Cognition and mental health in children and young people.

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Thesis Abstract

Background: Mental health difficulties are highly prevalent across adolescence and can change over the course of adolescent development. Left untreated, such difficulties can significantly impact an individual's health, income, and interpersonal relationships later in life, and create an enormous burden on social, healthcare, and economic systems. The factors implicated in the onset and maintenance of mental health problems include cognitive factors due to their importance in regulating emotions and behaviour.

Method: A systematic review and meta-analyses were conducted investigating the relationship between anxiety and attention and memory in children and young people. A data-driven approach with a large secondary data set was then used to explore changes in mental health profiles between mid- and late adolescence and their association with cognitive factors.

Results: The meta-analysis identified a significant bias towards threat when using an affective Stroop task, but not the dot probe task. The empirical paper found distinct profiles of mental health are identifiable and largely stable between mid- and late adolescence. An impaired ability to adjust risk-taking behaviours in response to contextual information was linked to profiles of persistent externalising symptoms and social difficulties. Poor spatial working memory was associated with persisting externalising problems.

Conclusions: Aspects of cognitive function are related to youth mental health difficulties. Childhood and adolescent anxiety are associated with attentional biases both towards and away from threat, and greater symptomology is possibly linked with biases towards recalling negative information over the long-term but not the short-term. These data suggest that mental health and cognition interact across development; anxiety can impact on the cognitive processing of

information, and cognitive control in mid-adolescence contributes to persistent patterns of mental health difficulties.

Access Condition and Agreement

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CHAPTER ONE

Introduction to the Thesis Portfolio

Introduction to the Thesis Portfolio

Overview

The broad aim of this thesis was to explore links between cognitive function and mental ill health in children and adolescents. The thesis contains a meta-analysis investigating memory and attention biases in anxious youth, and an empirical project using secondary data analysis to explore changes in mental health between mid- and late adolescence and their links to cognitive abilities. In this introductory chapter, I provide a broad overview of the prevalence of mental health problems among children and adolescents, the developmental trajectories of mental health difficulties from childhood to adulthood, and the potential role of cognition in the causes of these difficulties.

Mental health: prevalence rates

Mental health difficulties are more prevalent in late childhood and adolescence compared to any other stage of life (Gulliver et al., 2010; Kessler et al., 2005), with roughly 25% of young people experiencing psychological distress (Oksanen et al., 2017), and 17.4% of 6- to 16-year-olds in the UK having a probable mental health disorder (Newlove-Delgado et al., 2021). The first onset of mental health problems typically occurs in adolescence (Kessler et al., 2005), with more than half of all mental ill health starting by the age of 14 (Murphy & Fonagy, 2012). It is estimated that approximately 14% of 10- to 19-year-olds experience mental health conditions globally (Global Health Data Exchange, 2019), with anxiety disorders being most prevalent and occurring in 3.6% of 10- to 14-year-olds and 4.6% of 15- to 19-year-olds (World Health Organization, 2021). In England, one in six children aged six to 16 had a probable mental health condition in 2021, an increase from one in nine in 2017 (Peytrignet et al., 2022). An increase of 44% more patients

coming into contact with services in 2021 than in 2019 equates to an additional half a million children and young people in England with a probable mental health condition (Peytrignet et al., 2022). The reasons for these rises are complex and many. Increased recognition of mental health problems has certainly contributed, as has the social isolation, uncertainty and disruption caused by the global COVID-19 pandemic (e.g., Thorisdottir et al., 2021).

Left untreated, mental health difficulties can have a significant impact on an individual's health, income, and relationships in later life (Goodman et al., 2011; Green et al., 2005; Kowalenko & Culjak, 2018). The persistence of mental health problems and their economic and social burden drives the need to understand the development and progression of mental health difficulties. A better understanding of what predicts the development and maintenance of mental health difficulties, and how they change over time, is of paramount importance to aid the development of tailored interventions to reduce both individual distress and demands on health and social care systems.

Mental health: developmental trajectories

A wealth of literature covers the developmental trajectories of mental health problems from childhood through to adulthood. A few key trends and studies are presented below.

Diagnoses

Focussing first on the prevalence of diagnosed psychiatric disorders, Costello and colleagues (2011) observed that rates of depression, panic disorder, agoraphobia and substance use disorders increased from childhood to adolescence, while separation anxiety and attention-deficit hyperactivity disorder (ADHD) decreased. Exploring changes into adulthood, they reported that panic disorder, agoraphobia and substance use disorders continue to increase, while the prevalence

of social anxiety, ADHD, other phobias, and disruptive behaviours decrease. While rates of ADHD were noted to decrease, Moffitt and colleagues (2015) reported that the course of ADHD symptoms is variable, sometimes developing in adulthood, despite a prevailing belief that it is a child-onset neurodevelopmental disorder. Similarly, Copeland et al. (2014) reported the picture was more complex for anxiety, noting that longitudinal studies show diagnosis has a U-shaped prevalence, often presenting in late childhood, decreasing in early adolescence, and appearing again from mid-adolescence onwards. In an earlier meta-analysis of longitudinal studies, Copeland and colleagues (2013) found that behavioural disorders tended to precede anxiety in adulthood, with Oppositional Defiance Disorder (ODD) moderately predicting later depression and anxiety. Together, these studies show that the presentation of mental health problems changes across development.

Symptoms

Traditional approaches to understanding mental health difficulties typically use criteria-based diagnostic categories such as those outlined in the Diagnostic Statistical Manual of Mental Disorders (5th ed.; American Psychiatric Association [APA], 2013) to define mental ill health. While these approaches have many pragmatic benefits, they fail to account for high levels of symptom heterogeneity within a disorder category, similarities between disorders and high rates of comorbidity (Anttila et al., 2018; Constantino & Charman, 2016; Fried, 2015; Regier, 2013; Smoller, 2013; Wang et al., 2017; see Dalgleish et al., 2020 for a full review of these issues). In terms of capturing developmental change, diagnostic categories describe lists of behaviours that do not adequately account for variance due to developmental stage, beyond broad statements about age-appropriate behaviours.

To overcome these issues, transdiagnostic approaches are being increasingly adopted. These focus on symptoms of mental health and emphasise the importance of continuous factors that span the full range of functioning, from adaptive to maladaptive, that can cut across traditional categories of mental ill health (e.g., Caspi et al., 2014; Caspi & Moffitt, 2018; Lahey et al., 2017; Martel et al., 2017; Pataley et al., 2015). An increasing number of studies are using these approaches to capture how mental health symptoms change across development. Some recent examples are summarised here.

