiveTwo BioSemi system comprised of 64 electrodes inserted on a stretch-lycra cap in accordance with the 10/20 protocol. External electrodes were placed on the left and right mastoids. Electrooculogram (EOG) activity from eye saccades and blinks was recorded at FP1 and 4 external electrodes applied to the skin below each eye pupil and at roughly 1 cm from the outer canthi of both eyes. The Common Mode Sense active electrode and the Drive Right Leg passive electrodes formed the ground during data acquisition. Throughout data acquisition all signals were digitized at 2048Hz using ActiView software (BioSemi) and were later sampled at 512 Hz. Offline analyses were performed in BrainVision Analyzer 2.1 software (BrainProducts, Gilching, Germany). Scalp electrode recordings were re-referenced to the numeric mean of the mastoids and band-pass filtered with cutoffs of 0.1 and 30 Hz (12 dB/octave rolloff). Ocular corrections were conducted with the Gratton et al. (1983) method. In addition, physiological artifacts were identified and rejected using an algorithm built into BrainVision Analyzer 2.1 software. Trials were rejected where i) a voltage step exceeded 50 μV between adjoining sampling points, ii) within-trial voltage differences were in excess of 200 μV or iii) the maximum within-trial voltage was less than 0.5 μV.

ERN, CRN and ∆ERN - To extract that ERN from the Flanker tasks, response-locked data were segmented into epochs beginning 200 ms prior to flanker response onset until 800 ms post response. Baseline correction was based on average activity in the 200 ms window prior to response onset subtracted from each data point following the response. Following the recommendations of Luck (2005), ERPs were characterised using mean area amplitudes. The ERN was quantified as the average amplitude in the 0-100ms post response window across the five fronto-central electrode sites (Fz, F1, FCz, FC1 and Cz). In the training intervention reported in Chapter 5, having inspected the grand averages and observed where the ERN peaked, a narrower time frame of 0-50ms was also used to explore pre to post training changes in the ERN. This is discussed in the corresponding methods section of that chapter. ERPs were extracted for error (ERN) and correct responses (CRN) on flanker trials. The difference wave, ∆ERN, was quantified as the numeric difference in voltage amplitudes between error and correct responses. Statistical analyses were conducted on amplitudes at the electrode site where amplitudes were maximal.

P(e). The P(e) and its post correct response equivalent were quantified as the average amplitude (μV) in the 200-400 ms post-response time window at central parietal electrodes Pz and CPz. The error and correct response-locked waves were baseline corrected to the average of -200 ms prior to the response. Statistical analyses were conducted on the electrode site where P(e) amplitudes were maximal.

N2 and P3. Data pre-processing was as described as above. The N2 and P3 waveforms were time-locked to stimulus presentation on correct trials only in an emotional Stroop task. Stimulus-locked data for correct trials only were segmented into epochs beginning 200 ms prior to stimulus onset until 800 ms post response. The N2 was defined as the average activity in 200 - 300 post stimulus time window at fronto-central electrodes where deflections were maximal. The P3, also with a 200 ms baseline, was defined as the mean area amplitude within the 300-450 ms post stimulus time window at central parietal electrode sites.

2.4 Self-report scales

Psychopathology vulnerability was assessed in these studies using a variety of self-report assessments of anxiety, depression, general internalising symptoms, worry, rumination, perseverative thinking, trait effortful control, school burnout symptoms and negative life events. To avoid repetition, the following section contains descriptions and psychometric properties for all self-report scales.

2.4.1 **Trait anxiety**

Trait anxiety was assessed using the trait anxiety scale of the *State-Trait Anxiety Inventory* (STAI; Spielberger & Gorsuch, 1983). This self-report scale has been used widely in research and clinical settings. Participants respond to 20 items using a 4-point Likert scale. Responses assess the frequency of feelings, how people are "in general" rather than how they feel at this moment in time (e.g. I feel nervous and restless– where response options were [1] almost never, [2] sometimes, [3] often, and [4] almost always). Scores range from 20 to 80, where higher scores indicate higher trait anxiety. Studies have reported the STAI shows good internal consistency, Cronbach's alpha >.86 (De Anda et al., 1997).

2.4.2 **Anxiety, depression and internalising symptoms**

The Revised Child Anxiety and Depression Scales (RCADS, Chorpita et al., 2000) and the shortened version (Ebesutani et al., 2012) are self-report scales assessing anxiety and depression symptomology 8-18 year olds. The long version features 47 items which relate to six discrete subscales; Generalised Anxiety Disorder, Panic Disorder, Obsessive Compulsive Disorder, Separation Anxiety, Social Phobia and Depression. Answers to items are rated on a 4-point Likert scale, ranging from 0 (“never”) to 3 (“always”). It yields scores for each subscale, plus two composite scores - Total Anxiety (sum of the 5 anxiety subscales) and Total Internalising (sum of 5 anxiety plus 1 depression subscales – 6 in total). The subscales and composite scales are considered to have good reliability (Chorpita et al., 2005) and test-retest reliability at one week (Chorpita et al., 2000). There is evidence of good concurrent reliability with the Children’s Depression Inventory and the Revised Children’s Manifest Anxiety Scale (Chorpita et al., 2005). The shortened version of the questionnaire comprises 25 items, with 15 items relating to a broad anxiety scale and 10 items contributing to a Depression scale. Both scales can be combined to yield a total Internalising score. For both the long and short versions, raw scores yield scores standardised by age and gender. Higher scores indicate greater symptom severity. Although not previously validated in a typically developing UK sample, the RCADS is a reliable and valid instrument for measuring internalising symptoms in the general population and school samples in Australia, the Netherlands, Denmark and the US, and in clinical and school samples in Hawaii (Chorpita et al., 2002, 2005, Ebusetani et al., 2012; Kösters et al., 2015; Klaufus et al., 2020). The scales have moderate internal consistency, Cronbach’s alpha α = 0.70 - 0.85 (Klaufus et al., 2020) and good test-retest and convergent validity (Ebusutani et al., 2017).

The Strengths and Difficulties Questionnaire (SDQ; Goodman, 2001) youth self-report version, is a 25-item scale that assesses positive and negative emotional and behavioral characteristics in 11 – 17 year olds. It is comprised of five subscales determined by five contributing items. Subscales assess 1) emotional symptoms, 2) conduct problems 3) hyperactivity and inattention, 4) peer interaction and 5) pro-sociality. Items are responded to on a three-point Likert scale where 0 = not true, 1 = somewhat true, and 2 = certainly true. Subscale scores are calculated by summing the relevant 5 items and reverse scoring where appropriate. Scores range from 0-10, where higher scores on all subscales, bar the prosocial scale, indicate greater difficulties. The SDQ scale is reported to have reasonable psychometric properties with Cronbach's alpha usually $\alpha > .60$ (Muris & Meesters, 2009). Convergent validity is also good (Muris & Meesters, 2009) and test–retest reliability is satisfactory (Muris et al., 2003). The combined emotional and social subscales can be combined for a global 'internalising subscale' and the conduct and hyperactivity subscales can be combined into an 'externalizing subscale', both of which are reported to have good convergent and discriminant validity, particularly in non-clinical settings (Goodman et al., 2010).

2.4.3 **Worry**

The Penn State Worry Questionnaire for Children (PSWQ-C; Chorpita et al., 1997) is a 14-item questionnaire assessing self-reported worry in 7-17 year olds. Responses to each of the items are on a 4-point Likert scale (ranging from 0 = never true, to 3 = always true) and indicate the extent to which item statements about worry apply to respondents usually; for instance "Once I start worrying, I can't stop." Scores range from 0 to 42, with higher scores indicating greater worry. The scale has good internal consistency in both community and clinical samples with Cronbach's alpha $\alpha = .81$-.91 (Chorpita et al., 1997; Muris et al., 2001). The PSWQ child version is also reported to have good test-retest reliability and convergent validity (Chorpita et al., 1997).

Adult worry was assessed with the adult version of the *Penn State Worry Questionnaire* (PSWQ; T. J., Meyer et al., 1990). This 16-item questionnaire characterizes the pervasiveness and severity of worry symptoms and is similar to the child worry questionnaire described above. Reponses are on a Likert scale ranging from 1 ('not typical of me') to 5 ('very typical of me') with higher scores indicating more severe pathological worry. Scores range from 16-80, with higher scores indicating higher worry. The PSWQ has been shown to have good internal consistency in both clinical and non-clinical samples Cronbach's alpha α = .88-.95 (T. J., Meyer et al., 1990). Test-retest reliability and convergent and discriminant validity are also reported to be good. (Topper et al., 2014).

2.4.4 **Rumination and repetitive negative thinking**

The Children's Response Styles Questionnaire (CRSQ; Abela et al., 2004) is based on the adult Response Styles Questionnaire developed by Nolen-Hoeksema to assess patterns of response to depression symptomology (Nolen–Hoeksema & Morrow, 1991). The CSRQ is 25-item self-report scale asking children to indicate how they respond to situations in which they experience sadness or symptoms of depression. Each item corresponds to one of three subscales which represent different styles of responding (i) Ruminative Response subscale, ii) Distracting Response subscale, and (iii) Problem–Solving subscale. Our analyses focussed on Ruminative Response subscale (13 items) as the other two scales do not measure rumination, but rather alternative coping styles for dealing with sadness or depression. Items are responded to on a 4-point scale ranging from 0 to 3, where 0 = almost none of the time, 1 = some of the time, 2 = a lot of the time, 3 = almost all the time. Higher scores indicate higher rumination, with a maximum score of 39 and minimum score of 0. The scale is reported to have moderate internal consistency Cronbach's alpha α =.82, good test retest reliability (Abela et al., 2004; Lo et al., 2017) and convergent validity (Xavier et al., 2016).

Adult rumination was measured via the *Ruminative Response Scale* (RRS: Treynor et al., 2003) a 22- item scale with Likert scale ranging from 1 ('almost never') to 4 ('almost always)'. Items explore how respondents think and act when feeling sad or depressed. The total score ranges from 22 to 88, with higher scores indicating higher rumination. The scale has been shown to have high internal consistency with Cronbach's alpha ranging from α= .88 to .92 (Luminet, 2003), good test-retest reliability and excellent validity (Roelofs et al., 2006).

The Perseverative Thinking questionnaire (PTQ: Ehring et al., 2011) is a trans-diagnostic tool for examining repetitive negative thinking. Suitable for both adults and adolescents, this scale features 15 items that evaluate the central characteristics of repetitive negative thinking (repetitiveness, intrusiveness, and difficulty disengaging). Items are scored on a Likert scale ranging from 0 (never) to 4 (almost always), with higher scores indicating higher levels of repetitive negative thinking. The scale has been reported to have excellent internal consistency in international validation studies with Cronbach's alpha consistently above α= 0.90 (Devynck et al., 2017; Ehring et al., 2012). Validity and reliability are also reported to be good (Ehring et al., 2012).

2.4.5 **Temperamental attentional control**

The Early adolescent temperament questionnaire (EATQ-R; Ellis & Rothbart 2001) assessed self-reported temperamental effortful control. The EATQ-R was developed for assessing reactivity, self-regulation and emotionality in children and adolescents aged 10-15. It is a 65-item scale comprised of 10 subscales, loading onto 4 latent temperament factors Effortful Control, Surgency, Negative Affect and Affiliativeness. Participants respond to each item on a 5-point Likert scale ranging from 1 = almost always untrue to 5 = almost always true (e.g. It is easy for me to really concentrate on homework problems.). For the reverse-scored items, the converse is done. Of interest in study 3 was the Effortful Control factor, comprised of the 'attention control', 'inhibitory control', and 'activation control' subscales. Attention control refers to the ability to selectively shift and focus attention, whereas inhibitory control refers to the ability to quash automatic behaviour that undermine current goals, whilst activation control refers to the ability pursue a task oriented action in the face of innate opposition to it (Vijayakumar et al., 2014). Test-retest reliability of the EATQ-R is good, internal consistency is acceptable (Cronbach's alpha $\alpha >$ .60) and the scale has good convergent validity (Muris & Meesters, 2009).

2.4.6 **Burnout**

*The School burnout inventory (*SBI; Salmela-Aro et al., 2009) is a 9 item questionnaire that assesses self-reported burnout in an academic context in children and youth. The items measure three latent factors that contribute to overall school burnout, i) School exhaustion (4 items) (e.g. I feel overwhelmed by my schoolwork) ii) cynicism regarding the meaning/purpose of school (3 items) school (e.g. I feel lack of motivation in my schoolwork and often think of giving up) and iii) feeling of academic inadequacy (2 items) (e.g., I often have feelings of inadequacy in my schoolwork). Items are rated on a scale from 1 (*completely disagree*) to 6 (*completely agree*). Items can be summed to compute a composite school burnout score where higher scores indicate higher severity of overall school burnout. The school burnout inventory is reported to have adequate internal consistency Cronbach's alpha $\alpha > .60$, test-retest reliability and convergent validity (Koçak & Secer, 2018; May et al., 2020; Salmela-Aro et al., 2009).

2.4.7 **Negative life events**

Adolescent Life Events Questionnaire (ALEQ; Hankin & Abramson, 2002), is a youth self-report questionnaire for measuring a young person's exposure to stressful life events. It consists of 70 items related to negative life events. Participants indicate how often they had been exposed to the event referred to in each item (Never, Rarely, Sometimes, Frequently, Always) in the previous 3 months. For study 3, the scale was adapted to give the participants a binary choice from a) Yes, this has happened to me in the past 3 months or b) No, this has not happened to me in the past 3 months. Total numbers of events were summed for each of the four categories, with higher scores indicating greater exposure to stressful life events in that domain. A composite score was also computed which was the total sum of stressor exposure across all four domains.

CHAPTER 3

3 Study 1: Investigating the differential effects of age and WM load on the Error Related Negativity (ERN) and emotional reactivity following a worry induction. A behavioural and ERP study.

3.1 Chapter overview.

This Chapter describes a behavioural and ERP investigation into hypothesized hidden costs of compensatory effort on cognitive vulnerability to emotional disorder in adolescents and adults. The overarching aim of this study was to shed light on a potential neural and cognitive mechanism that could form a target of therapeutic action in attentional control training. The study explored if mental fatigue after a challenging cognitive task would increase susceptibility to negative thought intrusions and to what extent this was predicted by a neural index of compensatory effort, the ERN during the preceding task (Moser et al., 2013). Mental effort research suggests cognitive control decreases following periods of cognitive exertion (Baumeister et al., 2018; Dang, 2021; Schmeichel, 2007). It is unknown if individual differences in compensatory effort impact post-exertion cognitive control and subsequent intrusive thoughts. We hypothesized that working memory load (WML) would increase compensation costs, exaggerating emotional reactivity leading to impaired control over intrusive negative thoughts. We investigated effects of WML and age on the ΔERN, and emotional reactivity following a worry induction, and predicted larger ΔERNs commensurate with WML, but age-related differences in magnitude. We also predicted increased ΔERNs would drive emotional reactivity, namely increased negative thought intrusion post induction. Continuous EEG was recorded whilst adolescents and adults performed a flanker task under low or high WML. Half the blocks were standard arrow flanker trials and the remainder featured flankers interleaved with a WM task that was either easy (Low WML) or difficult (High

WML). Figure 3.2 shows the task design. The addition of dual task blocks was to augment cognitive fatigue for everyone, however to manipulate levels of fatigue between-groups, WM load in the WM component of the dual flanker task varied between high and low. This task was followed immediately by a breathing focus exercise during which thought intrusions were recorded before and after a worry induction.

Age, but not WML, impacted ΔERN magnitude, with adolescents displaying blunted dual-task ΔERN relative to baseline, whilst adult ΔERNs were similar across blocks. Although emotional reactivity due to the worry induction was unaffected by Age or WML, baseline ΔERN predicted emotional reactivity, but with developmental differences. A larger adult ΔERN significantly predicted increases in negative thought intrusions, whereas the association's direction was reversed in adolescents. In addition, a larger adolescent ΔERN significantly predicted lower school burnout and smaller worry increases in adolescents 18 months later, indicating a possible protective role for enlarged ΔERNs. These results support the CEMH of the ΔERN (Moser et al., 2013), and could highlight a mechanism explaining links between the ERN and emotional vulnerability which may differ across development. The possible implications of the findings for understanding causal mechanisms in emotional vulnerability, particularly during development, are discussed.

3.2 Introduction.

3.2.1 Bidirectional links between cognitive control and emotional vulnerability

The links between attention or cognitive control and vulnerability to psychopathology are complex and evidence points to bidirectional influences (Derakshan, 2020; Koster et al., 2017; Moran, 2016). Poor attentional control at one time can predict future psychopathology (Kertz et al., 2016), but there is also evidence that those who suffer from psychological disorders such as anxiety and depression experience significant cognitive and EF deficits (Joorman & Gotlib, 2010; Keller et al., 2019; Miyake & Hankin, 2015; Snyder et al., 2015; White et al., 2017). Mechanisms underlying bidirectional influences are poorly understood. The current study delineates a novel research question and addresses the hypothesis that inefficient cognitive control and concurrent compensatory neural effort known to be increased in worry and anxiety may have hidden costs following periods of sustained attentional effort or focus. The study was theoretically motivated by an integration of predictions from ACT (ACT; Eysenck et al., 2009), the resource model of control (Baumeister et al., 1998) and CEMH of the ERN (Moser et al., 2013). The hypothesized costs were subsequent control failures due to depleted cognitive resources leading ultimately to increased worry proliferation. This was addressed in a comparative study with adolescents and adults to examine this hypothesis from a developmental perspective.

3.2.2 Compensatory neural processing

Research has indicated that psychopathology is frequently associated with differential brain function and structure in neural networks associated with cognitive control (Besteher et al., 2017; Huchuan et al., 2018; McTeague et al., 2017; Shanmugan et al., 2016; Xia et al., 2018). One characteristic of differential neural functioning is hyperactivity and evidence of compensatory neural activation in executive function regions (Fales et al., 2008; Shanmugan et al., 2016). For example, in a large community sample of adolescents, Shanmugan et al. (2016) measured psychopathology via a structured diagnostic interview and categorized symptoms across orthogonal clinical dimensions using factor analysis. They derived a general psychopathology factor, plus four distinct categories of symptom representing 1) mood and anxiety symptoms, 2) psychosis-spectrum symptoms, 3) behavioral symptoms (conduct and ADHD), and 3) fear symptoms (phobia). The study found that a general psychopathology factor was associated with hypo-activation of executive control areas generally, however specific to the mood and anxiety dimension, there was hyper-activation across multiple executive control areas including the ACC, DLPFC and parietal cortices. Hyperactive fMRI activation in fronto-parietal, cingulo-opercular and ventral attention networks during cognitive control tasks has also been associated with individuals high in trait and clinical anxiety relative to controls in several other studies (Basten et al., 2011; 2012; Fales et al., 2008; Sylvester et al., 2012), and also in depressed relative to healthy individuals (Schöning et al., 2019). Similarly, patterns of hyper-activation in anxiety are also evident in EEG research examining event related potentials (ERP) associated with cognitive control (Ansari & Derakshan, 2011; see Berggren & Derakshan, 2013 for a review).

Neurocognitive studies indicate conflicting relationships between anxiety and attentional control. There is evidence that anxiety is associated with decreased prefrontal control over the bottom-up, stimulus-driven attention system (Bishop, 2007; 2009). However anxiety is also associated with increased activation in DLPFC during tasks tapping inhibitory control (Basten et al., 2011) and the central executive of WM (Basten et al., 2012) suggesting the possibility of decreased efficiency of attentional control processes. The Dual Modes of Control framework of cognitive control (DMC: Braver, 2012) can reconcile these apparently conflicting findings suggesting that anxiety is associated with decreased proactive cognitive control, which is more effortful and anticipatory, alongside increased reactive control which acts as a just-in-time corrective control function (Fales et al., 2008; Moser et al., 2013). This is consistent with Fales et al. (2008) who found differences in anxiety lay in the temporal dynamics of activation in the executive system. Compared to low anxiety, higher anxiety was associated with decreased sustained activity in the DLPFC alongside increased transitory activity in that region which reflected a bias towards reactive control to mitigate decrements in proactive control. Taken together, evidence suggests hyper-activation in executive brain regions appears to reflect compensatory cognitive control mechanisms in anxiety.

3.2.3 **Processing efficiency**

Although anxiety is frequently associated with difficulties in concentration, anxiety severity is not necessarily associated with poorer performance (Berggren & Derakshan, 2013). The processing efficiency and attentional control theories of anxiety can clarify seemingly discrepant effects of anxiety on cognitive performance (Derakshan & Eysenck, 2009; Eysenck & Calvo, 1992; Eysenck et al., 2007; Eysenck & Derakshan, 2011). They propose that perseverative worrisome thoughts occupy WM capacity and reduce the availability of cognitive control resources to inhibit the processing of irrelevant distractors, thus undermining task performance (Eysenck & Derakshan, 2011). As highlighted earlier in this thesis, there is a crucial distinction between performance effectiveness and performance efficiency. Anxiety may not always impair performance outcome (e.g. task accuracy) however the cost of task effectiveness in anxious individuals is frequently a loss of processing efficiency which may indicate a reliance on compensatory processing to meet task goals (Berggren & Derakshan, 2013). There is indirect behavioural evidence for this in studies where anxious people perform just as accurately as non-anxious or low anxious participants, yet differences emerge in terms of longer reaction times, task duration and self-perceived effort in a range of tasks engaging attentional control (Derakshan et al., 2009; Eysenck & Derakshan, 2011; Hepsomali et al., 2019).

Compensatory effort and processing efficiency has not been widely studied in developmental populations; however limited research mirrors some of the adult findings (Hadwin et al., 2005; Ng & Lee, 2010; Visu-Petra et al., 2010). For instance, high and low anxious 9-10 year-olds achieved similar accuracy in WM tasks, but individuals high anxiety were slower to respond on a backwards digit span task and reported greater subjective effort on a forward digit span task (Hadwin et al., 2005). Similarly, in a task measuring inhibitory control in the face of incongruent distractors, Kujawa et al. (2016) found clinically anxious 8-26 year-olds showed no differences in accuracy on a flanker task, but had significantly slower reaction times relative to controls. Similar to adults, some studies have found anxiety in adolescents is associated with longer anti-saccade latencies, alongside similar task accuracy to controls. Crucially these differences were detected during under reward and punishment, but not neutral, conditions indicating an important interaction with motivation systems in adolescents (Hardin et al., 2007; Jazbec et al., 2005).

3.2.4 The resource model of control and the cost of increased mental effort

Compensatory control mechanisms can be adaptive, if they facilitate effective performance. However, processing inefficiency implies comparatively greater effort to achieve comparable performance accuracy, but this extra effort could have maladaptive repercussions.

Research on mental fatigue has indicated that periods of prolonged cognitive exertion can deplete subsequent cognitive control (Baumeister et al., 2018; Boksem & Tops, 2008; Dang, 2021; Grillon et al., 2015). Schmeichel (2007) conducted several experiments demonstrating that initial cognitive control efforts impaired subsequent control in a variety of effortful tasks, including WM span and control of visual attention. Lorist et al. (2005) found cognitive depletion was associated with impaired performance monitoring, whilst evidence from Van der Linden et al. (2003) found fatigued participants had difficulty with sustained attention, planning and cognitive flexibility (reviewed in Boksem & Tops, 2008). Even temporary failures in cognitive control could undermine emotional regulation (Grillon et al., 2015; Hoffman et al., 2012), however there is an absence of work directly testing this (Hoffman et al., 2012).

Currently, the only study to explore directly the effect of differential mental fatigue on vulnerability to psychopathology was performed by Grillon et al. (2015) who examined fatigue and emotional regulation in adults using a physiological correlate of emotional regulation, the startleblink response, a defensive physiological response which is typically augmented during negative affective states (Lang et al., 1990; Pinkney et al., 2014). All participants took part in two experimental sessions each separated by 3 weeks (a depletion or control session). During the experimental sessions participants first performed an easy or an effortful cognitive depletion task. Afterwards they viewed negative emotional images and had to either down-regulate a spontaneous emotional response or allow it to unfold naturally. Startleblink responses to each condition were compared within participants. The startleblink response during negative images did not differ between the Fatigue and Control condition if participants were not instructed to downregulate their emotional response to the images. However significant differences between the control and the fatigue condition emerged when participants were instructed to engage control and downregulate their emotional response. The fatigue condition startle-blink remained elevated, whereas it decreased in the control condition, suggesting fewer control resources were available for successful emotion down regulation in the fatigue condition. The study was small and exploratory, did not control for anxiety, and the startle blink response serves as only a very indirect measure of emotional regulation and top down control. Nonetheless it has important implications for how a temporary hiatus in cognitive control can interfere with emotional regulation.

Exploring the potential costs of compensatory effort during cognitive processing may be important for understanding how processing inefficiency might exacerbate existing anxiety and increase risk of psychological burnout and depression. Furthermore, it may shed light on how such mechanisms might amplify adolescent vulnerably to anxiety and psychopathology. Whilst adolescents demonstrate adult-like abilities in inhibitory control and WM by early adolescence, they are less able to sustain consistent performance (Luna et al., 2010; Velanova et al., 2009). fMRI studies have shown age-related changes in prefrontal activation commensurate with improved cognitive control which are thought to reflect gains in overall efficiency (Geier et al., 2009; Luna et al., 2010; Scherf et al., 2006; Tamm, et al., 2002; Velanova et al., 2008). In this respect, adolescents relying on inefficient cognitive control processing relative to adults (Luna et al., 2010; Larsen & Luna, 2019) could be prone to greater cognitive depletion and emotional regulation impairment after periods of prolonged high load demands.

3.2.5 **The current study**

The aim of the current study was to explore i) if high relative to low WML impositions during a cognitive task would reduce subsequent ability to manage negative thought intrusions triggered by a worry induction due to differences in mental fatigue, ii) how depletion effects relate to a neural correlate of processing inefficiency, iii) developmental differences, iv) if the neural correlate of processing efficiency would predict psychological wellbeing 18 months later.

Working memory load was manipulated during a lengthy and attention-demanding dual task (adapted from Moran & Moser, 2012 and reported in Moser et al., 2013; see also Lavie & Defockert, 2005). Subsequent failures in cognitive control over endogenous emotional distractors was measured before and after a worry induction exercise. We employed a novel approach in which compensatory effort was assessed using the ERN as a proxy measure. As outlined in the methods chapter (Chapter 2), the ERN is negative deflection of the EEG waveform that peaks within the first 100 ms of an erroneous response and is typically detected at fronto central scalp positions (Falkenstein et al., 1999; Gehring et al., 1993). This ERP was selected because of its utility as an indicator of reactive cognitive control and known to be elevated in anxiety (Hajcak et al., 2003; Meyer, 2017; Moser at al., 2013; Olvet & Hajcak, 2008; Tamnes et al., 2013), in addition to its sensitivity to WML (Moser et al., 2013). As outlined in Chapters 1 and 2, an influential proposition to explain the links between anxiety and the ERN is that the enlarged ERN represents individual differences in cognitive control and compensatory processing to mitigate the distracting effects of anxious apprehension, worry and rumination on task performance (Moser, 2017; Moser et al., 2013; Zambrano-Vazquez et al., 2014; but see Proudfit et al., 2013 and Chapter 2 for an alternative view). In this context, the ERN was used to quantify processing efficiency and compensatory processing during the experimental task.

Intrusive thoughts and worry induction

According to Hirsch and Matthew's (2012) cognitive model of pathological worry, attentional control deficits represent a central cognitive component contributing to generalized anxiety disorders in adults, although a lack of high quality studies to date prevents strong conclusions about the role of attentional control in pathological worry during development (Songco et al., 2020). Anxiety and depression may persist, reoccur or escalate from subclinical to clinically problematic in part as a result of difficulty controlling proliferations of negative self-relevant thoughts, perpetuating a vicious cycle of rumination and worry (Allsopp & Williams, 1996; Borkovec et al., 1983; DeRaedt et al., 2015; Hirsch & Matthews, 2012; Hirsch et al., 2015; Joorman & Gotlib, 2010). Alterations in attentional control resulting from cognitive depletion and exacerbated by poor efficiency could temporarily reduce availability of attentional control resources to control negative thought intrusions. To investigate this further we examined how cognitive effort was associated with the ability to suppress everyday negative intrusive thoughts. Previous studies have used a worry induction procedure to demonstrate causal links between better attentional control and a reduction in everyday negative thought intrusions (Fox et al., 2015, Grol et al., 2018). No studies have examined possible transient effects of cognitive effort on the ability to suppress subsequent persistent negative thought intrusions following a worry induction exercise. Addressing this question would provide an important contribution to cognitive theories of vulnerability to emotional disorder in adults and adolescents.

Manipulating cognitive depletion

We recorded EEG during an hour-long experimental task which made demands on inhibitory control and WM. We manipulated cognitive depletion by varying WML during the task. Working memory load has been shown to have differential effects on cognitive depletion (Hofmann et al., 2012; Lavie et al., 2004) with higher WM load associated with greater subsequent depletion (Schmeichel, 2007). Immediately after EEG recording we measured the number and valence of unsolicited thought intrusions during a breathing focus task both before and after a procedure that induced personally significant worries. This task was adapted from Hirsch et al. (2009) and similar to Grol et al. (2018) who used this task to examine the effects of WMT on emotional reactivity.

Predicting future wellbeing and adolescent burnout

Another related factor in mental fatigue research is an association between situational cognitive control demands, control deficits and psychological burnout (Golonka et al., 2017; Linden et al., 2005; Schaufeli & Enzmann, 1998; Sokka et al., 2017). Studies have shown that greater self-regulatory demand at work increases burnout risk (Maslach & Jackson, 1981, 1986), especially where baseline executive control is low (Schmidt et al., 2007). In one study adults with non-clinical burnout reported impaired central executive functions of WM relative to healthy controls (van Dijk et al., 2020). Moreover, an association between an elevated ERN and burnout was found in two studies indicating an important role for compensatory cognitive control processes in adult burnout (Gajewski et al., 2017; Golonka et al., 2017), although these studies were cross sectional and did not test causal connections between the ERN and burnout. Nevertheless, these studies suggest that processing inefficiency and compensatory effort could increase risk for burnout, although longitudinal research is needed to assess if the ERN has causal influence on the development of burnout over time.

Research on cognitive fatigue and burnout in adolescents in limited. An adolescent-specific risk factor for emotional vulnerability is school-related stress and burnout (Salmela-Aro et al., 2009; Walburg, 2014), both of which could be exacerbated by processing inefficiency in anxious teenagers or those with control deficits. In fact, for many adolescents the academic and socio-emotional challenges of school represent a highly significant stressor (Anniko et al., 2019;

Lin & Yusoff, 2013). Consistent with exploring the hypothesis that compensatory processing may have hidden emotional costs, and in light of evidence from the adults, an additional aim of the current investigation was examine if the ERN would also predict vulnerability to current and future adolescent school burnout.

Participants completed a number of self-report scales to measure anxiety, depression, worry, perseverative thinking and school burnout. Participants were assessed approximately 18 months later by repeating self-reports on anxiety, depression and burnout. A self-report measure of negative life events permitted controlling for adverse experiences prior to follow-up. We hypothesized that both a larger ERN and greater emotional reactivity in the worry induction exercise would be associated with psychopathology vulnerability measures at follow up.

Hypotheses

In addition to predictions for burnout and emotional vulnerability at follow up, we hypothesized that higher WML leading to increased fatigue would impact ERN amplitudes, exaggerating emotional reactivity and increasing negative intrusions following the worry induction. We also hypothesised that differences in the magnitude of the ERN during the depletion task would be associated with negative reactivity, namely the increase in negative thought intrusions following the worry induction. To investigate developmental trajectories, we examined these effects separately for adults and adolescents, expecting that developmental limitations in cognitive control would render adolescents more prone to thought intrusions at baseline, and subject to greater reactivity due to the worry induction. As attentional control and processing efficiency theories have not been as comprehensively tested during adolescence as in adulthood, we did not make specific directional predictions for the adolescent group regarding the association between the ERN and emotional reactivity, however expected a larger ERN would be associated with greater negative reactivity in adults.

3.3 Methods

3.3.1 **Participants**

A total of n=79 participants took part in the study. Participants were 11-16 year old girls (*M* = 13.88 years, *SD* = 1.60) recruited through convenience sampling via flyers distributed on social media and in schools in London and SE England (n = 40). Women aged 21-45 (*M* = 26.68 years, *SD* = 6.68) were recruited via social media and from the student population at Birkbeck College and University College London. All were paid £25 for participation. Exclusion criteria were a current clinical diagnosis of anxiety and/or depression, ADHD or Autism Spectrum Disorder. All participants were right handed and had normal or corrected-to-normal vision. Those aged 16 and above gave written, informed consent in accordance with procedures approved by the ethics committees of the School of Psychological Sciences, Birkbeck College, University of London and the ESRC. Participants <16 years provided written informed consent, once parents/guardians had provided the same.

3.3.2 **Stimuli and procedures**

3.3.2.1 Working memory assessment

Working memory capacity was assessed using the shortened Operation Span (OSPAN) task developed by Foster et al. (2015) and presented in EPrime software. Participants memorised sequences of letters whilst also performing a distractor maths task. Letters are presented sequentially on a computer monitor. Between letter presentations, participants solve a simple equation and respond to a proposed solution by clicking ‘true’ or ‘false’. The alternating maths –

letter sequence ranges from 3 to 7 repetitions per trial, with unpredictable trial length. Participants retain each letter in the sequence in mind and at the end of sequence presentation recall each letter in order. To ensure validity of the distractor, participants had to attain ≥85% accuracy in the maths task. The experimenter explained the task verbally and the participants followed onscreen instruction to the practice trials. Scores were the sum of the letters accurately remembered in correct order, also known as the partial OSPAN score (Foster et al., 2015). The task was performed on a Dell latitude laptop with a 38 x 24cm monitor using built-in keyboard and mousepad.

Working memory capacity at follow-up was assessed using a Backwards Digit Span task (Massonnié, 2019) which was administered and hosted in Gorilla Experiment Builder (www.gorilla.sc). Participants were presented with lists of digits onscreen. They memorised and recalled the digits in reverse order by clicking the onscreen number pad. Following two practice trials, five lists of two digits were presented. Participants had to perform correct responses to these digits on at least four trials before graduating to the next level, where three digits would be presented. This procedure was repeated until participants reached maximum level – namely the sequence size at which they no longer met the target of four consecutive correct trials. The total number of correct answers and the level reached by the participant was recorded.

3.3.2.2 Self-report scales

The participants completed several self-report scales to measure dimensions of psychopathology vulnerability. Specifically, the scales measured trait anxiety, worry, rumination, perseverative thinking, anxiety and depression symptoms, and stressful life events. The measures are listed briefly below, but are described in detail in Chapter 2.

- Trait anxiety in all participants was assessed using the trait anxiety scale of the *State-Trait Anxiety Inventory* (STAI; Spielberger & Gorsuch, 1983).
- Adolescent anxiety and depression symptoms were assessed using the shortened version of-*The Revised Child Anxiety and Depression Scales* (RCADS, Ebesutani et al., 2017).
- Worry was assessed with *The Penn State Worry Questionnaire for Children* (PSWQ-C; Chorpita, et al., 1997) and the adult version, the *Penn State Worry Questionnaire* (PSWQ; Meyer et al., 1990).
- Adolescent and adult rumination was measured with *The Children's Response Styles Questionnaire* (CRSQ; Abela et al., 2004) and the *Ruminative Response Scale* (Treynor et al., 2003) respectively.
- Persistent negative thinking was assessed in both age groups with T*he Perseverative thinking questionnaire* (Ehring et al., 2011).
- *The School burnout inventory (*SBI; Salmela-Aro et al., 2009) assessed adolescent burnout.
- In the follow-up data collection only, adolescents responded to the *Adolescent Life Events Questionnaire* (ALEQ; Hankin & Abramson, 2002). This measure was used to control for stressful and adverse experiences in the 3 months prior to follow up.

With the exception of the ALEQ, participants responded to all other scales at the time of the experiment and also approximately 16-19 months after initial measurement. See Figure 3.1 for chart showing scales completed at each assessment.

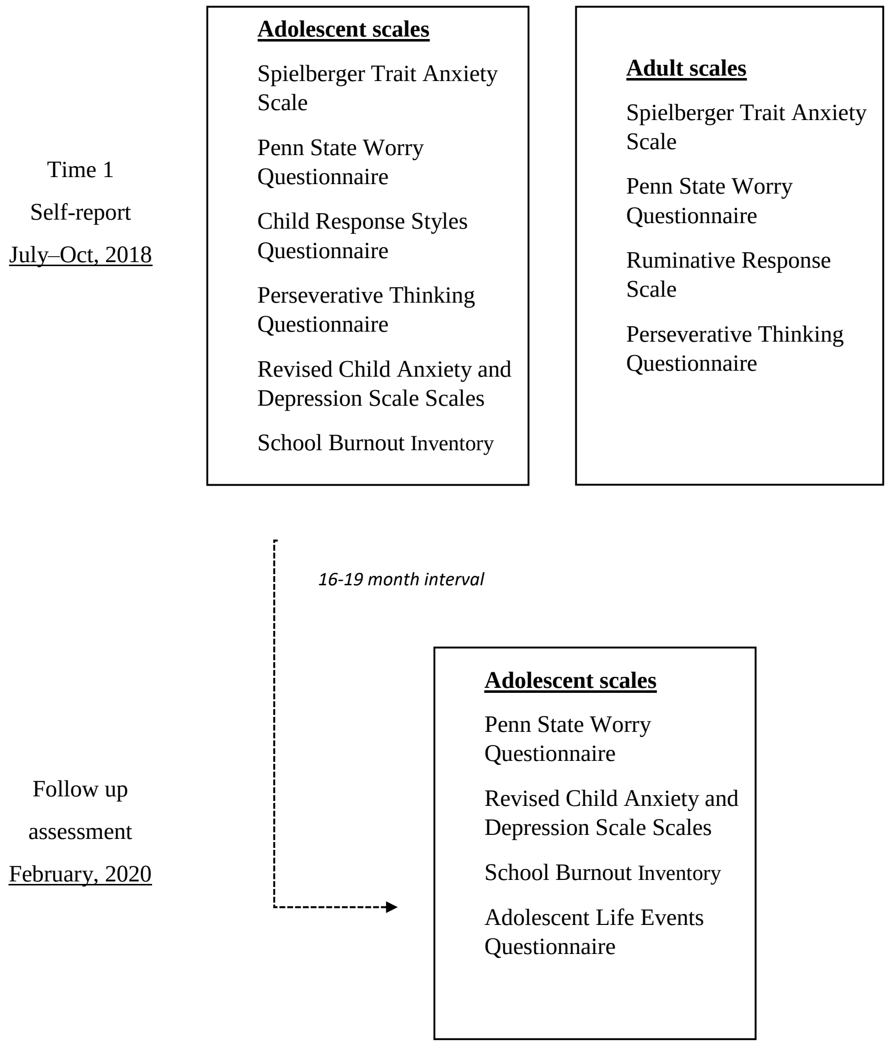


Figure 3.1 Overview of self-report scales administered at the first and follow up assessments. Note. Adults did not complete follow up assessments because the assessment period coincided with the early phases of the first wave of the 2020 pandemic

3.3.2.3 Flanker task and EEG recording procedures

3.3.2.3.1 Flanker task

EEG was recorded while participants performed a flanker task featuring 12 blocks (48 trials per block). The experimental task was comprised of two block types: Block type A which featured Simple flanker trials (Figure 3.4) and Block type B featuring Dual Working Memory (WM) flanker trials (Figure 3.5). This task was an adaptation of a standard arrow Flanker task (Eriksen & Eriksen, 1974), with the dual task element adapted from Moran and Moser (2012) and reported in Moser et al. (2013). Simple Flanker and Dual WM Flanker blocks alternated across the experiment, starting with a Dual WM Flanker block. There were six blocks of each type. The total task duration was approximately 60 - 70 minutes, including practice blocks. Figure 3.2 and Figure 3.3 provide comprehensive visualization of experiment design and block structure. For Simple and Dual trial procedures see Figure 3.5.

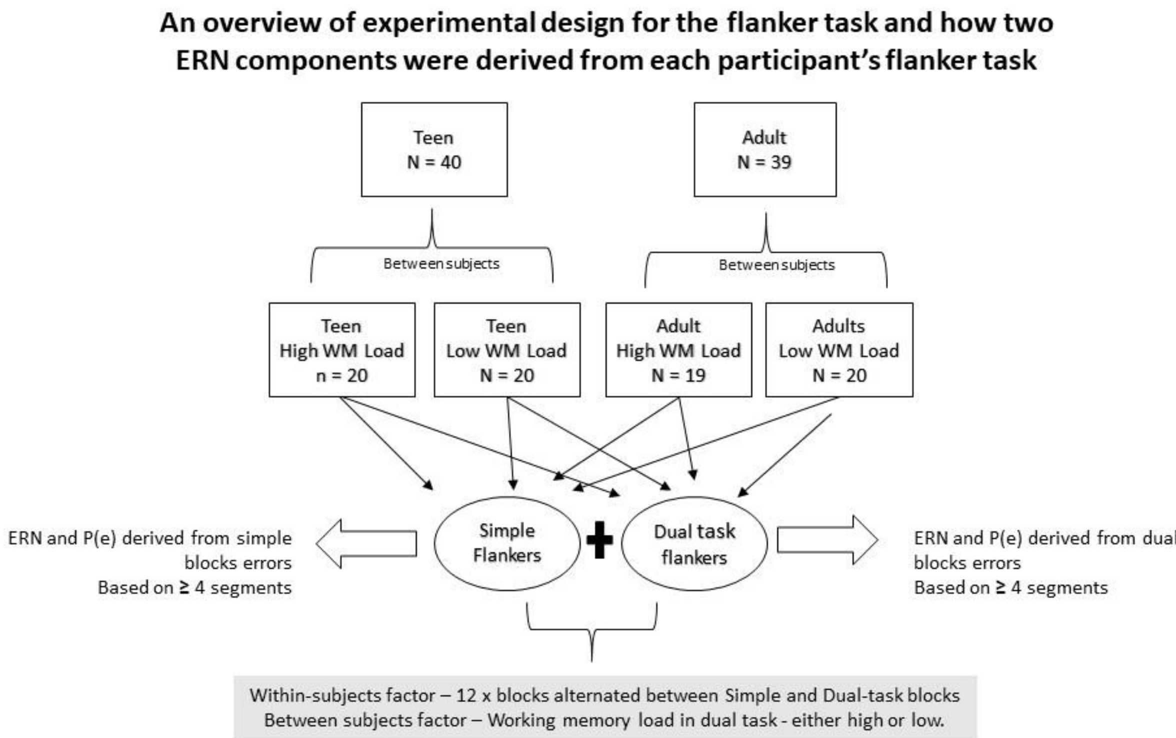


Figure 3.2. Overview of flanker task experimental design.

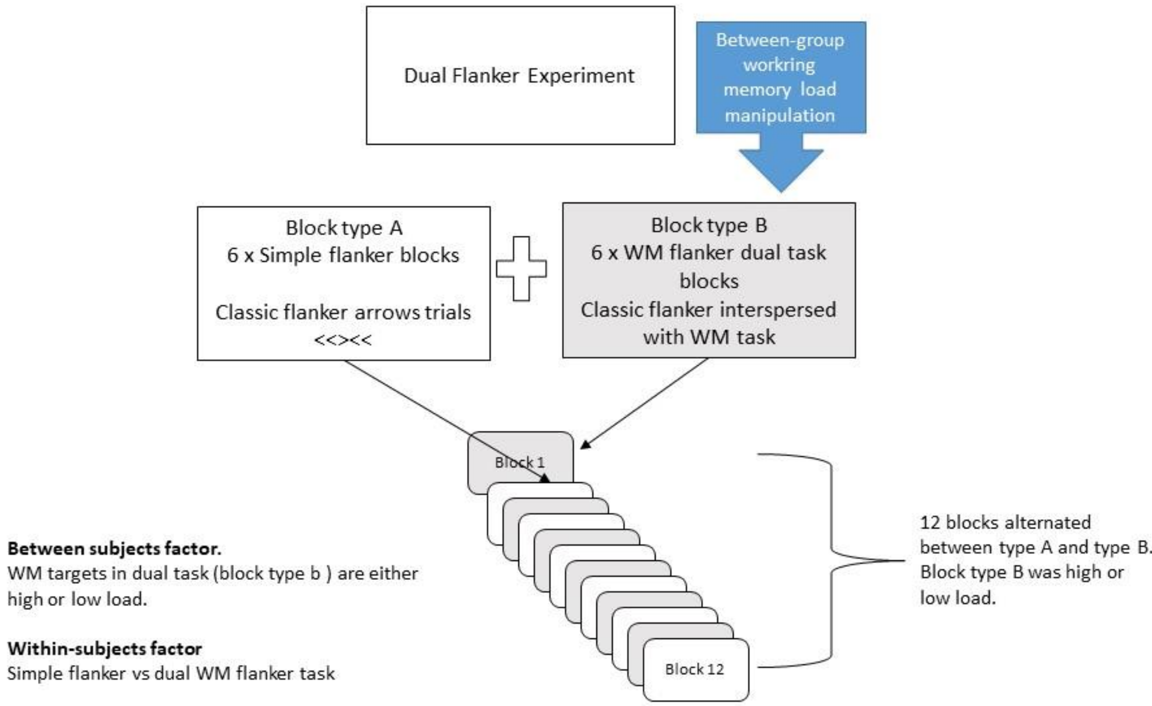


Figure 3.3 Overview of the structure of the flanker task experiment during which EEG was recorded.

3.3.2.3.1.1 Simple flanker – block type ‘A’

Participants saw a set of 5 arrows, horizontally oriented in the center of the screen e.g. < < > < <. Characters were displayed in white font on a black background. Pairs of distractor arrows were presented on either side of the central arrow and oriented in the same (congruent) or opposite (incongruent) direction. Participants indicated whether the central arrow pointed to the left or to the right, with responses made on the computer keyboard, ‘n’ for left and ‘m’ for right. Before each flanker presentation a fixation cross was presented during an inter-trial interval of variable duration (exposure times shown in Figure 3.4).