In 2019, Dugre et al. used a dimensional model of psychopathology to identify developmental trajectories, focussing on two well-established dimensions: an externalising dimension conveying risk for disorders characterised by disinhibition, and an internalising dimension conveying risk for mood and anxiety disorders (e.g., Achenbach & Edelbrock, 1981; Kendler et al., 2003; Krueger, 1999). Dugre et al. (2019) used longitudinal data from the Longitudinal Studies of Child Abuse and Neglect Consortium (LONGSCAN), which included four assessment points between the ages of 10 and 18 years. Group-based trajectory modelling was used to identify individual trajectories of anxious-depressive traits (ADT), or internalising symptoms, and trait aggression (TA), or externalising symptoms, across the 8-year period. Using this method, they identified four clusters of children, each following different trajectories for ADT: 1) consistently low-ADT (42.2% of the sample); 2) consistently moderate ADT (42.8%); 3) increasing ADT (11.9%); 4) consistently high ADT (3.1%). Two separate trajectories were identified for TA: consistently low TA (69.9%) and consistently high TA (30.1%). A joint model was then estimated to calculate the probabilities for each trajectory of one variable (e.g., ADT) to be in each trajectory of the second model (e.g., TA). This allowed the proportion of youth belonging simultaneously to ADT and TA trajectories to be estimated. Five trajectories were

identified: 51.8% of the total sample were characterised with low ADT and low TA; 13.3% with moderate ADT and low TA; 21.2% with moderate ADT and high TA; 10.5% with increasing ADT and high TA; and 3.2% with high ADT and high TA. None of the children had increasing levels of ADT and low TA, or low ADT and high TA. In the final step, logistic regression was used to predict which trajectory a child followed based on their ratings of different problems in childhood (e.g., childhood delinquency, symptoms of ADHD). The group with low ADT and low TA (i.e., those with no mental health symptoms) were used as a comparison group. The symptomatic groups were significantly more likely to display higher levels of childhood delinquency, social problems, and ADHD symptoms than the comparison group. Those in the low ADT and high TA and in the high ADT and high TA groups were significantly more likely to have reported more severe and frequent childhood abuse (both psychological and physical–sexual abuse) suggesting that those with high levels of externalising problems were likely to have experienced childhood adversity.

Recently, Bathelt et al. (2021) used a population-representative sample of 6,744 children drawn from the 1970 British Cohort Study (Butler & Bynner, 2016; Elliot & Shepherd, 2006) to identify common transitions in patterns of mental health symptoms as children move from childhood into adolescence. The young people were followed across a six-year period, from age 10 to age 16. They observed that problems with hyperactivity/impulsivity and conduct were prominent in childhood, while problems related to emotional control, anxiety and inattention were more common in adolescence. Overall, parent rating of behavioural problems decreased from childhood into adolescence, with the largest reduction observed in ratings of hyperactivity. A proportion of the population transitioned from no behavioural problems in childhood to exhibiting emotion problems in adolescence – a transition that was more common than transitioning to a profile of elevated inattention and hyperactivity. A large proportion of children with anxiety

problems showed emotional problems in adolescence, and children with problems related to emotion, motor control and hyperactivity mostly transitioned to difficulties related to inattention in adolescence. Finally, many of those with conduct problems in childhood experienced difficulties with anxiety, emotion, and inattention in adolescence. Bathelt et al. (2021) found that those who overcame behavioural problems by age 16 had better cognitive abilities in childhood.

Collectively, these two recent examples of transdiagnostic approaches to tracking developmental changes in mental health symptoms show that individual presentations can follow very different trajectories, which might be linked to both early childhood experiences and cognitive control.

Causes of mental health difficulties

Mental health difficulties have been associated with environmental factors, such as early deprivation and early adverse childhood experiences (e.g., Sheridan et al., 2020), social factors such as changes in social-emotional relationships (e.g., Foulkes & Blakemore, 2016), biological factors, including genetic factors, hormonal changes and neural development, and cognitive factors related to self- and emotional-regulation. A short overview of the social, environmental, and biological explanations for mental health problems is provided before a more detailed discussion of the cognitive theories, which are more central to this thesis.

Environmental

Adversity early in life is associated with increased risk of mental health problems. Explanations for these effects differ. While some suggest that each adverse exposure affects development through a specific pathway (e.g., Kessler et al., 1997), others suggest that the

accumulation of stress caused by multiple adversities leads to later mental health problems (e.g., Evans et al., 2013). A popular theory that attempts to reconcile these ideas and account for the timing of childhood adversity is the Dimensional Model of Adversity and Psychopathology (DMAP), which identifies two core domains of early experiences of adversity: threat (e.g., abuse) and deprivation (e.g., poverty, McLaughlin et al., 2014). According to this model, threat alters socioemotional functioning, while deprivation constrains learning and cognitive control (Lambert et al., 2017). Children who experience deprivation are more likely to show later cognitive difficulties (Rosen et al., 2019), while those who experience early threat are more likely to struggle with emotional reactivity (Dvir et al., 2014). Supporting this model, studies have found associations between threat and fear learning, and between deprivation and deficits in cognitive control (Lambert et al., 2017; Machlin et al., 2019; Miller et al., 2018; Sumner et al., 2019). More recently Sheridan et al., (2020) found that cognition clustered with socioecomonic status (a marker of deprivation), while emotional reactivity clustered with neglect, abuse, and trauma (markers of threat) in childhood.

Social

Social influences on mental health have their biggest impact during adolescence (the stage between 10 and 24 years). This is a period of life characterised by heightened sensitivity to social stimuli, changes in personal relationships, and a time when people are expected to embrace more adult societal roles in most cultures (Dahl, 2004; Orben et al., 2020). It has been proposed that the impact of puberty on the brain makes adolescents particularly sensitive to their social environments (Crone & Dahl, 2012), and that during this time they go through a period of social reorienting where the opinions of peers become more important than those of family members (Larson et al.,

1996), and where same sex peers become a more significant source of emotional support than parents (Furman & Buhrmester, 1992). This increased desire to be accepted by peers and avoid social rejection has been cited as a driver of adolescent behaviour (Sebastian et al., 2010), with studies showing that the rewarding nature of peer relationships during adolescence affects social decision-making processes (Dumontheil et al., 2010). These changes, which can be adaptive and positive, can also be aversive and stressful and confer increased risk for mental health problems (Blakemore & Mills, 2014).

Biological

Twin and family studies have shown that genetic factors contribute to risks of developing mental health difficulties (Boomsma et al., 2002; Polderman et al., 2015; Sullivan et al., 2012), with twin studies indicating significant genetic correlations across disorders (Derks et al., 2014; Kendler et al., 2003; Middeldrop et al., 2005; Ystrom et al., 2014). Moreover, genome wide association studies have identified a limited set of shared genetic risk factors that are associated with multiple mental health disorders (Malhotra & Sebat, 2012; Smoller et al., 2013).

Beyond genetic contributions, the increased vulnerability to mental health problems in adolescence is associated with hormonal surges (Pfeifer & Allen, 2021) and changes in brain development (Mills, 2016; Somerville et al., 2010; Tamnes et al., 2017) that disrupt mood stability (Maciejewski et al., 2015). Puberty is characterised by rapid increases in oestrogen in girls and testosterone in boys, marking a time when sex differences in mental health problems start to emerge. For example, rates of depression are similar in boys and girls before the onset of puberty, but twice as likely in girls than boys in adolescence. Boys are at greater risk than girls for substance abuse problems (Blakemore, 2019).

During adolescence, the brain undergoes continued development of both intracranial volume and whole brain volume and shows prolonged structural maturation of grey matter and white tracts supporting higher cognitive function (Dumontheil et al., 2016; Mills, 2016). These changes follow earlier puberty-driven maturation of sub-cortical regions supporting emotional and reward processing, and they are associated with increased cognitive control and better social cognition. This mismatch between early development of emotion and reward processing brain systems, and later development of systems supporting self-regulation and social cognition has been linked to increased sensation seeking and risk taking during adolescence, and greater sensitivity to social-affective contexts brain development. This is associated with increased vulnerabilities to mental health problems (Dumontheil, 2016).