Block type A - Example of a simple flanker trial sequence

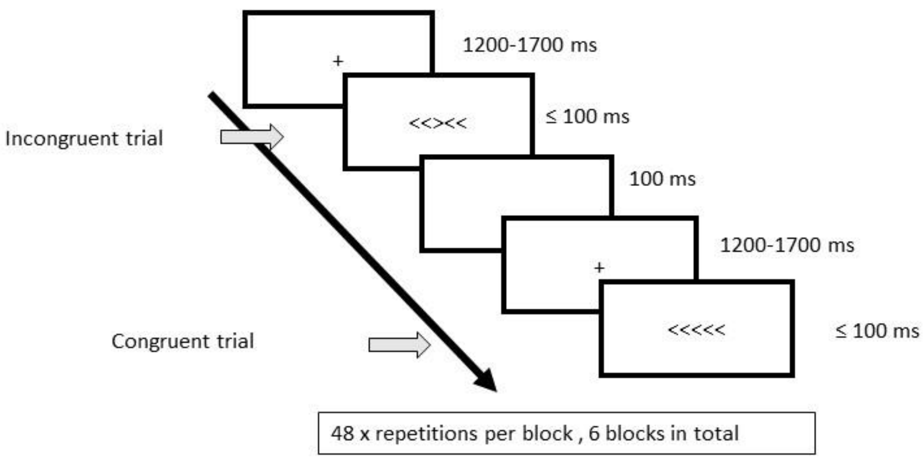


Figure 3.4 Example of trials that were presented in the Simple flanker blocks.

3.3.2.3.1.2 Dual Working Memory flanker – blocks type 'B'

These blocks featured flanker trials (as described above) interwoven with a digit sequence recall task. Prior to each flanker trial, participants saw a string of 5 digits (digits ranged from 1-9), and had to retain digit identity and sequence during the flanker trial. Trial stimuli and fixation exposure times are shown in Figure 3.5. Immediately after responding to a flanker, a randomly selected digit from the previous sequence (WM probe) appeared in the centre of the screen. Participants had to indicate the number that followed it in the earlier digit string. Responses were made on the number pad on the right side of the keyboard. There were two conditions; a high WML condition, where digits were in random order (e.g. 84397) and a low WML condition, where to-be-remembered digits strings were in sequential ascending or descending order (e.g. 54321, or 12345). The task was a between-subjects design, so participants did either a high or low load version of this task.

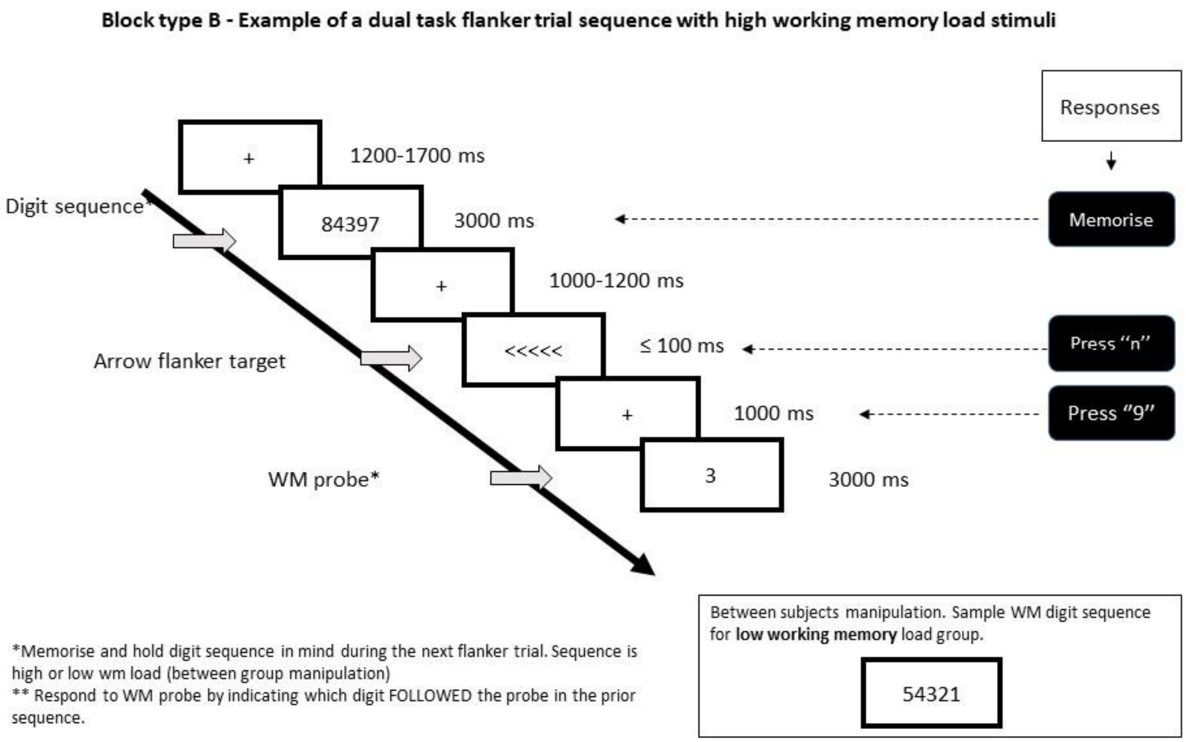


Figure 3.5 Example of dual task trial in Dual WM flanker blocks

3.3.2.3.2 EEG recording, processing and analysis

EEG recording and pre-processing followed the procedures outlined in full in Chapter 2. Participants were instructed to respond as quickly and as accurately as possible during the flanker trials with equal importance given to speed and accuracy. Participants were also instructed to avoid blinking or excessive movement during trial blocks, and encouraged to take brief breaks between blocks to rest eyes.

Epoch segmentation

Two sets of ERP components were produced for each participant, each time-locked to response errors during Simple flanker and Dual WM flanker blocks respectively. The following components were extracted - ERN, CRN, ΔERN and the P(e), each of which have been described in Chapter 2. Data were first segmented according to whether responses belonged to Simple Flanker blocks or to Dual flanker blocks. Response-locked data were then segmented into epochs of 1000 ms duration, commencing 200 ms before response onset and 800 ms post response. Simple flanker and Dual flanker blocks were analysed separately, and a set of ERPs extracted for each block type. ERPs were extracted where there were ≥ 4 error segments (per block type) surviving correction, and where performance accuracy on the flanker was at least 55%.

Analysis of variance (ANOVA) analyses were subsequently performed on data from the electrode sites where the ERN and P(e) voltages were maximal. In the 0-100ms post response window, the ERN was similarly maximal at FCz and Fz in the current study. We therefore calculated a pooled average across these two electrodes. Regression analyses utilized the ΔERN (i.e., the ERN - CRN = ΔERN) which has been reported to be more sensitive to neural responses to pure errors and distinguishes between general response monitoring processes common to both error and correct trials reflected in the CRN (Simons, 2010; Weinberg et al., 2016). The P(e) and its post correct response equivalent were quantified as the average amplitude (uV) in the 200-400 ms post-response time window at central parietal electrodes Pz and CPz. Statistical analyses were conducted on CPz amplitudes where P(e) was maximal.

3.3.2.4 Worry Induction/thought intrusion task

Immediately after flanker task completion participants performed the breathing focus exercise with the worry induction. This task was adapted from the Worry Task (Grol et al., 2018; Hirsch et al., 2008, 2013) and similar to Borkovec et al. (1983) and Fox et al. (2015). The worry induction component of the task was validated for adolescents by Frala et al. (2014) which found the induction procedure was effective for increasing future-oriented thoughts and elevating generalized negative affect in adolescents aged 12-17 years.

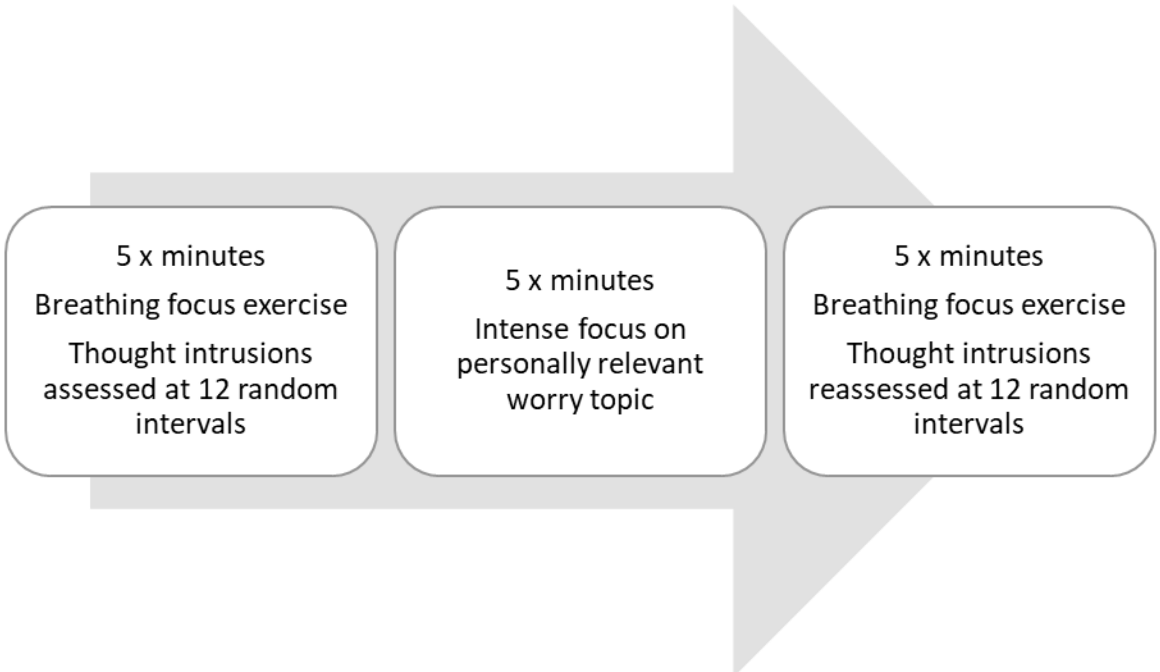


Figure 3.6 Flow chart of the worry induction task

The task featured three phases, each lasting 5 minutes (see Figure 3.6 above). In phase 1 participants sat quietly, closed eyes and focused attention on the breath. They were instructed that if their mind wandered, or they found themselves thinking about something, they should simply turn their attention back to the breath. A computerised application emitted 12 x loud beeps at random intervals during this period. This was delivered on a Dell Latitude laptop with built-in speakers. Following each beep, the participant told the experimenter if they had they been focussed on breathing or thinking about something when the interruption occurred. If there was a thought intrusion, they told the experimenter if it had been positive, negative or neutral. The experimenter noted each intrusion and its valence. During the task instructions, the experimenter explained that the negative intrusions related to topics/issues which worried, irritated or concerned them. Positive thoughts were thoughts related to pleasant things to which they had a positive attitude. Neutral thoughts meant something that did not have particular valence for that participant. Task instructions are provided in Appendix 1.

The phase 1 breathing focus and intrusion-counting exercise was followed by the worry induction procedure (phase 2). The experimenter asked the participant to identify a subject or issue that they worried about frequently. They were asked to avoid something that would upset them significantly. The experimenter briefly discussed the worry with the participant; why it worried them and what its current and future implications might be. The participant was then instructed to actively worry about this for five minutes, allowing themselves to have repetitive negative and unconstructive thoughts about the subject. They were explicitly told not to engage in constructive problem solving, such as developing a plan to tackle a problem. The experimenter left the room during this five-minute procedure. After this 5 minute worry period the experimenter returned to the room. The participant was instructed to close their eyes once again and repeat the breathing focus task for a further 5 minutes. Exactly as before, 12 x randomly spaced beeps interrupted the exercise and the experimenter noted if the participant had been focussed on the breath or experiencing a thought intrusion. The valence of intrusions was noted. The dependent measure was the intrusion count, and the valence of each intrusion. Negative thought intrusions before and after the worry induction procedure were counted and a difference score was calculated. Once the task was completed, to reduce persisting negative affect from the worry induction all participants watched a 1-minute comedy video to boost mood (Hair by Mr. Bean of London, Tiger Aspect Productions, 1995).

3.3.3 **Procedure.**

Figure 3.7 below provides an overview of the experimental timeline. Self-report assessments and experiments were conducted at the Department of Psychology and Human Development, at the Institute of Education, University College of London. Participants first completed self-report questionnaires and the computerised OSPAN WM capacity task. After random allocation to groups, participants completed either the high or low WML versions of the flanker experiment whilst EEG was continuously recorded. Immediately after the flanker, EEG electrodes were disconnected, the cap removed, and participants did the worry induction and breathing focus experiment. To minimise recovery from any cognitive fatigue, there was no break between tasks.

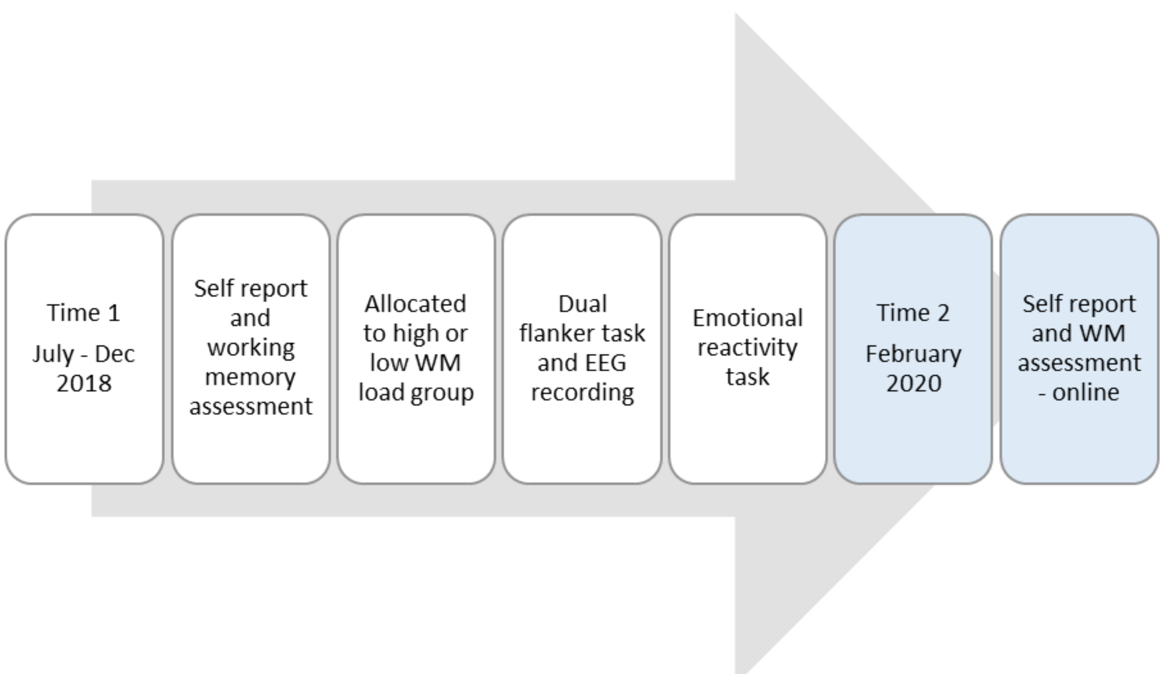


Figure 3.7 Flow chart of the experimental timeline.

Follow up assessments

16 - 19 months after the initial experiment, participants were contacted to take part in the online-only follow up assessment which was built and hosted via Gorilla Experiment Builder (www.gorilla.sc). Follow up measures were self-reported Anxiety, Depression, Worry, School Burnout and the Adolescent Life Events questionnaire. A backwards digit span assessed WM. The Coronavirus pandemic occurred during the follow up period and prevented complete data collection, as the effects of coronavirus were likely to bias responses making those before the pandemic unlikely to be comparable with responses afterwards. Responses were analyzed for n = 31 adolescent participants, who had responded by 18 March, 2020, the date of school closures due to the pandemic. We did not gather sufficient data from adults prior to lockdown on 23 March, so no adult data were analyzed.

3.3.3.1 Statistical methods

Analysis was conducted using SPSS version 25. To examine the effects of age and WM on ERPs and flanker task behavioural performance, we conducted a series of 2 x 2 x 2 mixed factorial ANOVAs. There were two between-subjects factors; age (adolescent vs adult), and Working Memory task load (high vs low). There was also a within-subjects factor; flanker block type (Simple vs Dual task). This within-subjects factor was used in the statistical analysis of the ERPs to investigate how the addition of a WML task during the flanker trial would alter error ERPs relative to a baseline measure (Simple) (a within-subjects manipulation), and if this would be further differentiated by WM load – high versus low load (a between-subjects manipulation).

A 2 x 2 x 2 mixed ANOVA was also conducted on thought intrusion scores to determine whether there were differential effects of age and cognitive load on thought intrusions after the worry induction. In these analyses the between-subjects factors were the same as indicated above (Age Group and WM load), but the within-subjects factor was Time (Pre, Post worry induction).

For each age group (adults; adolescents) Pearson correlation coefficients and regression models were used to analyze linear associations between Simple trial ERPs and susceptibility to negative emotional reactivity triggered by the worry induction, and also with cross sectional and longitudinal self-reported psychopathology vulnerability. We could not combine Dual task ERPs as Dual trial ERPs were subject to the differential WML in the flanker, whereas Simple task flanker trials were identical for all participants. Dual trial ERPs were therefore not used for correlational analyses as this would have necessitated further subdivision of the sample to conduct separate analyses for each WML group, in addition to age group.

3.4 Results

3.4.1 Self-report scales and WM assessment

Scores for all self-report measures and WM (OSPAN at T1; and Backwards Digit Span at T2) assessed at the time of the experiment (T1) and at follow-up (T2) are reported in Table 3.1. The groups did not differ from one another with respect to baseline trait anxiety $F < 1$, perseverative thinking $F < 1$, WM capacity $F(3, 75) = 1.10$, p = .31, worry (PSWQ adults; $F < 1$; PSWQ child $F(1, 38) = 1.64$, p = .21), rumination (Child RSQ; $F(1, 38) = 1.75$, p = .19; Adult RRS $F < 1$); school burnout or RCADS anxiety and depression symptoms (*Fs* < 1 *NS)*.

Adolescent worry and depression increased significantly between baseline and follow-up [worry, $t(28) = 5.87$, p <.001; depression $t(28) = 2.62$, p = .01], whereas anxiety and school burnout were not significantly changed [anxiety $t(28) = 1.26$, p = .22; school burnout, $t(28) = 1.19$, p = .24].

Table 3.1 Group means and standard deviations (in parentheses) for self-report scales and WM measures at time 1 and follow up (18 months later).

	Adolescents		Adults	
	High WML	*Low WML*	*High WML*	*Low WML*
First assessment				
Age	14.00 (1.56)	13.80 (1.70)	26.78 (6.63)	26.60 (6.90)
STAI	38.25 (11.15)	39.40 (9.21)	36.05 (11.27)	38.55 (8.83)
RCADS anxiety*	47.85 (9.55)	51.80 (7.88)		
RCADS depression*	49.65 (11.07)	50.80 (10.23)		
Worry**	16.70 (9.60)	20.45 (8.91)	46.05 (18.58)	49.20 (11.24)
Rumination**	13.85 (8.51)	17.16 (7.02)	37.68 (10.66)	43.30 (9.10)
Perseverative thinking	23.90 (11.19)	25.95 (9.18)	19.74 (12.31)	21.45 (8.22)
School Burnout*	29.00 (10.77)	30.05 (6.94)		
WMC Operation span	57.15 (9.70)	54.95 (9.79)	57.89 (14.27)	61.10 (12.57)
****Follow-up*				
RCADS anxiety	50.08 (11.45)	51.82 (6.75)		
RCADS depression	49.00 (12.92)	50.80 (10.23)		
Worry	26.25 (10.38)	26.20 (9.34)		
School Burnout	28.08 (12.21)	32.71 (7.36)		
Total NLE****	12.75 (6.08)	14.47 (6.89)		
School NLE	3.75 (1.91)	4.18 (1.78)		
Backwards Digit span	5.33 (1.30)	5.25 (1.69)		

*Notes. *Adolescent only measure. ** Separate scales for adults and adolescents for worry and rumination. ***Only adolescents were assessed at follow up. Adult follow up cancelled due to first wave of Covid 2020 pandemic. ****NLE = Negative life events.*

3.4.2 **Flanker task behavioural results.**

Means and standard deviations are shown in Table 3.2 Two 3-way mixed ANOVAs with Flanker Block type (Simple, Dual) as a within-subjects variable, plus Age Group (Adult, Adolescent) and Working Memory Load (High, Low) as between-subjects variables were performed on Flanker Accuracy (% correct) and Reaction Times on correct trials (ms).

Table 3.2 Means and standard deviations for behavioural performance in the flanker task by group

	Adolescent				Adults			
	M	SD	M	SD	M	SD	M	SD
	High WML		*Low WML*		*High WML*		*Low WML*	
Simple Accuracy	0.79	0.13	0.85	0.07	0.92	0.05	0.88	0.09
Simple RT	452.51	39.10	430.47	38.51	434.49	38.13	436.31	52.64
Dual Accuracy	0.85	0.17	0.90	0.11	0.96	0.03	0.96	0.04
Dual RT	588.91	77.20	525.03	71.58	509.32	55.36	504.62	76.56
Simple Accuracy Interference	-0.16	0.12	-0.14	0.07	-0.10	0.05	-0.11	0.07
Simple Accuracy RT interference	61.41	23.26	64.29	19.39	65.59	15.69	67.11	18.93
Dual Accuracy Interference	-0.09	0.07	-0.07	0.06	-0.05	0.05	-0.05	0.05
Dual RT Interference	80.36	34.81	71.79	27.54	68.32	23.00	71.52	20.87
Post error slowing simple flanker	49.66	43.19	47.29	26.22	55.22	43.56	42.51	48.36
Post error slowing dual flanker	16.50	64.83	-18.89	46.71	11.86	51.72	42.62	74.29

Accuracy: There was a main effect of block type, $F(1, 75) = 25.25$, $p < .001$, $\eta_p^2 = .25$ with higher overall accuracy on Dual trials ($M = .91$, $SD = .12$) compared to Simple trials ($M = .84$, $SD = .14$). There was also a main effect of age group $F(1, 75) = 22.68$, $p < .001$, $\eta_p^2 = .23$, such that adolescents ($M = .85$, $SD = .10$) were significantly less accurate than adults ($M = .93$, $SD = .05$). The main effect of WML was not significant $F(1, 75) = 2.02$, $p = .16$, $\eta_p^2 = .03$. However, there was a significant interaction between Age Group x WM load $F(1, 75) = 3.85$, $p = .05$, $\eta_p^2 = .05$. Simple effects analysis to decompose this interaction revealed that whilst adult accuracy did not differ between the low ($t < 1$) and high ($t < 1$) WML groups, there were differences between adolescents (High WML $M = .78$, $SD = .16$; Low WML $M = .85$, $SD = .10$) with better performance in the low relative to high WM load adolescents, however this difference missed significance, $t(38) = 1.84$, $p = .08$. The three-way interaction between Age Group, WML and Block type was not significant, $F < 1$, indicating that age interacted with WML similarly during the Simple and Dual trial types (i.e. regardless of whether there was a WM manipulation). The effect of WML on adolescents compared to adults, was therefore not exclusive to the blocks which contained the load manipulation.

Reaction times: There was a main effect of block type, $F(1, 75) = 200.23$, $p < .001$, $\eta_p^2 = .73$, such that reaction times (RT) were slower on Dual trials ($M = 533.23$, $SD = 85.42$) compared to Simple trials ($M = 439.60$, $SD = 44.77$). There was also a main effect of age group $F(1, 75) = 5.30$, $p = .02$, $\eta_p^2 = .07$, such that adolescents ($M = 504.47$, $SD = 62.22$) were significantly slower than adults ($M = 471.81$, $SD = 52.78$). There was a significant interaction between Age Group and Block type $F(1, 75) = 10.94$, $p = .001$, $\eta_p^2 = .13$. Adolescents ($M = 558.89$, $SD = 94.60$) were significantly slower than adults ($M = 506.91$, $SD = 66.24$) on the Dual trials, $t(77) = 2.82$, $p = .01$, whereas RTs were similar for Simple trials (Adolescent $M = 443.67$, $SD = 44.19$; Adult $M = 435.42$, $SD = 45.55$) $t < 1$. All other main effects and interactions were non-significant.

RT interference on correct trials: There was a main effect of block type, $F(3,75) = 8.68$, $p = .004$, $\eta_p^2 = .10$. Participants experienced greater slowing due to incongruence effects on Dual ($M = 72.88$, $SD = 26.70$) compared to Simple trials ($M = 64.67$, $SD = 19.16$). The interaction between Block type x Age Group was not significant, $F(1, 75) = 2.87$, $p = .09$, $\eta_p^2 = .04$. Furthermore, the interaction between Block Type x WML ($F < 1$) and the three-way interaction between Block Type x Age Group x WML were also not significant, $F(1, 75) = 1.33$, p = .25, $\eta_p^2 = .02$. All other main and interactions were non-significant (*Fs*< 1 *NS*).

Post error slowing: Overall response accuracy was *M* = .81, *SD* = .12, and this increased with age, *r* = .38 p < .001. Consistent with the literature, participants were faster on error (*M* = 428.57, *SD* = 94.42) than correct trials (*M* = 484.24, *SD* = 62.03), $t(61) = 7.16$, p < .001. Post error slowing was calculated for participants with at least 3 errors, and was the difference in average RT between pre-error and post error trials. Overall post error slowing was *M* = +29ms, *SD* = 30, with significantly greater slowing on Simple (*M* = 48.95, *SD* = 40.3) compared to Dual trials (*M* = 15.83, *SD* = 62.86), $t(52) = 2.58$, p = .01. Means and SDs by group are shown in Table 3.2.

There was a significant interaction between Age group x WML, $F(1, 49)= 6.30$, p = .02, $\eta_p^2 = .114$, such that in the low WML group, adults (*M* = 42.96, *SD* = 39.98) slowed significantly more than adolescents (*M* = 11.26, *SD* = 17.56), $t(27) = 2.92$, p = .02). There were no age related differences in post error slowing within the high WML groups $t < 1$. The three-way interaction between Age Group, WML and Block type was not significant $F < 1$, indicating that age interacted with WML similarly during the Simple and Dual trial types (i.e. regardless of WM manipulation). Differential effects of WML on adolescents compared to adults was therefore not exclusive to the blocks which contained the actual load manipulation.

Working memory component of the dual task

Accuracy: The main effect of Age Group approached significance. Adults (*M* = .87, *SD* = .12) were more accurate than adolescents (*M* = .82, *SD* = .14), $F(3, 75) = 3.73$, p = .06, $\eta_p^2 = .05$. There was a main effect of WML such that participants in the low WML group (*M* = .88, *SD* =

.11) were more accurate than the high WML group (*M* = .82, *SD* = .14), $F(3, 75) = 5.5$, $p = .02$, $\eta_p^2 = .07$. The interaction between Age group x WML was not significant, $F < 1$.

RT (ms) on correct trials; There was a main effect of Age Group, such that adolescents (*M* = 1407.08, *SD* = 235.63) were significantly slower than adults (*M* =1142.07, *SD* =233.81), $F(3, 75) = 26.72$, $p < .001$, $\eta_p^2 = .26$. There also a main effect of WML such that participants were faster in the low (*M* = 1205.30, *SD* =288.82) relative to high (*M* = 1340.44, *SD* =229.29) WML group, $F(3, 75) = 5.5$, $p = .02$, $\eta_p^2 = .06$. There was no significant interaction between Age group x WML, $F < 1$.

3.4.3 Flanker task ERP analysis

ERN. The combination of insufficient error segments and data loss due to artefacts or poor EEG recording, meant several participant exclusions were necessary. Table 3.3 shows numbers of participants with satisfactory ERPs eligible for analysis for Simple and Dual blocks. Statistical analyses were performed on mean area amplitudes in the 0-100ms post response window for both error (ERN) and correct (CRN) responses. There were significantly fewer errors of commission on the Dual (*M* = 7.00, *SD* = 9.28) compared to Simple blocks (*M* = 12.79, *SD* = 8.46), $t(71) = 4.95$, $p < .001$.

Table 3.3. Shows numbers of participants by group for whom there were sufficient of errors segment that survived correction.

Group	Simple Block	Dual Blocks
Adolescent High WML	16	6
Adolescent Low WML	17	9
Adult High WML	14	11
Adult Low WML	15	11

Consistent with predictions, error trials generated an ERN component with the maximal (i.e. most negative) amplitude at the midline fronto-central locations FCz and Fz. A pooled average across these electrode sites was calculated. ERN and CRN values confirmed a main effect of response type (error vs correct). The ERN amplitude was significantly more negative than the CRN for both dual $F(1, 32) = 5.41$. $p = .03$, and Simple flankers $F(1, 58) = 43.32$, $p < .001$. The ERN and CRN differed significantly for adults in both Simple ($t(28) = 4.08$ $p < .001$) and Dual blocks ($t(24) = .39$, $p < .001$), however for adolescents this difference was significant for Simple blocks only ($t(32) = 5.39$, $p < .001$). Dual was $t < 1$ *NS*.. Mean area amplitudes by Age and WML group are reported in Table 3.4. Topographical scalp maps and grand average waveforms for the ERN and CRN by Age group and Working Memory load are shown in Figure 3.8 – 3.10 (Simple blocks) and Figure 3.11-3.13 (Dual blocks).

Table 3.4. Mean area amplitude (mV) in the 0-100ms post response window pooled across Fz and FCz electrode sites for Simple and Dual flanker blocks, by age and WML groups.

		Dual Blocks						Simple Blocks					
		Pooled ERN		**Pooled CRN**		**Pooled ΔERN**		**Pooled ERN**		**Pooled CRN**		**Pooled ΔERN**	
		High	*Low*	*High*	*Low*	*High*	*Low*	*High*	*Low*	*High*	*Low*	*High*	*Low*
Adolescent	*M*	**1.46**	**-.19**	**.24**	**1.23**	**1.22**	**-1.42**	**-4.58**	**-4.26**	**-3.36**	**0.15**	**-1.22**	**-4.41**
High WML n = 6/ Low WML n = 9	*SD*	6.96	3.62	2.64	2.87	6.84	4.10	*3.77*	*2.76*	*2.08*	*3.24*	*5.00*	*3.34*
Adult	*M*	**-2.91**	**-1.07**	**1.33**	**1.51**	**-4.19**	**-2.59**	**-3.47**	**-1.43**	**0.54**	**1.08**	**-4.09**	**-2.51**
High WML n = 10/ Low WML n - 11	*SD*	*3.85*	*2.91*	*1.76*	*1.72*	*3.46*	*3.72*	*3.75*	*2.49*	*1.51*	*2.92*	*4.11*	*4.72*

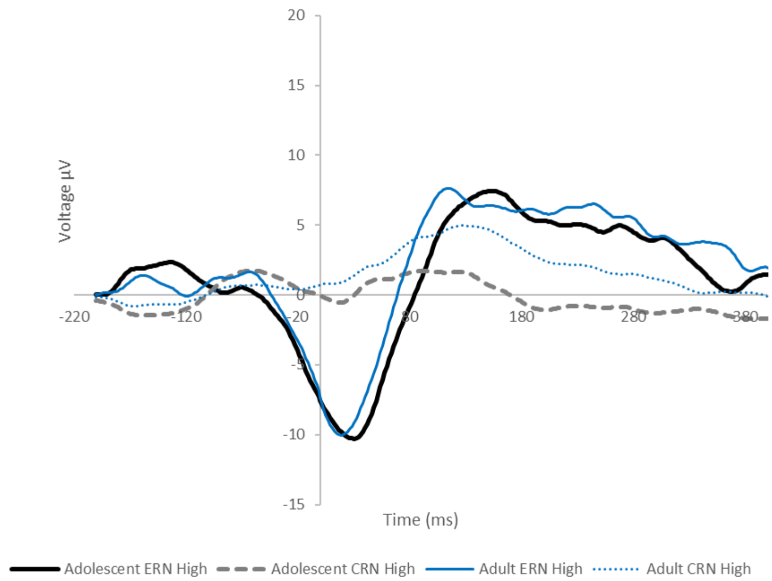


Figure 3.8 ***Simple blocks****. Response-locked ERP waveforms at FCz for errors (ERN) and corrects (CRN) comparing adults and adolescents in* ***high*** *WML groups.*

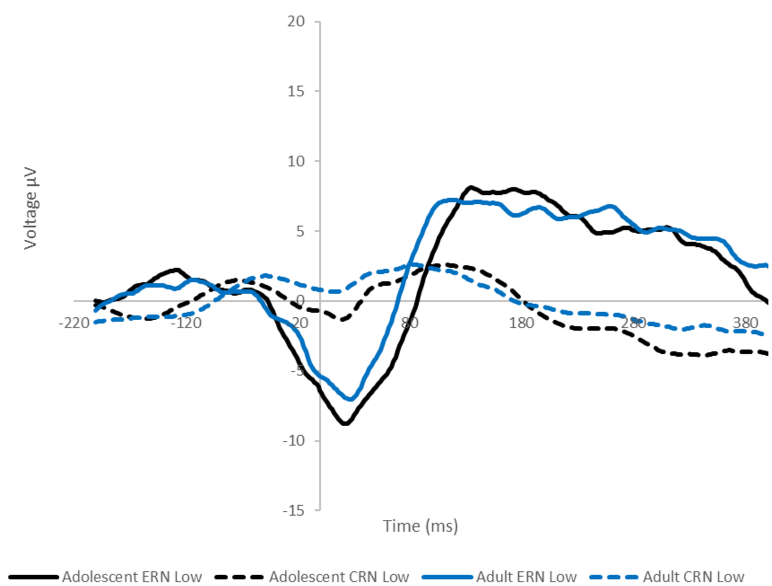


Figure 3.9. ***Simple blocks****. Response-locked ERP waveforms at FCz for errors (ERN) and corrects (CRN) comparing adults and adolescents in* ***low*** *WML groups.*

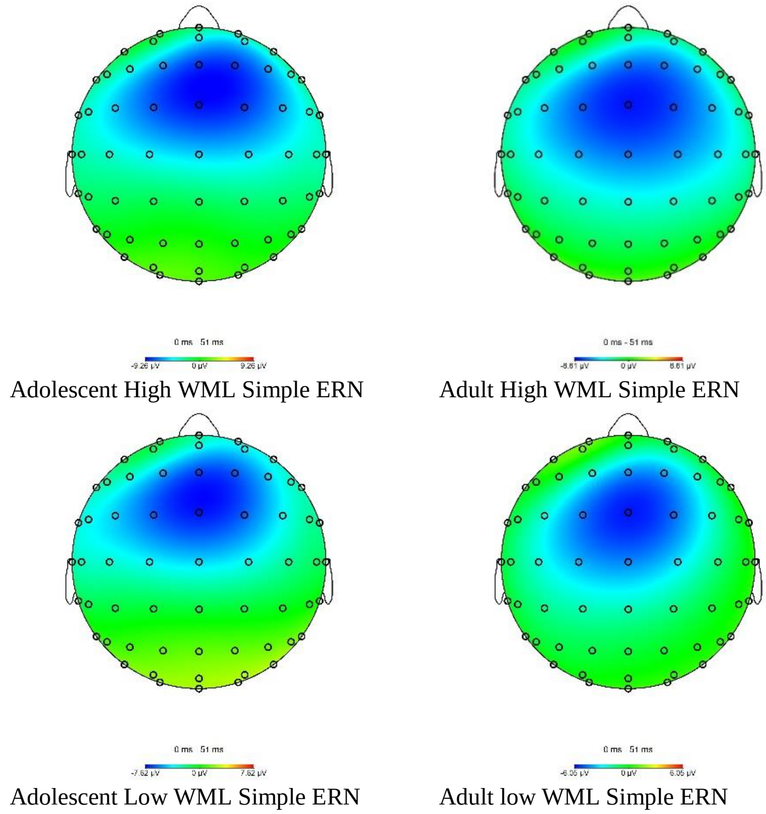


Figure 3.10 ***Simple blocks*** *Topographical scalp showing voltage distribution for the ERN by Age and WML*

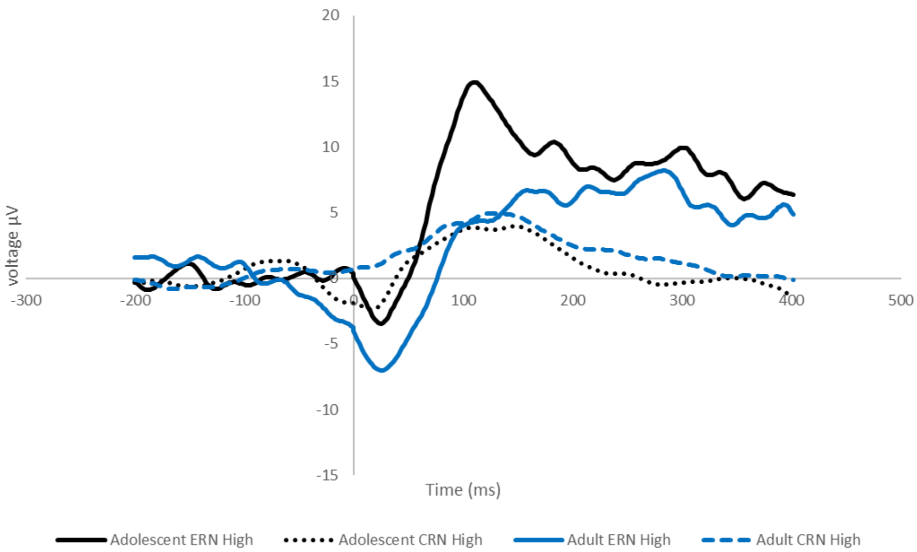


Figure 3.11 ***Dual blocks****. Response-locked ERP waveforms at FCz for errors (ERN) and corrects (CRN) comparing adults and adolescents in* ***high WML*** *groups.*

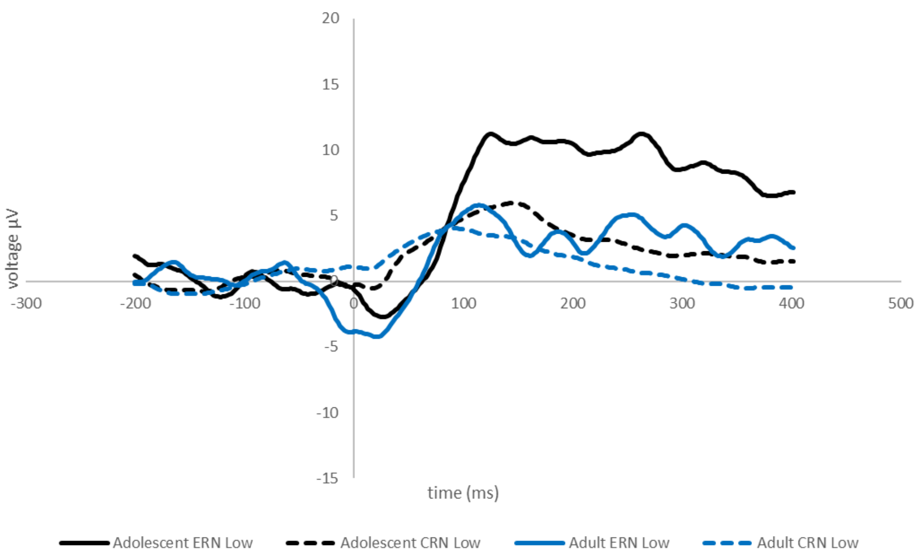
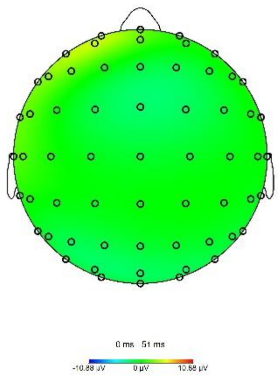
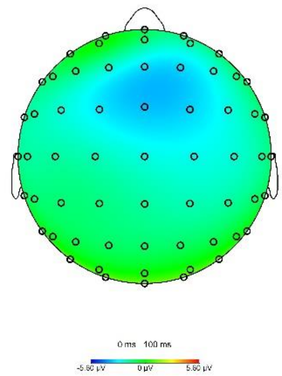


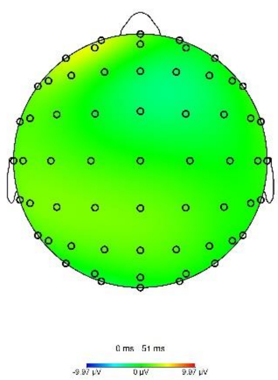
Figure 3.12 ***Dual blocks.*** *Response-locked ERP waveforms at FCz for errors (ERN) and corrects (CRN) comparing adults and adolescents in* ***low WML*** *groups.*



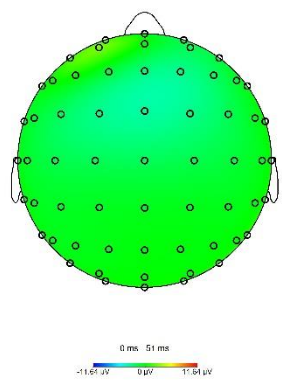
Adolescent High WML dual ERN



Adult High WML dual ERN



Adolescent Low WML dual ERN



Adult Low WML dual ERN

Figure 3.13. ***Dual blocks*** *Topographical scalp maps showing voltage distribution for the ERN during dual flanker blocks for each condition*

A 2x2x2 mixed ANOVA with Block type (Simple, Dual) as the within-subjects factor, and Age Group (Adolescent, Adult) and Working Memory Load (High, Low) as between-subjects factors tested the effects of Age group and WML on the ERN, CRN and ΔERN.

ERN: There was main effect of block type $F(1, 32) = 14.95$, p = .001, $\eta_p^2 = .32$, with a larger ERN on Simple flanker (M = -3.43, SD = .54) compared to Dual flanker (M = -.68, SD = .72 trials. There was a significant interaction between Block type and Age Group $F(1,32) = 10.43$, p = .003, $\eta_p^2 = .25$. See Figure 3.14. Follow-up tests revealed a significantly larger adolescent ERN on Simple (M = -4.39, SD = 3.08) compared to Dual trials (M = .47, SD = 5.05), $t(14) = -4.12$, p = .001, regardless of WML. The adult ERN (Simple M = -2.40, SD = 3.25; Dual M = -

1.95, *SD* =3.43) did not differ between Block type $t < 1$. The three-way interaction, and main effects of WML and Age Group were not significant (*Fs* < 1 *NS).*

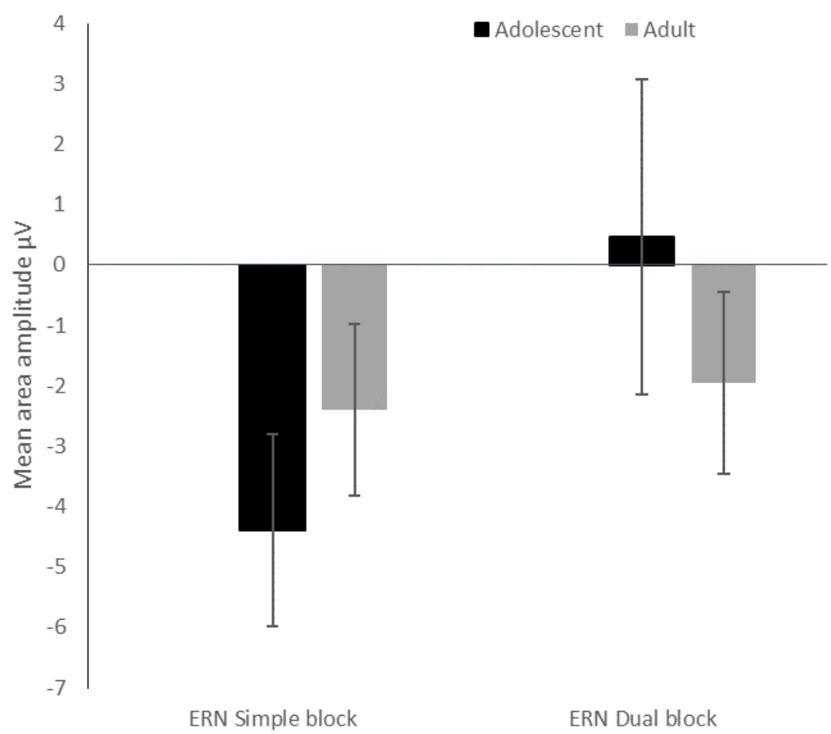


Figure 3.14. Depicts interaction between age group and block type on ERN mean area voltage in the 0-100 ms post response window.

CRN: There was a main effect of Block type $F(1, 32) = 18.44$, $p < .001$, $\eta_p^2 = .36$, with a larger CRN on Dual compared to Simple trials. The main effect of Age Group was significant $F(1, 32) = 4.27$, $p = .05$, $\eta_p^2 = .11$, and there was a trend towards a significant main effect of WML $F(1, 32)= 3.02$, $p =.09$, $\eta_p^2 = .08$. There was also a significant interaction between Block type and Age group $F(1, 32) = 6.31$, $p = .02$, $\eta_p^2 = .16$. Adolescent CRN amplitudes were significantly larger (*M* =- 1.25, *SD* = 3.45) than adults' (*M* =.81, *SD* = 2.28) during Simple flankers $t(35) = -2.19$, $p = .04$, whereas there were no differences between age groups on Dual trial flankers $t < 1$.

There was also a significant interaction between WML and Block type $F(1, 32) = 4.39$, p = .04, η_p^2 =.12. However, follow up t-tests found CRN amplitudes did not differ by WML on either block; Simple $t(35) = 1.5$, p = .21, Dual $t < 1$. There was no significant three-way interaction $F(1, 32) = 2.49$, p = .12, η_p^2 = .07 and no interaction between Age group x WML, $F < 1$.

Having observed a blunted adolescent ERN during Dual trials in the above analyses, we compared ERP responses on Correct versus Incorrect trials collapsed across WML (see Figure 3.15). There was a significantly larger (more negative) ERN compared to CRN in adults in both Simple flanker $t(20) = 4.08$ p < .001) and Dual flanker trials $t(21) = 3.39$, p < .001). However for adolescents, the difference was only significant for Simple flanker trials $t(15) = 2.87$, p = .01. The difference between ERN and CRN during Dual flanker trials was not significant for adolescents, $t < 1$.

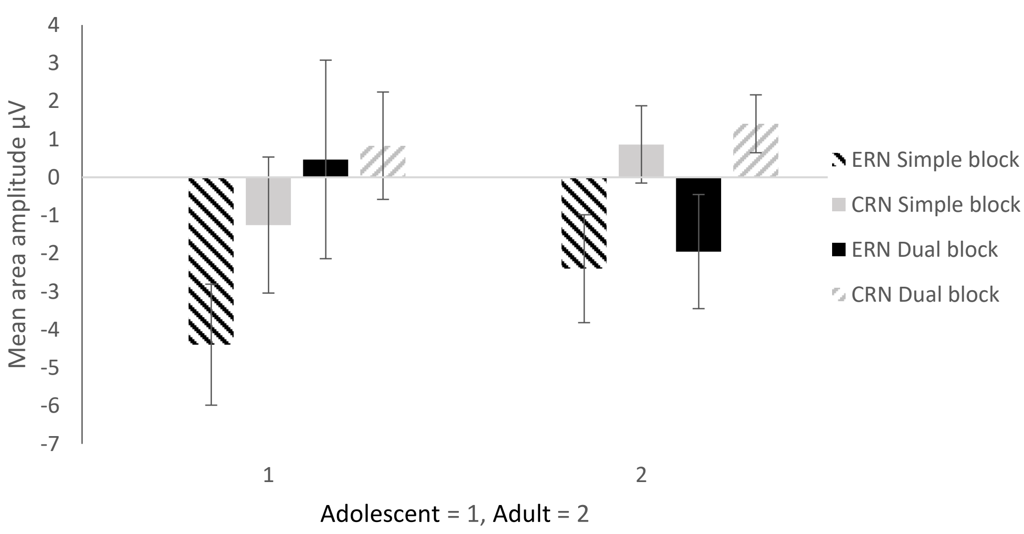


Figure 3.15. Bar chart comparing mean area amplitude in 0-100 ms post response window for error (ERN) and correct (CRN) by age group (adolescents and adults). Error bars represent +/- 2 SE.

ΔERN: There was a main effect of Block Type $F(1,32) = 3.99$, $p = .05$, $\eta_p^2 = .11$, with significantly greater negativity on Simple (*M* = -3.21, *SD* = 4.27) compared to Dual trials (*M* = -2.11, *SD* = 4.57), p = .05. The main effects of Age Group and WML were not significant, $F < 1$. There was a significant Age Group by Block-type interaction, $F(1,32) = 4.57$, $p = .04$, $\eta_p^2 = .16$, with adolescents showing a more attenuated ΔERN on the Dual trials, compared to adults $t(35) = 2.12$, $p = .04$, albeit not significant at corrected alpha p = .025. ΔERN was similar between age groups on Simple blocks $t < 1$, also irrespective of WML. There was a trend interaction between Age Group x WML, $F(1, 32) = 2.88$, $p = .09$, $\eta_p^2 = .08$, which showed, irrespective of block type, adults and adolescents in the low WML groups had a similar ΔERN, whereas adults had larger ΔERN than adolescents if in the high WML group. The effect was present in both Simple and Dual trials.

P(e): Means and standard deviations are displayed in Table 3.5 and grand averaged waveforms are shown in Appendix 2. There was no main effect of block type, $F < 1$. The P(e) was similar for Simple and Dual trials. The main effects of Age Group and WML were not significant, both were $F < 1$. The Age Group x WML interaction ($F < 1$) and the three-way interaction between Age Group x WML x Block type $F(1, 33) = 1.17$, $p = .29$, $\eta_p^2 = .003$ were also not significant.

Table 3.5. P(e) mean area amplitudes (µV) in 200-400 ms post error response window by age group and WML. Standard deviations in parenthesis

	Simple Blocks P(e) (error)		Dual Block P(e) (error)	
	High WML	*Low WML*	*High WML*	*Low WML*
Adolescent	5.01 (11.30)	4.22 (5.16)	2.98 (7.51)	4.60 (3.76)

Adult	5.62 (4.42)	4.68 (5.76)		6.28 (8.11)	2.74 (4.58)

3.4.4 **Worry induction and emotional reactivity task**

Means and SDs are in displayed in Table 3.6. A 2 x 2 x 2 mixed ANOVA explored the effects of Age Group and WML on responses following a worry induction during the Breathing Focus Task. The between-subjects factors were Age Group (Adolescent, Adult) and Working Memory Load (High, Low). The within-subjects factor was time (pre worry induction; post worry induction). The dependent variables of interest from the breathing focus task were 1) the total number of thought intrusions, and 2) the number of thought intrusions rated as negative by the participant and (3) increase in negative intrusions from pre to post induction.

Table 3.6. Mean numbers of thought intrusions during breathing focus task before (pre) and after (post) the worry induction.

	Adolescent				Adults			
	M	SD	M	SD	M	SD	M	SD
	High WML		*Low WML*		*High WML*		*Low WML*	
Total intrusions Pre	5.67	3.75	7.10	2.93	5.06	2.36	4.25	2.40
Total intrusions Post	6.41	3.86	7.79	3.57	6.22	2.76	6.05	2.58
Negative intrusions Pre	0.50	0.52	1.11	1.33	0.94	0.99	0.60	1.31
Negative intrusions Post	2.43	2.41	2.63	1.98	2.61	1.38	2.15	1.60
Neg intrusion change	1.69	2.06	1.45	1.90	1.67	1.19	1.55	1.39
Positive Intrusions Pre	1.71	1.73	2.26	1.63	1.39	1.24	1.05	1.32
Positive Intrusions Post	1.00	1.24	1.74	1.28	1.06	1.62	0.80	1.28
Neutral Intrusions Pre	3.86	2.98	3.63	2.19	2.72	2.37	2.60	1.93
Neutral Intrusions Post	3.43	3.41	3.42	2.89	2.56	2.15	3.10	2.32

Regardless of Age group or WML, there were significantly more thought intrusions after the worry manipulation [pre worry M = 5.47, SD = 2.30; post worry *M* = 6.63, *SD* = 3.27], *F*(1, 67) = 25.63, p <.001 η_p^2 = 27. The main effect of Age group approached significance *F*(1, 67) = 3.62, p = .06, η_p^2. = .05. Adolescents had more intrusions than adults before (adolescent *M* = 6.41, *SD* = 3.35; adults, *M* = 4.63, *SD* = 2.39) and after the worry induction (adolescent *M* = 7.18, *SD* = 3.83; adults *M* = 6.13, *SD* = 2.63). The interaction between Age Group x WML was not significant *F*(1, 67) = 1.78, p = .18, η_p^2 = .02. All other main effects and interactions were *F*< 1.

Negative emotional reactivity: Regardless of Age or WML group, there were significantly more negative thought intrusions after the worry induction [pre worry; *M* = .8, *SD* = 1.12; post worry; *M* = 2.45, *SD* = 1.81], *F*(1, 67) = 70.35, p <.001 η_p^2 = .51. The WML Group x Age Group interaction was not significant, *F*(1, 67) = *1.73 p =.19,* η_p^2 = .02. All others main effects and interactions were *F* < 1.

3.4.5 **Secondary analyses.**

Separate analysis by Age Group (adults, adolescents) examined ERP relationships with cognitive performance, emotional reactivity and with future school burnout and psychopathology symptoms.

3.4.5.1 <u>Adolescents</u>

Flanker task performance

Amongst adolescents, the ERN, CRN, ΔERN and P(e) were not correlated with accuracy or RT in the flanker task, ps > .1 *NS*. The P(e) was significantly correlated with frequency of commission errors (*r* = -.46, p = .01), such that a larger (more positive) P(e) response was associated with fewer errors (Figure 3.16).

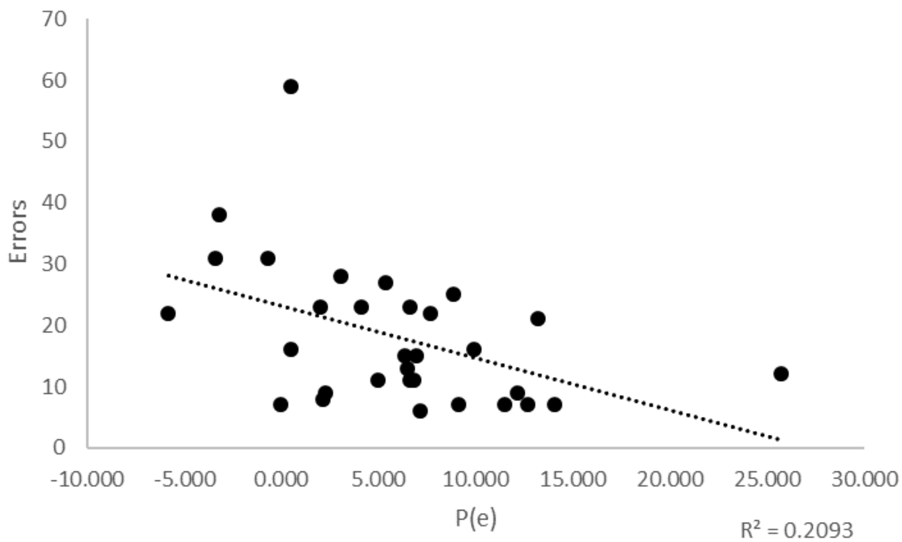


Figure 3.16. Scatterplot depicting significant association between adolescent number of errors of commission and P(e) on Simple trials.

Negative emotional reactivity and ΔERN

Simple block ΔERN accounted for 13% of variance in negative reactivity in adolescents, $F(1, 27) = 4.10$, R-squared = .13, p = .05 such that a smaller and less negative ΔERN predicted a greater increase in negative thought intrusions resulting from the worry induction, B = -.18, SE = .09, $t = 2.03$, p = .05. This relationship is plotted in Figure 3.17 (adolescents).

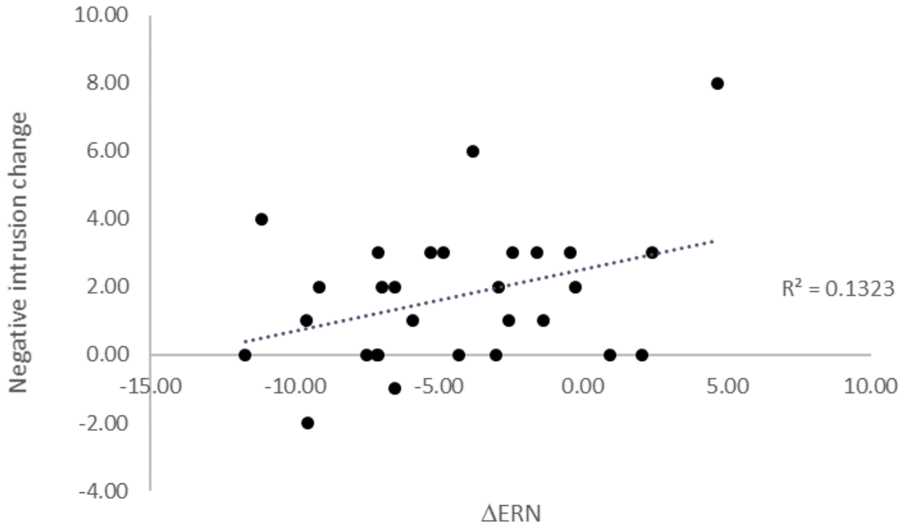


Figure 3.17. Scatterplot shows significant relationship between negative reactivity and ΔERN in adolescents. A larger, as in more negative, ΔERN was associated with smaller increases in negative thought intrusions after the worry induction.

ERP associations with OSPAN, psychopathology measures and school burnout

Neither the Simple Block ΔERN nor the P(e) was significantly associated with adolescent worry, anxiety, depression, rumination or preservative thinking at time 1, nor at the follow up assessment, p's > .1 *n.s.*. Having observed a significant increase in adolescent worry and depression over time, we examined whether these increases were associated with the ΔERN or P(e). The ΔERN predicted the increase in worry $F(1, 22) = 6.62$, p = .02, R-square = .23 such that a smaller/less negative ΔERN was associated with greater increases in worry over time, B = .70, SE = .28, $t = 2.58$, p =.02. The ΔERN was not correlated with depression increases $r = .12$, p = .57. The P(e) was not significantly associated with increases in worry, $r = -.05$, p = .83, or depression, $r = -.35$, p = .09.

There were no significant correlations between the adolescent ΔERN and OSPAN scores ($r = -.21$, p =.24) nor backwards digit span at follow up ($r = -.21$, p = .24). However, the P(e) was highly significantly correlated with OSPAN scores such that a larger P(e) was associated with better OSPAN performance, $r = .46$, $p < .001$. Neither the ERN nor the P(e) had significant associations with the backwards digit span at follow-up, (ΔERN r = -23., p =.25; P(e) r = 22, p = .29).

A hierarchical regression analysis explored the predictive power of ΔERN on future school burnout, whilst controlling for the effects of time 1 school burnout and frequency of negative life events associated with school (NLE-school) in the three months prior to follow up tests. These variables were controlled for as they were also expected to influence school burnout at follow up. When time 1 burnout and NLE-school were entered on step one, they accounted for 60% of the variance in burnout at follow up, $F(2,22) = 16.91$, $p < .001$. Time 1 burnout was a significant predictor of later burnout, ß = .65, $t = 4.95$, $p < .001$, whereas NLE-school was not, ß = .24, $t = 1.84$, $p = .12$. At Step 2, the addition of ΔERN explained additional variance in burnout, R-squared (change) = .09, and this change was significant, *Fchange* (1, 21) = 6.58, $p = .018$. ΔERN was a significant predictor of follow-up burnout symptoms, ß = .31, $t = 1.85$, $p = .018$, after controlling for the effects of the time 1 burnout and NLE. A larger, as in more negative, ΔERN was associated with lower burnout 16-19 months later. The association is shown in Figure 3.18 below.

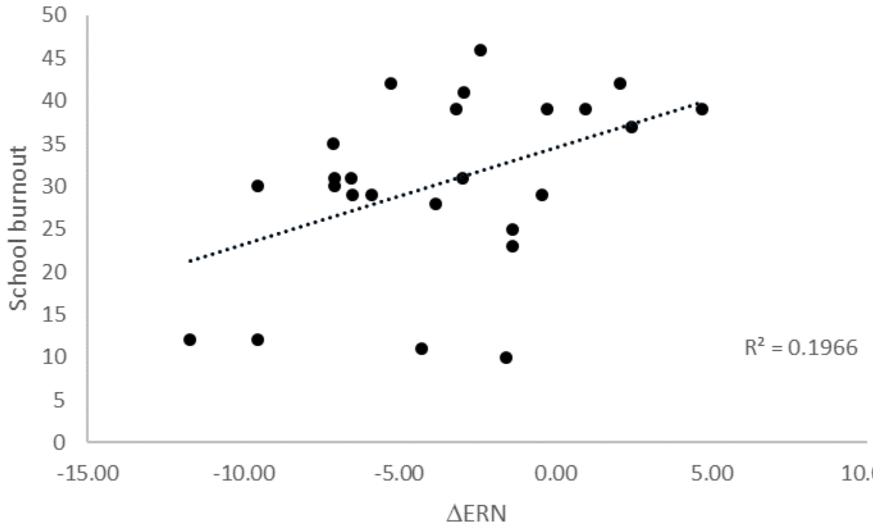


Figure 3.18. Scatterplot shows significant association between adolescent *ERN and School burnout 16-19 months later.*

3.4.5.2 Adults

Flanker task performance

Adult reaction times were significantly correlated with ERN (r = .42, p = .02), CRN (r = -.67, p < .001) and ΔERN (r = .62, p < .001), such that faster reaction times were associated with a larger ERN and ΔERN. Adult accuracy was not significantly correlated with any of the ERPs, p's > .1 *n.s*. The P(e) was significantly correlated with numbers of commission errors in adults (r = -.44, p = .02) such that a larger (more positive) P(e) response was associated with fewer errors of commission (Figure 3.19).

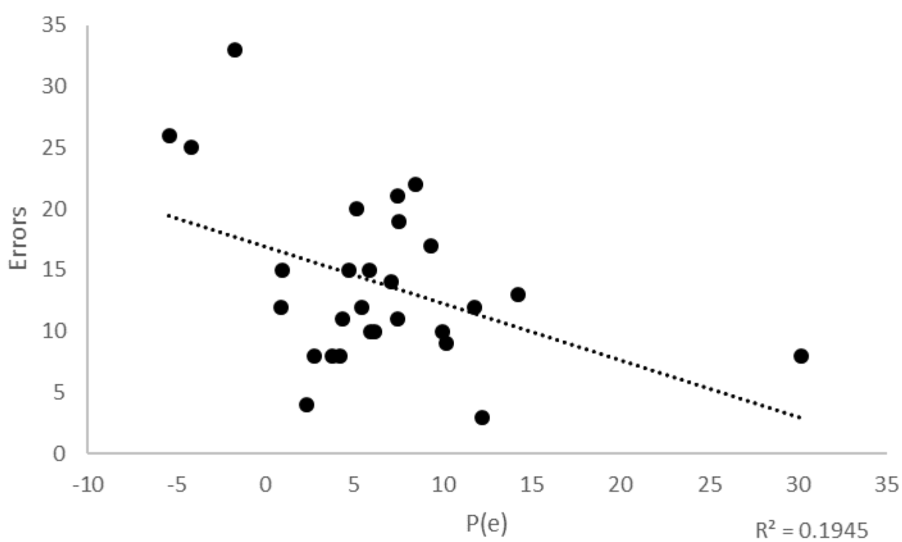


Figure 3.19. Scatterplot depicting significant association between adult's number of errors of commission and P(e) on Simple trials.

Negative emotional reactivity and ΔERN.

Simple block ΔERN accounted for 16% of the variance in adult negative reactivity, $F(1,26) = 4.99$, $p = .03$ and was a significant predictor $B = -.11$, $SE = .05$, $t = 2.23$, $p = .03$. The direction of the relationship was converse to that reported for adolescents. A larger and more negative adult ΔERN predicted greater increases in negative intrusions following the worry induction. This relationship is plotted in Figure 3.20.

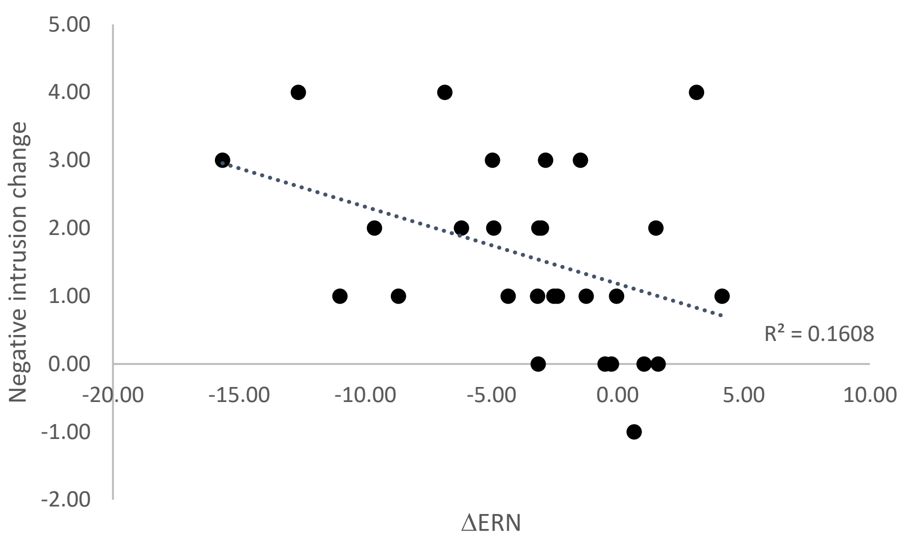


Figure 3.20. Scatterplot shows significant relationship between negative reactivity and ΔERN in adults. A larger, as in more negative, ΔERN was associated with a greater increases in negative thought intrusions after the worry induction.

ERP associations with psychopathology measures and WM OSPAN

Neither the Simple Block ΔERN nor the P(e) was significantly associated with worry, anxiety, depression, rumination or preservative thinking, $p > .1$ *n.s.*. The adult ΔERN was significantly correlated with OSPAN (r = -.53, p =.003) such that a larger ΔERN was associated with better OSPAN performance. Adult P(e) was not correlated with OSPAN, r = .19, p = .33, *n.s*.

3.5 Discussion

The primary aim of this study was to explore a novel hypothesis which predicted that cognitive depletion effects from a lengthy cognitive task that manipulated WML would lead to differential negative emotional reactivity as a function of load and that the effect would be more pronounced in adolescents compared to adults. We proposed the magnitude of cognitive effort in the earlier task would be signified by enlarged ERNs leading to greater subsequent fatigue and temporary reductions in cognitive control following the worry induction exercise. We hypothesized additionally that negative emotional reactivity would be elevated in participants with larger ERN amplitudes.

There was no effect of load on negative reactivity in either age group, nor was there an interaction between age group and load. All groups were similarly susceptible to increases in negative intrusions post worry induction, consistent with prior studies showing the worry induction increased negative intrusions during a breathing focus exercise (Grol et al., 2018; Hayes et al., 2010). Furthermore, adolescents were not more susceptible to the worry induction or load manipulation, although they had more intrusions than adults initally. Although previous research reported that tasks with high EF demands can lead to mental fatigue and temporary impairments of cognitive control (Dang, 2018; Hofmann et al., 2012; Schmeichel, 2007) which in turn can impede aspects of emotional regulation (Grillon et al., 2015), the hypothesis regarding group effects of depletion on emotional reactivity was not supported. Although these results are consistent with studies that do not find evidence of ego depletion (Hagger et al., 2016), there could be several reasons for the absence of direct group effects, which will be addressed later in the discussion.

Although there were no significant group-level behavioral effects on negative emotional reactivity, there were effects at an individual and neural level. There was a significant association between the ΔERN and negative reactivity in both adults and adolescents, but effects were in opposing directions. In adults, a larger ΔERN during Simple trials was linked to a larger increase in negative thought intrusions following the worry induction. In contrast, amongst adolescents, an elevated ΔERN was significantly associated with a smaller increase in negative reactivity following the worry induction. The results therefore supported the second hypothesis, that ΔERN magnitude would be associated with negative reactivity following the worry induction, albeit with developmental differences.

Cognitive control, the ability to engage with goal directed action whilst withstanding distractions, is central to a range of emotional regulation processes and, reduced engagement of control processes can increase negative affect (Cohen & Mor, 2018) and exposure to maladaptive rumination and worry (Beckwé et al., 2014). Individual differences in the adult ΔERN may have reflected differences in processing efficiency during the depletion task, with poorer efficiency leading to subsequently reduced cognitive control and impaired ability to maintain goal-directed attention in the breathing focus task and resist negative intrusions activated by the worry induction. Earlier work on cognitive depletion has demonstrated performance decrements in cognitive control following an effortful task and impaired self-regulation after executive function depletion (Dang, 2021; Garrison et al., 2019; Hofmann et al., 2012; Schmeichel, 2007). The findings are consistent with previous studies which have shown how cognitive depletion transferred to measures relevant to emotional regulation (Maranges et al., 2017). For instance Grillon et al. (2015) demonstrated that cognitive fatigue reduced ability to regulate emotion in a high relative to no cognitive fatigue condition. In the depletion condition there was an elevated startleblink response relative to control condition during an explicit emotion regulation exercise where participants were instructed to downregulate their emotions when viewing negative images, whereas the startleblink did not differ between conditions when participants were not downregulating emotional response to the images. That the startleblink response remained elevated after the downregulate instruction in the high fatigue condition, suggests that participants were less able to engage top down control to alter their emotional response. In the current study although the WML manipulation did not induce group differences in depletion effects, individual differences in the magnitude of the adult ΔERN may have reflected differing engagement of resources, where a larger ΔERN exaggerated control depletion and the triggering effects of the worry induction.

Pathological worry, meaning worry that elevates risk for anxiety disorders (Borkovec et al., 1991), emerges in part from an interaction between top-down attentional control processes and bottom-up stimulus-based biases (Basanovic et al., 2017; Goodwin et al., 2017; Hirsch & Matthews, 2012). Negative or threatening thoughts and stimuli receive preferential processing and poorer attention control allows them to flourish in WM, further limiting attentional resources needed to direct attention away from a stream of repetitive negative thoughts (Fox et al., 2015; Hirsch et al., 2015; Songco et al., 2020). In the current study overall thought intrusions and negative intrusions increased, whereas numbers of positive and neutral intrusions declined. The worry induction exercise therefore engaged repetitive worrisome thought patterns and during the subsequent breathing focus phase, attention control was required to maintain consistent focus on the breath whilst ignoring the recently activated negative thoughts. Previous task load and age did not induce differential worry proliferation, however a neural correlate of reactive cognitive control was predictive for both adults and adolescents.

Adults

Amongst the adults, enhanced reactive control evidenced by an elevated ΔERN during the flanker task may have temporarily reduced attentional control resources available to fight proliferation. Therefore, those who were more depleted as a result of inefficient processing could have experienced greater difficulty preventing negative intrusions from reaching consciousness. The ERN is increased in anxious individuals (Moser et al., 2013; Troller-Renfree et al., 2019) with substantial evidence linking it to anticipatory or worry-based anxiety (Moran et al., 2015; Moser et al., 2013). Whilst there is debate surrounding its functional significance (Meyer & Hajcak, 2019; Pasion & Barbosa, 2019; Weinberg et al., 2012), a prominent explanation for an elevated ERN in anxiety is that it represents compensatory neural processing to mitigate the effects of disruptions to proactive control by worry and rumination (Lo et al., 2017; Moser et al., 2013; Sari et al., 2017). This is consistent with ACT (Derakshan & Eysenck, 2009; Eysenck & Derakshan, 2011) and evidence that cognitive performance impairments in anxiety are frequently reflected in poorer task processing and neural efficiency (Basten et al., 2011, 2012; Berggren & Derakshan, 2013; Fales et al., 2008; Shanmugan et al., 2016, Shi et al., 2019). Moreover, state anxiety impairs proactive and enhances reactive control (Yang et al., 2018) and individuals demonstrating a bias for reactive over proactive control are also more likely to be anxious (Schmid et al., 2015; Troller-Renfree et al., 2019). The findings from the secondary analysis are therefore supportive of the CEMH in adults and extend attentional control and processing efficiency theories by demonstrating how compensatory effort to maintain high performance might contribute to future emotional regulation failures.

There was no differential effect of task load on reactivity, so we are cautious about concluding that adults with larger ΔERNs experienced more cognitive depletion than those with lower amplitudes. However, research on thought intrusions has shown cognitive control measures such as trait attentional control and WM capacity are negatively associated with the ability to suppress intrusive neutral and personally relevant negative thoughts (Bomyea & Amir, 2011; Brewin & Smart, 2005; Geraerts et al., 2007). Fox et al. (2015) found participants with poorer ability to resist emotional distractors in a modified flanker task were more susceptible to negative reactivity in a worry induction task that was almost identical to the task used in the current study. Another study from the same research group found WM performance increases during a cognitive training intervention were associated with reduced negative reactivity to the worry induction (Grol et al., 2018). If the adult ΔERN simply represented variation in task-related or trait cognitive control, then we should expect it to predict less negative reactivity. However, if a larger ΔERN represents compensatory neural activity linked to processing inefficiency, which depletes resources and temporarily impairs cognitive control, then it could explain the increase in adult negative reactivity observed in this study.

Adolescents

The adolescent results contradicted the adult findings. A larger, more negative ΔERN predicted a lower magnitude of negative intrusion gains following the worry induction, suggesting that a larger ΔERN may be linked to improved adolescent ability to maintain focus on the breath and guard against negative reactivity due to the worry induction. However, we could be more conclusive about this interpretation had the ΔERN been associated with time 1 worry, anxiety or depression. Nevertheless, a larger more negative ΔERN was associated with smaller increases in worry between time 1 and follow up 16-19 months later, lending support to interpreting a larger ΔERN as protective, or at least the correlate of a protective factor, in adolescents.

In light of evidence of elevated ERNs in anxious children and adolescents (Meyer, 2017; Moser, 2017), and the links between anxiety and processing inefficiency, it is therefore surprising that the relationship between the ERN and negative reactivity in adolescents was contrary to what we found for adults. Attentional control impairments and processing inefficiencies have been reported for children and adolescents with trait and clinical anxiety and there is evidence of compensatory effort using both behavioral and neural indices (Ng & Lee, 2015, 2016; Owens et al., 2008, 2012; Shanmugan et al., 2016; Shi et al., 2019). In addition, evidence suggests that a reliance on reactive compensatory cognitive control over proactive strategies also mediates the relationship between early childhood temperamental risk factors and later anxiety disorders (Troller-Renfree et al., 2019; Valadez et al., 2020). Our contradictory developmental findings may reflect a changing functional significance of the ERN over development. Shi et al.'s (2019) meta-analysis which examined evidence for key predictions of ACT included child and adolescent studies and explored the moderating effects of age. They found the strength of the association between anxiety and attentional control impairments increased with age, suggesting this compensatory mechanism evolves during development. Anxiety may disrupt the development of attentional control over time leading to compensatory processing strategies becoming more established over development (Moser et al., 2017; Shi et al., 2019).

It is also important to consider the normative development of the ERN and cognitive control to explain these findings. The ERN increases in amplitude across childhood and up until late adolescence (Buzzell et al., 2017; Davies et al., 2004; Hogan et al., 2005; Overbye et al., 2019; Tamnes et al., 2013), with considerable developmental adjustment between early and later adolescence (Ladouceur et al., 2007; Santesso & Segalowitz, 2008; Segalowitz et al., 2010; Taylor et al., 2018). This is accompanied by improvements in performance and consistency in executive functioning (Constantinidis & Luna, 2019; Dumontheil, 2016; Luciana et al., 2005; Luna et al., 2010, 2015), coinciding with major developmental changes in the cortical regions sub-serving conflict and error monitoring, including the ACC and PFC (Gee et al., 2013; Kujawa et al., 2016; Taylor et al., 2018; Velanova et al., 2008, 2009). Our data reflected this. ERN amplitudes were comparable between adults and adolescents on Simple blocks, but a blunted ERN emerged for adolescents during the more challenging Dual task trials, which was also mirrored by poorer adolescent performance on Dual trials, particularly in the high WML group. Although effects were small it indicated that differences between adults and adolescents only emerge in certain circumstances, such as increased cognitive load (Hogan et al., 2005).

Research on the developmental trajectory of cognitive control indicates there is a transition from a reliance on reactive cognitive control in early to late childhood to greater integration of proactive control during adolescence which is linked to increases in the efficiency and ease of employing pre-emptive cue-dependent top down control (Chatham et al., 2009; Chevalier et al., 2015; Killikelly & Szűcs, 2013; Lucenet & Blaye, 2014; Magis-Weinberg et al., 2019; Munakata et al., 2012; Troller-Renfree et al., 2016). Recent work indicates this transition is supported by the behavioral and neurocognitive development of WM (Troller-Renfree et al., 2020). Moreover, poor decision-making and risk-taking in adolescents has been linked to under-developed proactive control and compensatory transient activity in the ACC (Andrews-Hanna et al., 2011), which is also the neural source of the ERN (Tamnes et al., 2013; van Boxtel et al., 2005; Van Veen & Carter, 2002). Mature cognitive control involves the flexible interaction of reactive and proactive control to facilitate goal-directed action in a complex and changing environment (Braver, 2012). Thus aberrations in the development of dynamic and flexible interactions between temporally distinct control processes could emerge as processing inefficiencies in adulthood and compensatory neural activity associated with increased reactive control.

Extant evidence would therefore suggest a larger ΔERN predicting lower reactivity in adolescents may have reflected better overall cognitive control and a greater ability to resist distraction and interference from the worrisome thoughts triggered by the induction exercise. However, the ΔERN and behavioural performance in the flanker task were not correlated in adolescents, undermining this interpretation. This is difficult to account for, especially as better adult performance (faster RT on correct trials) was related to a larger ΔERN. There is evidence that better performance is associated with larger ERNs (Downes et al., 2017), however other evidence indicates that groups with larger ERNs do not necessarily perform better on EF measures than controls or low ERN groups (Lo, 2018; Meyer et al., 2016; Weinberg et al., 2012). The relationship between ERN amplitudes and cognitive control therefore remains unclear (Meyer et al., 2016). The ERN does not represent the execution of control itself but rather functions as an alert that conflict or an error has occurred, triggering the deployment of control events across several cortical and subcortical regions (Botvinick et al., 2001; Gehring et al., 1993; Holroyd & Coles, 2002; Holroyd & Yeung, 2012: Weinberg et al., 2016). As a correlate of reactive control, the ERN is rather indirect, so may not necessarily correspond to control outcomes (Meyer et al., 2016) and the neural processing that responds to the error signal and delivers control is likely to vary considerably between adolescent and adults. Therefore, although flanker performance was not associated with the adolescent ΔERN in the current study, it may not necessarily preclude that a larger ΔERN in our sample indexed better cognitive control and explained the association between reduced negative reactivity and a larger ΔERN.

This is not the first study with evidence of an elevated ΔERN linked to lower emotional vulnerability measures at one stage during normative development but a converse association in another (Meyer et al., 2012; Meyer, 2017; Weinberg et al., 2016). A number of studies in normative samples of children and adolescents examined the changing ERN-anxiety relationship over development and suggest this relationship may not emerge until later childhood or early adolescence (Bress et al., 2015; Meyer 2017; Santesso et al., 2006), though most studies feature older children (Meyer, 2017). One study that examined differences within a normative sample of 8-13 year olds found that an elevated ERN was associated with higher anxiety at trend level in older children, whereas in younger children there was no relationship (Meyer et al., 2012). In another study Weinberg et al. (2016) found scores on the checking behaviour subscale of the Inventory of Depression and Anxiety Symptoms were significantly related to the ERN in a sample of 515 girls. Younger girls displayed a blunted ERN in association with high checking symptoms, whilst older girls had an enlarged ERN. Our study did not have sufficient power to examine if the effect in the adolescent group was driven by younger participants in the sample but given the ages of the participants (M = 13 years) we might have expected a relationship to be evident already. However, the direction of the relationship between the ΔERN and negative reactivity in this normative developmental sample, albeit somewhat delayed in comparison to other studies, is roughly consistent with previous studies showing the relationship between an elevated ERN and higher anxiety in normative groups may not be fully established until later in adolescence (Meyer, 2017; Santesso et al., 2008).

Longitudinal findings

An important aim of this study was also to examine if our compensatory processing proxy, the ΔERN, would predict psychological burnout in adolescents longitudinally. We expected that individual differences in the ΔERN would result in greater psychological burnout in teenagers, which is speculated to be the result of more frequent depletion and persistent exposure to elevated emotional reactivity over time. Instead, we found that whilst the ΔERN predicted school burnout scores at follow-up, the association was in the opposite direction and contradicts the evidence of an association between burnout and the ERN that has been found in adults (Gajewski et al., 2017; Golonka et al., 2017). The larger the ΔERN at baseline, then the lower the burnout scores at follow-up, even controlling for baseline burnout and school-related negative life events. So, similar to negative reactivity, it appeared that a larger ΔERN was also protective from burnout long-term, which is consistent with studies showing elevated ΔERN in at-risk children predicting better academic and behavioural outcomes (McDermott et al., 2013; Moser, 2017; Troller-Renfree et al., 2016) and better academic performance in 19 year olds (Hirsh & Inzlicht, 2010). This is also consistent with one adult study that found a larger ERN was associated with lower reactivity to stress in everyday life (Compton et al., 2008), reflecting better control.

Our findings also showed that adolescent participants experienced a significant increase in worry symptoms between initial testing and follow up. The magnitude of this increased worry was predicted by ΔERN amplitudes, such that a smaller ΔERN at baseline predicted greater increases in worry 16-19 months later. Taken together with the results from the effect of the ΔERN on negative reactivity, this longitudinal evidence suggests that for typically developing adolescents, an enlarged ΔERN may be protective. Whilst it seems likely that this was linked to better overall cognitive control, as there was no association between the ERN and adolescent flanker performance we cannot conclude this with certainty.

Developmental differences

Our overall findings suggest that for adults at least, compensatory cognitive processing may increase negative reactivity and exposure to worry, providing a possible mechanism for how the ΔERN creates a vulnerability to anxiety, or anxiety maintenance (Moser et al., 2013). However the same neural measure indicated a different role in emotional vulnerability in adolescents (Moser, 2017). This is consistent with research indicating that other factors are likely to interact with the ERN to lead to anxiety disorders during development, e.g. harsh parenting and behaviorally inhibited temperaments (Brooker & Buss, 2014; Meyer et al., 2015), as well as studies which have found a larger ERN in institutionalized children is predictive of better outcomes longitudinally (McDermott et al., 2013, Troller-Renfree et al., 2016). Children rated as high on behavioral inhibition (BI) measures, where BI refers to a fearful and shy temperament in very young children (Kagan et al., 1988), are at risk for developing anxiety in later childhood or adolescence, but this is not an inevitable outcome (Lahat et al., 2011). Evidence suggests that cognitive control mechanisms and the ERN are likely to moderate the pathway that leads from behavioural inhibition to later psychopathology (Henderson et al., 2015; Lahat et al., 2014; McDermott et al., 2009).

We had expected that compensatory neural processing evident in larger ERN amplitudes would also be linked to vulnerability to emotional reactivity in adolescents, which would have been consistent with processing efficiency and attentional control theories. Many studies report evidence of processing inefficiency in relation to anxiety in adult samples (Berggren & Derakhsan,

2013) and there is some evidence that anxious children and teens are prone to decreased efficiency and a reliance on compensatory processing (Hadwin et al., 2005; Ng & Lee, 2010). However this remains to be addressed comprehensively in adolescents, particularly in more circumscribed age groups to establish developmental change in how processing efficiency might interact with anxiety vulnerability differently in adolescence. A recent review by Songco et al. (2020) indicated that attentional control plays less of a role in adolescent pathological worry compared to adults, indicating that models of worry, anxiety and cognitive control differ for adolescents compared to adults, but it remains unclear at what age the point of inflection occurs. Nonetheless, evidence that hyperactivity in the neural signatures associated with reactive control is linked to anxiety in adolescents (Shanmugan et al., 2016) indicates the complexity. Future studies should explore how the ERN and processing efficiency relate to dynamic interactions between reactive and proactive control in adolescents, and how this relates subsequently to worry, anxiety, and emotional reactivity measures.

It was also expected that high WML during the dual task would be associated with a larger ERN when compared to low WML (Moser et al., 2013), but this was not supported by our data. There was an interaction between age group and trial type where we found that irrespective of WML, teenagers had significantly attenuated ERN on the more challenging dual task in comparison with the adults. This was mirrored by the behavioural data, where adolescent reaction times were significantly slower than adults' on dual blocks. The Adult ERN did not differ significantly between Simple and Dual trials; thus error monitoring did not differ between trials types for adults, and adults and adolescents had similar ERNs on the simple blocks.

It appears that error monitoring on the flanker task was suppressed in the adolescents when engaged on a dual task. Differences between adult and adolescent cognitive processing were detectable only during the more demanding task, both at behavioral and neural levels. Cognitive control was engaged, but error monitoring and compensatory processes were diminished due to the dual tasks demands, leading to poorer overall performance in adolescents. As previously mentioned this is consistent with studies finding differences between the adult and adolescent ERN are only evident for challenging task conditions (Downes et al., 2017; Hogan et al., 2005). In the current study, the ERN and CRN differed significantly for adults in both Simple and Dual blocks, However adolescent ERN and CRN were not significantly distinguishable from one another during the Dual task, regardless of WM load, suggesting the dual task itself was already too difficult for adolescents. This was supported by the absence of post error slowing amongst adolescents on dual trials and implies attentional control was heavily occupied with the WM task component. It is possible that flanker errors lost their significance when coupled with possible aversion to errors in memorising the number sequences. This would be consistent with previous work that used a similar task to explore the influence of WML on ERN responses for errors that varied in their significance (Maier & Steinhauser, 2017). Cognitive load did not impair error detection per se, instead a reduced ERN was linked to reduced error evaluation which relied on central attentional capacity resources which were depleted by load. In the current study, developmental differences in the available central capacity impacting the evaluation of errors may explain why the ERN was blunted in the adolescents during the high WML dual task. Taken together, these results confirm previous findings that although adult and adolescent behavioural performance on executive function are frequently comparable, differences are apparent when challenge is increased, ERPs therefore reveal the continued maturation of error monitoring (Tamnes et al., 2013).

3.5.1 **Limitations**

There were several limitations to this study. Firstly as participants were all female and had no current or previous diagnoses of a psychological disorder, the results cannot be generalized to males or to clinical groups. Future studies should investigate if compensatory cognitive control mechanisms increase vulnerability to emotional dysregulation following demanding tasks in adolescents who are clinically anxious or high in trait anxiety or worry. Secondly, there was data loss due to artifacts and unexpectedly low errors rates on the dual task. This reduced the number of participants with sufficient artifact-free error segments for analyses, particularly in adolescents. To increase sample size for ERP analyses we applied a more lenient than usual threshold of $n = 4$ errors per participant, rather than the more common $n \geq 6$ errors (Grammer et al., 2014; Nayak & Tarullo, 2020). These conclusions are therefore tentative and the replication of the effects of the ERN on negative reactivity is highly desirable. Speaking to the absence of group effects of the WML manipulation on negative reactivity, the lack of a manipulation check was a limitation. Participants were not asked to report on how mentally fatigued they were by the task, therefore manipulating WM load may not have generated a sufficiently large effect of fatigue in the high WML participants to lead to group differences. Other studies that found an effect of depletion on cognitive performance used control tasks that made very limited demands on executive functions (Grillon et al., 2015; Schmeichel, 2007), which would have maximized depletion differences between groups. Furthermore, the absence of a manipulation check meant it was not possible to determine if or how much fatigue occurred, or to perform analyses taking individual differences in fatigue into account. Finally, we did not measure negative emotional reactivity prior to the flanker depletion task, so could not explore pre to post depletion changes in negative emotional reactivity. Nonetheless, there was an effect on a neural proxy of adult compensatory effort on negative reactivity, providing some support for our primary hypothesis, that variations in ERN amplitudes reflect differences in compensatory effort leading to resource depletion which may have influenced later control over worry proliferation.

3.5.2 Implications

These findings have several important research implications. In the first instance they provide further support for the CEMH explanation for the ERN in anxiety which proposes to explain elevated ERN amplitudes in adults, but also highlights developmental divergence. They also have implications for ACT in so much as they demonstrate how processing inefficiency could play a causal role in increasing exposure to negative thought intrusions after periods of intense cognitive effort. Taken together the findings suggest a mechanism for how an elevated ERN response in adults could pose a risk for anxiety over long term. Individual differences in the ERN may influence vulnerability to temporary control failures in real life, in particular where work or study make significant demands on limited cognitive resources. Future research will need to replicate these findings addressing some of the design limitations, ensuring for instance adequate differentiation between the depletion groups.

Finding a reversed effect in adolescents was unexpected. However a similar reversal of the relationship between anxiety and the ERN in prior studies, alongside evidence of that the ERN can predict better long-term socioemotional outcomes in some developmental groups, means this study further highlights the complexity in the ERN – emotional vulnerability relationship during development. The findings highlight that mechanisms in the development of error monitoring during adolescence could influence emerging mental health difficulties. This demonstrates a clear imperative for further research to characterize when and how compensatory cognitive control processing comes to predict emotional vulnerability during development? This should be addressed in studies that focus on much narrower age ranges than were included in the current study (Theodoraki et al., 2020) and combine both behavioural and neural measures.

Finally, one of the aims of this study was to elaborate on a neurocognitive mechanism that could be targeted via WMT interventions aimed at reducing emotional vulnerability. The findings suggest that adults with comparatively larger ERNs or who demonstrate bias towards reactive control could benefit from training interventions that would increase the efficiency of control, reduce the need for engaging reactive strategies, thereby supporting better emotional regulation. Although there were developmental differences in these findings, the findings suggest the ERN is also highly relevant to emotional regulation in adolescents and investigating the modulation of the ERN by WMT would provide important insights into the effects of training on adolescent emotional vulnerability to disorders. This question was addressed in study 3 which is presented in Chapter 5.

CHAPTER 4

4 Study 2. Training attentional control using dual nback WMT to reduce anxiety and depression symptoms in adolescents.

4.1 Chapter Overview.

Transdiagnostic research approaches using cognitive training have reported promising therapeutic effects of WMT on emotional vulnerability in adult populations. Some preliminary studies indicate efficacy in adolescents, whilst others have not. However, this is against the background of surprisingly scant research on WMT in adolescents generally, therefore data on adolescent responsiveness to training is lacking. Dual nback training is one of the most widely used WMT paradigms in adult studies and several studies have reported transfer effects of adaptive dual nback training on anxiety and worry symptom reduction and improved emotional regulation in adults (Diamond & Ling, 2019). No studies have investigated if dual nback training can reduce anxiety and depression vulnerability in adolescents. This chapter presents a proof of principle study to establish if training attentional control using adaptive dual nback training would transfer to reduced anxiety and depression in adolescents. Adolescent boys and girls were recruited from two London schools and randomly allocated to training on either an adaptive WM task or active control task for up to 20 days. Primary outcome measures were self-reported anxiety and depression symptomology before and after intervention, and at 1-month follow-up. Self-reported depression and anxiety decreased after training in the adaptive nback group relative to the non-adaptive controls in the intention-to-treat sample and these effects were sustained at follow-up. Findings constitute proof of principle evidence that WMT using the dual nback task may help reduce anxiety and depression vulnerability in a non-clinical adolescent population. The implications of the findings for reducing risk of internalising disorders in youth and the need for replication are discussed.

4.2 Introduction

Cumulative research points to the instrumental role of attentional control in vulnerability to anxiety and depression (Berggren & Derakshan, 2013; Koster et al., 2017), where attentional control refers to individual differences in the ability to regulate attention, awareness and concentration (Helzer et al., 2009; Rothbart & Bates, 2006). Many studies find evidence of associations between variation in the capacity to exercise voluntary control over mental resources and anxiety and depression in both children and adolescents (Kertz et al., 2016; Sportel et al., 2011). There is also evidence of a shared genetic aetiology for attentional control and anxiety, such that poorer attentional control may represent a phenotypic and genetic risk factor for anxiety disorders during adolescence (Gagne et al., 2017).

Attentional Control Theory (ACT: Eysenck et al., 2007) provides a productive theoretical framework for exploring links between attentional control and internalizing problems**.** According to ACT anxiety increases the influence of bottom-up over top-down attentional processes. Anxiety-related cognitions and worry exhaust attentional control resources, influencing critical executive functions and increasing demand for compensatory cognitive resources to mitigate the effects of poor attentional control (Berggren & Derakshan, 2013). Effects may be similar for rumination, the pattern of repetitive negative thinking about the past, which is characteristic and predictive of depression in adults (Nolen-Hoeksema, 2000). Reduced ability to intentionally direct attention away from worrisome thoughts or persistent negative self-talk may explain how worry and rumination increase vulnerability to anxiety and depression (Koster et al., 2017).