Cognitive

Cognitive impairments are implicated in the onset and maintenance of mental health difficulties (e.g., Carlson & Wang, 2007; Huang-Pollock et al., 2017; McTeague et al., 2016; Ochsner & Gross, 2005), and cognition and mental health interact across development (e.g., Furhmann et al., 2020). The cognitive reserve hypothesis suggests poor cognitive function impairs the downregulation of negative emotional responses, such as worry, fear or sadness, leading to poor mental health (LeMoult & Gotlib, 2019; Millan et al., 2012). Conversely, the interference hypothesis suggests psychological distress disrupts cognitive processing by shifting cognitive resources away from task-relevant information and onto negative thoughts (Llewellyn et al., 2008; Stawski et al., 2006), resulting in both short- and long-term cognitive difficulties (Dolcos et al., 2020). Finally, the dynamic mutualism hypothesis integrates these two opposing theories, arguing

that mental health and cognitive function interact reciprocally over time, leading to a dynamic cycle of exacerbation across the lifespan (Fuhrmann et al., 2020).

Adolescence is characterised by a maturation in cognitive abilities (Crone & Dahl, 2012; Dahl, 2004), in particular by rapid changes in skills related to emotional- or self-regulation, which are captured by executive functions (Best & Miller, 2010; Dumontheil et al., 2010; Rosenblum & Lewis, 2003; Silvers et al., 2012; van der Aar et al., 2018). These changes cause restructuring of emotion regulation strategies and their use (Zimmermann & Iwanski, 2014), increasing adolescents' vulnerability to mood variability and difficulties (Rosenblum & Lewis, 2003).

These changes, which are also linked to dramatic changes in brain development, are thought to be responsible for the increased risk taking and reward seeking behaviours in adolescence, especially when among peers (Steinberg, 2017). As stated in the section on biological causes, the development of the limbic system, which is associated with emotional processing and links the conscious functions of the cerebral cortex to the more automatic, unconscious functions of the brain stem, out-paces the development of the cortical circuitry associated with higher-level cognitive functions, resulting in increased reactivity to emotional stimuli (Urošević, 2012). As a result, emotional reactivity is not downregulated by slower-to-develop cognitive control areas, increasing the likelihood of risky and impulsive behaviours in adolescence (Powers & Casey, 2015).

There are various theories about the role of different cognitive functions in the onset and maintenance of mental health problems. Reviewing all of these theories is beyond the scope of the current thesis. Instead, a short overview of the role of the different cognitive skills explored

in the meta-analysis and empirical project is presented here and discussed more fully in the following chapters.

Attentional biases. Biased information processing has been linked to mental health difficulties. Cognitive models of anxiety highlight the link between attentional bias regarding threat and clinical and sub-clinical levels of anxiety (e.g., Beck et al., 1985, Beck & Clark, 1997; Eysenck et al., 2007, MacLoed & Mathews, 2012). Research has suggested that attention can be biased towards threat in the form of hypervigilance (Freeman et al., 2000), or away from threat, as in avoidance (Beck & Clark, 1997; Heuer, Rinck & Becker, 2007). This is explored further in Chapter Two of this thesis.

Working memory. Working memory refers to the ability to retain and manipulate information over a short period of time. It is used in many everyday activities as it enables people to hold goals in mind and reprioritise actions based on goal-orientated information. Working memory deficits have been linked with a range of mental health-related disorders, including ADHD (Martinussen et al., 2005; Willcutt et al., 2005), anxiety disorders (Bishop, 2009; Eysenck & Derakshan, 2011), depression (Paelecke-Habermann et al., 2005; Rogers et al., 2004), bipolar disorder (Quraishi & Frangou, 2002) and schizophrenia (Nieuwenstein et al., 2001), as well as autism (Hill, 2004; Hughes et al., 1994) and learning disabilities (McLean & Hitch, 1999; Willcutt et al., 2001). Given the prevalence of working memory deficits among individuals with mental health problems, it is not surprising that they have been referred to as a transdiagnostic risk factor for childhood psychopathology (Huang-Pollock et al., 2017). Associations between working memory and mental health in adolescence are considered in the empirical project presented in Chapter 4.

Inhibition. The ability to self-regulate, suppress automatic responses, control impulses, and inhibit distracting information to focus attention to make constructive choices is associated with success in many areas of life (Dillon & Pizzagalli, 2007). Deficits in inhibition are associated with increased anxiety in both adults (Reznick et al., 2008) and children (Henderson et al., 2015), and problems both inhibiting impulsive responses and delaying gratification are associated with elevated externalising symptoms across the lifespan (e.g. Barkley, 1997; Chaarani et al., 2017; Nigg et al., 2006; Pollak et al., 2019) and with increased impulsive and risky-decision making in adolescence (Crone et al., 2016; Dekkers et al., 2022; Rosenbaum & Hartley, 2019). The relationship between inhibition and mental health is discussed further in Chapter 4.

Thesis aims and clinical relevance

Clinical relevance

The current model for treating child and adolescent mental health is largely reactionary and difficulties are only identified and treated once they escalate. This contributes to both long waiting lists faced by young people trying to access services for mental health difficulties and to healthcare systems being overwhelmed (Clark, 2018, Crenna-Jennings & Hutchinson, 2020). To overcome some of these issues, healthcare systems are seeking to move towards more proactive models of prevention (Fenwick-Smith et al., 2018) and researchers have started to explore whether preventative interventions are cost-effective and easily and widely accessible through communities and schools (e.g., Kuyken et al., 2017). To design effective preventative interventions, it is vital to identify targets for intervention by understanding the factors that predispose individuals to mental health problems.

Aims

The overarching aim of this thesis was to explore the relationship between cognitive function and mental health in children and adolescents. I have chosen to focus specifically on cognition because cognitive models are heavily drawn upon for interventions for many psychopathologies, including anxiety (e.g., Wells, 1999), obsessive-compulsive disorder (O'Leary, 2007), post-traumatic stress disorder (Elhers & Clark, 2000) and depression (Beck, 2002). Cognitive therapies focus on thought processes and their impact on emotions and behaviour. Indeed, the most widely used therapy by the National Health Service (NHS) is cognitive-behaviour therapy (CBT), which has been shown to be efficacious in treating such psychological presentations in both adults and children (for a review see Hofmann et al., 2012).

The first piece of empirical work presented in this thesis is a meta-analysis and systematic review that reviews evidence for information processing biases in children and adolescents with anxiety. The second piece is an empirical project using secondary data analysis that adopts a transdiagnostic approach to explore how mental health profiles change between mid- and late adolescence, and how these changes relate to cognitive function.

CHAPTER TWO

Systematic Review and Meta-Analysis

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Memory and attention biases in youth anxiety: A meta-analysis and systematic review.

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Abstract

Despite extensive research, conclusions regarding cognitive biases in youth anxiety remain unclear. Building on previous meta-analyses, this study conducted separate analyses for tasks exploring attention biases in young people with anxiety. Twenty-two papers, reporting data from 877 children and adolescents with anxiety and 1,317 controls, aged 5 to 24 were included. Results found no significant bias towards threat in anxious children and adolescents as measured by dot probe tasks (congruent trials: $g = 0.02$, $p = 0.89$; incongruent trials: $g = 0.10$, $p = 0.57$; other: $g = -0.05$, $p = 0.74$). This is discussed in terms of vigilance and avoidance of threat. A significant bias towards threat in anxious compared to non-anxious children and adolescents was found when measured by the emotional Stroop task ($g = 0.50$, $p = 0.02$). Only two studies exploring memory biases were found; a narrative review of these offered insufficient data to draw concrete conclusions. Clinical implications and future directions are suggested.