Adolescence marks a period of significant developmental change and maturation in the neural networks associated with attention control and WM (Crone et al., 2006; Giedd et al., 1999, Nagy et al., 2004, Raznahan et al., 2011) and these cognitive processes may be under particular strain during this developmental period. Researchers have suggested vulnerability to mental ill-health in adolescents is linked to rapid changes in brain structure and function (Paus et al., 2008). Therefore, typically developing children and young people with emotional vulnerability may benefit from bolstering of these resources to reduce the risk of emotional disorders. In light of these clear links between attentional control and emotional vulnerability, establishing ways in which we can boost attentional control could have corollary salutary effects on some mental health metrics. We proposed that training attentional control via WM may be a viable way of doing so.

As highlighted in previous chapters, a large body of research has investigated if cognitive improvements following WMT, transfer to improvements in academic outcomes or performance on tasks relying on executive functions supported by attentional control. Several contradictory meta-analyses indicate there is no consensus on whether cognitive training improves performance on any measures beyond those practiced in training protocols themselves or on tasks that are very similar to the WMT paradigms employed in the study (Au et al., 2015, 2016; Gathercole et al., 2019; Melby-Lervåg et al., 2016; Shipstead, Redick et al., 2012; Soveri et al., 2017). However, this absence of consensus on transfer to academic measures, like reading or mathematics, or to attention in daily life does not preclude transfer to affective processes known to overlap with neural networks associated with attentional control, executive functions and WM (Goodkind et al., 2015; Schweizer et al., 2013).

Accumulative evidence shows promising effects for attentional control training via WM on internalising symptomology (reviewed in Derakshan, 2020; Koster et al., 2017; Motter et al., 2016), however most of this work has been undertaken amongst adults. Research amongst adolescents has begun to emerge, but as highlighted in Chapter 1, the evidence for the efficacy of WMT as an intervention to reduce adolescent vulnerability to emotional dysregulation or psychopathology remains inconclusive. Although dual nback training is one of the most widely used paradigms in WMT, there is surprisingly limited work on how adolescents respond to it. It is apt therefore to explore the potential of dual nback WMT as a preventative intervention aimed at reducing risk for internalising disorders during adolescence, especially as there is evidence of transfer to emotional vulnerability measures in several adult studies (Hotton et al., 2018; Pan et al., 2020; Sari et al., 2016; Swainston & Derakshan, 2018; Zhao et al., 2020).

There is evidence that many psychological disorders exist on a continuum from wellbeing to pathology in the general population (Ayuso-Mateos et al., 2010; Shevlin et al., 2017; Tebeka et al., 2018, 2021). Most cognitive training studies have not assessed adolescent's self-reported anxiety and depression symptoms, and none have done so in a typically developing unselected adolescent sample. In the context of investigating a role for WMT to support emotional regulation development and prevent the escalation of subsyndromal symptoms to pathological levels, important insight will be gained from assessing the immediate and sustained effects of WMT on participants' perception of their own anxiety and depression symptomology.

4.2.1 **The current study**

The goal of this study was to examine the immediate and sustained effects of a WMT intervention based on the adaptive nback task on self-reported anxiety and depression symptomology in a normative adolescent sample. A variety of WM and attentional control training tasks have been used to target affective processes (see Cohen & Ochsner, 2018; Koster et al., 2017; Barkus et al., 2020). One research group found evidence that WMT tasks may require an emotional dimension to be clinically effective (Schweizer et al., 2011), however the outcome measures in this study related to emotional regulation/affective control processes rather than psychopathology measures. Schweizer et al. (2017) found PTSD amelioration following emotional nback training, however it was not compared with a neutral training task. In general however, other groups have found cognitive training can lower psychopathology symptoms with neutral task stimuli (see Koster et al., 2017; Pan et al., 2020; Xiu et al., 2018). There is evidence that the adaptive dual nback task used in this study is an effective training task for increasing WM capacity (Jaeggi et al., 2008) and has already shown promise as a training intervention to target anxiety and depression vulnerability. Training using this paradigm has previously led to improvements in inhibition, WM capacity and cognitive control that were associated with reduced anxiety and depressive symptomatology (Course-Choi et al., 2017; Grol et al., 2018; Sari et al., 2016, 2020; Swainston & Derakhsan, 2018).

Training transfer was assessed using the Revised Child Anxiety and Depression Scale (RCADS: Chorpita et al., 2000) which features two composite measures (one for total anxiety and another for anxiety combined with depression), plus several subscales assessing different categories of anxiety and depression. We predicted that adaptive nback training compared with an active control group which trained on a non-adaptive version of the task, would lead to significant reductions in scores on the RCADS anxiety and depression scales directly following intervention with sustained effects at 1-month follow up.

4.3 Methods

4.3.1 Participants

Participants were pupils from two independent single-sex secondary schools in southeast England (one boy, and one girl). After an information evening and letter of invitation to parents and students, 254 pupils were recruited [141 boys (mean age = 12.8) and 113 girls (mean age =13.06)]. The mean age overall was 13.08 (SD = 1.7) and ranged from 10-18 years. Written informed parental and participant consent was obtained. Ethical approval was granted by the research ethics committee of the Department of Psychological Sciences at Birkbeck University of London. Participants were assigned to the nback training or active control groups via a system of sequentially alternating allocation to either condition (nback; n = 128, 58 = female: control; n = 126, 55 = female). Participants, parents, and the school staff involved in participant recruitment and adherence were all blind to group allocation.

4.3.2 The WMT intervention

The active group trained using the adaptive dual nback task: This task has been described in detail in the methods chapter (Chapter 2) so is not further decribed here. Participants in the control group trained using a non-adaptive version of this task where difficulty level remained constant at 1-back throughout the intervention period; namely participants only compared target trials with the immediately preceding trial.

Training procedure

The computerized training intervention was performed online daily using personal or school computers. Each participant had a unique URL to access the training and questionnaires. Training took place over a period of 4 weeks to permit participants to complete 5 days' training per week, with 2 days off, yielding a maximum of 20 days' training. This is roughly consistent with many previous WMT interventions providing opportunities to train for up to 25 days (e.g. Holmes et al., 2009; Klingberg, 2010). This time frame was also chosen to allow the study to be accommodated within the participating schools' schedule. Participants were therefore instructed to practice the task at least 5 days per week over a period of 4 weeks, at roughly the same time each day in a quiet space with no distractions. Participants could view their performance data at the end of each training session. Only one session per day was permitted, with all blocks completed in one attempt.

Participants were instructed in groups of 30 on the training tasks and questionnaires during half-hour training sessions and afterwards assigned to either the adaptive nback or control intervention. These sessions took place in classrooms. Participants were told we were testing different versions of the training, but not informed of a control. Participants were debriefed on hypotheses at the end of the study and all control participants were invited to do the adaptive training. On logging in for the first time, participants completed the RCADS self-report questionnaire (time 1). During the first session, participants performed as many practice blocks as desired before commencing the training blocks. After four weeks (time 2), and at one-month follow-up (time 3), participants completed the online RCADS questionnaire.

Training adherence and monitoring

Participants received a daily training prompt via email. Adherence was monitored by the researcher and missed sessions were communicated to school staff every other day. If training was missed, participants received a personal email of encouragement from the school. Reminders ceased after seven consecutive days where no training took place. This procedure was consistent across both schools, although the wording of emails was at the discretion of school staff.

4.3.3 **Outcome measures**

4.3.3.1 Self-Report scales

Emotional vulnerability was assessed using the long version of the Revised Child Anxiety and Depression Scale (RCADS, Chorpita et al., 2000). More extensive information on the RCADS scales can be found in Chapter 2. Of interest in the current study were scores on the two composite measures (Total Anxiety, Total Internalising) plus the Depression subscale, allowing us to capture overall anxiety and depression symptomology.

4.3.4 **Procedure.**

All participants completed the training intervention during the same 4 week period. Baseline and post training assessment took place immediately prior to the first training session and immediately after the final training session. Self-report questionnaires were completed online and participants were directed to them automatically when they accessed the training site. Approximately one month after the end of training participants were invited via school email to complete the third self-report assessment.

4.3.5 Statistical methods

Data were analysed using IBM SPSS Statistics, Version 25.0. Linear Mixed Effect Models (MLMs) compared groups on RCADS anxiety and depression measures across time. Fixed effects were specified for Group (nback, control), Time (time 1, time 2, time 3), and a Group x Time interaction. Data were analysed according to an intention-to-treat (ITT) principle whereby the initial sample with adequate training dosage (n = 120, nback = 59; control = 61) were analyzed, regardless of whether participants completed anxiety and depression scales across the entire intervention. Model estimation was with the maximum likelihood method. Cohen's d effect sizes were derived from the F test ($d = 2*\sqrt{}(F / df)$. In addition, a MLM was applied to the per protocol (PP) sample which included only the participants for whom there was anxiety and depression data at all three time points (nback, n = 27; control, n = 30).

4.4 Results

4.4.1 **Training adherence and data analysis approach.**

Figure 4.1 summarizes the flow of participants through the study. Of the 254 pupils who volunteered, 87 (nback n = 45; control n = 42) withdrew/completed no training. The remaining participants (n = 167) did not complete equal amounts of training, with adherence varying from 1-20 days. Figure 4.2 shows the distribution of completed training sessions across participants. The mean number of days trained was 10.81 days (*SD* = 6.36) and the mode was 20 days. Some research indicates nback training effects may emerge around 8 days (Jaeggi et al., 2008), while Peng and Miller's (2016) meta-analysis concluded training duration did not significantly influence training transfer effects. This evidence, combined with the fact that in the present study steepest improvements in adaptive nback performance occurred in the first 5 days of training (see figure 3), led us to regard ≥ 6 days' training as adequate dosage for analysis, resulting in an ITT sample of n =120 participants.

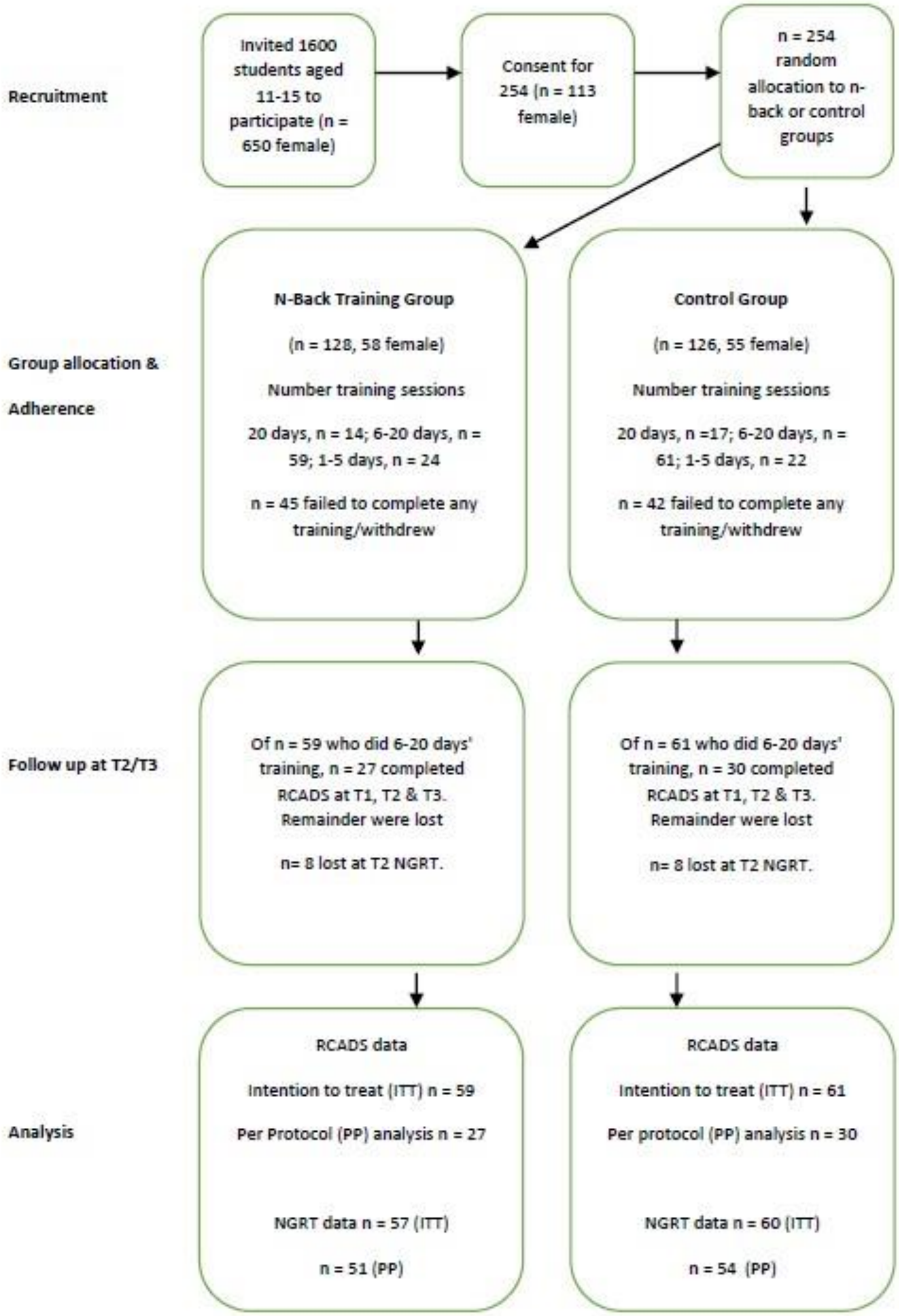


Figure 4.1. The flow of participants through each stage of the study

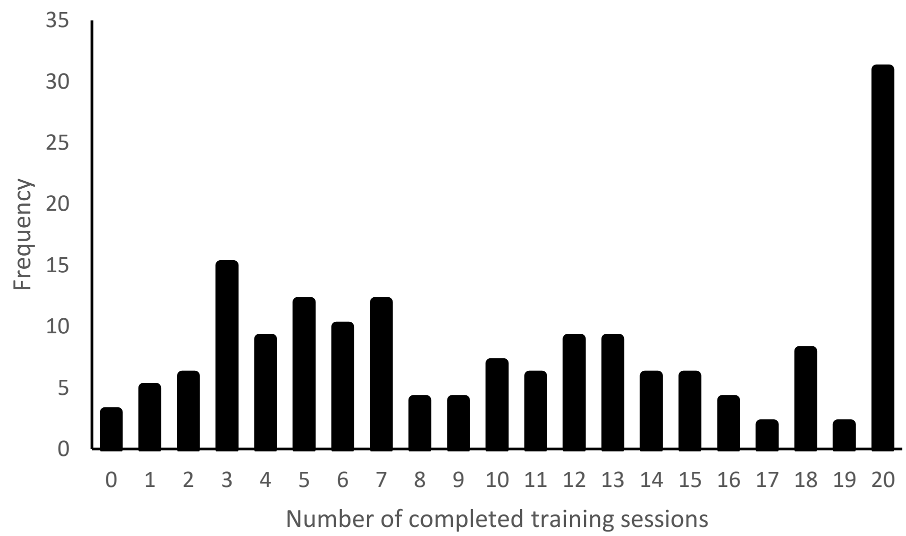


Figure 4.2 Distribution of number of completed training sessions across participants

The ITT group (nback n = 59; control n= 61) ranged in age from 10 to 18 years with a mean of 13 years (*SD* = 1.58 [nback], 1.71 [control]). Mean training dosage in the n-back training group was 13.31 days (SD = 4.95) and amongst the active controls was 14.13 days (*SD* = 5.1). The groups did not differ on training dosage $t(118) < 1$, *n.s.*. Age significantly predicted number of days' training $\beta = -0.809$, $t(119) = 22.97$, p = 0.004, and explained a small but significant proportion of training adherence $R = 0.07$, $F(1, 119) = 8.82$, p = 0.004. The gender of participants did not differ between the control and adaptive training group (nback, 27 males, 32 females; control, 28 males, 33 females) χ (1) < 1, *n.s.*, n = 120). Groups did not differ in age (nback, *M* = 13.2, *SD* = 1.58; control, *M* = 13.1, *SD* = 1.71), $t(118) < 1$, *n.s.*.

Amongst these participants n = 57 completed the psychopathology questionnaires 3 times. Per protocol (PP) sample analysis was conducted on this group. There were no significant gender differences between groups (nback; male = 11, female = 16: control; male = 6, female = 24) $\chi 2$ (1) = 2.92, p = .09 (n = 57). The mean number of training days for RCADS completers was *M* = 14.86, *SD* = 4.77 and the groups did not differ on number of days' training exposure (nback *M* = 14.63, *SD* = 4.85; control *M* = 15.07, *SD* = 4.76), *t*(55) < 1, *n.s.*.

47 participants completed 1-5 days training only, with similar numbers in each group (nback n = 24, control n = 23). The average age was 12.96 years (SD = 1.93). For this group of very poor adherers, the mean training dose was 3.36 days (*SD* = 1.30). The distribution of training adherence was bimodal with 3 (n = 15) or 5 (n = 12) days the most common dose. Within this group only n = 15 responded to the questionnaire at all three time points, while n = 5 did not respond to the questionnaires at all. Amongst the remaining poor adherers, n = 15 responded at Time 1 (T1) only, n = 7 completed T1 and Time 2 (T2) only, whilst n= 5 participants responded at T1 and Time 3 (T3) only.

4.4.2 Sensitivity analysis

To address variable training exposure a sensitivity analysis explored the relationship between training dosage and change in self-reported psychopathology from pre-intervention (T1) to both post intervention (T2) and follow-up (T3). There was no significant association between the number of training days and changes in symptomology, comparing T1 with T2 or T3 for Total Anxiety, Total Internalising and Depression, all p > .05, *n.s*. An identical analysis with the poor adherence group (≤5 training sessions) found all correlations were non-significant, all p > .05. *n.s.*

4.4.3 **Dual nback WMT performance**

Nback training - Figure 4.3 illustrates mean nback achieved by ITT group participants (n = 120) across the training period. WM performance improved significantly, evidenced by higher mean nback level on the last day of training (M = 2.36, SD = 1.03) relative to the first (M = 1.82, SD = 0.48) $t(58) = 4.84$, p < .001.

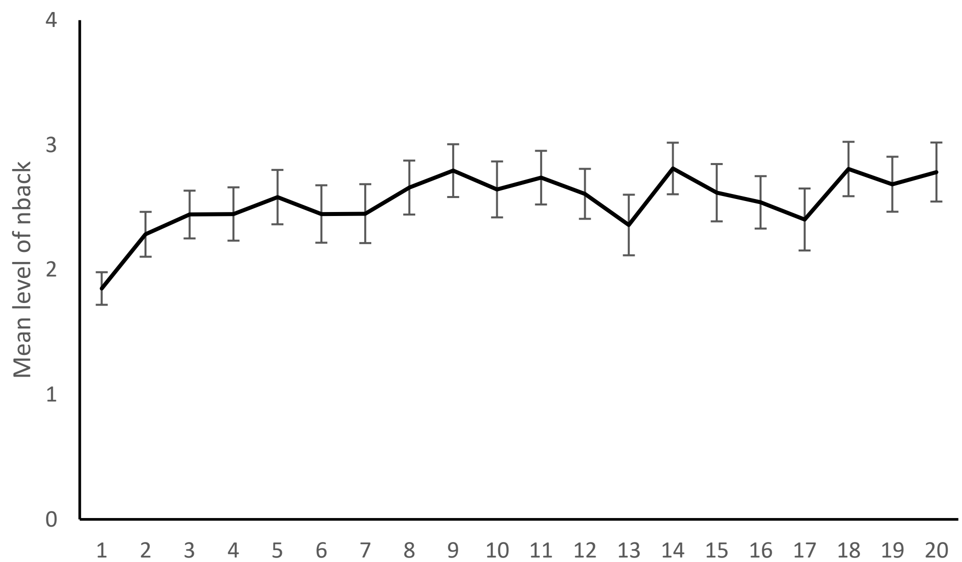


Figure 4.3 Shows mean daily nback level attained across days 1-20 of the training intervention period in the nback group. Error bars represent +/- 1SE.

1-back active control training - Percentage accuracy in 1-back performance amongst the active control group was unchanged between the beginning (M = 93.58, SD = 9.81) and end (M = 92.43, SD = 9.02) of training, $t(60) < 1$, *n.s.*.

The training improvement slope for the adaptive nback task was significantly negatively correlated with Total Internalising (r = -.243, p =.027, n = 83) at baseline T1, such that higher baseline internalising predicted poorer improvement on the nback training task.

4.4.4 **Effects of WMT on primary outcome measures**

Means and standard deviations for RCADS scores are presented in Table 4.1 for both ITT and PP samples respectively. The groups were not significantly different from one another prior to intervention on any measures, all t's ≤ 1, *n.s.*. Standardized RCADS scores ≥ 70 are clinically significant, whilst scores ≥ 65 are borderline clinically significant. The means for both the nback and the control groups in this study were below average. 5% of the ITT sample participants scored at borderline clinical or clinically significant levels of total anxiety, whilst 11.6% had internalising scores ≥ 65. Of these participants with borderline or clinical significant anxiety, the mean number of training days was 9.27 (*SD* = 1.64) with one of these participants completing fewer than 5 training days.

Table 4.1 Means and standard deviations (in parentheses) for self-reported RCADS scores for anxiety and depression symptomatology for nback and control groups at times 1, 2 and 3.

	Time 1		**Time 2**		**Time 3**	
	Nback	**Control**	***Nback***	**Control**	***Nback***	**Control**
Anxiety (PP)	47.04 (8.62)	46.84 (9.34)	44.67 (8.89)	46.41 (11.6)	42.81 (7.62)	45.47 (10.80)
Anxiety (ITT)	49.08 (11.42)	46.9 (8.67)	45.28 (8.33)	46.54 (10.85)	44.77 (9.80)	45.14 (10.51)
Internalising (PP)	46.78 (9.65)	46.88 (10.01)	44 (9.48)	46.66 (12.66)	42.78 (8.58)	46.19 (12.19)
Internalising (ITT)	49.32 (12.3)	47.2 (9.24)	45.2 (8.83)	47.08 (11.84)	45.05 (11.00)	45.72 (11.90)
Depression (PP)	5.96 (4.08)	6.53 (4.87)	5.04 (4.26)	7 (5.54)	4.41 (4.01)	6.81 (5.92)
Depression (ITT)	7.64 (5.55)	6.82 (4.28)	6.02 (4.06)	7.26 (5.33)	5.73 (5.5)	6.7 (5.65)

Total Anxiety symptomatology

Figure 4.4 shows that relative to the controls there was a decrease in RCADS Total Anxiety scores in the nback training group, which was sustained at follow-up. The MLM for the ITT sample confirmed this observation with a significant Group X Time interaction $F(2, 98.33) = 3.42$, $p = .04$, Cohen's $d = .37$ (ITT). The MLM for the PP sample missed significance $F(2, 66.33) = 2.61$, $p = .08$, Cohen's $d = .39$.

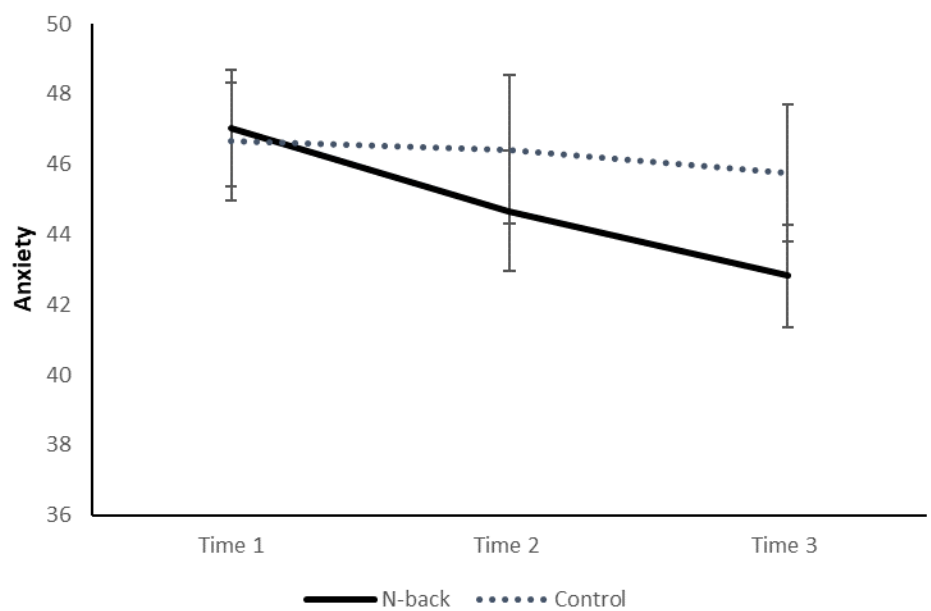


Figure 4.4 Changes in self-reported Total Anxiety symptomology as a function of training group across time.

Total Internalising symptomology

Figure 4.5 shows that relative to the controls there was a decrease in RCADS Total Internalising scores amongst participants in the nback training group, which was sustained at follow-up. The MLM confirmed this observation with a significant Group X Time interaction $F(2, 89.17) = 3.86$, $p = .03$, Cohen's $d = .41$ (ITT). The MLM for the PP sample missed significance, $F(2, 67.18) = 2.64$, $p = .08$, Cohen's $d = .39$.

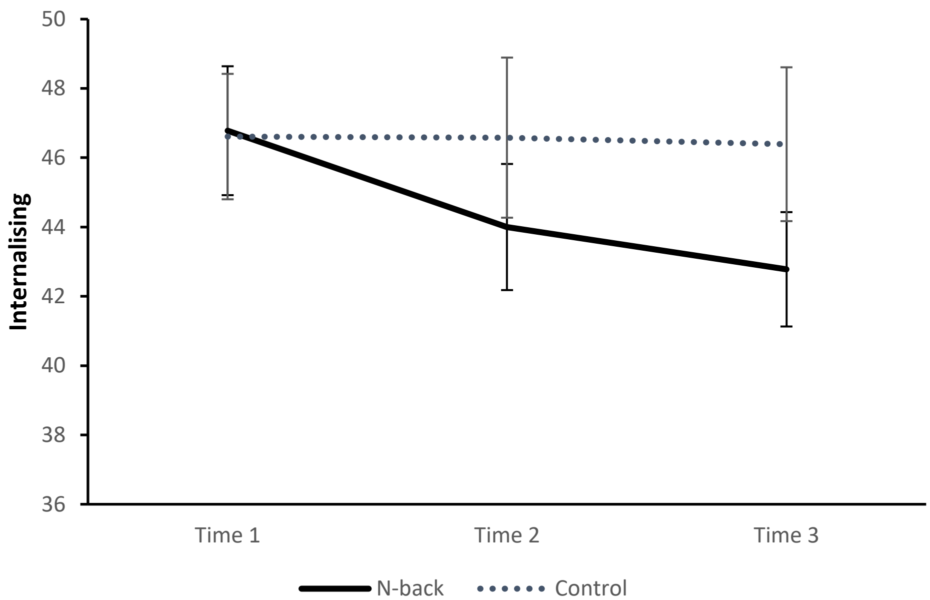


Figure 4.5 Changes in self-reported Total Internalising symptomology as a function of training group across time.

Depression

Figure 4.6 shows that relative to the controls, there was a considerable decrease in RCADS self-reported depression scores amongst participants in the nback training group, which was sustained at follow-up. This observation was corroborated in the MLM by a significant Group X Time interaction $F(2, 89.65) = 6.39$, p = .003, Cohen's $d = .52$ (ITT); $F(2, 65.94) = 3.93$, p = .02, Cohen's $d = .44$ (PP).

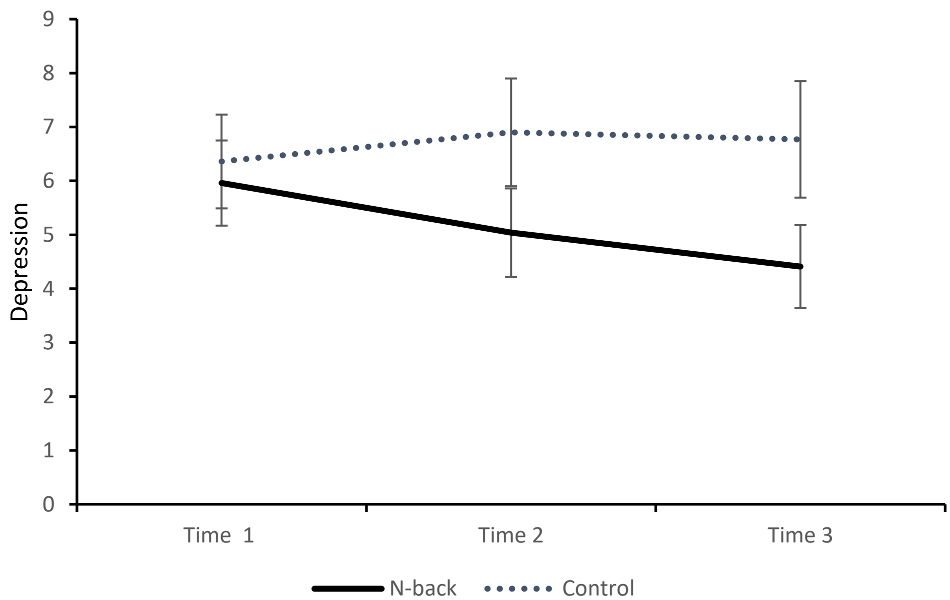


Figure 4.6 Changes in self-reported depression symptoms as a function of training group across time.

Symptom change at the individual level.

Figures 4.7 a, b and c below display individual participant's symptom change from T1 to T2 with mean group change in nback and control groups for Total Anxiety, Total Internalising, and Depression. In a post hoc analysis we explored the extent to which significant symptom reduction occurred at the individual level. Since our study instruments did not yield an objective measure for 'significant improvement' for an individual, we identified participants for whom difference scores were greater than the overall mean change which was -.04 across both groups. However -.04 was a low benchmark. Instead the mean difference in the nback group was chosen as the cut off. In the ITT sample, where 46 participants from the nback group completed the RCADS at T1 and T2, the mean Total Anxiety improvement was a reduction of 2.0 (SD = 5.66) and for Total Internalising a reduction of 2.3 (SD = 5.82). For both Total Anxiety and Total Internalising measures, n = 20 nback group members had improvement scores that exceeded the average improvement between T1 and T2.

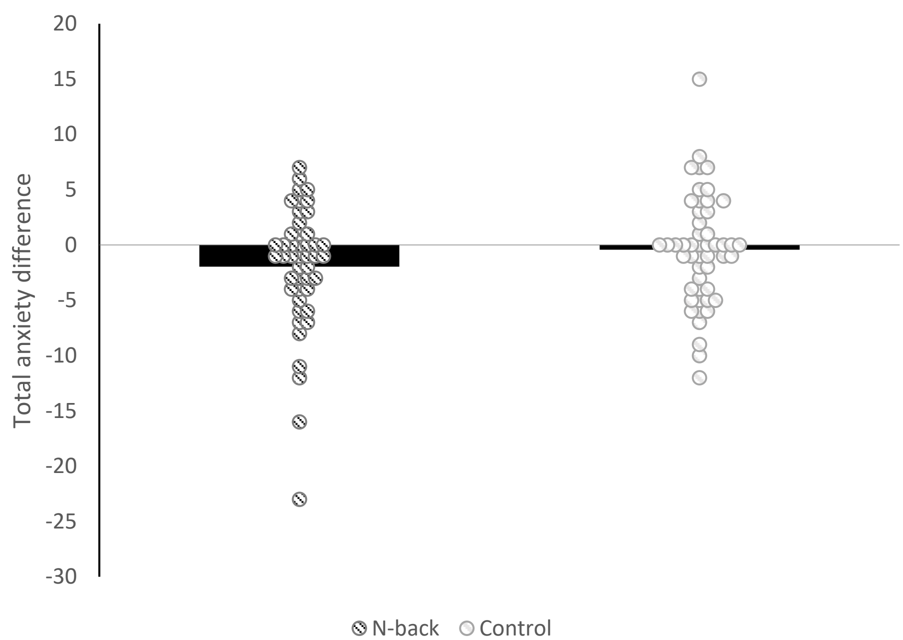


Figure 4.7a. Shows individual participant anxiety change scores by intervention group. Bars represents group means.

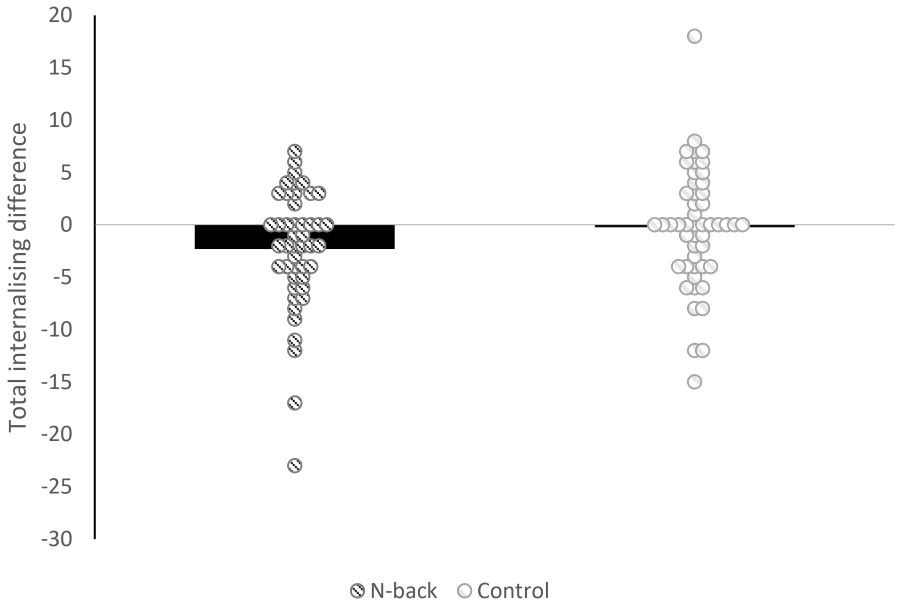


Figure 4.7b. Shows individual participant total internalising change scores by intervention group. Bars represents group means.

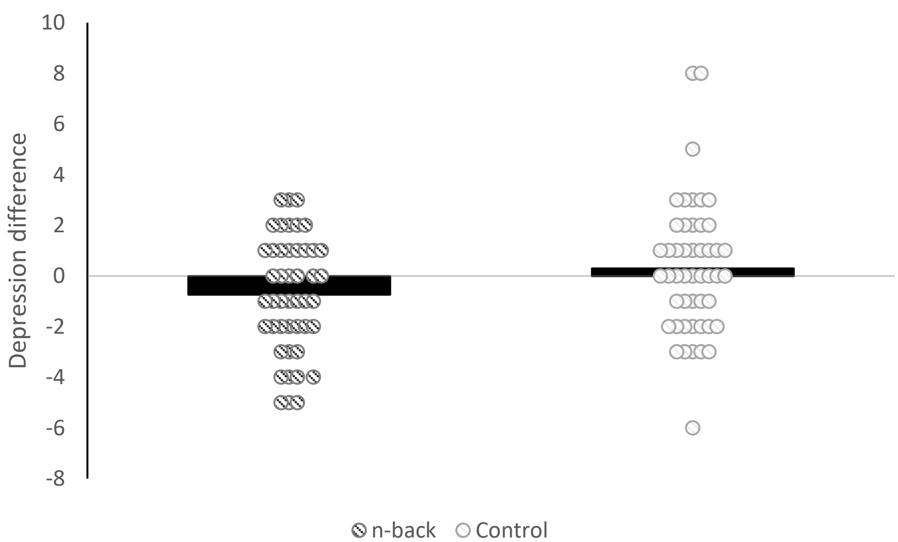


Figure 4.7c. Shows individual participant depression change scores by intervention group. Bars represents group means.

4.5 Discussion

Previous studies have shown that cognitive training may increase cognitive flexibility and reduce emotional vulnerability in clinically and sub-clinically anxious and depressed adults. The current study investigated if cognitive training using an adaptive dual nback WM task can reduce self-reported anxiety and depression symptoms in adolescence, when compared to a non-adaptive active control group. Nback training was significantly associated with reduced self-reported anxiety and depression symptomology relative to the controls directly following intervention and at one month follow-up. Our findings suggest that amongst adolescents it may be possible to reduce subclinical anxiety and depression symptoms using an intervention which is known to train WM (Au et al., 2016; Klingberg, 2010). Whilst WMT transfer to academic measures remains elusive, emotional processes may be more amenable to training transfer in this age group.

These findings are consistent with previous studies that found reduced self-reported anxiety (Hadwin & Richards, 2016) and teacher-reported emotional symptomology (Roughan & Hadwin, 2011) in school children following WMT using Cogmed, a computerized training package which targets attention and memory in academic underperformance and individuals with ADHD (Shipstead, Hicks et al., 2012). It is also consistent with adult studies which reported training-related improvement in anxiety and worry symptoms in high worriers (Course-Choi et al., 2017) and high trait anxious individuals (Sari et al., 2016). This study is however the first to find reductions in depression symptomology following adaptive dual nback training. Previous studies have found that nback training reduced anxiety symptoms in female breast cancer survivors (Swainston & Derakshan, 2018) and in high anxious individuals (Sari et al., 2016), but not depression in a moderately dysphoric sample (Owens et al., 2013). There is however evidence that cognitive training can reduce depression (Hoorelbeke & Koster, 2017; Brunoni et al., 2014) and depressive rumination (Hoorelbeke et al., 2015; Siegle et al., 2014; Vanderhasselt et al., 2015) in emotionally vulnerable and clinically depressed adults using other WMT paradigms.

These findings contrast with some recent studies that did not find transfer of WMT to anxiety and depression outcomes in adolescents (Hitchcock & Westwell, 2017; Mewton et al., 2020). It is unclear why this is the case, however our study differed from these studies in terms of the training tasks, participant ages and outcome measurement, which may have contributed to the different results. For instance Hitchcock and Westwell (2016) relied on teacher-reported social and emotional difficulties, which may not have captured true measures of participants' emotional vulnerability. Participants in the Mewton et al. (2020) study included young adults aged up to 24 years, therefore is possible that older adolescents and young adults do not benefit from training to the same extent as younger or middle adolescents. Notably, both these studies featured training programmes with multiple tasks, whilst our participants trained on a single task. Although Diamond and Ling's (2019) extensive review on training executive functions reported that interventions featuring variety in training tasks were most advantageous for increasing executive function, we have shown that training using a single WM task can improve emotional vulnerability.

Reductions in anxiety and depression symptomology were evident not just at the end of the training period, but persisted at follow up, one month post intervention. This suggests that the positive effects of nback training on emotional vulnerability were not short-lived and is evidence that adaptive training may have persistent lasting effects via cognitive plasticity in adolescence. Previously Swainston & Derakshan (2018) have shown that the positive effects of training persisted 18 month after intervention in a vulnerable adult population. Whilst our study suggests that sustainability of effects was also present here, further research using much longer-term follow up of adolescent participants is needed to address if the effects of nback training would persist beyond one month.

No previous study has explored the impact of adaptive WMT on depression and anxiety symptomology in a non-clinical adolescent population, and this study suggests a significant moderate effect of WMT on depression and anxiety. Anxiety and depression may have been reduced via an increase in cognitive control following training. Similar to adults (Borkovec et al., 1983; Nolen-Hoeksema, 2000) repetitive negative thinking in the form of high levels of rumination and worry are characteristic of depression and anxiety in children and adolescents (Abela et al., 2002; Muris, Roelofs et al., 2004; Schwartz & Koenig, 1996). Individuals with poorer attentional control may be prone to rumination and worry because of a greater susceptibility to intrusive negative thoughts, which are more difficult to control once worry or rumination has been initiated (Fox et al., 2015; Gotlib & Joorman, 2010). In this study, training may have increased attentional control reducing the prevalence of worrisome and ruminative thoughts. Although neither worry nor rumination were measured in this study, speculatively it may be the mechanism through which improvements in WM task performance reduced anxiety and depression.

The increase in WM following nback training may have reduced anxiety and depression symptoms via improved top down regulation of worry and ruminative thoughts due to increased prefrontal regulation of amygdala activity. Siegle et al. (2007) and Siegle et al. (2014) demonstrated normalization of fronto-limbic disruption in depression after WMT. Recent studies indicate the likelihood of a fronto-parietal network providing a hub for flexible regulation across several brain regions, including limbic, motor and visual systems, in the service of goal-directed action (Cole et al., 2014). In light of evidence of its disruption across diverse mental health disorders, Cole et al. (2014) propose the fronto-parietal control system as analogous to a psychological immune system. Healthy individuals may experience subclinical internalising symptoms but successfully regulate them via this fronto-parietal control hub. Of relevance to the current study, is that a central prediction of this hub system is that its integrity may be amenable to external manipulation via pharmacological or training interventions (Cole et al., 2014). Research on the neural correlates of WM and WMT suggest a potential overlap with this control hub. Evidence from fMRI and EEG studies have indicated that higher WM capacity is associated with greater fronto-parietal functional and structural connectivity (Constantinidis & Klingberg, 2016). Studies of the neural correlates of WMT indicate post-training changes in prefrontal and parietal cortical activity in adults and children (Astle et al., 2015; Klingberg et al., 2005; Olesen et al., 2004). Constantinidis and Klingberg (2016) reported increased fronto-parietal connectivity after WMT in children and suggested functional connectivity changes may result from increased myelination or stronger synaptic connectivity.

The behavioral and neural systems for WM undergo the most protracted development of all executive functions, not fully mature until late adolescence/early adulthood (Blakemore & Choudhury, 2006; Huizinga et al., 2006; Luna et al., 2010). Adolescence marks a critical period of maturation in the prefrontal cortex, which as previously described, is central to these systems. Increased vulnerability to mental health disorders in adolescence may be due to a culmination in maturational processes (Blakemore, 2008; Paus et al., 2008). This vulnerability is also an opportunity. Whilst training interventions in adults target an established neural architecture, training interventions in adolescents may act upon systems under construction with a salutary influence on development (Galván, 2010; Jolles & Crone, 2012). As such, the results of the current study suggest improving WM in adolescence may be a promising route for reducing anxiety and depressive vulnerability in adolescents.

The current study extends previous research in several ways. It is one of few studies to investigate WMT amongst typical adolescents. Thus research on effects in adolescence, particularly in typically developing samples, has been limited (Diamond & Ling, 2019; Jolles & Crone, 2012; Karbach & Unger, 2014; Wass et al., 2012). It also extends research on a potential causal role for WM in the maintenance of anxiety and depression symptomology in healthy adolescents, and the potential for WMT in anxiety and depression prevention (Hoorelbeke et al., 2016). Finally, the sustainability of the effects of training on anxiety and depression are both novel and important and suggest the potential for adaptive nback training to have lasting effects on mechanisms impacting cognition and emotion in adolescence.

4.5.1 **Limitations**

This study had a number of limitations. Participants were high academic achievers from independent schools, so results may not generalize to other adolescent groups. Secondly, there was poor training adherence and high attrition. It may be that the group who continued to train were self-selecting, thus biasing the results. However, equal numbers of participants were lost from each group, therefore any biases would apply to both intervention and control participants.

Whilst participants did not provide subjective feedback on their training experience, it is clear that many found it difficult to keep up their training over a prolonged period. This may be a reflection of the training task itself or a particular feature of undertaking intense cognitive training studies amongst adolescents, especially when participants have no clear incentives (participants were not paid in this study). Whilst parents might insist that younger children complete daily training exercises, this becomes more difficult as children enter adolescence and become less acquiescent to parental and experimenter wishes. This, combined with increased academic, extra-curricular and social commitments of adolescence, means daily training exercises may be low priority. This is hinted at in the negative association between age and training adherence in the present study. Future studies should improve how adolescent participants are incentivized to persevere in training interventions, whilst managing expectations regarding benefits of training itself and avoiding Hawthorne effects. This could include payment, although paying training participants is controversial and has been linked with lower rather than higher motivation and training effectiveness (Katz et al., 2018).

In the present study participants were briefed and recruited in fairly large groups and communications came via school staff rather than directly from researchers. Adherence might have been improved by a more ‘one-to-one’ relationship to promote a greater sense of participant’s personal responsibility. There is a fine line between encouraging participants who are falling behind in training and putting undue pressure on them. Perhaps more ethical would be better screening of participant motivation at the outset, however the cost might be an even more self-selecting sample. Alternatively, future researchers could develop better support systems to help participants anticipate and address boredom, loss of motivation or lapses in time management. These issues were all addressed in study 3 which is reported on in Chapter 5. In conclusion, motivation and adherence remain a major issue in this kind of study and future research should take this into account in study design and recruitment.

That not all participants entered into the analyses performed equal amounts of training is also limitation; however, the sensitivity analysis showed symptom change was not correlated with the number of completed training sessions. It is also important to acknowledge an additional limitation is that the analytic protocol and selection of a cut off at ≥ 6 days was not preregistered in this case. These findings need to be replicated and future replication attempts should be pre-registered, which was done in study in study 3. Finally, an attentional control measure and measures of worry and rumination would have permitted stronger conclusions on the mechanisms by which training WM might reduce anxiety and depression symptomology in adolescents. As it is, we may only speculate based on previous research that these mechanisms may have been involved.

4.5.2 Conclusion

Despite limitations, the study's preliminary findings are nonetheless informative. This is one of few studies to explore the effects of WMT on cognitive vulnerability in typically developing adolescents, and to demonstrate not only positive effects on emotional vulnerability at the end of training, but also sustained effects at one month follow-up. The significant effects on depression is an important and novel finding. Previously, Takeuchi et al. (2014) showed that WMT compared to a non-active control reduced negative affect in healthy adults indicating a potential clinical application in promoting cognitive functioning to support mental wellbeing. The current study provides preliminary evidence that targeting cognitive vulnerability to anxiety and depression in adolescence via WMT is a viable area for further research. This is of particular relevance to how we might address vulnerability to developing internalising disorders amongst adolescents in general, especially given widespread concerns about increasing prevalence of emotional disorders in this age group.

It will be essential to demonstrate that this finding can be replicated in a study that also provides insight on the cognitive and neurocognitive mechanisms underlying training-related reductions in symptomology in adolescents. To this end, Chapter 3 highlighted a candidate neurocognitive mechanism that could be targeted by training, and which formed a neural outcome measure in the WMT intervention study which is reported in Chapter 5.

CHAPTER 5

5 Study 3. A randomized control trial examining the effects of adaptive WMT on emotional vulnerability and neural correlates of cognitive control in adolescent boys. A behavioral and ERP study.

5.1 Chapter overview

Attentional control training shows promise as a universal or targeted intervention to reduce adolescent vulnerability to emotional or behavioral disorders. With interventions and procedures adapted from adult studies, further work is needed to understand how attentional control training plays out in adolescence specifically. Significant neurocognitive development in brain regions associated with attentional control during adolescence would suggest that adolescents may respond differently to adults and research is needed to understand how training impacts neural correlates of training-related change in emotional vulnerability in this age group.

The following chapter reports on and discusses the findings of a study to explore the effects of attentional control training on electrophysiological measures of cognitive control from two experimental tasks measuring attentional control and emotional regulation respectively. The study also aimed to replicate the findings of reduced anxiety and depression symptoms following WMT which were reported in Chapter 4. Adolescent boys, pre-screened for above-median worry, undertook two week's adaptive nback WMT or non-adaptive control training. Self-reported psychopathology vulnerability measures were recorded before and immediately after training and at 3 months follow-up. Prior to and directly after the training intervention, continuous EEG was recorded during a standard arrow flanker and emotional Stroop tasks from which several ERPs associated with different aspects and temporal stages of cognitive control processing (ERN, P(e), N2 and P3) were derived.

Results showed that despite improvements in performance on the adaptive WMT task, there were no improvements in self-reported symptoms of anxiety, depression, worry or rumination in the training group relative to the controls. Working memory capacity and performance during the flanker and Stroop tasks were also not differentially impacted by training. Statistical analyses also revealed there were no significant group differences on any of the ERPs as a result of training.

However, notable correlations were found in exploratory analyses, indicating a significant relationship between the rate of improvement on the adaptive training task and reduced emotional vulnerability at follow-up and a significant association between training improvement and a reduction in P(e) amplitudes. There were also significant associations between pre to post training changes in the P(e), N2 and P3 amplitudes and improvements in self-reported anxiety, worry and rumination at follow-up. There was no association between ERN change and any of the emotional vulnerability outcome measures. This tentatively suggested that training-related change in some neural indices of cognitive control were linked to improvements in emotional vulnerability at follow-up. Possible implications for the null findings at group level, alongside significant effects at the individual level are discussed.

5.2 Introduction

5.2.1 Background

Impaired attentional processes are regarded as an important cognitive contributor to the risk and maintenance of anxiety and depression (Derakshan, 2020; Eysenck et al., 2007; Joormann et al., 2007; Koster et al., 2017), where attentional control refers to the ability to direct and control attention towards and away from stimuli in the service of goal directed action (Eysenck et al., 2007; Rothbart & Bates, 2006). Studies show attentional control also plays a role in the development of emotional regulation influencing mental health across the lifespan (Cohen & Ochsner, 2018; Nigg, 2017; Ochsner & Gross, 2005; Schweizer et al., 2020), and can predict anxiety and depression in children and teens prospectively (Kertz et al., 2016; Sportel et al., 2011). It is not surprising therefore that researchers seek ways to train or augment attentional control to understand the causal role of attentional control in anxiety and depression vulnerability more widely, but also to explore its possibilities for therapeutic advantage. There is also increasing interest in employing cognitive training to address age or development-specific periods of vulnerability, particular during adolescence (Schweizer et al., 2020), however so far this has not been widely undertaken in adolescent samples. Although findings from study 2 (described in the previous chapter) suggest WMT can reduce emotional vulnerability in adolescents, results from other studies have been mixed (Boendermaker et al., 2018; De Voogd et al., 2016; Hadwin & Richards, 2016; Hitchcock & Westwell, 2017; Mewton et al. 2020; Rosenbaum et al., 2017) and much remains to be understood about the mechanisms involved in successful training transfer (Pergher et al., 2020; Smid et al., 2020). In particular, there has been limited work on the neural correlates of attentional control training targeting psychopathology vulnerability generally, and to date no work has addressed this in adolescent samples. The aim of the current study was firstly to replicate the effects of attentional control training on anxiety and depression found in experiment 2 (Chapter 4), and secondly to move beyond purely behavioral outcome measures to explore underlying changes in neural correlates of attentional control and emotional regulation.

5.2.2 **Neural mechanisms of WMT transfer to emotional outcome measures**

Although there is evidence that WMT can transfer to measures related to psychopathology and emotional regulation, the mechanisms for improvements to emotional functioning are not fully understood. See Barkus (2020), Derakshan (2020), Koster et al., (2017) and Motter et al. (2016) for reviews. Theoretically, if WMT alters attentional control, training-related change must be instantiated via changes in brain structure, function or connectivity (Klingberg, 2010). A limited number of studies examined neural change alongside alterations in emotional functioning or psychopathology outcomes following WMT interventions in adults (Liu et al., 2017; Lotfi, Ward et al., 2020; Owens et al., 2013; Pan et al., 2020; Sari et al., 2016; Schweizer et al., 2013; Zhao et al., 2020). Some of these studies suggest that changes in neural processes that support filtering efficiency and the orienting of attention may be linked to improvements in emotional functioning, or improved cognition in those prone to anxiety or worry (Liu et al., 2017; Lotfi, Ward et al., 2020; Owens et al., 2013). Liu et al. (2017) found improved orienting of attention, decreases in the Late Positive Potential (LPP) ERP amplitude during emotional regulation, and an association between individual differences in orientation and a subjective aspect of emotion regulation. Similarly, Pan et al., (2020) found nback training reduced anxiety and stress, improved self-reported positive refocusing and decreased the LPP during cognitive reappraisal. In another study, Owens et al. (2013) showed training led to increased neural filtering efficiency (FE) of distractors in WM in dysphoric individuals, with FE derived from EEG amplitudes in contralateral delay activity (CDA), indicating that attentional control impairments may be improved by training via filtering efficiency improvements.

Another study, employing an intervention that trained WM in an affective context, found transfer of WMT to emotion regulation was linked to functional activation change in the fronto-parietal network (Schweizer et al., 2013). Notably, there was decreased activation during an emotional WM task, alongside activation increases during an emotion regulation task which was linked to improved emotional regulation performance. This may have been because WMT enhanced the ability to engage the fronto-parietal network for more challenging emotional regulation tasks, whilst more automatic processing in the WM task explained reduced activation (Engen & Kanske, 2013). However, a recent study was unable to find links between dual nback WMT-related improvements in social anxiety symptoms and significant changes in a variety of ERP components (Zhao et al., 2020), so delineating clear therapeutic mechanisms remains a challenge. Taken together evidence from adult WMT studies suggest that improvements in emotional outcome measures are accompanied by changes in neural measures associated with higher order cognitive control and emotional regulation.

In general, despite optimism about cognitive training to boost emotional functioning in adolescence, there are gaps in the literature regarding specific mechanisms underlying the effects of training in typically developing adolescents, especially with regard to psychopathology vulnerability. The overwhelming majority of WMT studies feature younger or pre-adolescent children in their samples (Sala & Gobet, 2017) with some exceptions for younger adolescents (Kun, 2007; Pugin et al., 2014; Rosenbaum et al., 2017; Shavelson et al., 2008) or focused on adolescents with developmental disorders associated with WM impairments (Sala & Gobet, 2017; Stevens et al., 2016). As a consequence, there is a paucity of research on how WMT impacts cognitive and behavioral outcomes in typically developing adolescents, and to date, no studies have examined training-related neural alterations alongside measures of emotional vulnerability**.**

5.2.3 **The current study**

The aim of the current study was to replicate findings from the study in Chapter 4 and explore the effect of adaptive dual nback training on neural processing associated with cognitive control and emotional vulnerability in adolescents using an RCT design. Several ERPs are known to vary according to attentional control demands and emotional content, therefore represent an ideal way to explore changes in higher-level cognitive processing. The study examined training-related change in response-locked ERPs linked to error processing during a flanker task - the ERN and the P(e) - in addition to changes in the stimulus-locked ERP correlates of conflict monitoring and attention control (N2, P3) during an emotional Stroop task. A central aim of the study was to explore how changes in ERPs following WMT relate to sustained longitudinal changes in vulnerability to anxiety and depression.

Extant research has shown that the adult ERN may be amenable to WMT, evidenced by training-related gains in WM performance and increases in ERN amplitudes following WMT (Horowitz-Kraus & Breznitz, 2009; Lotfi, Ward et al., 2020). To date, no studies have reported the effects of training the P(e). Lotfi, Ward et al. (2020) found emotional WMT increased the ERN and reduced worry symptoms and trait anxiety in adults, suggesting that improved anxiety may be linked to improvements in attentional control and changes in error processing. WMT effects on the ERN may be especially useful to study alongside emotional vulnerability changes, because of well-documented links the ERN and proneness to worry, anxiety and negative affect in adults (Hajcak et al., 2003; Moser, et al., 2013). Developmental research indicates a more complex relationship, and this was borne out in the findings from Study 1 (Chapter 3). The direction of associations between anxiety and the ERN varies across childhood and adolescence, such that adult-like patterns emerge later in childhood and in older adolescents (Bress et al., 2015;

Ladouceur et al., 2008; Meyer, 2017; Moser, 2017). There is also evidence that in developmental populations, an elevated ERN in anxiety is more likely to be detected in between-group comparisons between high versus low anxiety participants, or clinical versus non-clinical groups, than in linear associations between the ERN and symptom severity common in the adult literature (Meyer et al., 2012).

To enhance power to detect effects, participants in the current study were pre-screened for elevated worry. It was hypothesised that worry, rumination, anxiety and depression should decrease immediately following training and be sustained at follow up 3 and 6 months later. Although WMT can enhance adult ERN amplitudes (Horowitz-Kraus & Breznitz, 2009; Lotfi, Ward et al., 2020), it is not clear how ERNs in adolescent high worriers would be impacted by WMT, given evidence of elevated ERN as a potential marker for anxiety disorders, and findings that the ERN continues to change during development. This is further complicated by prior work in both adults and developmental clinical populations where ERN amplitudes remain elevated or unchanged following successful treatments with Cognitive Behaviour Therapy (CBT) or Selective serotonin reuptake inhibitors (SSRI) medication (Hajcak et al., 2008; Ladouceur et al., 2018). However, there is some evidence the ERN may moderate the effectiveness of some treatments (Gorka et al., 2018). Expectations therefore regarding effects of training on the ERN and P(e) were non directional and exploratory.

As outlined in Chapter 2, the N2 is a negative going waveform that occurs approximately 200-350 post stimulus onset at fronto-central electrodes (Yeung et al., 2005), whereas the P3 typically peaks 300-500 ms post stimulus onset at central parietal sites (Hajcak et al., 2010). These components represent higher level cognitive control processing of task stimuli, where the N2 has been associated with conflict detection, assigning attention to a stimulus and response inhibition

(Donkers & van Boxtel, 2004; Falkenstein et al., 1999; Ladouceur et al., 2007) and the P3 is related to more elaborate stimulus processing (Polich, 2004; Segalowitz & Davies, 2004). The N2 and P3 are frequently modulated by emotional stimuli during inhibitory control and conflict monitoring tasks (Hum et al., 2012; Righi et al., 2009; Sehlmayer et al., 2010) and therefore suitable for tracking electrophysiological and neural change associated with higher order cognition and emotional regulation.

Studies examining the effect of WMT on the N2 and P3 components suggest that WMT can enhance the N2 (Wang & Covey, 2020; Zhao et al., 2020) and P3 (Liu et al., 2017; Oelhafen et al. 2013; Pan et al., 2020; Shiran & Breznitz, 2011; Wang & Covey, 2020), suggesting that training may enhance spatial attention allocation and conflict monitoring. Of these studies only Zhao et al. (2020) explored links between ERP modulations and changes in emotional vulnerability. These authors found that dual nback training transferred to improved WM performance (Ospan task) and reduced social anxiety symptoms post training. However although reductions in social anxiety post training were significantly mediated by increased WM performance, improvements in emotional vulnerability were not explained by increases in the N2, although low power may explain why these changes were not significantly correlated. These studies broadly suggest that training-related improvements in attentional control may be reflected in modulations of the adult N2 and P3, and are suitable outcome measures in adolescent training studies aimed at exploring neural mechanisms of training change.

This study employed an emotional variant of the Stroop colour-word paradigm (Perez-Edgar & Fox, 2003) which is amenable to performance improvements following WMT (Schweizer et al., 2011). EEG was recorded while participants indicated the text colour of words presented on a computer monitor. Words were either neutral or threat-related, but word-meaning was task irrelevant, with differences in speed of response for threat stimuli representing the ability to avoid attentional capture from irrelevant threat distractors. We predicted that training-related improvement in attentional control should transfer to a reduced emotional Stroop interference effect with performance improvements accompanied by modulation of the N2 and P3 responses to threat stimuli from baseline to post training. The ERN on the other hand was derived from errors on a standard arrow flanker task.

We also conducted post hoc analyses to examine if alterations to ERPs would relate to long-term symptom change in the training relative to control groups, predicting that symptom alleviation would be associated with training-related modulation of these ERPs. Finally, a frequently overlooked consideration in training studies is whether and how much differential engagement and training task progress may impact outcomes in intervention studies. Researchers also cite difficulties with training adherence and sustaining motivation among adolescents (Mewton et al. 2020), and levels of training engagement within the training task may influence outcomes, even where group differences are absent (Hotton et al., 2018; Sari et al., 2016, 2020). With this in mind,we also examined how improvement on the training task would relate to changes in neural and emotional outcomes, predicting that more improvement in the adaptive dual nback training task would be associated with symptom improvement and neural plasticity indexed by ERP modulations.

Participants trained using the adaptive dual n-back task, which was the same as the training task used in study 2 and previously described in Chapters 2 and 4. Participants were randomly allocated to either the active training or an active control group and all participants were required to undertake the training over the same two week period in October 2019. Although the training and the control task paradigms were consistent with study 2, the duration of the intervention was shortened to two weeks with participants expected to train 6 days per week. This alteration was made in response to the attrition observed in study 2.

5.2.4 **Summary of hypotheses**

The following predictions were made.

- Working memory performance in the adaptive training group would increase over the course of the intervention.
- Relative to the control, adaptive nback training-related WM performance increases would transfer to attentional control measured at a behavioural and neural level. Specifically, we predicted training would lead to increased WM capacity, improved inhibition of distractors in the flanker task, alongside modulations in ERN and P(e) amplitudes, plus a reduced threat-word interference effect in the emotional Stroop task accompanied by modulation of N2 and P3 amplitudes for threat words.
- Sustainability of effects are of paramount importance. Previous work has shown sustained efficacy for up to 15 months post training (Borella et al., 2013; Swainston & Derakshan, 2018). It was expected that relative to the active control, attentional control improvements in the adaptive nback group would ultimately transfer to reduced post-training worry, rumination, anxiety and depression scores sustained at 3 and 6 months follow up.

Post hoc analyses explored if sustained improvement in psychological vulnerability were associated with the rate of improvement in the nback training task performance and ERP change. We predicted higher improvement rates would correlate with reduced emotional vulnerability and ERP modulations. A priori hypotheses were preregistered with the open science framework, whereas the post hoc analysis were not. The preregistered study had also included a 6 month follow up to test longer term effects of training, however this follow up was cancelled due to school closures during the 2020/21 pandemic.

5.3 Methods

5.3.1 Participants

Participants were recruited from an independent boy's secondary school in SE England and pre-selected for high worry using the Penn State Worry Questionnaire – Child version (PSWQ-C Chorpita et al., 1997). N = 75 completed the screening questionnaire and n = 46 with ≥16 above-median worry scores were invited to take part in the training study. An a priori power analysis using G*Power determined a sample size of minimum n = 34 to achieve .80 power to detect a small effect. A final sample of N=36 consented to participation, with n = 5 dropping out just before testing began. Participants were aged 11-16 years (*M* = 13.31, *SD* = 1.76). Screening took place between May and June, 2019 and training intervention and pre and post training assessments, took place the following autumn. Follow-up testing was in February, 2020. All participants were right handed and had normal or corrected to normal vision. Exclusion criteria were a current diagnosis of a developmental or psychological disorder. Data from n = 1 participant was excluded as they disclosed they were undergoing pharmacological treatment for a mood disorder. Participant details are shown in Table 5.1.

Table 5.1 Participant demographic and pubertal status information

	Control Group (n = 15)	**Training Group (n = 16)**
Age in years Mean (SD)	13.46	13.25
	Number (%)	Number (%)
English as first language	14 (93.33)	16 (100)
English spoken for at least 10 years	15 (100)	16 (100)
British Nationality	13 (73.33)	12 (75)
Pubertal Status		
Voice has not broken	7(46.67)	8 (50)
Voice has broken	8 (53.33)	7 (43.75)
Months since beginning puberty	23.12	23.83
Do not know if voice broken	0	1
Right -handed	15 (100)	16 (100)
Left handed	0	0
Mother's Education		
University	9 (60)	14 (87.5)
Father's Education		
University	10 (66.67)	14 (87.5)
Ethnicity		
Asian/British Asian	4 (26.66)	4 (25)
Arab/Middle East	0	1 (6.25)
Black	0	0
White	8(53.33)	10 (62.5)
Mixed	3 (20)	1 (6.25)
Other	0	0

Ethical approval was granted by the research ethics committee of the Department of Psychological Sciences at Birkbeck University of London as well as the ESRC. Written parental consent was sought prior to baseline testing and participant written consent was obtained on the day of baseline tests.

5.3.2 **The WMT intervention**

Participants were randomly allocated to an active training group or a control. The active group trained using the adaptive dual nback task: This task was equivalent to that used in the previous study (Chapter 4) and has been described in detail in Chapter 2. Similar to Chapter 4, the control group trained on the non-adaptive 1back version of the task.

Training procedure

Training procedures were almost identical to the previous study (Chapter 4), but with some important differences. Study duration was shortened to reduce attrition and because it was observed that participant's nback improvement plateaued after around 6 days in the prior study (Chapter 4). Training took place over a period of 2 weeks to permit participants to complete 5 days' training per week, with 1 day off, yielding a maximum of 12 days' training. Preregistered analyses stated that analysis would include all participants who completed at least 10 days' training. Participants accessed the training online from home using a personal computer during the October half-term, 2019. Participants received automatic daily reminders and countdown information to the end of the training. Wording of emails was the same for all participants. Adherence was monitored by the researcher and if a session was missed participants were emailed and reminded to catch up. One participant missed three training sessions near the beginning of training due to a religious holiday, but was permitted to return to training and start over.

Recruitment and training task instruction

Participants were invited to participate in the study during a presentation delivered by researchers at a school assembly. Specifically, students were informed the study was an investigation of training on brain activity. EEG was explained and the procedure was carefully described. Parents were informed about the study in written communications from the head teacher. There were also additional information sessions hosted by the researcher where parent questions were answered. In contrast to study 2 where the training task was introduced to participants in group information sessions, the nback task was demonstrated on a one-to-one basis at the baseline testing session. Participants understood the researchers were testing different versions of the training and were not informed of a control. Finally, participants received a £25 gift voucher after completing post training tests. This was given as a reward and was not offered as an incentive during recruitment.

5.3.3 **Outcome measures**

5.3.3.1 Self-report measures of emotional vulnerability

The self-report scales used in this study have been described in detail in Chapter 2, but are set out in brief below. The following scales were assessed at pre, post and 3 months follow-up to training; anxiety and depression symptomology was assessed using the *Revised Child Anxiety and Depression Scales* (RCADS, Chorpita et al., 2000) shortened version (Ebesutani et al., 2012), whilst worry and rumination were assessed using the *Penn State Worry Questionnaire for Children* (PSWQ-C; Chorpita et al., 1997) and the *Children's Response Styles Questionnaire*

(CRSQ; Abela et al., 2004) respectively. Adolescent burnout was assessed using the *School burnout inventory (*SBI; Salmela-Aro et al., 2009).

The Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997; Goodman et al., 1998), which assesses positive and negative emotional and behavioral characteristics, and *The Early adolescent temperament questionnaire* (EATQ-R; Ellis & Rothbart 2001) which assesses temperamental effortful control were assessed at baseline only. It had been intended to re-administer these scales at the 6 month follow-up to examine longer term consolidation of the far transfer of training on mental health and temperament, however this final assessment session was cancelled due to the pandemic.

5.3.3.2 Behavioural Tasks

Shortened Operation Span (OSPAN)

Working memory capacity was assessed using the shortened operation span task (OSPAN) Foster et al. (2015) and presented in EPrime software on a Dell latitude laptop with a 38 x 24 cm monitor using a built-in keyboard and mouse pad. This task was also used in Study 1. As it was previously described in Chapter 3, it is not discussed further here.

Emotional Stroop task

Continuous EEG was recorded during an emotional colour-word Stroop task designed according to recommendations in Ben-Haim et al. (2016). The task was presented with Eprime software (Psychology Software Tools, Inc., Pittsburgh) on a 23 inch monitor with participants seated approximately 70cm from the screen. The experiment consisted of word stimuli in 25-point Verdana font on a grey background in the centre of the display. Target stimulus font colour was blue, green or yellow. As quickly and accurately as possible, participants indicated the font colour of the word stimulus. Response keys were the bottom three keys on the keyboard's number pad (1 = blue, 2 = green, 3 = yellow) and, as a guide, each key was overlaid with a corresponding coloured sticker.

There were two practice blocks followed by three experimental blocks featuring 63 trials per block. In the first practice block the corresponding keypad numbers were displayed on screen to train participants on colour-to-button correspondence. Practice stimuli were 'fruit' words. (e.g. apple, pear etc.). On the second practice block, only target words appeared on screen. Participants were instructed to respond as quickly and as accurately as possible. Feedback on accuracy and reaction time followed each practice trial. Active blocks contained equal numbers of neutral (n = 21) and threat words (n = 21). Each word was repeated a total of three times and appeared in each colour once. Threat and neutral words and colour order were dispersed pseudo-randomly throughout blocks. Each word appeared once in each colour. Trials began with a central fixation cross (duration 300 ms) replaced by the target word (duration 1000 ms) and followed by an ITI which varied randomly between 1500 and 2000 ms.

Neutral words comprised a list of common household objects, whilst threat words were negative words selected from stimuli used in previous experiments with children, youth and adults and likely to be threatening to adolescents. The word list is shown in

Table 5.2. Stimuli were matched for word length, log frequency and orthographic neighbourhood, however threat words frequency was higher for threat than neutral words $t(19)$ =

2.89, $p = .01$. The final word list was piloted on $n = 12$ adolescents and a stroop interference effect was observed, reaction times were slower on threat compared to neutral trials, $t(11) = 4.61$, $p < .001$.

Table 5.2 Threat and neutral word stimuli used in the emotional Stroop task

Threat words		Neutral words	
dead	bullied	door	curtain
hate	doom	hall	dish
hurt	anxious	iron	kitchen
loser	failure	bench	toaster
alone	divorce	table	bathroom
panic	helpless	plate	lightbulb
scared	nightmare	shower	bookshelf
terror	depressed	mirror	lampshade
attack	frightened	kettle	dishwasher
cancer	murder	carpet	mirror

<u>Flanker Task</u>

Flanker task stimuli were presented on a 23 inch monitor with a sitting distance of 70cm. The task was built with Eprime software (Psychology Software Tools, Inc., Pittsburgh). Task stimuli were white on a black background. Stimuli presentation times were based on Tamnes et al. (2012). The task objective was to indicate the orientation of a centrally located horizontal arrow (< or >), whilst ignoring distractor arrows on either side at 180°. Each trial began with a jittered central fixation cross + (1200 - 1800ms), and replaced by the target arrow flanked on either side by two distractor arrows eg. < < > < <. (duration 60ms). The flanker distractors appeared 80 ms prior to the target stimulus and pointed either in the same or the opposite direction. This was to augment the distractor effect (Overbye et al., 2019). Target stimuli presentation was followed by a black screen which remained for up to 1000 ms or until a response was made. Participants responded by indicating the direction of the central arrow using the ‘M’ and ‘N’ buttons on the keyboard; N if the arrow pointed to left < , and M if it pointed right >. Target and flanker arrows disappeared simultaneously as soon as a response was made. The direction of the arrow was random with each direction occurring with equal frequency. Consistent with other studies using the flanker task to elicit the ERN in adolescents (Ladouceur et al., 2007; Meyer et al., 2018), half the trials were congruent e.g. <<<<<, i.e. the distractor arrows matched the target arrow and half the trials were incongruent, e.g. <<><< the distractor’s direction was opposite to the target.

The experiment consisted of two practice blocks followed by 10 experimental blocks featuring 48 trials per block. There were 480 trials in total. In the first practice block participants had an infinite response time to allow them learn the task without time pressure. In the second practice block, trials were identical to true blocks. Participants were instructed to respond as quickly and as accurately as possible, with equal emphasis on speed and accuracy. To maximise EEG recording quality participants were instructed to minimize eye blinks and physical movement during the blocks. There was an enforced break between blocks when participants were instructed to relax eyes, blink and move feet or stretch out legs if necessary.

5.3.3.3 ERPs

EEG data acquisition and preprocessing

Continuous EEG activity was recorded during the Flanker and Emotional word Stroop tasks, with Flanker data used to extract error response locked ERPs [ERN and P(e)] whereas the stimulus-locked N2 and P3 ERPs were extracted from the emotional Stroop task. Data was recorded and preprocessed according to methods outlined in Chapter 2. In line with the preregistered analysis the ERN was quantified as the average amplitude in the 0-100ms post response window across the five fronto-central electrode sites (Fz, F1, FCz, FC1 and Cz). ERPs were extracted for error (ERN) and correct responses (CRN) on flanker trials. Statistical analyses were conducted on amplitudes at Fz, the site where amplitudes were maximal. The difference wave ΔERN was quantified as the voltage amplitude difference between error and correct responses. On inspection of the grand average waveform (see figure 5.5) we observed a substantially more pronounced ERN component peaking in a 0-50 ms window. Guided by the data, we also quantified an ERN based on mean area amplitudes within this unplanned window, with statistical analyses reported for this ERP, as it was reasoned it would have greater power to detect effects of training if they were present. Analyses for the 0-100 ms window are reported in Appendix 3, but consistent with regard to group and individual difference effects of training. The P(e) and its post correct response equivalent were quantified as the average amplitude (uV) in the 200-400 ms post-response time window at central parietal electrodes Pz and CPz. Statistical analyses were conducted on CPz amplitudes where P(e) was maximal.

N2 and P3 ERP waveforms were time-locked to stimulus presentation on correct Stroop trials only, with a -200ms baseline. Separate ERPs were derived for threat and neutral stimuli.

Data processing followed the procedure described in Chapter 2. The N2 was defined as the average activity in 200 - 300 ms post stimulus time window at fronto central electrodes where deflections were maximal (FCz). The P3, also with a 200ms baseline, was defined as the mean area amplitude within the 300-450 ms post stimulus window at central parietal sites and was maximal at CPz.

5.3.4 **Procedure.**

All participants completed the training intervention during the same two week period. Baseline and post training testing took place within two weeks either side of the start and end dates. Self-reports were completed at baseline, post training and 3 months follow up. Cognitive tasks and EEG recordings were administered at baseline and post training only. These experimental sessions took place at the UCL, Institute of Education, London. Participants were excused from lessons and attended either a morning or afternoon testing session. To ensure all testing sessions were accommodated within two weeks either side of the intervention, most participants attended the lab in pairs and were tested in parallel, although scheduling also had to accommodate single participant testing sessions. All participants completed training in parallel during the October 2019 half-term. At baseline and post training test sessions, half the participants completed the self-report questionnaires and OSPAN task first, followed by EEG recordings during flanker and Stroop tasks in an adjacent room. The remaining participants completed the study in reverse order. Order of testing was the same for participants at both sessions. This ordering of tasks allowed the accommodation of two participants per testing session.

At the 3 month follow up, only self-report questionnaires were administered and this was online only. Gorilla Experiment Builder (www.gorilla.sc) was used to create and host the follow-up questionnaires.

After all baseline tasks had been administered, participants were allocated to either the training (n = 16) or control (n = 15) groups. Participant's unique study identification codes were first ordered randomly using an online randomization service, www.random.org. The first 16 participants appearing in this randomly ordered list were allocated to the nback training group and remaining participants to the control group. There were no significant differences between groups prior to training on outcome measures, age or pubertal status prior to training ($ps > .05$ *n.s.*). Participants, their parents, school staff and EEG lab assistants were blinded to groups. To prevent participants deducing which group they were in, they were informed that several different versions of the memory task were being trialed.

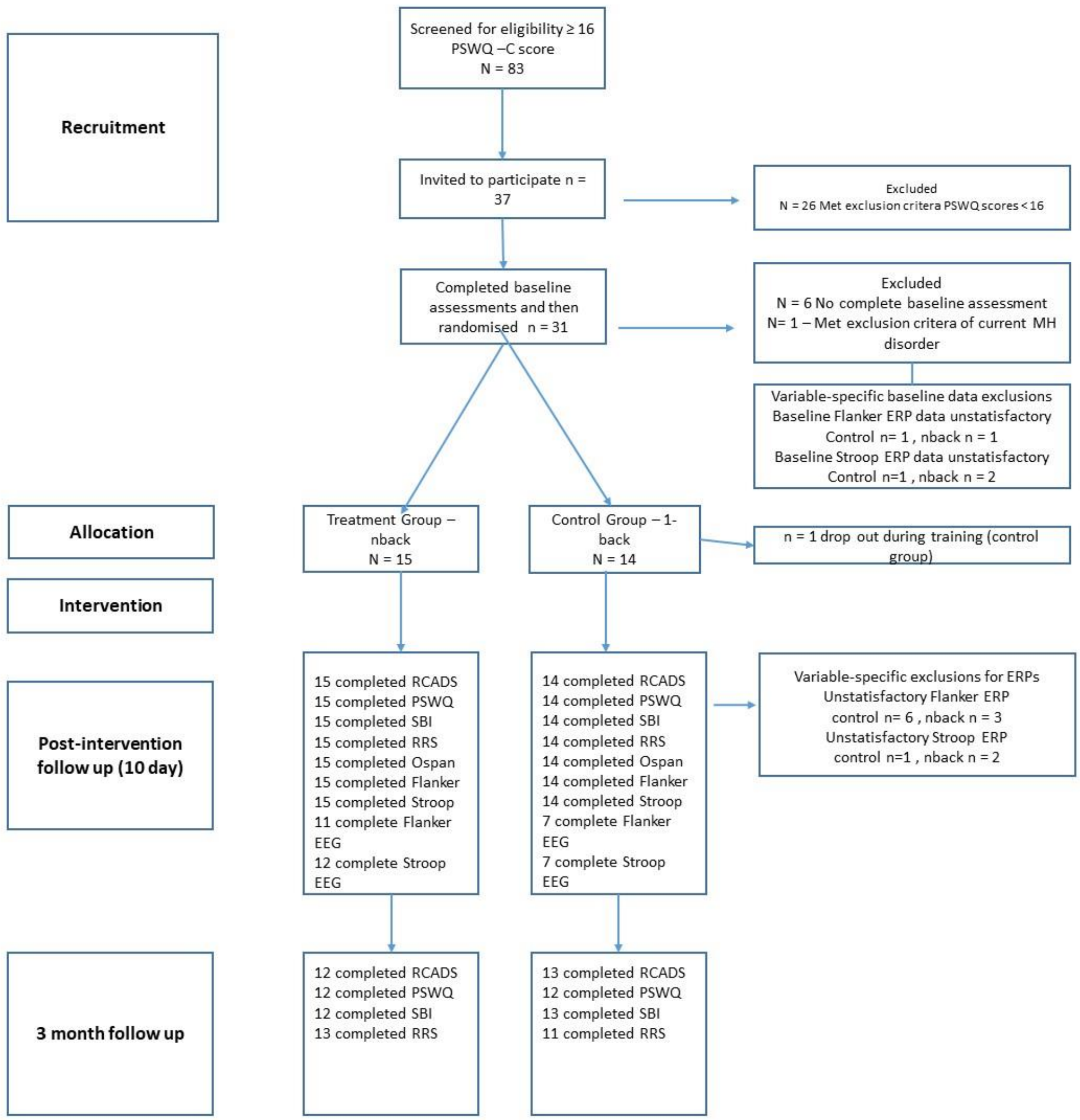


Figure 5.1 Consort diagram shows flow of participants through the study from recruitment through to follow up.

5.3.5 Statistical methods

Figure 5.1 above outlines the flow of participants through the study and sample sizes eligible for statistical analysis. Data were analyzed according to an intention- to-treat (ITT) principle, a gold standard approach in which all participant's data are analysed, regardless of compliance (Gupta, 2011). This is designed to maintain the integrity of randomization and avoid over-estimation of treatment effects (Gupta, 2011). Data were analyzed using IBM SPSS Statistics, Version 25. Linear Mixed Effect Models (MLMs) compared groups on the self-report scores across time. Fixed effects were specified for Group (nback, control), Time (time 1, time 2, time 3), and a Group x Time interaction. Additional 2 (Group: n-back, control) × 2 (Time: pre training, post training) MLMs compared group ERPs and behavioural task outcomes from pre to post training. Model estimation was with the maximum likelihood method.

5.4 Results

5.4.1 Training adherence and improvement.

All participants completed 10 or more of the 12 training sessions. Figure 5.2 illustrates mean daily n-back level reached by nback group participants (n = 15) across the training period. Participants improved significantly on the nback training across time as evidenced by a main effect of time $F(1, 126) = 4.18$, $p < .001$, $\eta_p^2 = .23$. Percentage accuracy in 1-back performance amongst the active control group was unchanged between the beginning (M = 96.72, SD = 2.41) and end (M = 96.59, SD = 3.01) of training, $t(13) < 1$, *n.s.*.

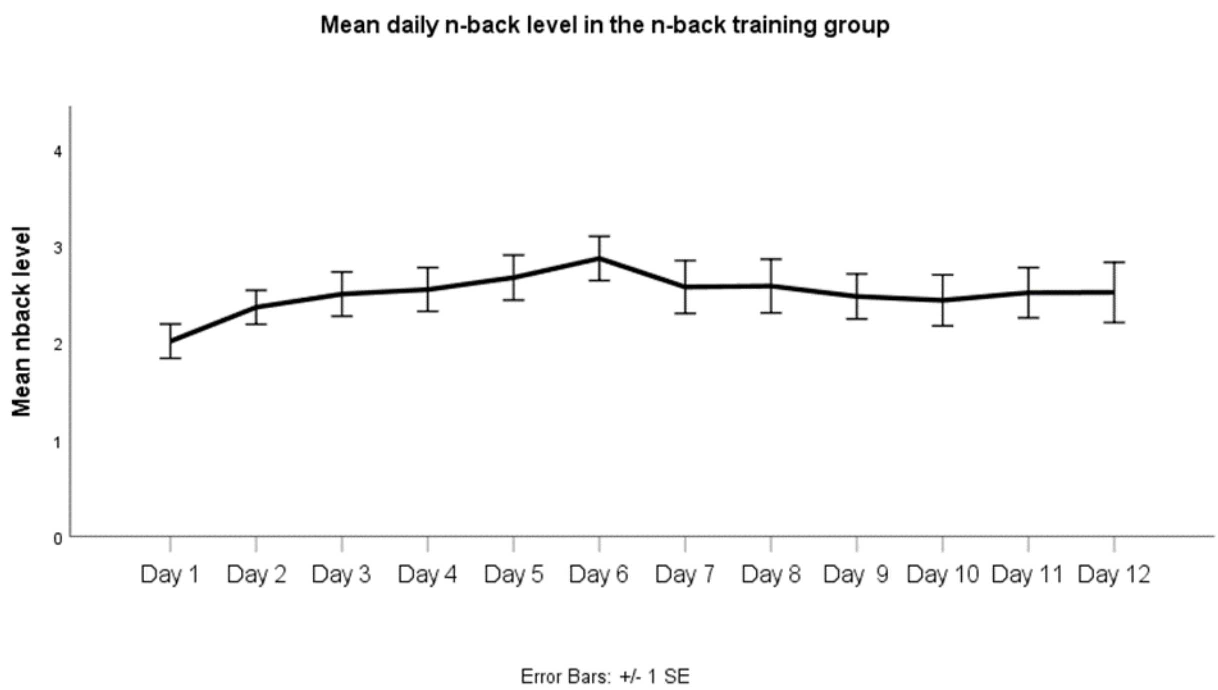


Figure 5.2 Mean level of nback on each daily training session throughout the training period.

On average participants in the nback group improved from the beginning to the end of training reaching a higher mean nback level at the end (M = 2.4, SD =.96) relative to the beginning (M =

2.05, *SD* = .66) of training *t*(28) = 2.00, p = .05. To explore individual differences in training improvement and WM performance increase, two additional scores were calculated: 1) A rate of improvement score was derived from the slope of a participant's daily increase in nback level over the training period. Improvement slope ranged from -0.07 to 0.18, M = .04, *SD* = .08, and 2) WM performance gain, which was the difference between an individual's Day 1 and Day 10 nback level, that ranged from -.70 to 1.55, M = .4, SD = .74. A negative score indicates where performance actually declined during a training.

5.4.2 Emotional vulnerability outcomes

Group means and standard deviations for age-standardised scores on the RCADS Anxiety and Depression scales, Penn State Worry Questionnaire, Rumination Response and School burnout inventory scales at pre-training, post training and at 3 months follow up are shown in Table 5.3. RCADS scores ≥70 are clinically significant, whilst scores ≥65 are considered borderline clinically significant. No participant had clinically significant depression scores, whilst 16.66% of the sample were had depression scores that were borderline significant. For anxiety, one participant scored within the clinically significant range and 6.7% of the sample (n=2) had borderline significant anxiety scores.

Table 5.3 Intention to treat (ITT) sample means scores for all self-report measures pre and post training and 3 months follow up. Standard deviations in parenthesis.

	Nback			**Control**		
	Pre training	Post training	3 months	Pre training	Post training	3 months
	n =15	*n= 15*	*n = 12*	*n = 14*	*n = 14*	*n = 13*
School Burnout	26.53 (9.80)	2660 (12.29)	26.25 (10.19)	26.43 (7.91)	27.28 (8.29)	27.00 (8.88)
Worry	18.33 (10.19)	18.33 (6.1)	19.92 (7.42)	21.75 (7.52)	22 (9.03)	20.83 (6.29)
Rumination	26.07 (7.01)	25.80 (6343)	25.61 (7.10)	31.21 (7.64)	31.79 (6.78)	29.64 (1.27)
Anxiety	51.13 (8.40)	47.73 (9.71)	48.00 (11.60)	52.57 (10.42)	52.64 (8.97)	49 (7.02)
Depression	49.40 (8.85)	50.00 (11.63)	46.08 (7.74)	54.43 (9.04)	51.36 (10.92)	53.00 (7.96)
Effortful Control	3.67 (.54)	n/a	n/a	3.73 (.43)	n/a	n/a
SDQ internalising	4.71 (2.73)	n/a	n/a	5.86 (3.35)	n/a	n/a
SDQ externalising	5.43 (3.44)	n/a	n/a	5.71 (2.76)	n/a	n/a

5.4.2.1 Group comparisons

The training groups were not significantly different from one another prior to intervention on any psychopathology vulnerability measure, all were $t < 1$, *n.s.*. MLMs showed there were no significant main effects of group, time, nor Group X time interactions on any of the psychopathology outcome variables. The results of these MLM analyses are summarised in Table 5.4

Table 5.4 Summary of the results of Mixed Linear Models exploring differential effects of training intervention group across time for self-report scales assessing psychopathology vulnerability.

Outcome	Main effect of group	Main effect of time	Group*Time interaction
SBI	$F < 1$	$F < 1$	$F < 1$
PSWQ	$F(1, 36.57) = 2.54$, p = .12	$F < 1$	$F < 1$
RRS	$F(1, 43.05) = 2.76$, p = .10	$F < 1$	$F < 1$
Anxiety	$F < 1$	$F < 1$	$F < 1$
Depression	$F(1,41.82) = 1.124$, p = .29	$F < 1$	$F < 1$

5.4.2.2 Correlational analyses

Associations between rate of nback performance change and baseline emotional vulnerability.

Correlational analyses first investigated associations between individual differences in rate of training improvement (training slope), WM performance gains (nback performance differences between first and last day of training) and baseline psychopathology vulnerability. The rate of improvement (slope) was significantly correlated with baseline depression, $r(14) = -.62$, p = .01, and baseline school burnout inventory scores, $r(14) = -.56$, p = .03, such that higher baseline scores on these measures were met with a poorer rate of WM improvement over the training period in the nback group (Figure 5.3). Similarly, nback gain scores (difference between first and final day of training) were correlated negatively with pre-training Strengths and Difficulties Questionnaire internalising, $r(14) = -.53$, p = .05, and at trend with baseline depression, $r(14) = -.46$, p = .08, such that higher internalising scores were associated with subsequently smaller nback improvement gains across training. Correlations between training improvement and other baseline measures are summarised in Table 5.5.

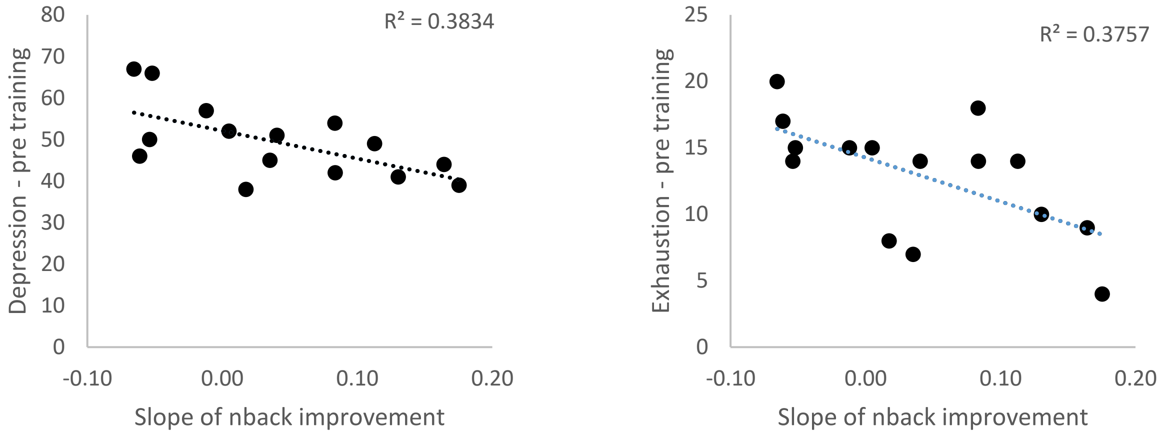


Figure 5.3 Scatterplots showing relationship between slope of training improvement and pre training scores for the exhaustion subscale of the school burnout inventory (right) and depression (left).

Table 5.5 Pearson correlation coefficients for associations between nback training slope and nback training gains with ***baseline self-report measures*** *and cognitive task performance. Nback only (n = 15)*

	1	2	3	4	5	6	7	8	9	10	11	13	14	Mean	SD
1. nback slope	_													0.04	0.08
2. nback gain	.708**	_												0.4	0.74
3. Worry	-0.033	-0.122	_											18.33	6.1
4. SchooI Burnout	-.557*	-0.163	0.073	_										26.53	9.8
5. SBI_Exh	-.613*	-0.148	0.107	.908**	_									12.93	4.42
6. Rumination	-0.102	-0.046	0.243	0.274	0.150	_								26.07	7
7. Efforful Control	0.385	0.138	-0.010	-.679**	-0.491	0.080	_							3.67	0.54
8. SDQ Extern	-0.438	-0.132	-0.058	.653*	.610*	0.197	-.886**	_						5.43	3.44
9. SDQ Intern	-0.067	-.534*	.610*	-0.075	-0.136	-0.261	-0.064	0.039	_					4.71	2.73
10. Depression	-.619*	-0.461	0.315	.724**	.739**	0.307	-.600*	.565*	0.374	_				49.4	8.85
11 Anxiety	-0.130	-0.284	0.437	0.016	0.170	0.499	0.246	-0.060	.657*	0.285	_			51.13	8.4
12. OSPAN	0.408	0.362	0.297	0.024	-0.031	-0.321	-0.313	0.341	0.147	0.032	-0.131	_		58.87	14.13
13. Stroop	0.024	0.138	-0.004	.593*	.604*	0.043	-0.382	0.518	0.049	0.514	0.050	.562*	_	4.49	29.52
14. Flanker	-0.187	-0.068	-0.396	0.111	0.290	-0.417	-0.183	-0.429	0.099	-0.295	-.590*	0.002	-0.016	83.85	20.16

*Note: *p< .05, **p < .01 2-tailed. Variable notes SBI-Exh = exhaustion subscale of School Burnout Inventory; SDQ Extern = SDQ externalizing scores, SDQ Intern = SDQ internalising; Flanker = Flanker task RT interference; Stroop = Stroop task RT interference. Shading highlights significant correlations between training improvement and baseline emotional vulnerability measures.*

Association between training improvement and emotional vulnerability change

We also explored associations between the rate of nback training improvement (slope) and changes in self-reported emotional vulnerability from pre training to three-months follow up (summarised in Table 5.6). Improvement rate was significantly correlated with change in one variable only; it was associated with greater reductions in anxiety symptomology $r(12) = -.59$, p = .04 three months post training (Figure 5.4). Nback training gain was also correlated with rumination at follow-up such that greater training improvement gains was associated with lower rumination scores $r(12) = -.61$, p = .03.

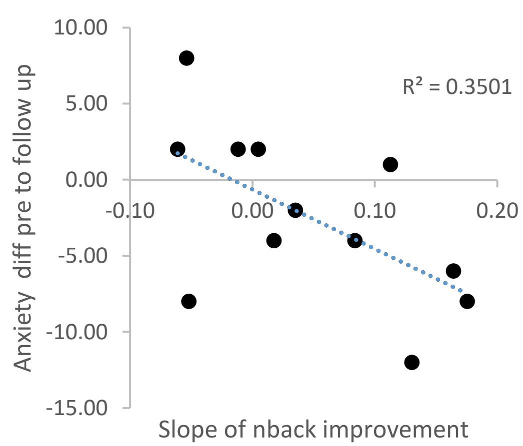


Figure 5.4 Scatterplot of change in anxiety scores from pre training to 3 months follow up against 10 day improvement slope (nback group).

Table 5.6 Pearson correlation coefficients for associations between ***nback training slope*** *and* ***nback training gains*** *and* ***follow up self-report measures*** *(t3) and* ***changes*** *in self-reported psychopathology from* ***baseline to follow up****. Nback only (n = 12)*

	1	2	3	4	5	6	7	8	9	10	M	SD
1 Nback slope	-										0.04	0.08
2 Nback gain	.708**	-									0.40	0.74
3 Anxiety change	-.592*	-.304	-								-2.42	5.65
4 Depression change	.337	.434	.304	-							-1.33	5.21
5 Rumination change	-.213	.049	.567	.268	-						-1.49	3.36
6 Worry change	-.255	-.351	.344	.320	-.058	-					2.00	5.29
7 SBI change	.480	.497	-.207	.258	.098	-.567	-				1.58	4.21
8 T3 Anxiety	-.413	-.548	**.645***	.319	.352	.514	-.411	-			48.00	11.60
9 T3 Depression	-.391	-.260	.471	.271	.144	**.582***	-.233	**.630***	**-**		46.08	7.74
10 T3 Rumination	**-.609***	-.389	.538	-.177	.235	**.635***	**-.649***	**.642***	**.759***	-	25.67	7.10
11 T3 Worry	-.237	-.493	.340	.260	-.047	.496	-.065	**.748****	**.741****	**.637***	19.92	7.42

*Note: *p< .05, **p < .01 2-tailed. M = Mean*; SD = standard deviation. Shading highlights significant correlations between training improvement and changes in emotional vulnerability measures.