Introduction

Anxiety is highly prevalent in young people. A recent meta-analysis of 29 studies, including 80,879 youth, reported that, from January 2020 to February 2021, 25.2% of children and 20.5% of adolescents experienced clinically elevated symptoms of anxiety (Racine et al. 2021). Racine et al. (2021) highlighted that prevalence estimates have increased during the COVID-19 pandemic, but, even prior to this, rates were as high as 11.6% (Tiirikaninen et al., 2018), with up to 23.5% experiencing clinically significant levels before the age of 21 (Copeland et al. 2011).

Cognitive models of anxiety suggest that biased patterns of information processing could be instrumental in the aetiology (Beck & Clark, 1997; Eysenck et al., 2007, MacLeod & Mathews, 2012) and maintenance (Beck, 1976; Mogg & Bradley, 1998, Williams et al., 1997) of problematic anxiety. Such models propose that a hypervigilance for threat – such as increased attention towards perceived danger in the environment or selectively remembering threatening stimuli – causes anxiety (Muir & Field, 2008). These biases lead to avoidant behaviour that precludes opportunities to disconfirm threatening beliefs, resulting in the maintenance of anxiety (Beck & Clark, 1997; Heuer, Rinck & Becker, 2007).

Attention bias

Attentional biases towards threat have been reported extensively in anxiety disorders (Dalgleish & Watts, 1990; Williams et al., 1997), and several meta-analyses have been published. The consensus is that individuals with anxiety have threat-related biased attention (Bar-Haim et al., 2007; Dudeney et al., 2015), although with varying effect sizes. Most meta-analyses have been conducted with adults. The seminal meta-analysis that involved children

(Bar-Haim et al., 2007), included data from 172 studies with adults and children. Attentional bias for threat-related content was reliably demonstrated across different experimental paradigms (dot probe and emotional Stroop tasks), with an effect size of $d = 0.45$ in participants with anxiety. However, child studies made up only 10% of the total studies.

More recently, Dudeney et al. (2015) conducted a meta-analysis that included 28 articles concerned with attentional bias towards threat in children. They found that children with anxiety, as defined by either a clinical diagnosis or scoring above a cut-off point on a self-/parent-report validated measure of anxiety, showed a significant bias towards threat compared to controls ($d = 0.21$) and a significant bias towards threat-related over neutral stimuli ($d = 0.15$). Their data revealed that differences between anxious and non-anxious youth were only reliably observed when attentional bias was measured by the emotional Stroop paradigm ($d = 0.44$), not when measured by the dot probe task ($d = 0.18$). This was true for both pictorial and linguistic stimuli, and differed to Bar-Haim and colleagues (2007) results that reported significant biases in attention towards threatening stimuli in anxious participants over controls in both emotional Stroop ($d = 0.48$) and dot-probe ($d = 0.34$) studies.

Memory bias

There is comparatively little research into the biased recall of threatening information in anxiety relative to that on attention bias. Evidence for memory biases in adults with anxiety is mixed. Dalgleish et al. (1994) reported no evidence for memory biases in people with anxiety using a homophone spelling task or an anagram solution task. Similar results were reported by Baños et al. (2001), Harrison and Turpin (2003), and Wenzel and Holt (2002), who also found no anxiety-related memory biases. In contrast, Coles et al. (2007) reported a memory bias for

ideographically selected threat words in people with generalised anxiety disorder (GAD). A meta-analysis by Mitte (2008) attempted to resolve inconsistent findings by integrating data from 165 adult studies. They reported a memory bias in adults with anxiety for recalling threat-related stimuli, though this finding did not reach significance. In a more recent meta-analysis, Herra et al. (2017) compiled data from 171 studies and found an anxiety-related memory bias in free recall tasks, but not in cued recall, recognition, or lexical decision tasks. These results suggest that memory biases might be task-specific, like that reported by Dudeney et al. (2015) for attention biases.

Very few studies have investigated memory biases in children and adolescents, and again, the findings are mixed. For example, Visu-Petra et al. (2012) found that anxious children recalled more angry than happy or neutral faces, whereas low-anxious children showed the opposite pattern. In contrast, Daleiden (1998) found that whilst anxiety predicated a memory bias towards negative relative to neutral information during conceptual tasks (e.g., presented with a semantic cue and asked to recall a word with a similar meaning which they had previously seen in the task), none was found in perceptual tasks (e.g., word fragment completion task). Meta-analyses investigating general memory performance in specific populations, such as those with specific types of anxiety (e.g., mathematics anxiety, Namkung et al., 2019) or attention deficit hyperactivity disorder (e.g., Martinussen et al., 2005) have been conducted, but to date no meta-analyses have explored biased recall for threat-related information in children and adolescents with and without anxiety.

The present study

The aim of this review was to conduct meta-analyses exploring memory and attention biases in anxious youth. The first set of meta-analyses investigated whether there was an attentional bias toward threat in anxious vs non-anxious children and adolescents; an updated version of Dudeney et al.'s (2015) meta-analysis. A limitation highlighted by Dudeney et al. (2015) of their meta-analysis was the high level of heterogeneity of study variables. This review addressed this by conducting separate meta-analyses for studies with samples and variables as homogenous as possible, e.g., separating different tasks. The emotional Stroop and dot probe tasks are most commonly used to measure attentional bias. The emotional Stroop task measures attentional bias as an interference effect by examining the difference between colour naming speed with affective vs neutral stimuli; colour naming latencies are typically longer for emotional stimuli. In the dot probe task participants are presented visually with stimulus pairs (words or pictures) that disappear and are replaced by a probe in the location of one of the stimuli. Participants are required to press a button indicating the location of the probe. Shorter reaction times when the probe appears in the same location as the emotional stimuli (congruent) compared to when it replaces the neutral stimuli (incongruent) reveal attentional biases towards threat, under the assumption participants were already attending to this location (Hadwin et al., 2006). In an extension to Dudeney et al.'s (2015) review, we explored whether bias towards threat was present in both congruent and incongruent trials of the dot probe paradigm. Previous research (e.g., Strauss et al., 2005) has suggested that there is low test-retest reliability among interference scores calculated by subtracting performance in one condition from performance in another. Thus, this review will complete meta-analyses using only latencies, where available, for the separate trials. We hypothesised that young people with anxiety would show an attentional

bias towards threat, as measured by the dot probe and emotional Stroop tasks, greater than that of controls. The aim of the second review was to investigate whether anxious youth show biased recall for threat-related information compared to controls. We predicted that they would. Across both reviews, anxiety was measured by clinical diagnosis and/or self-/parent-reports of elevated levels of anxiety. Given the high rates of comorbidity between anxiety and depression (Kalin, 2020), and the reported prevalence of information processing biases in people with comorbid anxiety and depression (Mogg et al., 1995), we included studies with participants with comorbidities.