5.4.3 **Effects of training on cognitive task performance and neural outcome variables.**

Results are first presented for group comparisons before and after training, followed by analyses of correlations between performance and neural change, and with self-reported vulnerability to psychopathology at follow-up.

5.4.3.1 OSPAN

Descriptive statistics for OSPAN scores are shown in Table 5.7. There was a main effect of time on OSPAN performance, $F(1, 29) = 4.19$, $p = .05$. Participants had significantly higher scores post training (M = 62.72, SD = 11.36) compared to pre (M = 58.83 SD = 12.32) regardless of group. There was no main effect of training group $F < 1$, and no group X time interaction $F(1, 26) = 2.11$, $p = .16$.

Table 5.7 Intention to treat (ITT) sample means scores for Flanker task performance and OSPAN scores, pre and post training. Standard deviations in parenthesis

	N-back (Mean/SD)		**Control (Mean/SD)**	
	Pre training	Post training	Pre training	Post training
Flanker Performance	ITT (N=15)	ITT (N=15)	ITT (n=14)	*ITT (N = 10)*
Total accuracy	.85 (.13)	.86 (.14)	0.87 (.13)	.91 (.04)
Accuracy Congruent	.94 (.09)	.91 (.16)	.94 (.14)	.96 (.04)
Accuracy Incongruent	.75 (.17)	.82 (.15)	.80 (.15)	.86 (.12)
RT (ms) Congruent	436.23 (104.95)	463.62 (105.23)	375.11 (68.83)	409.77 (69.59)
RT (ms) Incongruent	520.08 (103.39)	527.42 (102.71)	446.26 (79.74)	466.18 (57.18)
Error Count	73.27 (61.45)	64.93 (70.11)	62.79 (64.08)	42.30 (33.44)
Error RT (ms)	260.68 (58.39)	195.13 (83.09)	294.44 (51.94)	261.98 (68.94)
RT Correct (ms)	472.87 (101.56)	493.93 (103.54)	407.62 (73.52)	436.14 (64.60)
OSPAN	58.87 (14.13)	60.20 (14.87)	58.79 (10.63)	65.43 (4.94)

5.4.3.2 Flanker task

5.4.3.2.1 Behavioural results

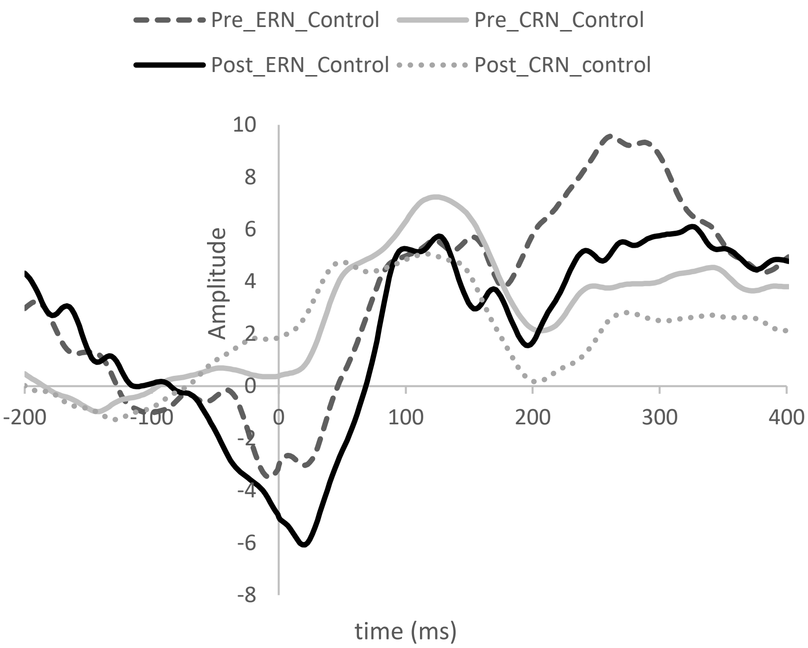
Statistical analyses were conducted on overall flanker task percentage accuracy interference and reaction time (RT) interference (ms), where interference was the difference between scores on congruent vs incongruent trials. Descriptive statistics are shown in table 6 above. MLM found there was no group x time interaction in Flanker accuracy interference scores, RT interference, Fs < 1. There was a main effect of time, such that RT interference declined significantly from pre to post training $F(1, 23.38) = 18.99$, $p < .001$, regardless of group. There was also a main effect of time on accuracy interference, $F(1, 23.38) = 19.42$, $p < .001$, such that accuracy interference declined significantly from pre to post training.

5.4.3.2.2 ERP results

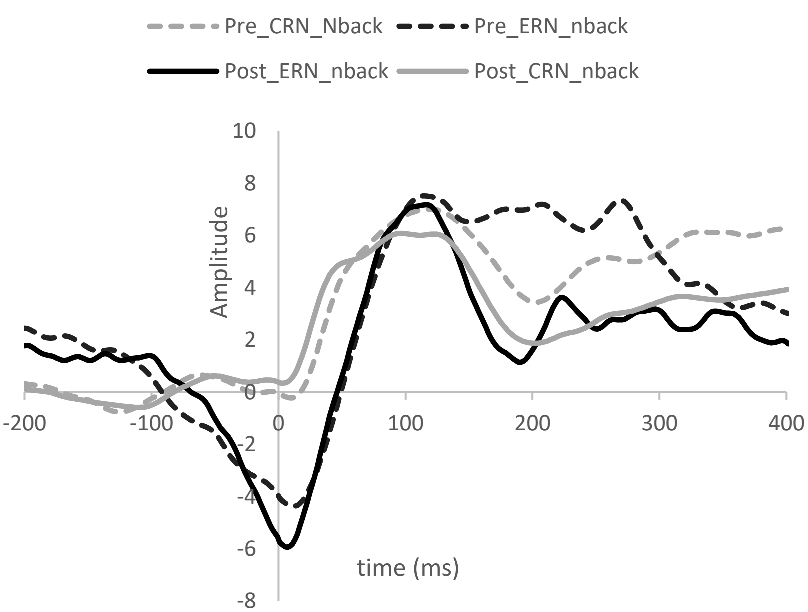
Means and standard deviations for the ERN, CRN and difference wave ΔERN are shown in Table 5.8. Details on number of participants included in the analyses were shown earlier in the consort diagram (Figure 5.1). Grand averaged waveforms by group are shown for the ERN in Figure 5.5a (control) and Figure 5.5b (nback). Scalp maps showing topographic voltage distribution are shown in Figure 5.6.

Table 5.8 Mean scores for error ERP measures pre and post training. Standard deviations in parenthesis

	N-back (Mean/SD)		**Control (Mean/SD)**	
	Pre training	Post training	Pre training	Post training
Flanker task ERPs	*(N = 14)*	*(N=11)*	*(N=13)*	*(N = 7)*
ERN (μV) 0-50	-3.57 (3.43)	-3.81(3.63)	-3.77 (*4.68)*	-5.02 (4.27)
CRN (μV) 0-50	.97 (4.00)	2.34 (4.09)	1.91 (*3.37)*	3.01 (3.20)
ΔERN (μV) 0-50	-4.54 (2.68)	-6.15 (3.42)	-5.68 (5.30)	-8.03 (5.65)
Pe error (μV)	8.55 (8.23)	3.66 (4.51)	10.40 (6.88)	7.44 (9.25)
Pe correct (μV)	-2.24 (3.92)	-3.58 (2.81)	-6.12 (6.56)	-7.53 (3.94)

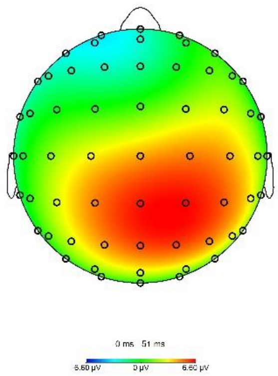


5.5a <u>Control group</u> *grand average waveform for ERN and CRN pre (time 1) and post (time 2) training intervention.*

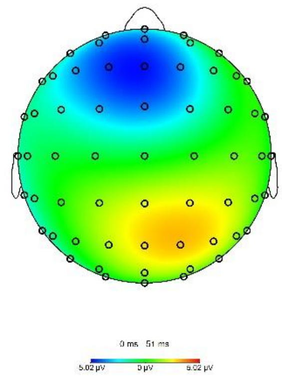


5.5b. <u>Nback group</u> *grand average waveform for ERN and CRN pre (time 1) and post (time 2) training intervention.*

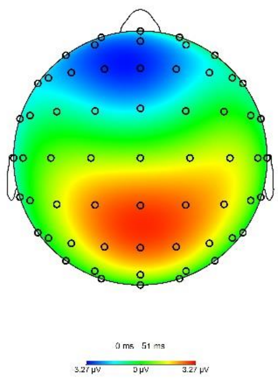
Figure 5.5 *Grand average waveforms for ERN and CRN pre and post-training for control (5.5a) and nback (5.5b) groups at Fz.*



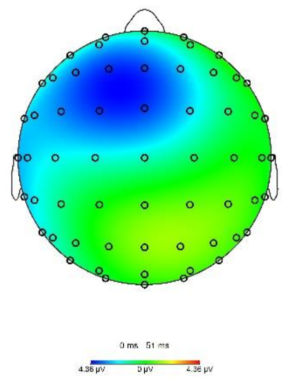
Pre training control group



Post training control group



Pre training nback group



Post training nback group

Figure 5.6 Topographic maps depicting voltage distributions across the scalp in the time range of the ERN (0–50 ms) by intervention group (control, nback) and by time (pre, post intervention).

Effects of training on ERN and P(e) - group comparisons

ERN: The bar chart below (Figure 5.7) compares mean amplitudes of error (ERN) versus correct (CRN) response in nback and control groups pre and post training. Amplitudes were more negative following erroneous compared to correct responses at pre (*mean difference* = -5.09, *SD* = 4.11, $t(26) = 6.43$, $p < .001$) and post training (*mean difference* = -6.88, *SD* = 4.36, $t(17) = 6.69$ $p < .001$). MLMs explored the effect of training group on the ERN from pre to post training. The MLM with ERN amplitudes as the dependent variable found there was no significant group X time interaction, $F < 1$. Similarly, the MLM on ΔERN amplitudes also found the group X time interaction was non-significant, $F < 1$. There were no significant main effects of time or group on either the ERN or the ΔERN. All main effects were $F < 1$.

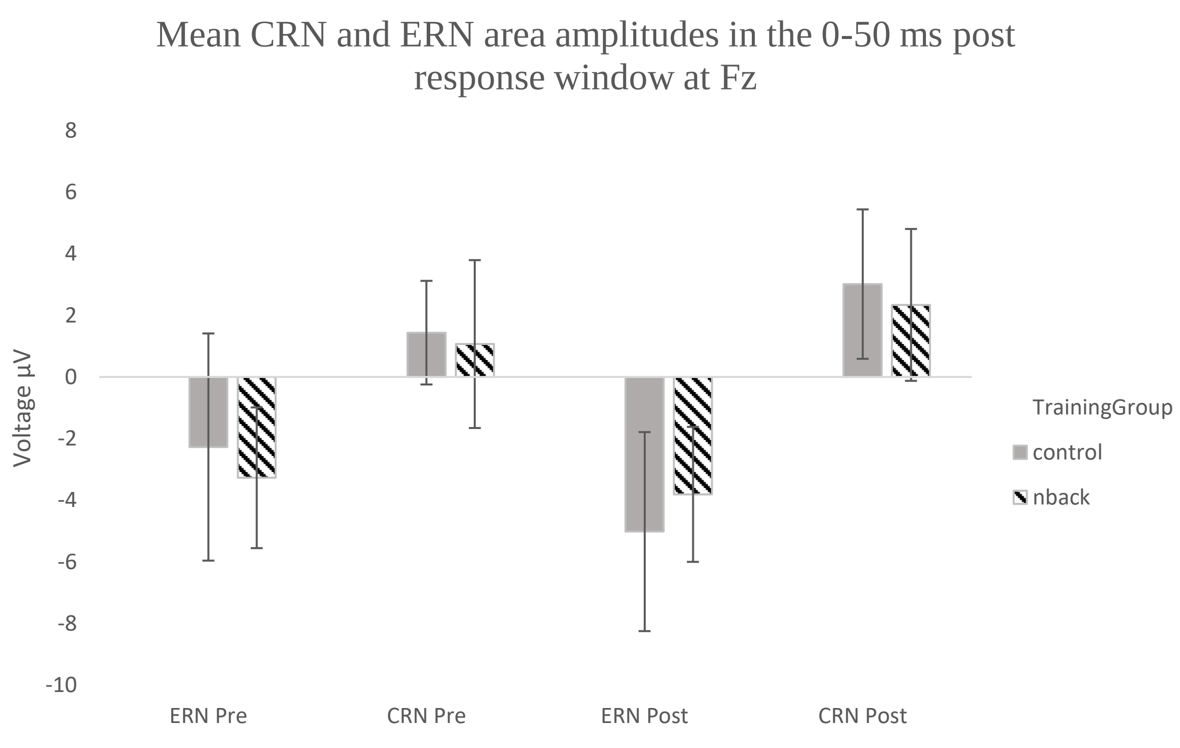


Figure 5.7 Bar chart of mean area amplitudes for ERN (error response) and CRN (correct response) in 0-50ms post response ERN window by group, pre and post training.

P(e)

P(e) means and standard deviations are shown in Table 5.9. Grand averaged waveforms by group, and scalp maps showing topographic voltage distribution are shown in Figure 5.8 Figure 5.9 respectively.

Table 5.9 Intention to treat (ITT) sample means scores for P(e) on flanker trial responses pre and post training. Standard deviations in parenthesis.

	N-back (Mean/SD)		**Control (Mean/SD)**	
	Pre training	Post training	Pre training	Post training
Pe error (μV)	8.55 (8.23)	3.66 (4.51)	10.40 (6.88)	7.44 (9.25)
Pe correct (μV)	-2.24 (3.92)	-3.58 (2.81)	-6.12 (6.56)	-7.53 (3.94)

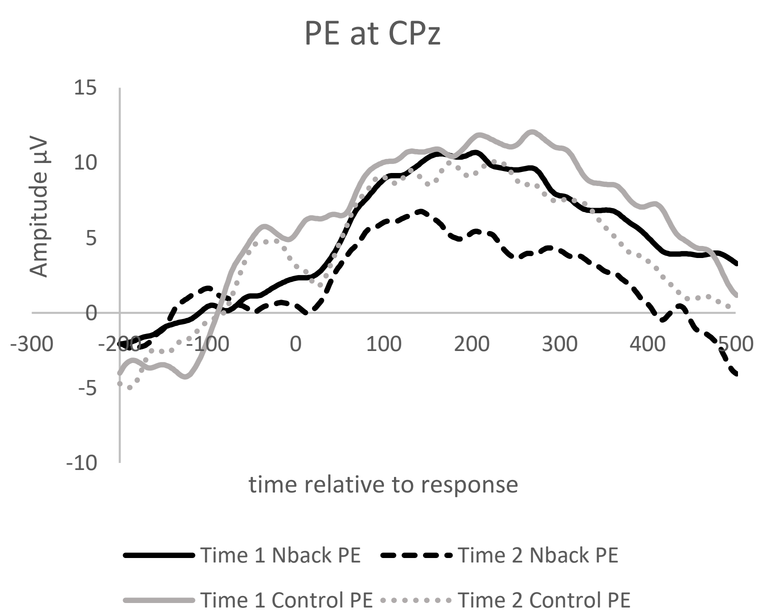


Figure 5.8 Grand average waveform for P(e) error positivity following erroneous responses pre (time 1) and post (time 2) training intervention for control AND nback groups at CPz, where P(e) was maximal.

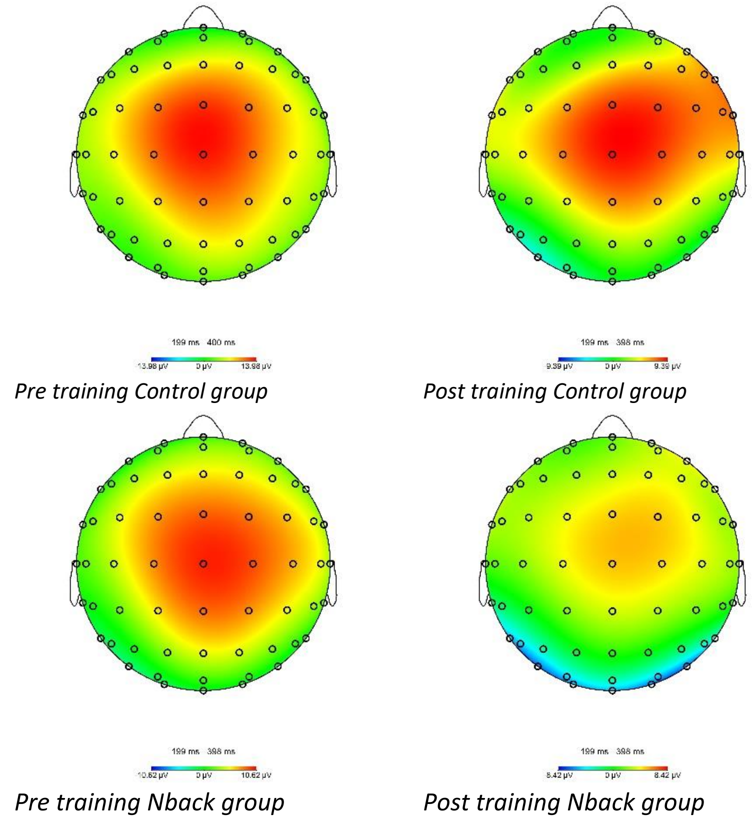


Figure 5.9 Scalp topographies depicting voltage distributions in the 200-400 ms post error response window of the P(e), by intervention group (control, nback) and by time (pre, post intervention).

P(e) amplitudes were more positive following erroneous compared to correct responses at pre (*mean difference* = 13.55, *SD* = 8.44, $t(26) = 8.45$, $p < .001$) and post training (*mean difference* = 10.24, *SD* = 7.92, $t(17) = 5.48$ $p < .001$. Figure 5.10 shows that P(e) amplitudes declined from pre to post training in the nback and control groups with a bigger amplitude decrease in the nback group (*Mean difference* = -5) compared to the controls (*Mean difference* = -2.96). This is also depicted in the grand averaged waveforms and the scalp maps (Figure 5.8 and Figure 5.9). MLMs tested the effect of training group on the P(e) amplitudes across time. There was no main effect of group, $F(1, 27.86) = 1.24$, $p = .28$, but the main effect of time was significant, $F(1, 22.51) = 5.96$ $p = .02$ with smaller P(e) amplitudes post training relative to pre. There was no significant group x time interaction $F < 1$ indicating that P(e) amplitude reductions were not significantly affected by training group.

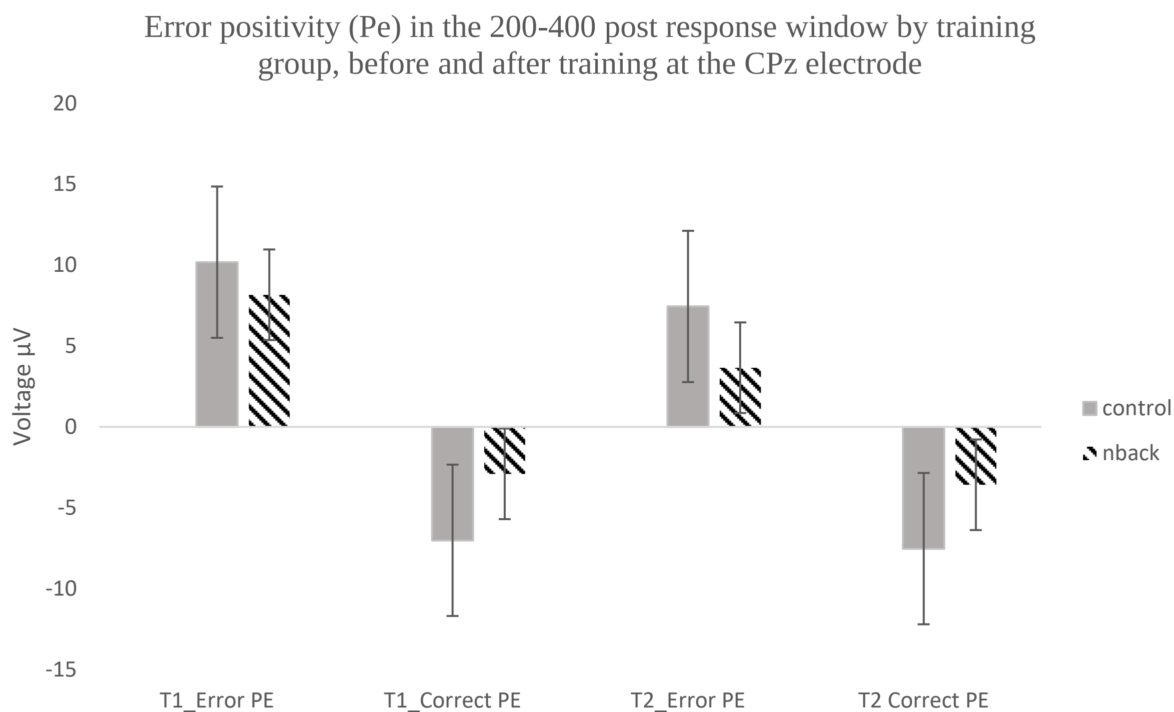


Figure 5.10 Bar chart of mean area amplitudes (µV) for Pe (error response) and corresponding correct response in 200-400ms post response window by group pre and post training.

5.4.3.2.3 Post-hoc correlational analyses

Correlation analyses investigated associations between training-related changes in neural processing of errors and 1) training task improvement and 2) change in self-reported psychopathology symptoms at 3 months follow up.

ERN: There were no significant associations between the ERN post-training, and sustained changes in self-reported psychopathology between pre-training and 3 months follow-up in either group. Correlations are reported in Table 5.10 (nback) and Table 5.11(controls).

Table 5.10 Nback group - Pearson correlations for the associations between nback training improvement, self-reported emotional vulnerability change and error ERPs.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	M	SD
1 Nback slope																0.04	0.08
2 Nback gain	**.708****															0.40	0.74
3 Anxiety change	**-.592***	-.304														-2.42	5.65
4 Depression change	.337	.434	.304													-1.33	5.21
5 Rumination change	-.213	.049	.567	.268												-1.49	3.36
6 Worry change	-.255	-.351	.344	.319	-.058											2.00	5.29
7 SBI change	.479	.497	-.207	.258	.098	-.567										1.58	4.21
8 T3 Anxiety	-.413	-.548	**.645***	.319	.352	.514	-.411									48.00	11.60
9 T3 Depression	-390	-.259	.471	.271	.144	**.582***	-.233	**.630***								46.08	7.74
10 T3 Rumination	**-.609***	-.389	.538	-.178	.235	**.635***	**-.649***	**.642***	**.759***							25.67	7.10
11 T3 Worry	-.237	-.493	.339	.260	-.047	.496	-.065	**.748****	**.741****	**.637***						19.92	7.42
12 T3 SBI	-.314	.055	.236	.195	.029	.280	.272	-.034	.620*	.342	.368					26.25	10.20
13 ΔERN	.247	-.062	-.275	-.102	-.410	.334	-.224	.015	-.311	.063	.083	-.422				-4.54	2.68
14 ΔERN change	-.081	-.053	-.424	-.084	-.112	-.413	.039	-.104	-.304	-.417	-.385	-.166	-.406			-1.81	3.34
15 T1 PE	**.652***	**.561***	-.576	.224	-.041	-.255	.120	-.224	-.153	**-.634***	-.268	-.195	-.180	.577		8.56	8.23
16 PE change	**-.708***	-.525	.644	-.336	.026	**.760***	-.581	.502	**.716***	**.799****	**.762***	.185	.094	**-.614***	**-.867****	-4.51	8.85

*Note: *p< .05, **p < .01 2-tailed.*

Table 5.11 Control Group - Pearson correlations for the associations between control group changes in psychopathology and error ERP change.

	1	2	3	4	5	6	7	8	9	10	11	12	13	M	SD
1 Anxiety change														-2.85	8.74
2 Depression change	**.672***													-1.08	6.64
3 Rumination change	.374	**.613***												-1.17	6.52
4 Worry change	**.882****	**.770****	.342											-0.17	4.75
5 SBI change	**.554***	**.612***	.498	**.687***										0.92	6.97
6 T3 Anxiety	.132	.402	-.018	.104	.194									49.00	7.02
7 T3 Depression	.289	.197	.167	.258	.322	.504								53.00	7.96
8 T3 Rumination	-.399	-.314	.258	-.535	.069	-.126	.263							29.64	7.27
9 T3 Worry	.009	.331	.135	.008	.141	**.760****	**.719****	.223						20.83	6.29
10 T3 SBI	.002	.226	.010	.099	.498	**.682***	.475	.329	.474					27.00	8.89
11 DERN	.169	.355	.476	.386	.224	.287	.511	-.418	.350	.247				-5.68	5.30
12 DERN change	-.235	-.022	.094	-.043	.491	-.355	-.061	.655	-.185	.579	-.305			-4.32	4.48
13 T1 PE	-.092	.090	-.228	-.098	-.025	-.035	-.545	.028	-.152	.143	-.482	.585		10.40	6.88
14 PE change	.258	.216	-.035	.087	.360	.547	-.173	-.134	-.378	.623	-.340	.083	.242	-2.74	4.88

*Note: *p< .05, **p < .01 2-tailed.*

P(e): There were no significant associations between change in P(e) amplitudes and follow-up self-report measures in the control group participants (Table 5.11). However, amongst the nback group there was a significant correlation between pre-training P(e) and the rate of improvement in the nback training task $r(13) = .652$, p = .01, such that a larger P(e) at baseline was associated with greater training task improvement. The rate of adaptive nback improvement was in turn associated with subsequent reductions in the P(e), $r(13) = -.71$, p = .02. This association is plotted in Figure 5.11 and shows that participants who did not improve on the training task had increased P(e) post training, whereas all others had a decreased P(e) which was associated with training improvement.

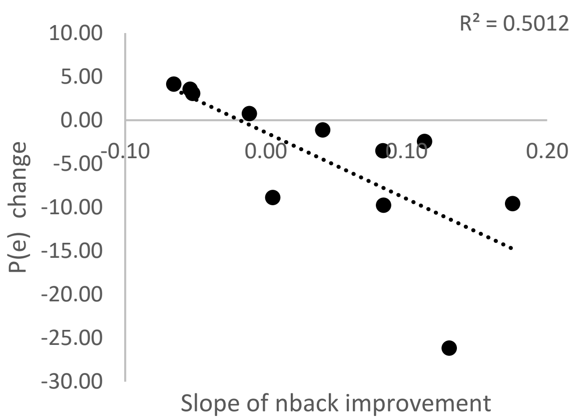


Figure 5.11 Scatterplot showing the correlation between the rate of nback training improvement association with reductions in P(e).

Reductions in the amplitude of the nback group P(e) were in turn significantly associated with lower worry $r(7) = .76$, p = .03, rumination $r(7) =.79$, p = .006) and depression $r(7) =.72$, p = .05 at follow up. P(e) reductions in the nback group were also significantly associated with smaller increases in worry from pre to follow up $r(7) = .76$, p = .03, and there was a trend association between reduced anxiety from pre-training to follow up *r*(7) = .64, p = .09. These correlations are plotted in Figure 5.12 and Figure 5.13.

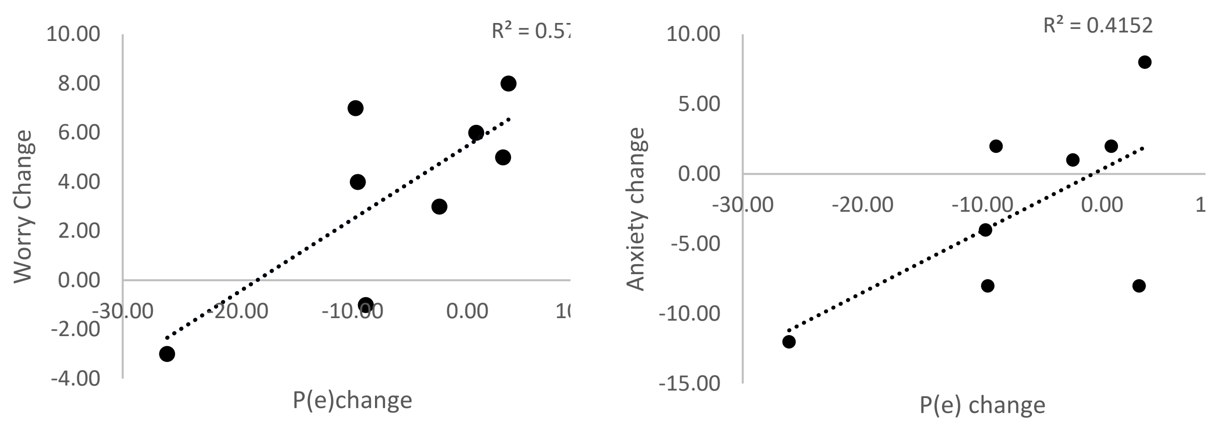
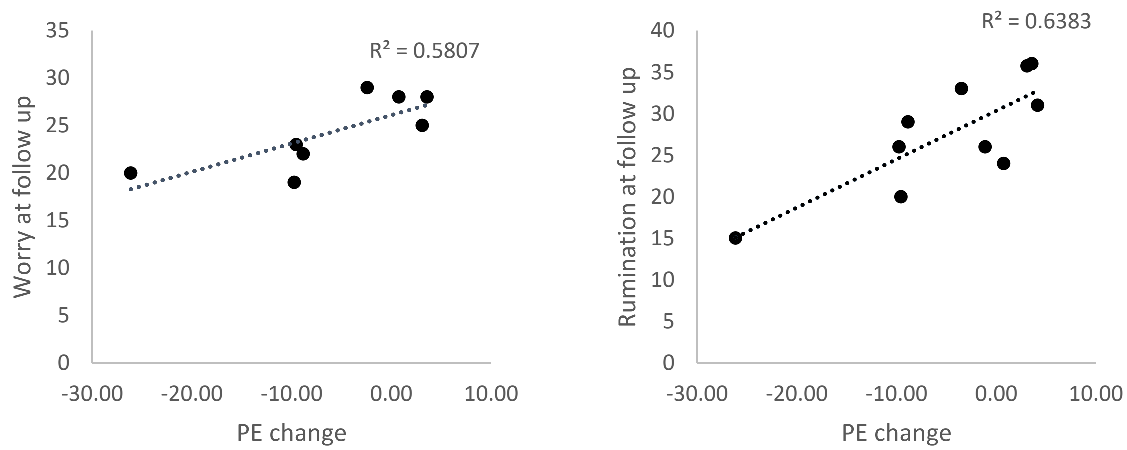


Figure 5.12 Scatterplot shows the correlation between reductions in P(e) from pre to post training and changes in self-reported worry (left) and anxiety (right) between baseline and follow up



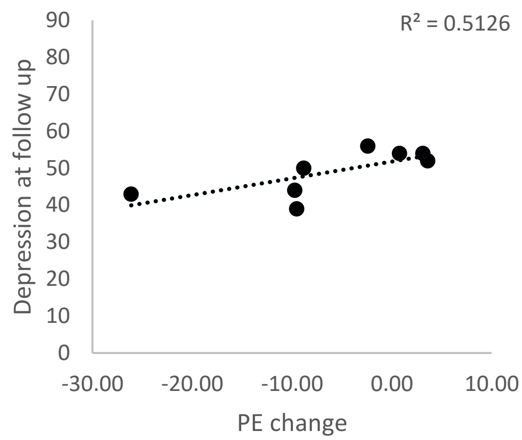


Figure 5.13 Scatterplots showing relationship between changes in the P(e) and Time 3 worry (top left), rumination (top right) and depression (bottom)

5.4.3.3 Emotional Stroop

5.4.3.3.1 Behavioural results

Table 5.12 Intention to treat (ITT) sample means scores for Stroop performance. Standard deviations in parenthesis.

	N-back (Mean/SD)		**Control (Mean/SD)**	
	Pre training	Post training	Pre training	Post training
Stroop performance	(N=15)	(N=15)	(n=14)	(n=12)
Threat RT	586.77 (68.00)	595.56 (88.23)	576.89 (85.76)	618.87 (147.97)
Neutral RT	582.28 (82.6)	614.56 (76.43)	566.01 (82.79)	634.81 (167.27)
Interference (RT threat - neutral)	4.49 (29.52)	-18.99 (35.96)	10.87 (23.57)	-15.94 (31.69)

Pre and post training descriptive statistics for emotional Stroop task performance are shown in Table 5.12 above and plotted in Figure 5.14 below. To ascertain the hypothesised emotional Stroop effect (slower RT on threat compared to neutral trials) we conducted a mixed 2 x 2 x 2 ANOVA with valence (threat vs neutral) and time (pre and post) as within-subjects variables and group (control, nback) as the between-subjects variable, on reaction times. There was a main effect of time $F(1, 25) = 6.93$, p = 02, $\eta_p^2 = .20$ with significantly slower RTs post training relative to baseline (*mean difference* = 38.20). There was a main effect of Stroop stimulus valence, $F(1,25) = 6.40$, p= .02, $\eta_p^2 = .20$ which was qualified by a significant interaction between time x valence $F(1,25) = 7.89$, p = .01, $\eta_p^2 = .24$. Post-training responses were significantly faster for threat than for neutral stimuli (*mean difference* =17.63, *SD* = 33.52, $t(26) = 2.73$, p = .01 (significant at corrected alpha p = .01). Whereas conversely, RT to threat stimuli were slower than for neutral prior to the intervention (*mean difference* = 7.57 *SD* = 26.53), $t(28)$ 1.54, p = .14. Participants were significantly slower on neutral trials post training, (*mean difference* = 48.75 *SD* = 86.44), $t(27) = -2.01$, p = .006 (significant at corrected alpha p = .01), whereas, although slower post training, there was no significant change in threat trial RTs across time, $t(27) = 1.88$ p = .12 *n.s.* (*mean difference* = 23.72, *SD* = 76.83).

Relative to the control group, the nback training intervention did not differentially impact reaction times, evidenced by the absence of a two-way group x time interaction, three-way group x time x valence interaction, all *F*s < 1. The main effect of group was not also not significant, $F < 1$.

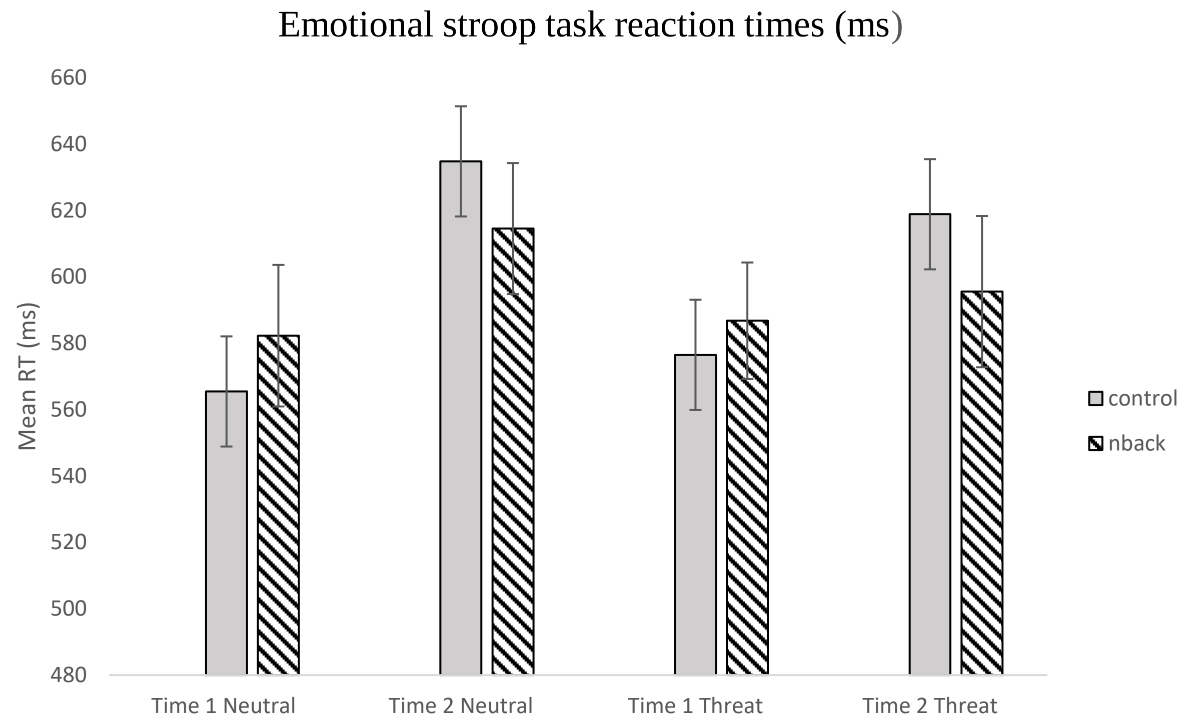


Figure 5.14 Compares control vs nback group response reaction times to Neutral and Threat stimuli in Stroop task, before (time 1) and after (time 2) training. Error bars represent 1 SE.

Correlations between Stroop performance change and emotional vulnerability.

Neither post-training emotional Stroop interference nor changes in interference from pre to post training was associated with changes in self-reported psychopathology sustained at 3 months follow-up in either group, ps > .05, *n.s.*.

5.4.3.3.2 <u>ERP results - training effects on the N2 and P3.</u>

<u>Group comparisons</u>

N2: The N2 was time-locked to stimulus presentation with a -200 ms baseline, and defined as the mean area amplitude in the 200-300 ms post stimulus time window at electrode FCz, where it was maximal. The grand average waveform for the N2 is shown in Figure 5.15. Means and standard deviations for the N2 by group and stimulus valence are reported in Table 5.13 and plotted in Figure 5.16.

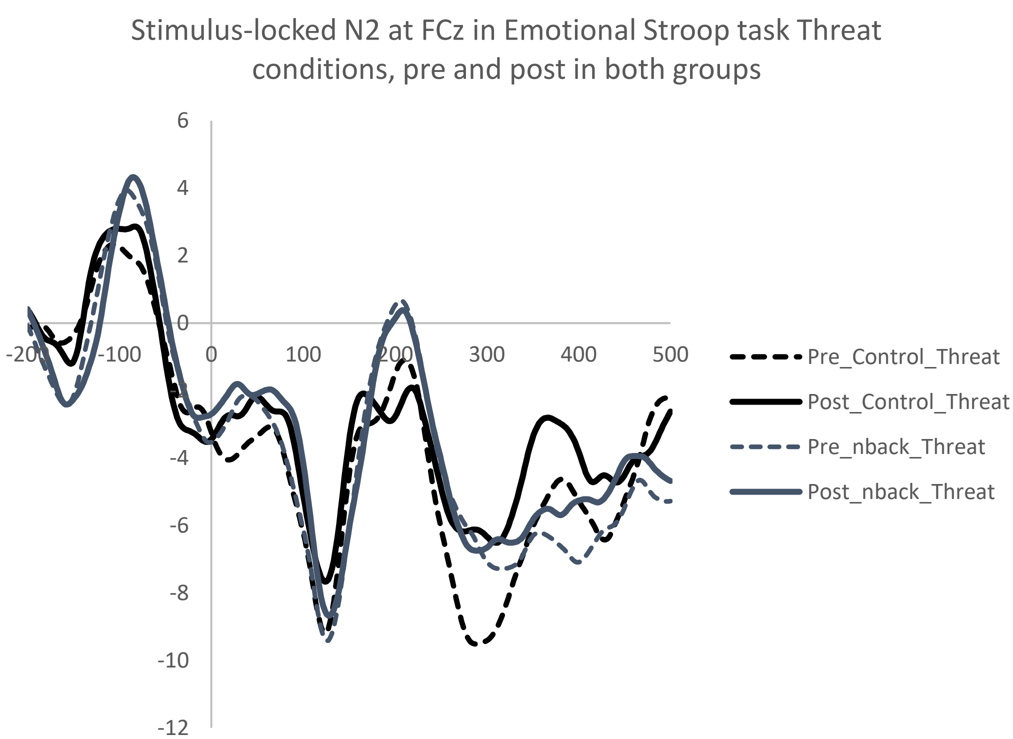


Figure 5.15 Grand average waveform at FCz for N2 in 200-300ms window following threat stimuli pre (time 1) and post (time 2) training intervention for control AND nback groups

Table 5.13 Intention to treat (ITT) sample mean scores for N2 amplitudes pre and post training. Standard deviations in parenthesis

	N-back (Mean/SD)		**Control (Mean/SD)**	
	Pre training	Post training	Pre training	Post training
	(N=13)	(N=12)	(N=13)	(N=7)
N2 Threat at FCz (μV)	-3.07 (5.57)	-3.48 (5.80)	-4.53 (4.86)	-4.95 (3.69)
N2 Neutral at FCz (μV)	-3.62 (6.09)	-5.40 (5.21)	-3.7 (5.67)	-6.32 (4.61)
N2 interference	.38 (3.89)	2.18 (3.67)	-.83 (4.39)	1.37 (2.68)

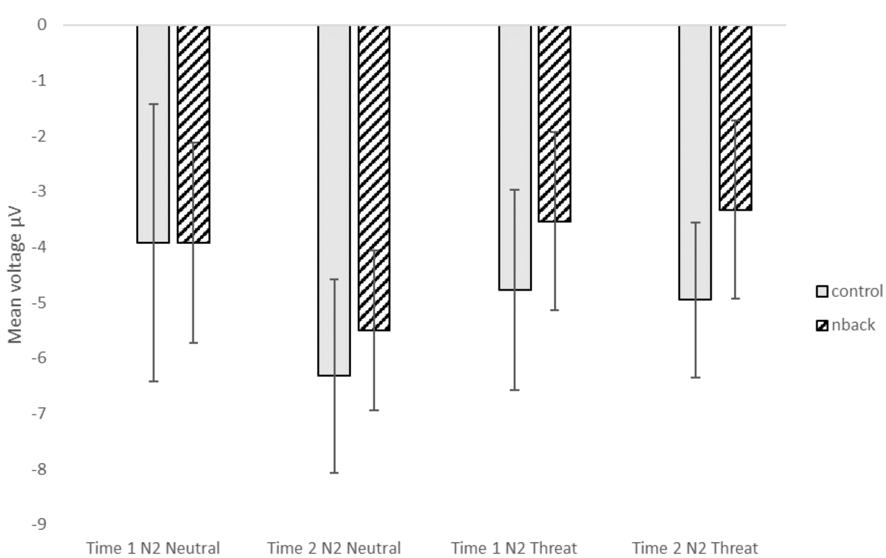


Figure 5.16 Compares control vs nback group N2 response for mean area amplitudes in the 200-300 ms post stimulus onset window for neutral vs threat stimuli in Stroop task, before (time 1) and after (time 2) training. Error bars represent 1 SE.

We were interested in the differential effects of training intervention (control vs nback) on participant's neural responses to threat stimuli. Hence MLM analyses focused on N2 responses to threat stimuli and the associated interference (threat – neutral) and examined the effect of group and time. The MLM found that the main effects of group on the threat N2 and the N2 interference effect were not significant. Moreover, the group x time interaction was not significant for the N2 response to threat, nor for the N2 interference effect, *Fs* < 1.