Method

Study Protocol and Search strategy

A systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009). The study protocol was pre-registered on PROSPERO (CRD42021262394) on 21st June 2021. Three electronic databases (Scopus, PsycINFO, and PubMed) were searched, from 1st January 1980 up to 30th June 2021. The search terms are included in Table 2.1. Terms were searched in titles and abstracts in peer-reviewed articles. Opinion articles, reviews and other meta-analyses were excluded. Other filters included human studies with participants aged 5 to 24, featuring a control and an anxious group, and those published in the English language.

A greater number of search terms was used comparative to the Dudeney (2015) paper to ensure the highest possible number of papers were identified. An earlier cut off date than used by Dudeney and colleagues (2015) was used to be more in line with when such computerised tasks

were first employed. A wider age-range was also used to capture the full neurological developmental period, rather than the typical cut-off of 18 years.

Two of the electronic databases used were different than those used by Dudeney and colleagues (2015). These were chosen due to their large mutidisciplinary libraries and their relevance to the field of interest.

Table 2.1

Search terms

Category	Search Terms
Information processing bias	cog*bias*, cog* process*, cog* process* bias*, cog* factor*, information process* bias*, emotion process* bias*, cog* model*, information process* model*, attention* bias*, interpret* bias*, memory bias*
Executive Function	attention*control, executive function*, cog* control, inhibit* control, executive control, emotion* control, working memory, inhibition, updating
Anxiety	anxiety*, generalised anxiety disorder*, GAD, separation anxiety, social anxiety, panic, panic disorder, obsessive compulsive disorder, OCD
Age	youth*, child*, adolescen*, young people, young adults, youth

Note: **Indicates where truncation was used to find singular and plural forms of words and variant endings.*

Study selection

Papers retrieved through the initial search were divided equally between authors J.P. and M.V. for title and abstract screening. Each reviewed a random selection of 15% of the other's articles to provide additional checking in line with the inclusion criteria. One discrepancy was

resolved by the senior author. A full text screening was conducted by J.P. and M.V. of their remaining articles, for inclusion.

Studies were included if they met the following criteria: (a) included human participants aged five to 24, (b) administered a standardised measure of anxiety, (c) included a nonpsychiatric control group or a comparison group of participants with low levels of anxiety, (d) featured a measure of attention or memory using emotional stimuli, (e) reported quantitative data that could be transformed into an effect size to quantify differences in performance between anxious and non-anxious individuals, and (f) were published in English in peer-reviewed journals between January 1980 and June 2021.

Studies featuring only populations with specific phobias (e.g., arachnophobia, agoraphobia, etc.), Post-traumatic stress disorder (PTSD) and social anxiety were excluded due to the specific focus of the participants' anxiety. Studies capturing generalised anxiety or where a mix of anxiety diagnoses reported together, were included. Studies focussing on anxiety in a specific group (e.g., asthmatics or individuals with learning disabilities) were also excluded due to the narrow population focus. Association studies (e.g., those reporting correlations between cognitive performance and anxiety, or predicting anxiety from cognitive task performance) were excluded as they did not meet the study aims (to compare cognitive bias between anxious and non-anxious youth). Finally, studies reporting only accuracy data for the different conditions of the attention bias tasks were excluded. Accuracy is generally very high on interference tasks, pointing to ceiling effects (e.g., Penner et al., 2014; Strauss et al., 2005). For this reason, only studies reporting reaction times (RTs), or bias scores calculated from RTs, were included.

Data extraction

Data was extracted for all studies meeting the inclusion criteria by the principal investigator and second author. Sample characteristics (n, age range, mean age, standard deviation) and the measures of anxiety and cognition were extracted. The cognitive tasks were categorised according to: i) type of cognitive bias investigated (attention or memory), ii) type of task (dot probe or emotional Stroop – applicable to attention bias only), and iii) type of trial for dot probe (congruent and incongruent, or other, where other referred to the difference between two conditions). The sample size of the anxious and control groups, and each group's performance on the cognitive tasks (mean RT and standard deviation, or standard error where standard deviation was not provided) and the effect size of the difference between groups (where provided) was extracted (tables 2.2, 2.3 and 2.4).

Risk of bias

The quality of the included studies was assessed using a risk of bias tool (Appendix B) that was developed from The Critical Appraisal Skills Programme (2018), The Scottish Intercollegiate Guidelines Network (SIGN) Methodology checklist (2012) and The Cochrane Collaboration's tool for assessing risk of bias (2011). The risk of bias assessment tool comprised 15 questions assessing the design, measurement, analysis, and participant details of each study. Based on these questions, each study was allocated a risk of bias rating by the first or second author (0–4 = high risk, 5–9 = medium risk, 10–15 = low risk; see Table 2.2).

Data synthesis

Where studies reported group comparisons for multiple conditions (e.g., conditions with different stimuli exposure times), the data most consistent with the other studies were extracted.

For example, if a study reported group performance for stimuli exposures of both 1000ms and 750ms on a dot probe task, the data for the 750ms condition was extracted as this exposure time was closer to the 500ms exposure time used in all other studies. Where studies counter-balanced trials, average mean RTs and standard deviations were calculated. RTs were converted to milliseconds for all studies. Where bias scores were calculated for both negative vs neutral and negative vs positive stimuli, the data from the negative vs neutral trials were included, consistent with most studies in the field. Where multiple timepoints were reported (e.g., in an intervention study), data from the first assessment point (baseline data) was used.

Statistical analysis

All analyses were performed in R using the metafor package, version 4.1.2 (R Core Team, 2021). A series of random-effects meta-analyses were conducted, with the I^2 statistic used to assess the heterogeneity of effect sizes. Random effects (RE) models were run because the studies included investigated cognitive biases in youth with anxiety with different comorbidities, meaning the variability across studies was anticipated to be at least moderate. The standard errors of study effect estimates are adjusted in a random effects model to incorporate this heterogeneity (Borenstein et al., 2011).

Of the papers included regarding attentional biases, only two tasks were used – the dot probe and emotional Stroop. Four meta-analyses were conducted: three for dot probe (congruent, incongruent, and other) and one for emotional Stroop. The Hedges' *g* effect sizes of the difference in performance on the task between the anxious and non-anxious group was calculated. Hedges' *g,* an amended version of Cohen's *d,* adapts effect sizes for smaller samples, making it more appropriate to use in this study. Effect sizes were converted to the same

direction: a positive *g* value indicated that the attentional bias towards threat was larger in the anxious than the control group, and a negative *g* value indicated an attentional bias away from threat in the anxious group, greater than that of the control group. It was not possible to run meta-analyses on memory studies due to a lack of appropriate studies.

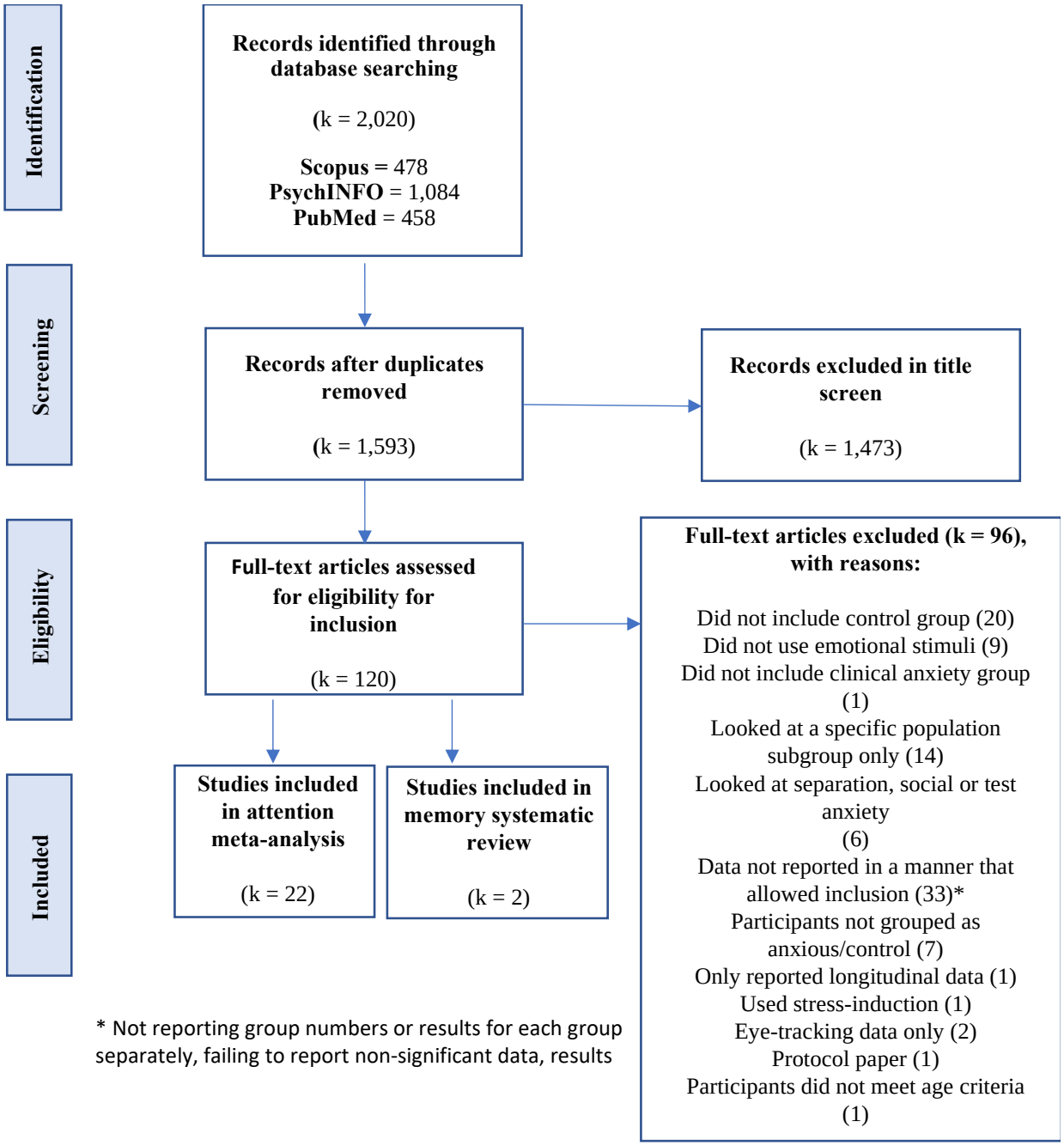
Results

Included studies

Figure 2.1 presents a PRISMA flowchart (Moher et al., 2009) of the study selection and exclusion process. Electronic data searches identified 2020 citations. After removal of duplicates, 1,593 articles were screened by title and abstract. A total of 120 full-text articles were assessed for eligibility, resulting in 24 studies being selected for inclusion in the review. Of these, 22 compared attention biases between anxious and control groups and only two compared memory biases. Due to the sparsity of papers meeting inclusion criteria for memory biases, these results are described as a narrative synthesis.

Figure 2.1

Prisma flowchart



Attentional bias as measured by Dot probe – congruent and incongruent

There were 10 articles in the meta-analyses for the dot probe congruent and dot probe incongruent trials. Susa et al. (2008) reported data separately for two age groups, meaning data for eleven independent groups are included. The characteristics of the included studies and the effect size differences between the anxious and control groups for both trial types are presented in Table 2.2. The overall age range for participants was five to 18 years. Across the studies there were 346 anxious participants and 287 controls. Diagnoses included OCD (Wang et al., 2021) and GAD; comorbidities included separation anxiety, phobia, social anxiety, and depression. The majority (k = 9) used emotive faces as stimuli, and two used other pictorial images. Exposure time was 500ms in all studies, except in Price et al. (2013) who used a stimuli exposure time of 750ms.

Across the studies, the combined effect sizes were non-significant, meaning there was no significant difference between anxious and non-anxious groups (congruent trials: $k = 11$, $n = 633$, $g = 0.02$, $p = 0.89$; incongruent trials: $k = 11$, $n = 633$, $g = 0.10$, $p = 0.57$). Forest plots summarising these results are presented in Figures 2.2 and 2.3.

Table 2.2

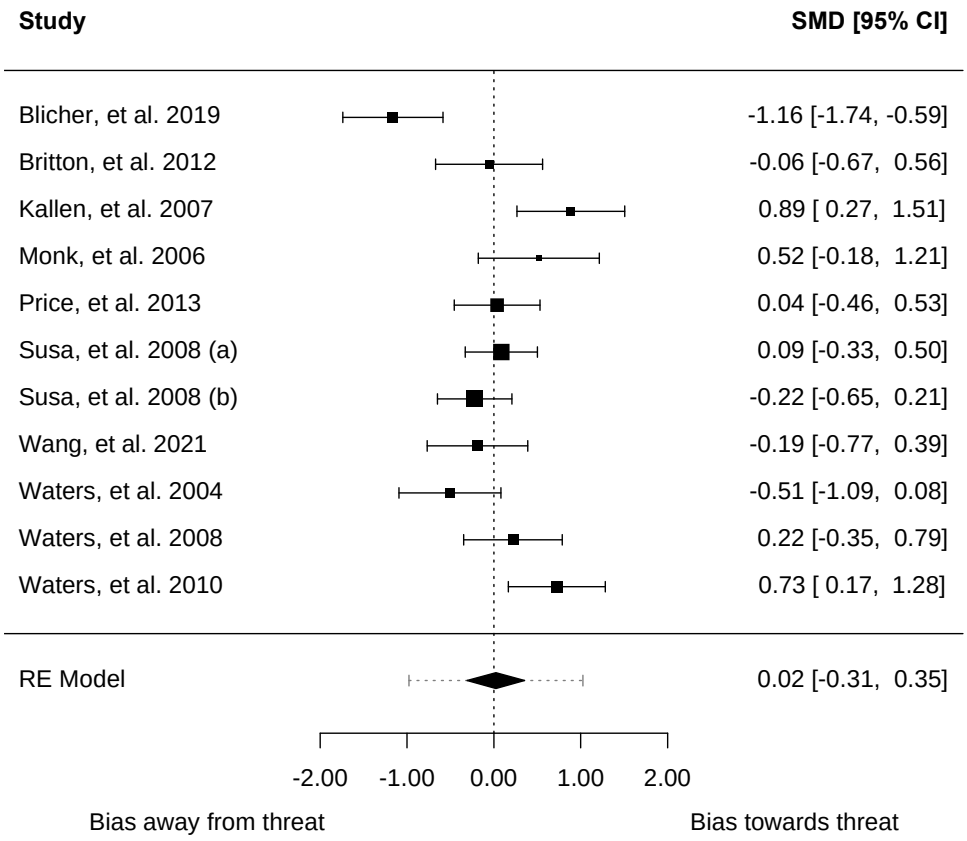
Study characteristics and effect sizes for dot probe congruent and incongruent trials