P3**:** The P3, also with a -200 ms baseline, was defined as mean area amplitude within the 300-450 ms post stimulus time window at central parietal sites and was maximal at CPz. Grand-averaged waveforms for the P3 are displayed in Figure 5.17. Means and standard deviations are reported in Table 5.14 and plotted in Figure 5.18

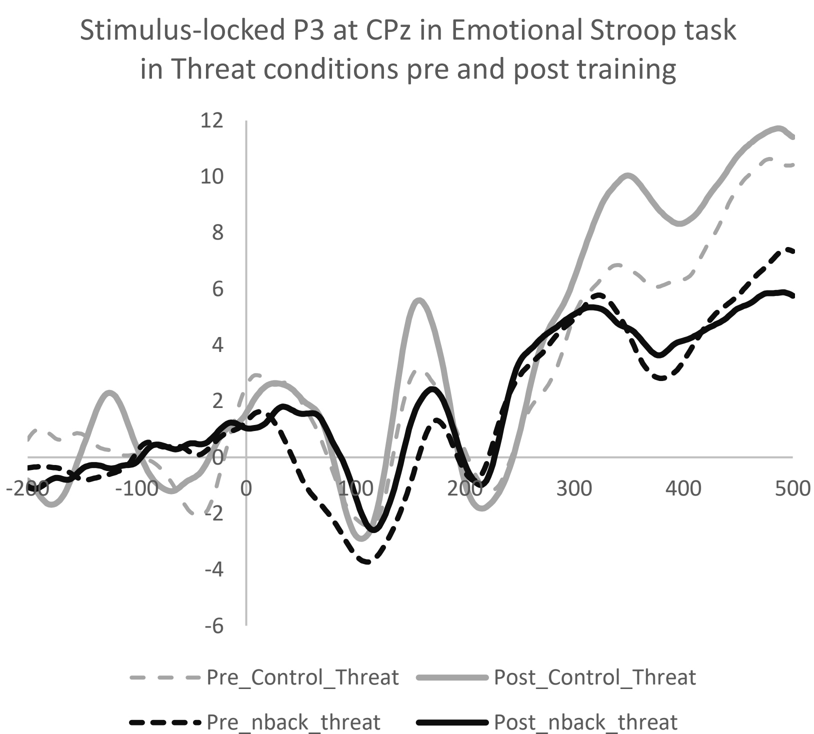


Figure 5.17 Grand average waveform for P3 in the 300-450ms window following threat stimuli pre (time 1) and post (time 2) training intervention for control AND nback groups

Table 5.14 Intention to treat (ITT) sample mean scores for P3 amplitudes pre and post training. Standard deviations in parenthesis

	N-back (Mean/SD)		**Control (Mean/SD)**	
	Pre training	Post training	Pre training	Post training
P3 Threat (µV) at CPz	4.39 (4.75)	4.39 (7.12)	5.47 (5.78)	8.34 (7)
P3 Neutral (µV) at CPz	4.07 (4.33)	3.90 (4.32)	6.49 (6.10)	7.02 (8.85)
P3 interference	.23 (3.40)	.50 (3.51)	-1.02 (3.27)	2.12 (5.65)

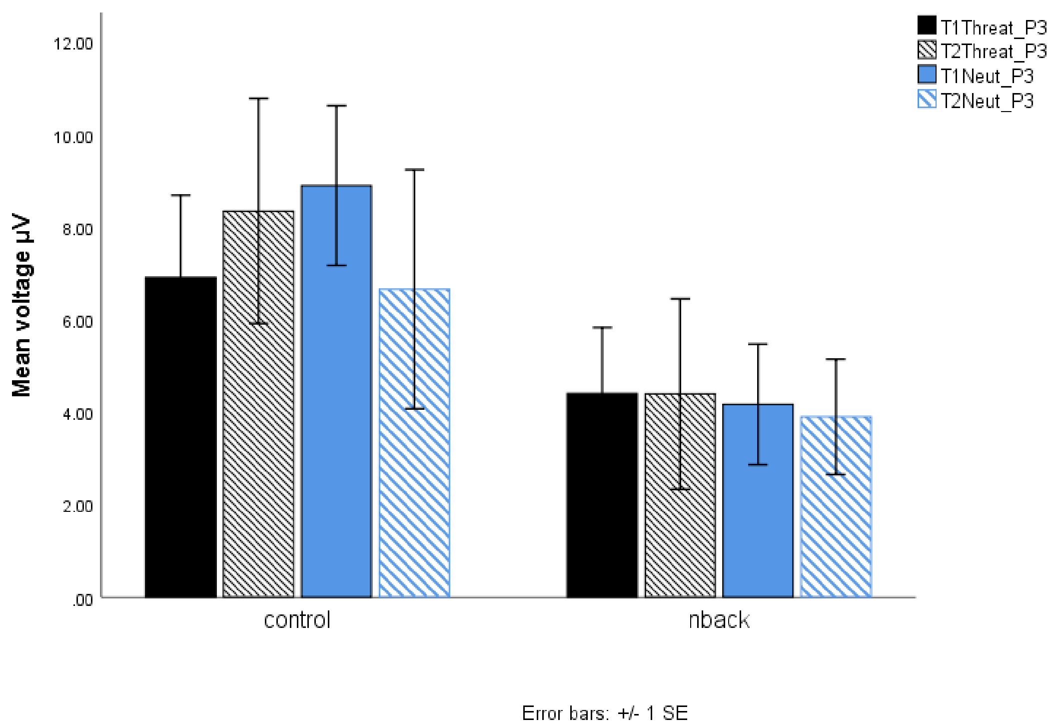


Figure 5.18 Compares control vs nback group response P3 amplitudes for neutral vs threat stimuli in Stroop task, before (time 1) and after (time 2) training. Error bars represent 1 SE.

MLM analyses tested for an effect of intervention group over time on the P3 threat response and the associated interference effect (threat – neutral). The MLM found the main effects of group and time on both P3, and P3 interference were not significant, $F < 1$. Moreover, the group x time interaction was not significant for the P3, $F < 1$, nor P3 interference effect $F(1, 32.44) = 1.47$, $p = .23$.

5.4.3.4 Post-hoc correlational analyses

Correlation analyses investigated associations between training-related changes in N2 and P3 and 1) training task improvement and 2) change in self-reported psychopathology symptoms at 3 months follow up. The N2 post-training was associated with the rate of nback training improvement (slope) at trend level significance, such that a steeper rate of nback improvement was associated with an increase in the magnitude of the threat N2 (N2 became increasingly negative), *r* =.51, p = .09 (Figure 5.19). The rate of nback improvement was not significantly associated with the P3, *r* = .28, p =.11 *n.s.*.

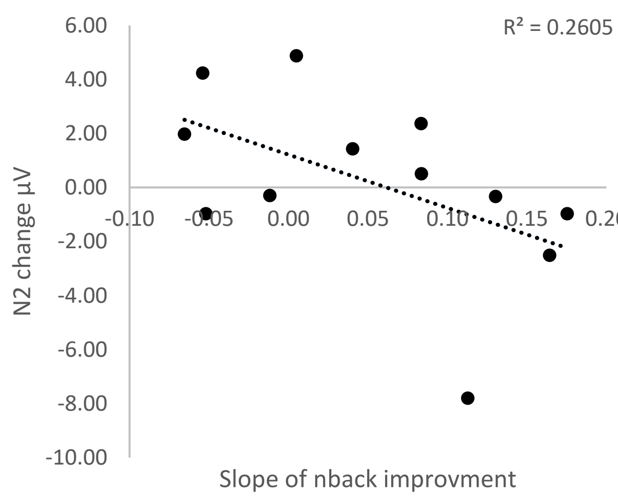


Figure 5.19 Scatterplot show relationship between changes in N2 amplitude and slope of nback improvement.

Nback group: Change in the threat N2 was significantly associated with rumination change from pre-training to 3 months follow-up, *r*(8) = .68, p = .04, such that an increase in N2 amplitude (greater negativity) was associated with a reduction in rumination (Figure 5.20). Associations of similar magnitude were found between change in the interference effect on N2 amplitudes and rumination differences from pre-training to follow up, $r(8) = .78$, $p = .01$, such that a decrease in rumination was associated with a reduction in the threat interference effect.

Changes in P3 amplitude were significantly associated with changes in rumination from pre-training to follow-up in the nback group, $r(8) = .82$, $p = .01$ such that a decline in P3 amplitudes from pre to post training was associated with a decrease in rumination from pre-training to 3-month follow-up (Figure 5.20). No significant associations between P3 interference effects and changes in symptoms were found, although a trend association emerged for rumination change at follow up $r(8) = .62$, $p = .07$.

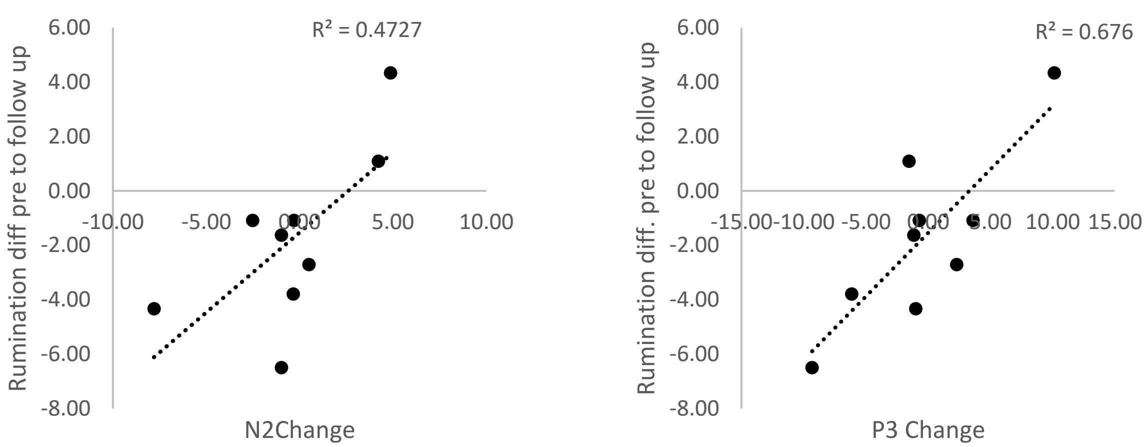


Figure 5.20 Scatterplots show correlations between changes in N2 and P3 amplitudes over time AND the change in rumination scores from pre training to follow up three months later

Control group. Changes in the magnitude of the P3 and N2 from pre-training to follow up were not significantly associated with changes in any of self-report measure in the controls (Table 5.16).

Table 5.15 ***Nback group*** *- Pearson correlations for the associations between nback training improvement, self-reported emotional vulnerability change and Stroop task ERPs.*

	1	2	3	4	5	6	7	8	9	10	Mean	SD
1 nback slope	_										0.04	0.08
2 nback gain	**.708****	_									0.4	0.74
3 P3 Interference change	-.206	-.161	_								0.27	5.5
4 P3 Change	-.239	-.081	**.939****	_							-0.01	5.34
5 N2 Change	-.510	-.236	.078	.362	_						0.21	3.33
6 N2 Interference change	-.033	.008	**.577***	**.663***	.406	_					1.79	3.47
7 SBI change	.480	.497	.431	.254	-.501	-.015	_				1.58	4.21
8 Worry change	-.255	-.351	.051	-.052	.073	.000	-.567	_			2	5.29
9 Rumination change	-.213	.049	.621	**.822****	**.688***	**.782***	.098	-.058	_		-1.49	3.36
10 Anxiety change	**-.592***	-.304	.551	.546	.309	.362	-.207	.344	.567	_	-2.42	5.65
11 Depression change	.337	.434	.342	.266	-.259	.064	.258	.320	.268	.304	-1.33	5.21

*Note: *p< .05, **p < .01 2-tailed. Variable notes; SD = standard deviation.*

Table 5.16 ***Control group*** *- Pearson correlations for the associations between control group changes in psychopathology and Stroop task ERPs.*

	1	2	3	4	5	6	7	8	Mean	SD
1 P3 Interference change	_								3.79	6.85
2 P3 Change	0.499	_							1.08	5.73
3 N2 Change	0.473	0.214	_						-0.17	3.88
4 N2 Interference change	.803*	.767*	0.576	_					2.23	5.23
5 SBI change	0.125	-0.18	0.627	0.038	_				0.92	6.97
6 Worry change	-0.19	-0.4	0.572	0.041	.687*	_			-0.17	4.75
7 Rumination change	0.019	0.06	-0.27	-0.21	0.498	0.342	_		-1.17	6.52
8 Anxiety change	-0.54	-0.66	0.367	-0.43	.554*	.882**	0.374	_	-2.85	8.74
9 Depression change	-0.17	-0.74	0.315	-0.4	.612*	.770**	.613*	.672*	-1.08	6.64

*Note: *p< .05, **p < .01 2-tailed. Variable notes* ; SD = standard deviation.

5.4.4 **Summary of correlational findings**

Figure 5.21 summarizes the correlational findings, where there were significant relationships between slope of improvement on the nback training, ERP change and long-term emotional vulnerability outcomes in the nback group.

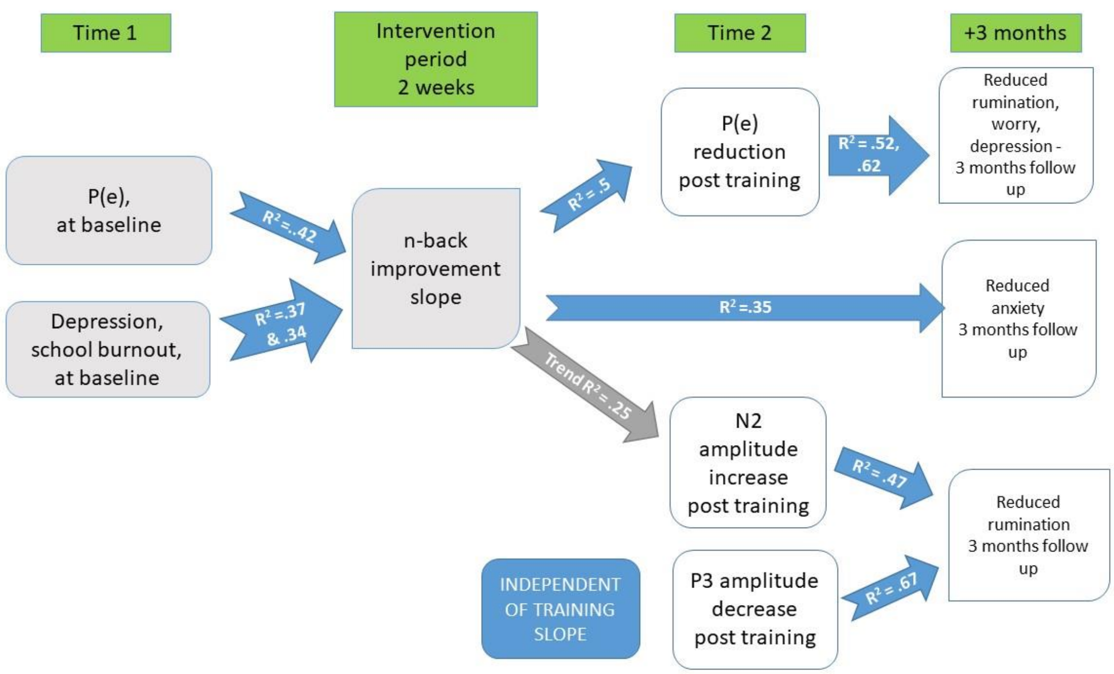


Figure 5.21 Summarizes relationships between nback group training improvement slope, neural change and sustained reduction in symptomology at 3 months follow- up compared to pre-training. Blue arrows indicate significant correlations. Grey arrow indicates at trend

5.5 Discussion

The study was a single-blind RCT to examine the effects of adaptive dual nback WMT on self-reported psychopathology and ERP indices of attentional control and emotional regulation in worry-prone adolescent boys. Both groups demonstrated similar effects of training on performance across time in the flanker, Stroop and OSPAN tasks. Post training, there was increased accuracy on incongruent flanker trials alongside reduced incongruence interference effects on reaction times and accuracy in both groups, indicating increased inhibition of distractors regardless of training group. Similarly, there was a significant increase in partial OSPAN scores, irrespective of group. Behavioural performance on the Stroop task was not differentially affected by group. Overall, in both control and nback groups there was slower Stroop task reaction times across all trials post training. However, whilst there was a typical albeit non-significant emotional Stroop effect, of slower RT on threat compared to neutral trials prior to training, this effect was reversed post training with significantly faster reaction times to threat relative to neutral stimuli in both training groups, suggesting that training resulted in better inhibition of a threat relative to neutral trial stimuli following training (Perez Edgar & Fox 2005).

Although there was evidence of increased attentional control in flanker task and WM performance in the OSPAN task as a result of both the control and adaptive WM intervention, this did not transfer to any self-report measures. There were no differences between the control and adaptive nback training groups' anxiety and depression symptomology, worry, rumination or school burnout scores post training, and in addition, no significant changes in either group from pre to post, or pre-to-follow up. The findings therefore did not support our hypothesis that adaptive nback training would reduce self-reported symptomatology in adolescent boys pre-screened for above-median worry.

These findings are consistent with the null group effects on training reported in three large RCTs which found no significant effects of WMT on self-reported or carer-reported psychological vulnerability in adolescents (Hitchcock & Westwell, 2017; De Voogt et al., 2016; Mewton et al., 2020), although De Voogt et al. (2016) found trend level increases in self-esteem in unselected Dutch adolescents with emotional nback training. Nonetheless, the current study's findings contrast with a number of previous studies exploring effects of cognitive training on psychopathology vulnerability in teens. For instance the findings reported in Chapter 4 found significantly reduced anxiety and depression post training, and at three months follow-up in typically developing adolescents using the same WMT task, while Schweizer et al. (2017) reported a significant reduction in PTSD symptoms in traumatised teens following training with an emotional nback task. Rosenbaum in et al. (2017) found a WMT group was less susceptible to peer influence on risk taking, a behaviour which is typically elevated in adolescence and associated with problematic behaviours (Steinberg et al., 2008). However, in Rosenbaum et al. (2017) training did not improve cognitive control and the study reported in Chapter 4 did not have an attentional control measure, so could not show a clear mechanism for change.

This is the first study to examine neurocognitive change and psychopathology vulnerability in adolescents. We selected the flanker task error response locked ERN and P(e) and Stroop threat stimulus locked N2 and P3 for their role in distinct neural processes that instantiate cognitive control and support emotional regulation. Adaptive dual nback training did not lead to significant ERN, P(e), N2 or P3 differences relative to controls following training, suggesting that training did not alter neurocognitive indices of error processing, conflict monitoring or elaborate stimulus processing in the flanker or emotional Stroop task respectively. However, there was a main effect of time on P(e) amplitudes with significantly reduced P(e) post training. The group means indicated that the P(e) was in fact more reduced in the nback group after training although this did not lead to a significant interaction. In other recent studies, Lotfi, Rostami, et al. (2020) reported increased P3b amplitudes in dyslexic children following visuospatial WMT, whilst Zhao et al. (2020) found adaptive dual nback training resulted in increased N2 amplitudes and reduced social anxiety symptoms in adults, although change in the N2 and other ERPs was not associated with symptom change, so the neural mechanism for the reduction in social anxiety was unclear, although the study was likely underpowered for mediation analysis. Our findings also contrasted with Lotfi, Ward, et al. (2020) which reported that emotional nback WMT led to increased ERN amplitudes alongside significant amelioration of both anxiety and depression symptoms. Zhao et al. 2020 and Lotfi, Rostami, et al. (2020) both administered training tasks featuring non-emotional stimuli, so our use of neutral training stimuli does not explain the absence of an effect.

Characteristics of the emotional Stroop task may have contributed to the absence of training-related changes in the N2 and P3 threat response. There was no significant threat interference effect at baseline, which was reflected in both the behavioural and neural measures, so it is possible that the baseline N2 threat response was insufficiently differentiated from the neutral and therefore any effects of training would not be detectable in this task. Perhaps more aversive threat stimuli would have revealed greater pre to post training differences. Although, we found no effects of training on emotion processing during a task that required regulation, this contrasts with some studies using fMRI which have found training resulted in changes in fronto-parietal networks and limbic areas associated with emotion (N. Cohen et al., 2016; Schweizer et al., 2013). For instance, Schweizer et al. (2013) reported that emotional nback training-related benefits on emotional regulation were associated with greater activity in fronto-parietal regions. N. Cohen et al. (2016) reported executive control training led to suppressed amygdala response to emotionally aversive images and increased functional connectivity between the amygdala and the prefrontal cortex. In another study Li et al. (2016) explored if nback training could improve impaired hedonic processing, an emotion processing deficit common in schizophrenia. They found evidence of training-related modulations of the ACC, precuneous and dorsal striatum during an affective incentive task, and DLPFC during a monetary incentive task. Notably, changes in activation represented a normalisation of hedonic processing for impaired participants, with no significant neural change in the control group (Li et al., 2016).

The present study is the first to assess neurocognitive change after adaptive dual nback training in typically developing adolescents, so despite the null group effects of training, it represents a first step towards understanding training-related neural change in this age group. Previous research amongst children and adolescents using fMRI and magnetoencephalography (MEG) to examine the neural correlates of WMT have shown mixed results. Some studies have found training related increases in WM led to increased functional connectivity between fronto-parietal areas (Astle et al., 2015), improved resting state connectivity (Barnes et al., 2015) and increased fronto-parietal activations (Jolles et al., 2012) in typically developing children and young adolescents. Other studies have found both increases and decreases in fMRI activation, but as participants were from different clinical groups and studies were not RCTs it is difficult to draw firm conclusions (Everts et al., 2017; Stevens et al., 2016; Yoncheva et al., 2017). Our findings are consistent with Kelly et al. (2020) who found null effects of CogMed training relative to controls on brain structure and function in low birthweight children when comparing pre and post training imaging data, although there were small but significant increases in neurite density in several white matter regions in both groups.

Taken together with the behavioural and self-report findings, our study suggested that adaptive WMT improvements did not transfer to group level differences in emotional, behavioural or neural outcomes. However increasingly, developmental neuroscience points to limitations in between-group comparisons of adolescent neural measures based on evidence of significant variation in the rate and trajectory of brain and cognitive development (Becht et al., 2020; Becht & Mills, 2020; Foulkes & Blakemore, 2018). For instance, one study examined individual developmental trajectories and grey matter volume (GMV) across the amygdala, nucleus accumbens and prefrontal cortex. Whilst there were general patterns of increase and decrease in GMV during development, there was substantial variation in how and whether these general patterns applied to individuals (Mills et al., 2014). This may have two-fold consequences: first, developmental differences may influence the extent to which adolescents are able to perform and engage with the training in the first place, and secondly, variations in individual participants' position along a developmental trajectory could make it difficult to detect training-related change using within-group comparisons. It is possible that the combination of small sample size, individual variation in neurocognitive development and relatively low baseline vulnerability scores contributed to the absence of support of our main hypotheses.

To address the potential effect of individual differences in training outcomes as well as baseline characteristics that predicted improvement in the training task, we conducted post-hoc exploratory analyses. The results were summarised in Figure 5.21. There was evidence that baseline depression and school burnout scores predicted the rate of improvement in the WMT task. Higher depression and school burnout were significantly associated with poorer training improvement, suggesting a magnification effect of training in those who were less vulnerable, whereas boys with higher emotional vulnerability were less able to benefit from training. This study is not the first to find that poorer baseline mental health measures influence intervention behaviours. Firstly, these findings were consistent with study 2 where there was also a significant association between baseline internalising and nback improvement, although this may be specific to adolescents, as it has been recently shown that adults with greater emotional difficulties benefited most from nback training (Ciobotaru et al., 2021). These results are also consistent with other intervention approaches. An online CBT intervention for teens comparing outcomes in school and community settings found higher anxiety predicted poorer engagement when the intervention was managed via school, although a reverse effect was found for depression scores in a community rather than school-centred intervention (Neil et al., 2009). Studies of mindfulness interventions for mental health protection also find that worry and rumination predict poorer engagement with the intervention and reduced overall benefit (Banerjee et al., 2017, 2018; Crane & Williams, 2010), although to the best of our knowledge no evidence is available for adolescent samples.

It is not clear why depression or burnout impacted training improvement. Depression may impact training via general cognitive impairments (Shilyansky et al., 2016), which could have made the training task more cognitively challenging and reduced the rate of task improvement. A related finding was that higher school burnout, particularly the exhaustion subscale of the school burnout inventory, was also significantly associated with poorer nback performance gains. School burnout is also linked cognitive impairments (May et al., 2015), which may have hindered training progress in higher burnout individuals. A third possibility is that depression and burnout may relate to training progress via another variable not measured in our study; for instance via self-efficacy and perceived competence which in turn could have interfered with training progress and engagement (Quiroga et al., 2013). Recent cross lagged analyses indicated that depression is more predictive of self-efficacy and perceived competence that the other way round (Ohannessian et al., 2019). Our findings indicate baseline depression and burnout have a bearing over how well participants engage with cognitive training and therefore are highly relevant for developing interventions designed to support emotionally vulnerable young people going forward. Future studies are needed which can elucidate which participant characteristics help or hinder progress with WMT itself and how individual differences in these characteristics interact with different components of the study design, such as training duration or the levels of training task difficulty (Schmid et al., 2020; Shani et al., 2019).

Although there were no group differences on psychopathology outcome measures between adaptive nback training and control groups on post training, the slope of WM improvement during training was correlated with long-term reductions in anxiety such that increases in the WM improvement slope were significantly associated with reductions in anxiety from baseline to 3 months follow up. Nback gains (difference between beginning and end of training) were also significantly associated with rumination at follow up. These associations emerged at 3 months follow-up post training, suggesting that effects of training took time to consolidate. It is possible that low overall baseline psychopathology scores may explain non-significant group effects which has been indicated as a possible explanation for different effects of training on emotional vulnerability outcome measures in other studies (Mewton et al., 2020).

The results of the post hoc analyses demonstrate that analysis of individual variation may be important for understanding training transfer in this age group. This is a notable finding and shows that the level of engagement with the training intervention may be critical for change. That the rate of improvement was associated with therapeutic change is consistent with Sari et al. (2016), who also found that increases in training engagement predicted reductions in anxiety post training, and also in the absence of group differences (see also Hotton et al., 2018). Siegle et al., (2014) employed a physiological measure of training engagement in the PASAT WMT and found that the magnitude of rumination reduction in depressed participants was predicted by engagement with the training task and furthermore these improvements arose from increased recruitment of the DLPFC. This finding contributes to understanding the importance of motivation and effort in the effectiveness of training on therapeutic outcomes (Sari et al., 2016) and that this is relevant for adolescents similar to adults. Caution about this finding is nonetheless warranted as it is unclear why this relationship would only occur for anxiety and not any of the other self-report measures. Moreover this sample size was restricted and results would need to be replicated in a larger sample.

The slope of improvement in the nback training task was also associated with pre to post training changes in one of the ERP measures. Although the ERN response to errors was not associated with the improvement slope, the P(e) was, and in two ways. Firstly, baseline P(e) predicted improvement such that higher baseline P(e) amplitudes predicted greater nback improvement across the training period. In addition, training slope increases were also associated with a reduction in P(e) amplitudes from pre to post training which was consistent with the non-significant group effects of bigger P(e) reductions in the nback group post training. Notably, reduced P(e) was in turn associated with worry, depression and rumination at follow up, and smaller increases in worry (significant) and anxiety (trend) from baseline to 3 months follow up. In contrast, there were no significant associations between post training P(e) and any of the psychopathology measures in the control group. Prior work has not consistently pointed to associations between the P(e) and psychopathology vulnerability (Endrass et al., 2008; Hajcak et al., 2008; Ladouceur et al., 2006; Meyer et al., 2012), although Santesso et al. (2006) found an enlarged P(e) was associated with OCD symptoms in pre-adolescent children. Studies of the functional significance of the P(e) consistently find that it represents conscious awareness of errors, whereas the ERN is involved in earlier non-conscious error processing (Endrass et al., 2007; Hewig et al., 2011; Nieuwenhuis et al., 2001). Furthermore, the amplitude of the P(e) has been linked to changes in error aversion such that amplitudes decline when the error has lower motivational significance (Overbeek et al., 2005; Ridderinkhof et al., 2009). Indeed Paul, et al. (2017) recently found that compared to neutral mood, a happy mood reduced the P(e) whilst the ERN was unaffected, because the motivational salience of errors was reduced under positive affect. A possible explanation for our findings is that whilst greater sensitivity to the motivational significance of errors boosted training engagement itself, the resultant changes in neural function linked to greater training improvement, instigated a decrease in the significance of conscious errors which subsequently boosted overall psychological wellbeing by the time of follow-up testing.

Training improvement was somewhat associated with change in the N2 associated with threat stimuli during the emotional Stroop task, evidenced by a trend towards a significant correlation. We were interested in the extent to which training impacted the regulation of emotional distractors in particular, and we found that the training improvement slope was associated at trend levels with increases in N2 amplitudes in response to task irrelevant threat. Importantly, increases in N2 amplitudes from pre to post training were in turn associated with subsequent decreases in rumination from baseline to follow-up, suggesting that training-related increases in attention control in the context of threat-related distractors were associated with lower rumination in adolescents. This is further supported by our finding that the N2 interference effect was also associated with rumination. This provides some tentative support that changes in neural indices of inhibitory control were associated with reduced rumination in the nback group. Although training improvement did not correlate with P3 amplitudes, decreases in the P3 from pre to post training were significantly associated with subsequent reductions in rumination at follow-up compared to baseline, suggesting a reduction in attentional biases to threatening information and subsequent elaborative processing, although this cannot be attributed to training improvement. It is possible that the reductions in the P3 may indicate reduced elaborative processing of the threat stimulus via attentional gating at an earlier stage in the processing stream.

Overall these findings were consistent with several other studies showing that when cognitive interventions led to clinical improvements they were accompanied by increases in N2 amplitudes and a combination of the increased and decreased P3s. For instance, the direction of effects in this study were similar to Zhao et al. (2020) who found an nback training group had significantly increased N2 amplitudes compared to a control group post training, although these N2 increases were not associated with the improvements to social anxiety also reported in that study. In a related finding, the ERPs of clinically anxious children were assessed before and after CBT. Those who improved clinically had an increased N2 after the intervention, whereas N2 amplitudes remained unchanged in non-improvers (Hum et al., 2013). There is also evidence from other interventions for clinical groups which reported differing effects of therapeutic interventions on the N2 and P3 amplitudes. For instance, in one study in which participants were trained to allocate their attention away from threating stimuli, anxious but not control participants showed a decrease in P3 amplitude and an increase in the N2 (Eldar & Bar-Haim, 2010). Somewhat different trajectories of change were reported for the P3 following an intervention study that featured a combined protocol featuring a form of cognitive training (mindfulness meditation) and physical exercise amongst depressed participants and controls (Alderman et al., 2016). Training reduced depressive symptoms and led to increases in both P3 and N2 amplitudes in all participants. These increases were more pronounced in depressed participants and represented a normalisation of impaired N2 and P3 function in the clinical group. The differing P3 outcome for Alderman et al. (2016) may have been due to the differing clinical populations and differing mechanisms of action for the training interventions.

Taken together our results provide some tentative support consistent with earlier work, that where there is sufficient improvement in the training task, adaptive dual nback training can instantiate some changes in ERP indices of cognitive control which was most evident on the P(e). Bearing in mind the absence of an effect of training improvement on the P3, we should be especially cautious in interpreting the trend level effect for the N2. Nonetheless, that we found an association between training improvement and reductions in the P(e), which was in turn associated with reduced self-reported psychopathology measures in the nback group only, indicates further research is warranted to elucidate the effects of WMT on the P(e) and error processing in adolescents.

It is worthwhile to consider these findings in the wider context of the developmental change in the N2 and P3 ERPs and how differences in these ERPS are also related to clinical vulnerability, as it highlights that interpreting increases and decreases in their amplitude is challenging. Studies in adults have reported that anxiety is associated with both increases (Owens et al., 2015; Righi et al., 2009; Sehlmeyer et al., 2010) and decreases (Dennis & Chen 2009; Kim et al., 2007) in N2 amplitudes. There are also mixed findings for how these ERPs change during development. A recent meta-analysis concluded that most evidence indicates the N2 decreases between childhood and adolescence (Espinet al., 2012; Lo, 2018) with decreasing N2 amplitudes indexing improved cognitive control (Lamm et al., 2014), in particular the improved ability to filter out distracting task irrelevant information (Lo, 2018). However other researchers have found evidence of an increasing N2 over development (Enoki et al., 1993; Ladouceur et al., 2004, 2007). Research on the developmental trajectory of the P3 is inconclusive with evidence of both increases and decreases in amplitude throughout childhood and into late adolescence (Riggins & Scott, 2020; van Dinteren et al., 2014). This may reflect differences in the P3 for visual and auditory domains, but could also reflect early maturation of the frontal sources of the P3 alongside more protracted development of the posterior parietal P3 which is associated with WM and executive attention (Downes et al., 2018; Overbye et al.; 2018). Researchers exploring risk factors for the development of psychological disorders find evidence that differences in N2 and P3 responses mediate the links between an early childhood temperament risk factors for anxiety and subsequent development of anxiety disorders (Henderson et al., 2015; Lahat et al., 2014; Reeb Sutherland et al. 2009; Thai et al., 2016; White et al., 2011). Therefore the relationships between cognitive control ERPs, training-related change and psychopathology vulnerability during development are complex, and future studies examining effect of WMT on N2 and P3 ERPs will require careful design to elucidate genuine effects of training.

A final point to consider when interpreting the ERP results in this study is that in contrast to the N2, P3, and ERN each of which undergo steady change over the course of development, the latency and amplitude of the P(e) does not change beyond late childhood. The P(e) has been detected in pre-schoolers and numerous studies report maturation in late childhood with no age-related changes in P(e) amplitudes during adolescence (Davies et al., 2004, Overbye et al., 2021), although one study has reported higher P(e) in late adolescence relative to adults (Ladouceur et al., 2007). Such stability could make it easier to detect neuroplastic changes due to WMT and explain why there were stronger effect of training on the P(e) compared to the other ERPs.

5.5.1 **Limitations**

This study had a number of limitations. The sample size was small, so may have had insufficient power to detect group differences on psychopathology and neurocognitive outcome measures. A larger sample size would have permitted more complex regression analyses and a more comprehensive exploration of the links between training engagement and psychopathology outcomes via neurocognitive change. The sample size limitations also extend to all correlation analyses. Whilst there were notable and significant correlations between individual differences in training improvement, ERP changes and changes in self-reported symptomology, we must be cautious about the conclusions we can draw. Moreover, the observed coefficients were large, so again caution is warranted as these effect sizes likely overestimate the true effect sizes due to the small sample size.

The study participants were exclusively male, so these findings cannot be generalised to adolescent girls. This is especially relevant as boys are less likely than girls to report anxiety and depression (Van Droogenbroeck et al., 2018) and also have been shown to gain fewer benefits from other interventions, including mindfulness meditation and suicide prevention programmes (Bluth et al., 2017; Hamilton & Klimes-Dougan, 2015; Katz & Toner, 201).

There was a main effect of time on OSPAN and Flanker task performance indicating training related increases in both the adaptive training and the control groups. There were also changes in Stroop task performance shared across participants, regardless of group. These may have been practice effects or linked to reduced anxiety in participants on their second visit to the lab, however placebo or expectancy effects may also have influenced post training performance. Whilst it may be possible with younger children, it remains a challenge to maintain the naivety of participants in training study designs and a measure of participant expectancy would have allowed us unpick this effect (Masurovsky, 2020).

The emotional Stroop task did not produce a significant threat interference effect in either group, reducing the reliability of the Stroop task findings and the associated N2 and P3 threat ERPs, although others have shown sensitivity to threat on ERP measures despite no behavioural effects (Thomas et al., 2007). A significant interference effect was confirmed during piloting of the task in a small community sample of mixed gender adolescents. Sample characteristics may explain this lack of sensitivity in the Stroop task, as the sample was male only and recruited from a single sex independent school. Studies using Stroop tasks indicate threat word sensitivity is very person-specific, and have recommended a procedure where a participant rates a selection of words prior to the task with only the most threatening selected used with that participant (Thomas et al., 2010). Personalised threat stimuli might have improved ability to detect changes in emotional regulation. Additionally a more pronounced emotional Stroop interference effect might also have been elicited had we manipulated state anxiety (Dresler et al., 2009).

High attrition was an issue in study 2 (Chapter 4) and this was also reported as a challenge in other WMT intervention studies with adolescent participants (Mewton et al., 2020, Sweeney et al., 2018). Indeed, high attrition rates are common in adolescent intervention studies generally (Boys et al., 2003; Yeager et al., 2018). Some intervention studies distinguish between physical and psychological engagement, where physical engagement refers to the act of doing the practice and homework, whereas psychological engagement reflects deeper engagement and effort during practice (Banerjee et al., 2018). Only one participant dropped out of this study. It is possible that efforts to reduce attrition; including stressing the importance of finishing the training, preparing participants for inevitable motivation dips, close monitoring and very regular contact with participants boosted physical engagement only, but failed to deal with psychological engagement. Perhaps those who might otherwise have dropped out, continued to train but with poorer psychological engagement, which might have undermined training effects, and also explained why some participants had a negative improvement slope. This is potentially an important factor in training studies in this age group and future research will need to introduce measures to enhance and monitor psychological, as well as physical engagement.

5.5.2 Concluding remarks

Contrary to pre-registered hypotheses, adaptive WMT did not significantly reduce psychopathology vulnerability in adolescent boys selected for high worry, and did not lead to changes in several neural correlates of cognitive control. Nonetheless there was tentative evidence that individual differences in training engagement was an important predictor of neural change and improved psychological vulnerability, with strongest effects for an ERP indexing the motivational significance of errors. Future research should explore how individual differences in training performance and engagement differentially impact neural and emotional vulnerability outcomes, as this is likely to be an important feature of training benefit, especially during adolescence when neurocognitive systems governing cognitive control and socio-emotional development are experiencing such flux.

CHAPTER 6

6 General Discussion.

6.1 General overview of thesis

This thesis set out to explore neurocognitive mechanisms of vulnerability to emotional disorders in typical adolescents alongside the efficacy of cognitive training as an intervention method to improve emotional regulation and reduce symptoms and trait vulnerabilities to disorder. Adolescence is a remarkable life phase, characterized by significant physiological, cognitive and psychological development alongside substantial changes in the social context. Adolescence is also recognized as a sensitive period of cognitive and socioemotional maturation driven by enhanced neural plasticity. A corollary of this plasticity may be a vulnerability to perturbations during the development of higher order cognition, contributing to a cascade of events that increase risk for emotional disorders.

Accumulating evidence points to aberrations or impairments in inhibition, shifting and WM as a source of vulnerability to emotional disorders generally (Berggren & Derakshan, 2013; Grahek et al., 2018). These processes are intricately involved in regulating how much negative or emotional information gains access to the mind and how long it stays active there. They also govern how we actively guide our behaviour and our affective responses to emotional or motivationally significant stimuli. Multiple sources of evidence indicate many emotional disorders are associated with dysfunctional activations in fronto-parietal and executive brain networks and in their interactions with subcortical regions involved in cognitive processes (Etkin et al., 2009; Hilbert et al., 2014; Roy et al., 2013).

A characteristic of emotionally resilient adolescents may be better cognitive control abilities. Although attentional control abilities develop linearly, the ability to execute efficient attentional control under affective conditions is more protracted and may not follow a unitary developmental trajectory, as a recent review has indicated (Schweizer et al., 2020). This ability is increasingly identified as a driver of emotional regulation and variation in control under affective conditions and may be a particular source of adolescent vulnerability to mental health difficulties (Schweizer et al., 2020). Nevertheless, there is evidence that adolescents and children with high to relative low trait and clinical anxiety, as well as depression, experience attentional control impairments even in non-emotional contexts (Jazbec et al., 2005; Waszczuk et al., 2015). Together this suggests that adolescents predisposed to emotional disorders (e.g. genetically or via early childhood adversity) may be protected from disorder by more efficient or effective engagement of attentional control.

Motivated by accumulating evidence of a tight coupling between emotional and cognitive processes, intensive cognitive training interventions may offer a way to improve emotional wellbeing and reduce negative affect (Shani et al., 2021). Theoretically driven investigations have strategically targeted the cognitive mechanisms involved in WM using computerized WMT interventions (Derakshan, 2020). Studies in adults have shown indeed that training WM can have a positive therapeutic effect in clinically and sub-clinically vulnerable populations leading to symptom reduction and improved cognitive functioning (Barkus, 2020; Derakshan et al., 2020; Koster et al., 2017).

A principal aim of the current thesis was to capitalize on this research by exploring the efficacy of WMT interventions amongst typically developing adolescents. The theoretical motivations were similar to the studies with adults, but included a developmental perspective recognizing that training should interact with the dynamic restructuring of cognitive control processing during adolescence (Klingberg, 2010). Some early studies had provided tentative evidence that training might support adolescent emotional wellbeing (Hadwin & Richards, 2016; Roughan & Hadwin, 2011) although results from research undertaken in parallel to studies reported in this thesis are mixed. The work in this thesis has however focused on a training intervention that has shown promise in adult interventions, but not previously investigated amongst adolescents. It aimed to explore the effect of training not only on emotional regulation, but on self-reported symptoms of anxiety and depression. The efficacy of cognitive training has been widely debated generally (Redick, 2019), however the emphasis to date on behavioral measures, limits the understanding of training efficacy. A notable gap in the literature has been a dearth of studies examining the effects of training on neural outcomes in this age group, and investigating neural measures relevant to emotion processing would permit better understanding of the impacts of training on emotional regulation and symptoms. Even in the absence of direct transfer to task performance, there may be evidence of a modulation in neural activations pointing to changes in efficiency or strategy. In summary, the first aim of the thesis was to build on prior training work targeting affective processes in adults, employing the previously untested nback training task in typically developing adolescents, with an emphasis on assessing symptom change, emotional vulnerability and neural outcomes.

A second aim of the research was to build on previous work in the Attentional Control (Derakshan & Eysenck, 2009; 2011; Eysenck et al., 2007) and the Resource Model of Control (Baumeister, 1998; Muraven & Baumeister, 2000) theories to explore if processing inefficiency in attentional control tasks necessitating compensatory cognitive processing might have hidden emotional costs. Numerous studies indicate poorer inefficiency during attentional control tasks is linked to mental health vulnerabilities in adults and adolescents (Berggren & Derakshan, 2013; Shi et al., 2019), although the volume of research in adolescents is limited. Moreover, developmental studies have also indicated that adolescents may be less efficient per se than adults in inhibitory control and WM task performance (Spronk et al., 2014; Velanova et al., 2009). An intriguing question arising from these findings is whether the combination of processing inefficiency and compensatory effort with high situational cognitive load is cost neutral. No studies have attempted to explore possible consequences of compensatory tendencies and how that might impact affective control generally, although previous authors have speculated that individuals who persistently need to compensate will be drained of resources and experience significant real-world difficulties and impairment (Moser et al., 2013). By addressing this question directly, I aimed to elaborate on a mechanism through which cognitive training interventions might improve emotional wellbeing using combined behavioural and EEG methods.

6.2 Summary and discussion of the main findings

6.2.1 Exploring hidden costs of compensatory effort on negative thought proliferation in adolescents and adults

The aim of study 1 (Chapter 3) was to a) investigate the differential age effects of cognitive depletion on negative thought proliferation triggered by a worry induction and b) measure the association between an electrophysiological measure of compensatory reactive cognitive control during a depletion task and concurrent emotional reactivity and school burnout, in addition to longer term burnout and emotional vulnerability assessed 18 months later. It has been hypothesized that engaging higher order cognitive control functions, either through self-regulation or in tasks with high attentional control demands, depletes limited control reserves leading to a temporary hiatus in resource availability resulting in impaired cognitive control (Muraven & Baumeister, 2000). Attentional Control Theory predicts that attentional control impairments due to interference from worrisome or ruminative thoughts can be mitigated though extra effort, evidenced by disruptions to task efficiency rather than effectiveness (Derakshan & Eysenck, 2009). By marrying these two theoretical perspectives it was hypothesized that a depletion task with high rather than low WML would increase negative thought intrusions when worry was induced directly after the depletion task. In light of lower inhibitory control efficiency in adolescents relative to adults, adolescents in the high load group were expected to be most vulnerable to depletion effects on induced negative intrusions.

Age and WML had neither independent nor interacting effects on emotional reactivity due to the worry induction, and therefore results did not support the hypothesis that a more demanding cognitive exercise would impair subsequent ability to resist negative thought intrusions when triggered by the worry induction. Although adolescents were significantly more susceptible to thought intrusions prior to the induction, this is likely to have reflected general age-related attentional control differences rather than depletion effects. However, there was partial support for the prediction that expending more processing effort during the task would result in subsequent impairments to task-focus and resistance to negative thought intrusions triggered by the worry induction. The correlational analysis focused on the predictive power of the ERN, as this ERP has robust associations with mental health vulnerabilities and is hypothesized to index compensatory cognitive processing during performance monitoring (Moser, 2017; Moser et al., 2013). Amongst the adults, larger ΔERN amplitudes were associated with bigger increases in negative thought intrusions triggered by the worry induction, consistent with research showing internalizing disorders are associated with hyper-activation in executive and salience networks (Fales et al., 2008; Sha et al., 2019; Shanmugan et al., 2016).

The findings from study 1 extend previous work supporting the compensatory monitoring hypotheses of the ERN in anxiety (Moser, 2017; Moser et al., 2013) by demonstrating that an elevated ΔERN was associated with subsequent attentional control failures operationalized in increased proliferations of negative intrusive thoughts. Critically this was in adults only. Participants were not selected for elevated anxiety, thus extending the usefulness of the compensatory effort hypothesis to explain how healthy adults, but not adolescents, can be at risk for mental health problems when relying on less efficient cognitive control. There were no significant group effects of depletion on negative thought intrusions triggered by the worry induction, appearing to substantiate evidence countering the existence of ego depletion phenomena in adults (Hagger et al., 2016) and adolescents (Gullo et al., 2017) and which reflects conflicting findings and inconclusiveness in that literature as a whole (Friese et al., 2019). However this study extends prior findings with an additional level of analysis. Recording the ERN during the depletion exercise, permitted an examination of the underlying cognitive effort applied during the experimental task and the relationship between that effort and subsequent cognitive control impairments in the worry induction exercise. The study also extends prior studies in so much as it demonstrated that manipulating WML in half of the blocks was insufficient to drive significant group differences in resource depletion. Future studies will need to devise computerized task adaptations which more effectively discriminate between high and low/ no depletion effects, but remain suitable for extracting ERPs.

Contrary to predictions, the study found no evidence that adolescents were more prone to the effects of depletion than adults. In addition, the correlation analysis showed an enlarged ΔERN did not indicate greater susceptibility to the triggering effect of the worry induction on negative thought intrusions and task effectiveness. In fact, the converse occurred. Adolescents with an elevated ΔERN were more resistant to the triggering effect of the worry induction on negative thought intrusions. Moreover, and providing further support for interpreting an elevated ERN as protective, a smaller ΔERN was associated with worry and school burnout increases between time 1 to follow-up 18 months later. If interpreting the ERN as a marker of efficient processing or effort, it suggested that larger ΔERNs in adolescents indicate more efficient or at least more effective cognitive control. The latter is consistent with studies showing a larger adult ERN is associated with higher WM capacity (Coleman et al., 2018; Miller et al., 2012), and that ERN amplitudes increase during development alongside gradual improvements in performance monitoring (Overbye et al., 2019; Tamnes et al., 2013).

The specific patterns of ΔERN activation in relation to emotional vulnerability in adolescents substantiates prior evidence that the anxiety-ERN relationship may be reversed in younger relative to older adolescents who do not have a disorder, indicating a flip in the ERN – emotional vulnerability relationship during development (Meyer et al., 2012; Moser 2017; Weinberg et al., 2016). Moser (2017) has suggested that a developmental reversal in this relationship could be linked to developmental changes in the neural generators of the ERN. Although the source of the ERN is largely attributed to the ACC and PCC, generators in the fronto-parietal and limbic regions are also implicated. The ACC and PCC sources of ERN are relatively stable in development, but the contribution of the inferior frontal gyrus, insula and orbitofrontal cortex increase with age and are related to the integration of motivation and salience information in error monitoring (Buzzell et al., 2017; Moser, 2017). Whilst earlier in development, worries may disrupt attentional control allocation, the lack of salience or motivational input from the IFG, OFC and insula is reflected in smaller ERNs. As development progresses, input on salience and motivation may boost control processing and increase the ERN (Moser, 2017). In the current study adolescents with less well developed error monitoring systems may have been less able to regulate the effects of the worry induction on behaviour and thus experienced increased negative intrusions relative to those with larger ERNs. Speculating on this developmental reversal, as motivational and salience information become more established and integrated with error processing some individuals may acquire habits of overcompensation in a variety of contexts where they fear failure or exposure to criticism or disapproval (Moser, 2017).