Author, year	*Country*	*Anxiety measure(s)*	*Total N*	*Age range*	*Mean age (SD)*	*Stimuli*	*Risk of bias (/15)*	*Anxious Group*		*Control Group*		*Cohen's d*	
								N	Mean age (SD)	N	Mean age (SD)	Congruent	Incongruent
Blicher et al., 2019	Denmark	RCADS ADIS-C	54	7-13	9.5 (1.6)	Faces	Low (12)	27	10.1 (1.6)	27	9.0 (1.5)	-1.16	-1.22
Britton et al., 2012	USA	PARS K-SADS SCARED-C	42	8-18	13.85 (2.62)	Faces	Low (11)	17	13.3 (2.9)	25	14.4 (2.3)	-0.06	0
Kallen et al., 2007	Netherlands	MASC	44	10-13	11.6 (DNR)	Items, animals, scenes, people	Low (10)	23	DNR	21	DNR	0.89	0.9
Monk et al., 2006	USA	K-SADS	33	9-17	12.91 (2.24)	Faces	Med (9)	18	13.53 (2.41)	15	12.28 (2.05)	0.52	0.29
Price et al., 2013	USA	K-SADS	94	9-13	10.55 (1.3)	Faces	Low (10)	74	10.6 (1.4)	20	10.5 (1.2)	0.04	-0.02
Susa et al., 2008 (a)	Romania	SCAS	89	5-9	7.5 (1.85)	Faces	Med (9)	46	DNR	43	DNR	0.09	0.05
Susa et al., 2008 (b)	Romania	SCAS	84	10-11	10.6 (0.71)	Faces	Low (10)	44	DNR	40	DNR	-0.22	-0.2
Wang et al., 2021	China	YBOCS Hamilton Anxiety Scale	46	13-19	15.93 (1.61)	Faces	Med (9)	22	16.36 (1.59)	24	15.5 (1.64)	-0.19	0.2
Waters et al., 2004	Australia	ADIS-C	46	9-12	DNR	Items, animals, scenes, people	Low (10)	23	DNR	23	DNR	-0.51	-0.25
Waters et al., 2008	Australia	ADIS-C SCAS	48	7-12	9.85 (DNR)	Faces	Low (10)	23	10.2 (DNR)	25	9.5 (DNR)	0.22	0.38
Waters et al., 2010	Australia	ADIS-C SCAS	53	8-12	10.12 (1.61)	Faces	Low (11)	29	10.02 (1.33)	24	10.21 (1.2)	0.73	1.07

Note: *N = number; SD = standard deviation; DNR = did not report; RCADS = Revised Children's Anxiety and Depression Scale; ADIS-C = Anxiety Disorders Interview Schedule – child version; PARS = Personal Adjustment and Role Skills; K-SADS = Kiddie Schedule for Affective Disorders and Schizophrenia; SCARED-C = Screen for Child Anxiety Related Disorders – child version; MASC = Multidimensional Anxiety Scale for Children; SCAS = Spence Children's Anxiety Scale; YBOCS = Yale-Brown Obsessive-Compulsive Scale.*

Figure 2.2

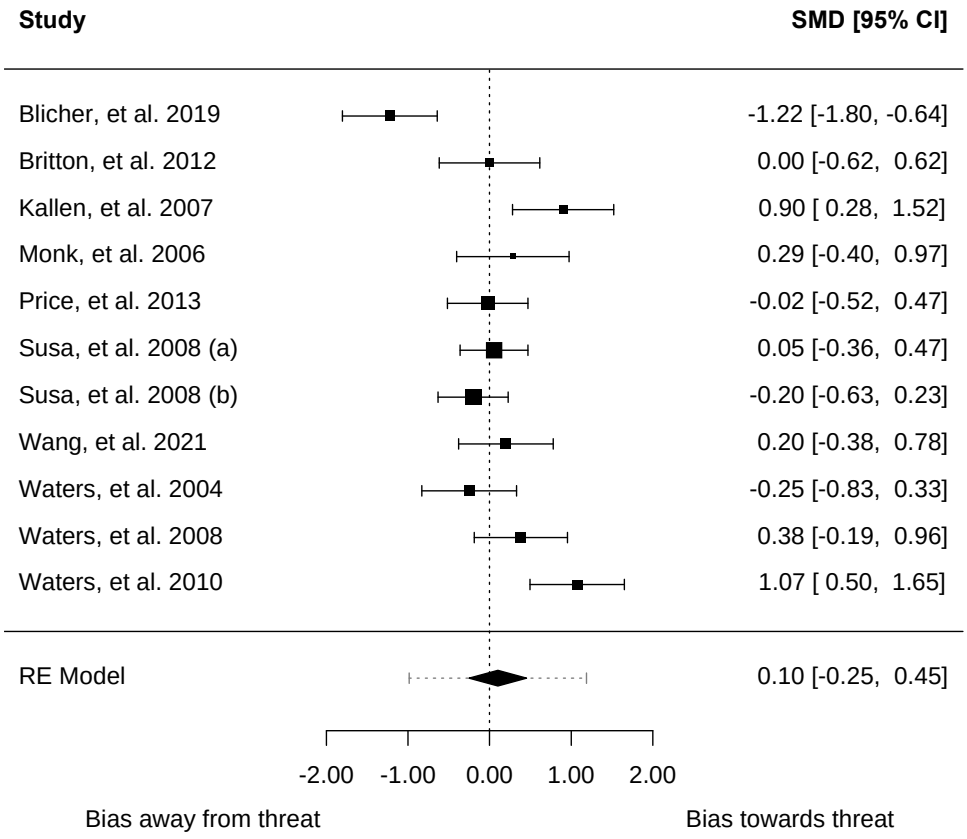
Forest plot of effect sizes for dot probe task, congruent trials



The Q statistic was significant for congruent and incongruent trials (congruent trials: Q = 37.15, df = 10, p <0.0001; incongruent trials: Q = 42.13, df = 10, p <0.0001) indicating considerable heterogeneity between effect sizes across the studies (congruent I^2 = 75.21%; incongruent I^2=78.14%).

Figure 2.3

Forest plot of effect sizes for dot probe task, incongruent trials



Attentional bias as measured by Dot probe – other

Eight studies used the dot probe task to measure attention bias but did not report data separately for congruent and incongruent trials. Both Gamble et al. (2009) and Reinholdt-Dunne et al. (2012) reported data separately for two age groups, resulting in 10 independent groups. The characteristics of the included studies and the effect size differences between the anxious and control groups are presented in Table 2.3. The overall age range for participants was seven to 18 years. Across the studies there were 371 anxious participants and 863 controls. All studies used

emotive faces as stimuli. Exposure time was 500ms in most studies, with Brown et al. (2013) using a stimulus exposure time of 1000ms. A sensitivity analysis was run, excluding data from the Brown et al. (2003) study to reduce heterogeneity across the studies. This did not significantly change the overall effect size, thus only the full meta-analysis including data from Brown et al. (2013) is reported.