It remains unclear when the reversal occurs. Evidence from previous studies suggest it occurs between late childhood and very early adolescence (Meyer et al., 2012) or between 13.5 and 15.5 years (Weinberg et al., 2016). The results of study 1 extend the age at which larger ERNs predict emotional resilience rather than vulnerability and that the ERN may not reflect compensatory functions until later adolescence for some individuals. Further research using within-person longitudinal designs is needed to clarify the changing trajectories in the relationship between the ERN, processing efficiency and emotional vulnerability, and these studies should incorporate motivational and salience manipulations to clarify their contribution to this relationship. The inclusion of both adults and adolescents in this study was a notable strength, permitting the identification of a potentially important developmental difference and a target for future research into how vulnerability to emotional disorders may emerge during development.

6.2.2 Targeting attentional control using dual nback WMT to reduce emotional vulnerability in adolescents.

The aim of the study 2 (Chapter 4) was to investigate the impact of a four week regime of dual nback WMT targeting anxiety and depression symptomology in adolescent boys and girls. Anxiety and depression symptoms were assessed using self-report, before, directly after, and at one month post intervention follow-up to investigate the sustainability of transfer effects. Firstly, the study found that daily engagement with the WMT task improved over the course of the training period demonstrating that adolescents can successfully engage with and increase performance on the dual nback training paradigm. Secondly, relative to the control group, the training group had significantly reduced anxiety and depression symptoms at post training which was sustained at one month follow up, demonstrating the first evidence that dual nback training can reduce depression as well as anxiety symptoms in adolescent participants.

Findings from study 2 build on two previous studies which showed CogMed WMT could reduce anxiety symptoms and emotional difficulties in at-risk adolescents (Hadwin & Richards, 2016; Roughan & Hadwin, 2011) extending prior work to show training-related reductions in self-reported anxiety and depressive symptoms at a subclinical level in typically developing adolescents. This finding shows that in addition to at-risk young people, even adolescents without a disorder may benefit therapeutically from WMT. This is a notable finding, as it demonstrates how WMT might support adolescents to manage age-typical emotional ups and downs and prevent the escalation of subclinical symptoms to more serious clinically significant levels. This is also the first study to find group differences for effects of nback training on depression symptoms. Prior WMT studies with adults have reported post training reductions in rumination and brooding, both critical in the etiology of depression, but to date there were limited effects on depressive symptomology (Koster et al., 2017; Wanmaker et al., 2015, 2018). Previously, Onraedt and Koster (2014) found no differences in depression between the training and control groups after a short (6 day) intervention, however improved dual nback training task performance was correlated with depressive symptom reduction post intervention, suggesting a more intensive training programme might have been more effective (Schwaighofer et al., 2015). The duration of the current training intervention may have played a role in depression reduction, indicating that whilst shorter interventions may be sufficient to promote reductions in anxiety, worry or rumination (Course-Choi et al., 2017; Sari et al., 2020; Swainston & Derakshan, 2018), transfer to depressive symptoms may demand longer interventions.

An important difference between this study and more recent investigations into the effects of WMT on adolescent mental health (e.g. Mewton et al., 2020) was the adoption of a training paradigm that has already shown some promise in targeting emotional vulnerability in healthy and vulnerable adult populations. Researchers have trialed a variety of training paradigms in adolescents, which include several investigations using CogMed training which have had mixed results, and a heterogeneous set of other paradigms which had limited transfer on emotional measures, although with some exceptions (Rosenbaum et al., 2017; Schweizer et al., 2017). One of the only studies to find reliable effects of training in an RCT used a version of the nback task featuring emotional distractor stimuli (Schweizer et al., 2017). It is therefore possible that shared elements of WM updating in emotional and neutral nback tasks is an important therapeutic ingredient in training paradigms. The current study also adds more broadly to the literature on WMT with adolescents. Only a few prior studies have trialed dual nback training in developmental samples targeting cognitive performance (Jaeggi et al., 2011; Pugin et al., 2014, 2015). These studies indicated that children and early adolescents found nback training difficult, suggesting the lack of training transfer could have resulted from limited training engagement, which was supported by evidence of training transfer in participants who had improved training performance in those two studies. Study 2 (Chapter 4), and indeed study 3 (Chapter 5) provided evidence that adolescents can however engage with and improve WM performance using the dual nback task, despite finding it challenging. Nevertheless it must be acknowledged that across the two studies successful nback improvement was not universal.

6.2.3 Effects of adaptive WMT on emotional vulnerability and neural correlates of cognitive control in adolescent male worriers

The aim of study 3 (Chapter 5) was to replicate the findings from study 2, this time in a vulnerable, albeit non-clinical, adolescent sample, using a broader range of behavioral and emotional regulation outcome measures, in addition to internalizing symptomatology. Moreover, the study also aimed to explore the neural correlates of training transfer using a variety of ERP indices of cognitive control relevant to emotion processing. Contrary to the findings in study 2, two weeks' dual nback training did not transfer to reduced anxiety and depression scores relative to controls, nor did it transfer to worry, rumination, WM capacity, interference in a flanker task, nor emotional interference in a Stroop task. This is consistent with several adolescent studies which did not find direct effects of adaptive WMT transfer on cognition or emotional vulnerability relative to controls (Hitchcock & Westwell, 2017; Mewton et al., 2020). Nevertheless, in a manner highly consistent with a growing number of adult studies (Grol et al., 2018; Hotton et al., 2018; Koster et al., 2017; Sari et al., 2016; Shani et al., 2021) there was a significant association between the rate of improvement in the training task paradigm over the course of the intervention and reduced anxiety at three months follow-up, further testimony to varied trainability, motivation and propensity to benefit from WMT seen in other studies.

There are a number of differences between the two training studies reported in this thesis which may speak to why group differences in transfer of training were found in study 2, but not study 3. The second study had a smaller sample. Sample selectivity (participants were screened for above median worry five 5 months before training) and an a priori G*power analysis recommended a mimumum n = 34 participants. As a result of participant drop out directly before training, the final sample was n = 31, which was admittedly underpowered. Secondly, in light of participant attrition in study 2, a shorter intervention was decided upon for study 3, which minimized attrition. That there was a correlation between training improvement and anxiety reduction suggests that for some participants a two-week intervention was sufficient to find transfer effects, however for effects to be more widespread, the weight of evidence from these two studies favours a longer training dose, particularly to improve depression symptoms. The third major difference between the studies lies in the gender of participants. Whereas study 2 featured boys and girls, study 3 featured boys only. Emotional disorders are more prevalent amongst girls (Collishaw & Sellers, 2020), which could indicate we should expect to see weaker effects on vulnerability measures amongst boys generally, although selecting boys who were high worriers was intended to maximise the chance of detecting effects of training.

Study 3 is currently among the first to investigate neural correlates of adolescent WMT targeting wellbeing, so these findings provide a first step towards understanding the impact of nback training on underlying neural processing at the intersection of affect and cognition in this age group. Extant work with adults and younger children has found WMT to be associated with changes in fMRI task activations and resting state within fronto-parietal and salience networks

(Astle et al., 2015; Barnes et al., 2016; Constantinidis & Klingberg, 2016; Salmi et al., 2018), as well as modulation of a variety of ERPs involved in cognitive control and emotion processing which have neural generators within these same networks (Pan et al., 2020; Salmi et al., 2019), although interpretation of activation increases or decreases can be speculative (Salmi et al., 2019).

With respect to findings from study 3, consistent with the behavioral measures, evidence for neuroplastic effects of training on ERPs associated with affect and cognitive control were minimal for the ERN, N2 and P3, but there was some evidence of neuroplasticity in the P(e). There were no significant pre to post training differences between the adaptive dual nback and control groups for the response–locked ERN on flanker errors, nor on the N2 and P3 responses to threat stimuli in the emotional Stroop task. However the nback group showed a marked decline in P(e) amplitudes from pre to post training relative to the control group, although did this not reach significance in group comparisons. Moreover there was a notable and significant correlation between the rate of improvement on nback training task performance and subsequent P(e) amplitude reductions. Additionally, a decrease in the nback participants' P(e) amplitude was significantly correlated with reduced worry, rumination and depression from pre-training to follow up, in contrast to no significant or even marginally significant associations between the P(e) and any measure in the control group.

Results therefore did not substantiate previous findings of training-related increases in ERN amplitudes in adults following WMT (Horowitz-Kraus & Breznitz, 2009; Lotfi et al., 2020), indicating that unlike adults with dyslexia or anxiety, the ERN of adolescent boys was not altered by WMT. Instead, it was consistent with previous work which found the ERN was resistant to change following cognitive training, CBT and psychotherapy, despite treatment efficacy (Grützmann et al., 2021; Hajcak et al., 2008; Ladouceur et al., 2018; Riesel et al., 2015).

Additionally, the study did not corroborate findings from several studies where there was modulation of the adult N2 and P3 following WMT (Küper et al., 2017; Turtola & Covey, 2021; Salmi et al., 2019; Zhao et al., 2020).

There was a marginal association between training improvement and pre to post training increases in the threat N2, which was in turn associated with reduced rumination at follow up. Independent of training improvement, a decrease in P3 amplitude was also associated with reduced rumination. This provided some tentative support that changes in neural indices of inhibitory control and attentional bias to threat were associated with reduced rumination in the nback group. It is prudent however to be cautious in attributing significance to this finding, as the correlations were not significantly linked to training improvement and there were no behavioural interference effects for threat relative to neutral stimuli in the Stroop task.

As only the P(e) was significantly associated with training improvement it may offer insight regarding a possible mechanism of training transfer and anxiety reduction at follow-up in this study. Moreover, it may not be a coincidence that the N2, P3 and ERN all undergo linear changes in their amplitudes during development, whereas the P(e), the only ERP to show pre to post training changes, is stable in amplitude from age seven (Davies et al., 2004), further substantiating the reliability of the P(e) finding. Other studies which examined effects of training on the error processing ERPs only examined the ERN (Horowitz-Kraus and Breznitz, 2009; Lotfi et al., 2020), therefore to the best of my knowledge, this is the first to report on WMT related modulations in the P(e). If dual nback training had improved functioning of fronto-parietal networks underlying WM we might have expected an increase in P(e) amplitudes in line with previous studies indicating higher WMC is associated with an enlarged P(e), reflecting improved goal maintenance, conscious error identification and strategic adjustment to remediate performance (Coleman et al., 2018; Miller et al., 2012). Yet the opposite occurred. A reduced P(e) can indicate that training may have lessened the emotional and affective significance of errors (Overbeek et al., 2005; Ullsperger et al., 2010).

It is not clear why this should be and also how this reduction can also be linked to lower worry, rumination and depression. On the one hand, familiarity with the task and testing environment could have meant that participants were less anxious about making mistakes on their second visit to the lab, however this should have applied equally to both groups. P(e) reductions in the control group were marginal, and unrelated to the emotional vulnerability outcomes, thus familiarity is an unlikely explanation. Considering the training intervention more broadly, another variable which was not measured in the study could have altered participants concern about errors. One possible explanation for the reduced motivational significance of errors post training may be linked to the relationship between P(e) amplitudes and error frequency. Studies have shown the magnitude of the P(e) is associated with error frequency, such that more frequent errors are associated with a smaller P(e) (Falkenstein et al., 2000). P(e) amplitudes are also related to autonomic nervous system response (Hajcak et al., 2003; Larson, Steffen et al., 2013; Wessel et al., 2011). Errors not only activate the cognitive control system but are also registered in amygdala activations which are coupled with post error activations in the neural generators of the P(e) (Pourtois et al., 2010). Together this indicates coupling between error awareness and visceral emotional responses.

The dual nback training task is challenging, and training using the adaptive task necessarily involves repeated exposure to mistakes. Over the course of training, daily exposure to errors may have reduced the physiological and emotional impact of errors in the nback, which could potentially generalize to errors on the flanker task, thus lowering the P(e). If this were the case, perhaps the altered motivational significance and reduced attention to errors may also generalize to less harsh self-judgement which could have ultimately driven reductions in rumination and worry. This is highly speculative given limited overall understanding of the functional significance of the P(e), but it offers a tentative explanation for how WMT related reductions in anxiety could arise in the absence of training transfer to behavioural and other neural measures of cognitive control.

Finding P(e) differences between the training and control group demands further investigation. The only other intervention study to find such an effect was with a brief mindfulness meditation intervention which resulted in reduced systolic blood pressure and a reduced P(e) (Larson, Steffen et al., 2013), which was unexpected and conflicted with a prior evidence that mindfulness meditation increased rather than decreased attentional orientation to errors and boosted P(e) amplitudes (Teper & Inzlicht, 2013). Finally, although some studies report relationships between the P(e) and negative affect or emotional vulnerability indicators (Hajcak et al., 2004; Holmes & Pizzagalli, 2010) many studies do not (Clayson et al., 2012; Larson, Gray et al., 2013; Larson, Steffen et al., 2013; Pfabigan et al., 2013). So whilst the effect on the P(e) is intriguing, replication is needed and further research would need to monitor and manipulate error salience and awareness throughout the training period itself, as well as in pre to post-training assessments, in order to illuminate the effect of WMT on P(e).

Building on findings from study 2, where higher overall internalizing at baseline predicted the rate of nback training improvement, pre-training depression and school burnout amongst this sample of boys were associated with significantly poorer rates of training task improvement. This mirrors findings from research on other psychotherapeutic interventions, in particular those using online delivery, which found symptom severity influenced participant engagement with the intervention (Banerjee et al., 2018; Crane & Williams, 2010; Neil et al., 2009). The findings from these two interventions do not allow us to disentangle precise reasons why symptom severity impacts engagement, but it points towards a need to explore adaptations to WMT that better account for the limitations of individuals at the more severe end of the spectrum. This is particularly pertinent when considering the application of cognitive training interventions in universal settings, such as schools.

6.2.4 **Limitations**

Study 1 had several limitations which recommend cautious interpretation of its results. The experimental design did not permit the assessment of susceptibility to the worry induction before the depletion exercise, therefore the study only partially captures the depletion effects of this exercise. Had a pre-depletion assessment been included, it would have been better able to detect group differences and could provide a more conclusive answer to the research question on ego depletion and permitted more casual interferences. Instead the study interpretations are reliant on correlational findings.

The wide age range in the adolescent sample is also a limitation. Participants ranged in age from 11 to 16, so were at varying stages in brain and cognitive development. Within this relatively small sample size, individual variation in brain development is likely to have contributed noise to the ERN data and as a result the findings may not be as reliable as they would had been with a more circumscribed age range. The sample size was further restricted by the exclusion of data from participants with very low error commission. Moreover, to counter these low error rates across the sample, a lenient threshold for error averaging was adopted, which is a further limitation.

The samples in all studies are not widely generalizable. The training study samples were pupils from independent fee paying schools, therefore not generalizable to adolescents in the state school system or from low socioeconomic groups. Similarly, the participants in study 1 were recruited via convenience sampling and were predominantly white middle class girls attending a range of comprehensive, grammar and independent schools. Nevertheless, recent evidence suggests that pupils from middle class families attending high achieving schools are especially vulnerable to emotional disorders resulting from excessive pressure to succeed and excel in school and extracurricular activities (Luthar et al., 2020). A recent review reported the incidence of clinically significant anxiety and depression in pupils at high achieving US schools was 6-7 times the national average (Luthar et al., 2020). Therefore the findings from these studies are highly informative for this vulnerable demographic.

It is important to draw attention to some limitations in the training interventions studies which impede their interpretation. Study 2 suffered from high participant attrition which may have contributed to bias in the analyzed sample. This should have been mitigated partially by the decision to analyse data for participants who completed at least 6 days' training, however a limitation of the analysis is that not all participants received the same training dose. Adjustments were made to participant recruitment and participant instruction in study 3 in order to reduce attrition. As a result, training attrition was minimal amongst those who began the study, however some last minute drop outs just prior to the start of training resulted in a somewhat underpowered sample. Finally, some technical issues disrupted post-training ERP recordings for a few participants, further reducing sample size at posttest. Nonetheless mixed linear models analysis deals well with missing data in intervention studies and should have mitigated this limitation in the group comparisons, although the correlational analyses were performed on relatively small sample sizes.

For study 2 including at least one attentional control measure would have permitted stronger conclusions, not only regarding a mechanism for the significant improvement in anxiety and depression symptoms in that study, but also in making comparisons across the two interventions. For instance, it would have enhanced the interpretability of finding training- related symptom improvement and P(e) reductions in study 3. An additional limitation, particularly with regard to advancing understanding of the effects of training on attention control in emotional contexts, was that the emotional Stroop task did not result in significant interference effects from the threat stimuli, so behavioral and neural measures from this task may not reliably reflect emotional interference control. Finally, although ERPs offer excellent insight to the temporal unfolding of brain activations, they say little about where in the brain this differential activity is coming from. Activations in the limbic systems are highly relevant to this research and ERPs cannot offer insight into subcortical activity during emotional tasks, and which may have been impacted by WMT (Olesen et al., 2004).

6.3 General Implications and Future Directions

6.3.1 Implications of Study 1

The finding that the adult ERN predicted proneness to increased negative thought intrusions triggered by the worry induction is important. It points to a mechanism wherein compensatory effort during task performance might play a causal role in enhancing rumination, worry proliferation and prolonged contact with personally salient negative content. When cognitive control is measured in the lab, we typically gather measures at one point in time and therefore cognitive tasks may provide a poor or misleading indication of how cognitive control unfolds over extended periods or in real world situations. This experiment connected performance on the consecutive task via ΔERN associations, which indicated that cognitive control was especially undermined in the worry induction amongst those with larger adult ΔERNs. It was important to note that the ΔERN was only associated with negative intrusion changes due to the worry induction and not performance pre or post, so the cognitive control differences arose when the worrisome thoughts were deliberately activated.

There is a large weight of evidence indicating cognitive processing inefficiencies in those vulnerable to mental health difficulties. The elevated ERN in anxiety is thought to reflect a reliance on reactive and stimulus-driven control processing to sustain performance, alongside a reduced preference for planful proactive control instantiated through top down maintenance of goal information (Filippi et al., 2021; Moser et al., 2017). For individuals with high levels of anxiety, this finding points to the causal involvement of processing inefficiency in the maintenance of anxious or depressive symptomology. Processing efficiency theory has previously accounted for cognitive impairments associated with anxiety, but the current findings indicate that this theory might be extended to explain how individuals biased towards more reactive rather than proactive cognitive control strategies, could become vulnerable to control failures after periods of cognitive effort, when they are less motivated to sustain high control.

These findings also signify that mechanisms in the development of error monitoring during adolescence could influence emerging vulnerabilities for emotional disorders. Much remains to be learned about the drivers of the apparent reversal in the relationship between the ERN and anxiety vulnerability and what this means for models of psychopathology. This could have important implications for mental health of older adolescents. Whilst there was no evidence of depletion effects on adolescent control nor that the ERN indexed compensatory functioning, the findings suggest a transition occurs between late childhood and adulthood. This implies a need to consider cognitive load placed on adolescents and how different aspects of the school environment might stimulate or sustain maladaptive and compensatory processing and lead to regulatory control depletion. Recent research has highlighted that emotional disorders are now more prevalent and more severe amongst older adolescents, and girls in particular (Collishaw & Sellers, 2020; Vizard et al., 2020). The timing of the deterioration coincides with onerous and high stakes state exams in this country. 16-year olds sit upwards of 24 individual GCSE exams in the UK. It is therefore important to consider cognitive processing efficiency and compensatory effort in the context of high situational cognitive load on adolescents studying for high stakes exams. Increasing evidence demonstrating the role of academic stress in adolescent mental health deterioration, particularly amongst girls, is a case in point (Giota & Gustafsson 2017; Högberg et al., 2020).

Another important implication of study 1's findings is that adults with comparatively high ERNs or who demonstrate bias towards reactive control may benefit from training proactive control strategies to increase the efficiency of control and reduce the need for engaging reactive strategies and the resultant impact on emotional regulation. Although an enlarged ERN may be associated with better mental health in younger children and adolescents, study 1 has shown this relationship may reverse, therefore there is an imperative to promote the development of better proactive control strategies and discourage the emergence of a processing style relying too heavily on inefficient reactive control. In light of evidence that development of proactive control is underpinned by developmental improvements in WM (Troller-Renfree et al., 2020), and that higher adult WMC is associated with control strategies that favour proactive control (Braver, 2012;

Redick, 2014; Wiemers & Redick, 2018), interventions to enhance WM represent a promising route to support individuals, young and old, to develop more effective and efficient cognitive control processing. The findings of study 1 validated the investigation of WMT to target emotional vulnerability and identified that error processing ERPs should represent informative neural outcome measures.

6.3.2 Implications of Working Memory Training Studies

The findings from the training intervention studies 2 and 3 have several implications for future research and practice. They demonstrate that targeting the developing prefrontal mechanisms involved in top-down proactive control and goal maintenance has the potential to reduce symptoms of adolescent anxiety, depression, rumination and worry, substantiating evidence from recent research conducted in clinically vulnerable adults. Nevertheless training effects on emotional outcomes in adolescents were neither clear cut nor consistent. Whilst study 2 found significant group effects of training relative to controls on both anxiety and depression in a reasonably robust sample, a shorter intervention in a smaller sample did not replicate this effect, consistent with a number of studies finding no effects of training on negative affect in adolescents (e.g. Mewton et al., 2020). Nevertheless the rate of training improvement in study 3 was significantly correlated with anxiety reductions between pre-training and follow up indicating that for at least some participants WMT engagement was related to reduced negative affect.

The modest increase in nback level attained over the course of the training and a decline in nback for some participants indicated poor psychological engagement with this training. Previous work has shown very young children can attain excellent nback gains in training (Peng et al., 2017), so it is unlikely that the nback task exceeded participants' cognitive ability. Despite feedback at the end of each training session and daily motivational emails, the task failed to engage and motivate many participants. Adaptations to the training paradigm whilst retaining its core feature of WM updating are needed. Feedback and rewards throughout the task, more engaging graphics and introducing gamification elements represent several areas where improvements could be made (Vermeir et al., 2020). The involvement of adolescent focus groups in future task and intervention adaptations is highly desirable and arguably essential for developing a more effective training task.

The lack of consistency in the group comparisons and the correlation between training improvement and emotional outcomes draws attention to inter-individual variation in trainability. This was brought into relief by finding that in both studies participants with higher depression, internalising and school burnout were less able engage with the training, rendering some of the most vulnerable amongst the least likely to benefit. This has important implications. Firstly, it highlights a limitation in most cognitive training research, which is that most studies focus analyses on group comparisons exclusively, which means some important details may be lost (Smid et al., 2020). As the number of cognitive training intervention studies has grown, increasing numbers of studies have reported associations between training improvement/engagement and positive therapeutic outcomes, suggesting a one-size-fits-all may not be the best approach (Smid et al., 2020; Shani et al., 2019, 2021). A particular constellation of intervention characteristics or components (duration, task, difficulty) may suit some participants better than others, and the goal of ongoing research must be to understand how to match the right training characteristics to the individual. An additional challenge will be to take into account the substantial individual variation in the trajectories of brain and cognitive development which must likely influence outcomes and trainability of children and adolescents (Becht & Mills, 2020; Foulkes & Blakemore, 2018). A recently published protocol has outlined plans for an individual-level meta-analysis of cognitive training studies aimed at enhancing wellbeing (Shani et al., 2021). The goal of this research is to apply machine learning algorithms to the combined data from multiple training studies to identify which participant characteristics are most responsive to training generally, and determine a best match of training type to individual. Incorporating brain imaging, including fMRI, into study designs would permit insight into how differences in brain development interact with training. Together, these approaches would provide a more nuanced understanding of the effects of training during development than has been possible to date.

6.3.3 Implications of the Neural Findings in Working Memory Training

Adult studies have demonstrated that ERPs can be altered as a result of training and cognitive interventions, however research in adolescents is limited. The findings in this thesis suggest there was limited evidence that neural activations underlying attentional control were modulated by two weeks' WMT, although we cannot rule out that effects on neural processing take time to consolidate and are not immediately detectable directly after training. Although there were associations between the N2 and P3 and reduced rumination, pointing towards increased cognitive control and reduced attentional bias towards threat, there was little to relate this to training. The association between training-related reductions of the P(e) and subsequent associations with a reduction in several emotional vulnerability measures is difficult to interpret as a neural change that supported improvements in attentional control, because training was not associated with behavioural change. It was nonetheless intriguing that the motivational and emotional significance of errors was related to WMT improvements, and this could have implications for how we view modes of therapeutic action in training. We have taken for granted that the only mechanism of action could be alterations in top-down control, however this finding warrants reflection on other ways that WMT could have exerted an effect on adolescent's wellbeing, such as a desensitization to errors over the course of the training generalizing to reduced self-criticism and rumination about negative aspects of the self. Future training studies for instance could incorporate experiential sampling over the course of training (Csikszentmihalyi & Larson, 2014) to assess sensitivity to errors and self-criticism and linking this to the frequency of error commission during training practice.

The lack of clear transfer effects could indicate that WMT does not alter neural processing underlying attentional control in adolescents, however a further implication of these findings may be the unsuitability of small developmental samples to address research questions regarding training transfer on ERP measures. Previous adult studies have found group differences in similar sized samples (e.g. Covey et al., 2018). However most adolescent ERPs are still developing and highly variable, therefore variations in individual participant's rate and trajectory of development could mask any training-related change in between-group comparisons (Foulkes & Blakemore, 2018).

Lastly, it could be that, with the exception of the P(e), the ERPs selected in the current work are not sensitive to WMT and change in emotional vulnerability. Other ERPs should also be explored. In particular, recent work has demonstrated that WMT can reduce amplitudes of the adult Late Positive Potential (LPP), an ERP which reflects attention to emotional stimuli and is larger when viewing emotional relative to neutral images (Pan et al., 2020; Xiu et al., 2018; Dennis & Hajcak, 2009). Typically LPP amplitudes can be attenuated by implementing emotional regulation strategies such as reappraisal and distraction (Veloso & Ty, 2021), therefore future investigations using the LPP could shed light on an alternative neurocognitive pathway through which WMT might reduce emotional vulnerability in adolescence.

In summary, whilst the work in this thesis extends our understanding of the neural effects of training, considerably more work is needed in much larger samples and taking into account individual differences in the trajectory of development to clarify if and how WMT instigates neuroplastic change in adolescents. Additionally, further clarification of the functional significance of the P(e) is required to allow a more comprehensive interpretation of training-related changes in the P(e) and improved worry, rumination and depression.

6.3.4 **Future Directions for Research**

The findings from the training studies presented in this thesis provide preliminary evidence and a proof of principle that a remote computerised training intervention using the nback task is appropriate for use with adolescents and can alleviate symptoms of depression and anxiety and contribute to reduced worry and rumination. The next step will be to replicate this in a much larger sample using study designs that can account for differential responsiveness and ability to engage with training. For instance, addressing the finding that participants with higher depression and school burnout scores made poorest progress across both studies, it is imperative that components of training interventions are examined more closely to determine whether WMT per se is not appropriate for these young people or if certain components might be adapted in order for them to benefit. For example, adjustments to stimulus exposure time in the training task or criteria for moving between nback levels could potentially impact whether individuals can engage with training. It would also be advantageous for researchers to involve young people with lived experience of depression and anxiety in the adaptation of tasks and training interventions to maximise their efficacy and usability. This could be preceded by qualitative research to investigate experiential accounts of training amongst adolescents. This would enable a better understanding of how the trajectory of training improvement and transfer effects could be modulated by baseline depression. In addition, whilst remote computerized WMT may work for some adolescents, supervised sessions may be more helpful for those with poorer concentration or motivation. As already highlighted, the introduction of training task features that encourage and motivate adolescents to want to increase their performance also represents an essential next step if we are to progress this research. Looking further ahead, it will also be important to reflect on WMT in the context of the myriad other interventions under investigation which may also benefit adolescent mental health, including but not limited to mindfulness meditation (Kuyken et al., 2017), attention bias modification training (Ollendick et al., 2019) and physical exercise (Biddle et al., 2019). Cognitive training interventions are time intensive so there are opportunity costs for individuals who undertake them but do not benefit, although this is the case with all therapies, none are universally effective. Linking back to the imperative for personalized interventions, future studies will need to compare the efficacy of WMT against alternative evidenced-based interventions and where universal prevention is the goal, begin to understand which individual is most likely to benefit from which intervention.

Building on the findings from study 1, the first step will be to replicate these findings addressing the limitations in the cognitive depletion manipulation and adjusting the study design to incorporate measurements of negative emotional reactivity before and after the cognitive depletion exercise. This will be essential to establish if there is a causal rather than purely correlational relationship between higher ERN and negative emotional reactivity. There is also the possibility that the ERN may not be a reliable or sensitive indicator of compensatory effort in adolescents, suggesting other ERPs also associated with cognitive effort and compensatory cognitive control, such as the N2 (Owens et al., 2015) or the Contingent Negative Variation (CNV) (Ansari & Derakshan, 2011) should be explored in adolescent research.

There are two complementary avenues of future research which could expand on the main findings from study 1. The first focusing on the changes in the relationship between emotional vulnerability and the ERN during development, and the second to focus on elaborating a model that integrates predictions from ACT and the resource model of control to clarify how variations in the efficiency of cognitive control processing increase exposure to negative thought intrusions and perseverative negative thinking as a consequence of resource depletion. For the former, future work should incorporate within-person longitudinal designs tracking how the ERN and anxiety relationship unfolds from mid-childhood through to adulthood. This should also include studies that examine the emerging integration of motivation and salience information in error processing during development and test how motivation might mediate or moderate associations between anxiety and the ERN. For the latter, research should prioritize studies that address the causal role of compensatory effort on emotional regulation performance directly after depletion exercises. There will also be a need for studies that can capture how this plays out in real world applications and if differences in compensatory effort ultimately influence the development or maintenance of emotional disorders in longitudinal examinations. The emergence of wearable and portable EEG means that it will be increasingly possible to implement studies that monitor neural activity and processing effort in real world scenarios (Lau-Zhu et al., 2019).

6.3.5 Contribution of findings to the study of attentional control in adolescents and its relationship to mental health.

The findings presented in this thesis make a contribution to a central question in the emerging field of WMT to target mental health-related outcomes, which is to elaborate on mechanisms of action of training in adolescents. This question can be addressed in part through improving our understanding of how differences in the underlying neural processing that gives rise to attentional control skills relates to mental health-related outcomes in adolescents. Research has shown that mental effort is aversive and that cognitive systems favour an economic approach to effort evidenced by fatigue effects on attentional control over time (Boksem & Tops, 2008; Shenhav et al., 2017). Few studies consider the role of motivation, effort and efficiency in the performance of experimental computerised attentional control tasks (e.g. flanker, nback, anti-saccade), or how these infuences may be important when assessing cognitive training (Ganesan & Steinbeis, 2021). Additionally, studies typically provide only a snapshot of attentional control performance in time and may not reflect how individuals engage control in real life situations. For instance, experimental conditions may motivate some participants to try hard to impress researchers meaning behavioural performance may equally reflect effort and motivation as it does inherent capacity. It also remains unclear attentional control is sustained over protracted periods and if fluctuations following earlier effort may impact the regulation of thought and emotion (Grillon et al., 2015).

Study 1 demonstrated that the ERN ERP, which reflects neural activations underlying attentional control in the context of performance monitoring and error correction, predicted increased emotional reactivity in the subsequent meditation exercise which engaged attentional control in a different way. Moreover this neural activity predicted long term mental health relevant outcomes, but with developmental differences. These results provide a starting point for considering whether fatigue effects could impact emotional vulnerability via differential processing efficiency. Moreover, it may shed light on one possible mechanism through which the efficiency of neural activations supporting attentional control could be altered by training to reduce emotional vulnerability. Study 3 found however that the ERN was not impacted by WMT, despite the findings in study 1 and the salutatory effect of WMT on anxiety and depression reported in study 2. This was in contrast to adult studies which have found alterations to the ERN as a result of WMT. The absence of WMT transfer to the ERN could reflect poor progress in the training itself, but could also arise from the developmental differences in the direction of the effects that were observed in study 1, where this study suggested that a negative association between the ERN and mental health vulnerability may develop during adolescence. Alternatively, the mechanism of action for improving mental health outcomes in adolescents could lie elsewhere and be unrelated this particular error response.

The thesis' findings also highlight the need to examine broader measures of adolescent attentional control not only when considering the impact of WMT but when exploring the role of attentional control in adolescent emotional vulnerability more generally. There was evidence that WMT can reduce anxiety and depression (study 2), and for a significant association between training improvement and better long term mental health outcomes (study 3). However, improvements in these outcomes were not accompanied by transfer effects to behavioural measures of attentional control. Yet what mechanism can explain the findings from study 2? To make further progress, researchers may need to re-evaluate how we measure attentional control in adolescents, and in particular give attention to the contexts where attentional control may be differentially engaged amongst this age group. It should include developing tasks that better capture how attentional control is engaged in real world situations, taking into account context, motivation and effort (Ganesan & Steinbeis, 2021). Central to this will be to capture how attentional control abilities might fluctuate as a function of executive load and effort expended to meet prior task demand using both behavioural and neural measures.

6.3.6 Contribution of studies to advancing knowledge on the capacity for WMT to modify neural substrates of attentional control.

One of the advantages of ERPs is that they permit exploration of the neural correlates of cognition at numerous and precise timepoints in the processing stream. An important contribution of the findings in this thesis is they provide insight on effects of WMT on the neural correlates of attentional control at early (ERN) and later (N2, P3, P(e)) stages of processing. Speaking to the capacity for dual nback training to modify neural substrates of attentional control, the findings were not conclusive. Although there were no significant group differences in the effects of training on any of the ERPs examined, the rate of daily improvement on training task performance was modest, at best. We should not judge the effects of WMT on neural activations if the training itself was not engaged with adequately. The findings therefore cannot be interpreted as evidence that training does not modify the neural signatures of attentional control assessed in this thesis. It remains an important and highly relevant area for further research. Study 1 demonstrated there was a significant association between a neural substrate of early stage attentional control processing in response to errors (ERN) and the ability to control negative thought intrusions in a subsequent task, even though there were no significant associations between the ERN and concurrent attentional control performance in that task. This highlights that just because WMT may not show evidence of far transfer to behavioural measures of attentional control, exploring change beyond behaviour is essential for us to understand effects of training on mental health relevant outcomes. It may be that training can boost efficiency and reduce the amount of effort needed in attentional control tasks and this alone could contribute to improved mental health without a need for significant capacity gains. Linking back to Study 1's research questions and the implications of high effort in combination with high attentional control demands on adolescent emotional regulation, the mental health benefits of WMT could come from improved efficiency and future research should examine training outcomes which capture effort and efficiency gains rather than simply focusing on whether or not there were capacity increases.

The only ERP showing some evidence of modification by WMT was the P(e). This manifested in a significant association between training improvement and a reduced P(e) which in turn predicted better mental health outcomes longitudinally. As already highlighted, the association between training improvement and reduced P(e) amplitudes was unlikely due to changes in attentional control but rather a reduction in the motivational or emotional significance of errors in the flanker task. An implication of this finding for the field of cognitive training is that researchers must retain an open mind about the mechanisms of change in cognitive training. The training task itself may do more than simply train WM capacity. Participating in WMT is a complex experience for young people, and many aspects of this experience could contribute to change in emotional outcomes. Gradual performance increases may boost confidence or provide a sense of purpose. Alternatively, as the finding in study 3 suggested, greater engagement with the training task itself reduced the emotional significance of making errors, which speculatively, could generalise to less harsh self-judgement leading to better mental health outcomes. The P(e) findings taken together with no significant effects of training on the other ERPs or on behavioural measures of attentional control, yet clear evidence for an effect of training on anxiety and depression in study

2, emphases the importance for future research to pursue a broad range of neural indices to expand our understanding of the mechanism of therapeutic action in WMT. A further implication from these findings is that researchers need to develop innovative study designs that can control for demand characteristics and participant expectations in training studies.

6.4 Concluding Remarks

Together these findings show that training WM using a paradigm based on the adaptive dual nback task can reduce subclinical anxiety and depression symptoms in adolescents. However, the efficacy of WMT is varied, and in its current form, as a one size fits all prophylactic, is unlikely to be suitable for universal intervention amongst adolescents. Future research should address how training paradigms can be adapted to meet the needs of a wider range of adolescents, particularly those who are most vulnerable. The findings did not clearly elucidate the neural mechanisms of training transfer to emotional vulnerability outcomes, pointing instead to a training-related decrease in the motivational significance of errors, which was difficult to reconcile with attentional control improvements. The findings could indicate the mechanism of WMT transfer may not be limited to effects on attentional control, however replication and further research are needed to clarify this. Furthermore, the current findings also provide novel insight into a potential neurocognitive mechanism underlying vulnerability to the onset and maintenance of emotional disorder, showing that, for adults at least, compensatory cognitive control is associated with increased risk of exposure to the proliferation of negative thoughts after a period of cognitive effort. Whilst a reverse relationship was observed for adolescents, we can expect that development will ultimately lead to adult-like associations, although it unclear when this transition occurs. A key conclusion to be drawn from this finding is the likely benefit of adopting more proactive cognitive control strategies, and its theoretical support for cognitive control training to increase the efficiency of cognitive control. However there is a wider implication of this finding, which is a consideration of how much cognitive load is placed on individuals and how this might contribute to their emotional vulnerability. Rather than focus on maximizing cognition to meet the demands of the environment and increasing demands on the cognitive system, part of the solution to mental health challenges facing adolescents and young people may be to look towards adaptations to the wider cultural and social environment that will reduce cognitive load and mitigate depletion effects. From a broader perspective on the science of intervention, these findings therefore highlight the importance of applying findings from cognitive and affective psychology to foster environments that are in harmony with the human cognitive and emotional system.

Although the field of cognitive training research remains controversial and some have argued further research is futile (Sala & Gobet, 2020), the findings in this thesis demonstrate that many questions remains unanswered. There is a clear need for new approaches, including but not limited to developing more engaging and motivational WMT methods for adolescents, innovative and ecologically valid measures of attentional control that might better capture training effects than existing tasks, and for study designs to have a strong theory-driven focus on mechanism of action which ought to be considered from both a behavioural and neural perspective. In conclusion, a rich seam of knowledge on WMT remains to be uncovered and it would be premature to dismiss the potential role of WMT for improving mental health outcomes in adolescents at this stage.

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Appendix 1

Appendix 1 – Instructions for breathing focus task with worry induction used in Experiment 1.

1. <u>Verbal Explanation of Task</u>

"I'll just give you a quick overview of how this next task's going to run. First you will be asked to focus your attention on your breathing for a short time. Then you will be asked to focus on your normal thoughts, followed by another period of focusing on your breathing. While you are focusing on your breathing we will ask you about your thoughts on a few occasions".

"We'll start by practicing focusing your attention on your breathing for a short time. Try not to think about anything except your breathing. It is completely normal for thoughts to wander, but if this happens try to refocus your attention back on your breathing again."

Ok, so if you'd like to start practising (focusing on your breathing), I'll let you know when to stop after 20 seconds. (Just concentrate on breathing in and out)" (leave them for 20seconds). *"That's great." (N.B brackets represent optional statements)*

"When the task begins I'll ask you to direct your thoughts to your breathing.

Then, at random intervals, the computer will make a beep sound.

If you are thinking about breathing at that point simply say "breathing".

However, if your thoughts have wandered, I would like you to tell me whether your thoughts were positive, neutral, or negative.

Set the computer for **45 seconds**, with intervals of **10-20**.

2. Practice

“I want you to start focussing on your breathing and over the practice you will hear beeps at random intervals. As I mentioned before, when you hear a beep signal, if your thoughts at that moment are focused on breathing, just say “breathing”. If your thoughts have wandered at that point, I’d like you to first tell me whether your thoughts are positive, neutral, or negative.

For example you might say ‘Positive’.

Try not to predict when the beep will come, just think about your breathing.

There is no need to wait for me to prompt you, just go ahead and make your rating as soon as you hear a beep. If you are comfortable to do so you can close your eyes.

There should be 3 beeps. When the 45secs is up you may need to explain briefly again what is required if they aren’t quite getting it right

Set the computer for **5 minutes (300secs),** with intervals of **20-30 seconds**.

3. Main Task

“Ok, that was great. Now we are going to begin the main task. It will last 5 minutes with beeps at random intervals. As before we would like you to focus on your breathing and then make a response after each beep.

Remember to try not to think about anything except your breathing. It is completely normal for thoughts to wander but if this happens try to refocus your attention back on your breathing again. Are you ready?

If necessary, press pause on the computer after each beep while they give their answers and then resume again once they have finished talking [avoid pausing as much as possible]. Note the (i) Affective Ratings and (ii) Descriptions of thoughts given by the participants at each beep.

4. Worry

What I'd like you to do now is identify the topic which you currently find yourself worrying about the most, for example, financial, social or relationship worries.

You should also choose a worry that you are happy to share with us a little bit. Don't choose something that you think would be very distressing to think about.

Ok, if you are comfortable sharing, could you just briefly tell me what your worry topic is about? [you may need to help the participant to think about the worry topic a little bit and explore the negative aspects that they have been worrying about – prime 3-4 issues].

Downward Arrow Technique: *What worries/concerns you about that? What would that mean for you?*

Topic: *Future oriented; Negative/threatening; would create stress/anxiety*

Summarise

Hmm, that sounds understandably worrying (show empathy)

I'm now going to give you 5 minutes to worry about this topic.

During this time I am going to leave the room, and I'll return in 5 minutes.

So all you have to do is continue to worry about this topic.

5. Leave room → Time 5 minutes → Return.

OK, that's the end of the 5 minutes.

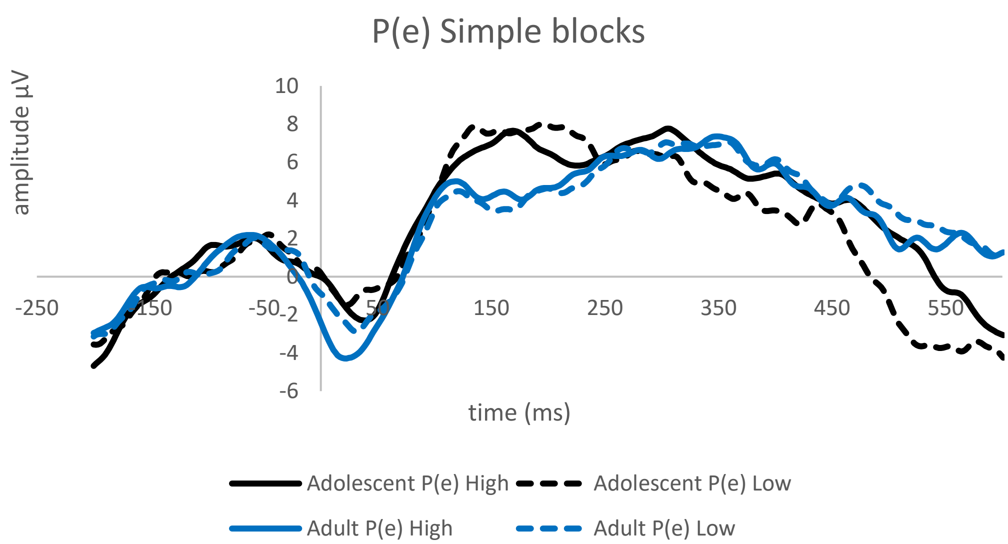
6. <u>Second Five Mins</u>

You will now be given 5 minutes in which to focus your attention on your breathing again. As before, try not to think about anything except your breathing. It is completely normal for thoughts to wander but if this happens try to refocus your attention back on your breathing again.

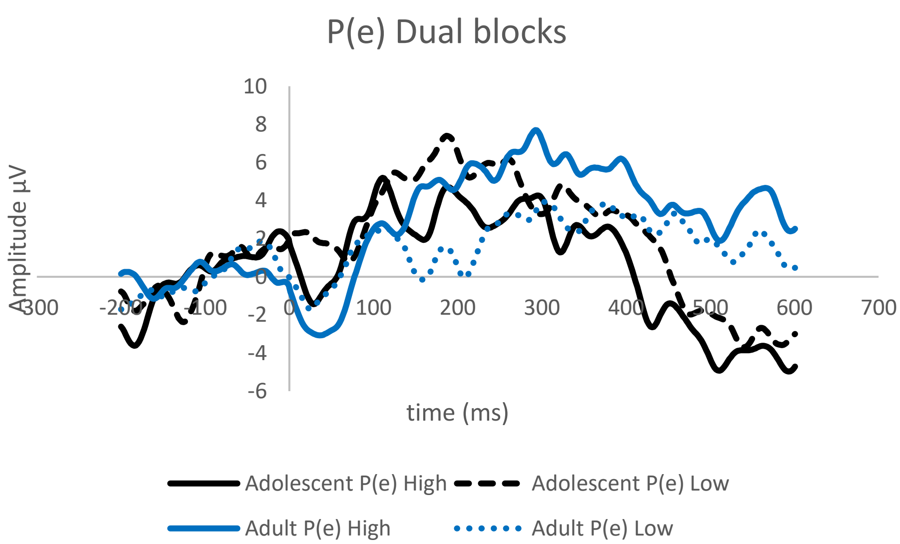
Again, at random intervals the computer will make a beep. If you are thinking about your breathing at that point simply say "breathing". However, if your thoughts have wandered I would like you to first tell me whether your thoughts are positive, neutral or negative, and then give a brief description of your thoughts at that moment.

***END OF WORRY TASK –**

Appendix 2



Supplementary figure 3.1a. Grandaverage waveforms for the P(e) by age group and WML in Simple blocks



Supplementary figure 3.1b. Grandaverage waveforms for the P(e) by age group and WML in dual blocks

Appendix 3

Results of group comparisons for of the Flanker task ERN in the 0-100 ms post response window.

Supplementary Table 4.1 Means and standard deviations for error voltages in the 0-100 ms post response time window.

	N-back (Mean/SD)		**Control (Mean/SD)**	
	Pre training	Post training	Pre training	Post training
Flanker task ERPs	*(N = 14)*	*(N=11)*	*(N=13)*	*(N = 7)*
ERN (μV)	-1.53 (5.63)	-.005 (4.47)	-.86 (5.07)	-2.10 (3.23)
CRN (μV)	2.89 (4.24)	4.14 (4.07)	4.17 (4.52	3.77 (3.94)
ΔERN (μV)	-4.43 (4.60)	-4.14 (4.03)	-5.03 (6.47)	-5.87(4.56)

Supplementary Table above shows means and standard deviations of error ERPs before and after the WMT intervention. MLMs were conducted to explore the effect of training group on the ERN from pre to post training. The MLM with ERN amplitudes as the dependent variable found there was no significant group X time interaction, $F(1, 24.65) = 2.69$ $p = .16$, *NS*. Similarly, the MLM on ΔERN amplitudes also found the group X time interaction was non-significant, $F(1, 19.53) = .73$, $p = .40$. There were no significant main effects of time or group on either the ERN or the ΔERN. All main effects were $F < 1$.