Table 2.3

Study characteristics and effect sizes for dot probe other

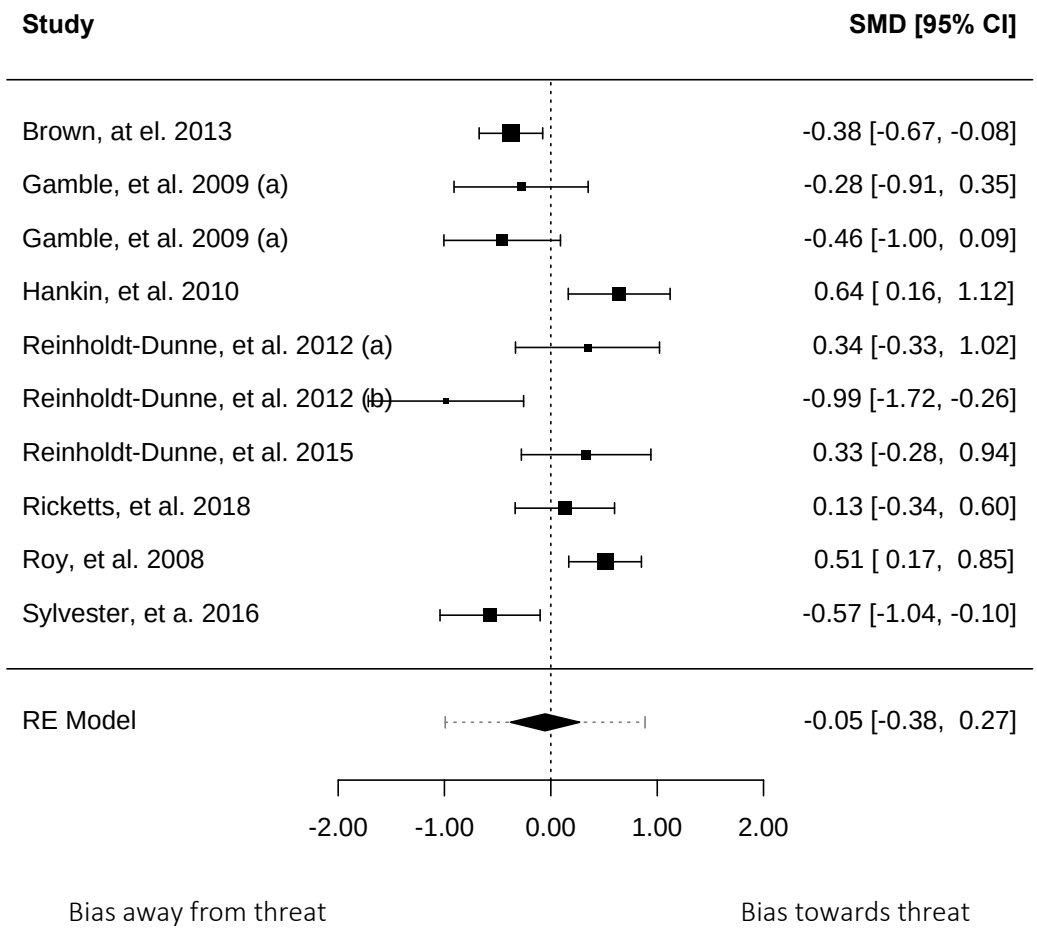
Author, year	*Country*	*Anxiety measure(s)*	*Total N*	*Age range*	*Mean age (SD)*	*Stimuli*	*Risk of bias (/15)*	*Anxious Group*		*Control Group*		*Hedges' g*
								N	Mean age (SD)	N	Mean age (SD)	
Brown et al., 2013	UK	DAWBA	600	8.24 – 8.92	DNR	Faces	Low (11)	47	DNR	553	DNR	-0.38
Gamble et al., 2009 (a)	Australia	ADIS-C SCAS	39	7-11	10.23 (1.04)	Faces	Low (10)	19	9.82 (1.1)	20	10.64 (0.98)	-0.28
Gamble et al., 2009 (b)	Australia	ADIS-C SCAS	53	12-7	13.82 (1.31)	Faces	Low (10)	24	13.99 (1.5)	29	13.65 (1.08)	-0.46
Hankin et al., 2010	USA	ADIS	118	9-17	12.68 (2.16)	Faces	Med (9)	21	12.97 (2.55)	97	12.93 (2.06)	0.64
Reinholdt-Dunne et al., 2012 (a)	Denmark	RCADS	34	7-10	9.35 (0.71)	Faces	Med (8)	17	9.6 (0.6)	17	9.1 (0.8)	0.34
Reinholdt-Dunne et al., 2012 (b)	Denmark	RCADS	33	11-14	11.8 (0.77)	Faces	Med (8)	14	11.7 (0.6)	19	11.9 (0.9)	-0.99
Reinholdt-Dunne et al., 2015	Denmark	ADIS	42	7-12	9.8 (1.75)	Faces	Low (10)	22	9.6 (1.7)	20	10 (1.8)	0.33
Ricketts et al., 2018	USA	PARS SCARED	90	9-14	11.28 (1.49)	Faces	Low (10)	66	DNR	24	DNR	0.13
Roy et al., 2008	USA	PARS	152	9-18	12.55 (2.75)	Faces	Med (9)	101	11.5 (2.8)	51	13.6 (2.7)	0.51
Sylvester et al., 2016	USA	MASC SCARED	73	11-14	12.9 (1.16)	Faces	Low (10)	40	13.2 (1)	33	12.6 (1.3)	-0.57

Note: *N = number; SD = standard deviation; DNR = did not report; DAWBA = Development and Well-Being Assessment; ADIS-C = Anxiety Disorders Interview Schedule – child version; SCAS = Spence Children's Anxiety Scale; ADIS = Anxiety Disorders Interview Schedule; RCADS = Revised Children's Anxiety and Depression Scale; PARS = Personal Adjustment and Role Skills; SCARED = Screen for Child Anxiety Related Disorders; MASC = Multidimensional Anxiety Scale for Children.*

The combined effect size was non-significant across the dot probe other studies (k = 10, n = 1234, g = -0.05, p = 0.74). Figure 2.4 shows the forest plot of the effect sizes across these tasks.

Figure 2.4

Forest plot of effect sizes for dot probe, other



The Q test result was significant (Q = 39.94, df = 9, p <0.0001), again indicating considerable heterogeneity between the results of the studies (I^2 = 77.29%).

Table 2.4

Study characteristics and effect sizes for emotional Stroop

Author, year	*Country*	*Anxiety measure(s)*	*Total N*	*Age range*	*Mean age (SD)*	*Stimuli*	*Risk of bias (/15)*	*Anxious Group*		*Control Group*		*Hedges' g*
								N	Mean age (SD)	N	Mean age (SD)	
Bashford-Largo et al., 2021	USA	SCARED	69	13-17	15.61 (1.62)	ms, animals, scenes, peo	Low (11)	35	15.32 (1.75)	34	15.9 (1.47)	0.35
Reinholdt-Dunne et al., 2012(a)	Denmark	RCADS	34	7-10	9.35 (0.71)	Faces	Med (8)	17	9.6 (0.6)	17	9.1 (0.8)	0.48
Reinholdt-Dunne et al., 2012(b)	Denmark	RCADS	33	11-14	11.8 (0.77)	Faces	Med (8)	14	11.7 (0.6)	19	11.9 (0.9)	-0.2
Richards et al., 2007	UK	STAIC	50	10-11	11 (3.71)	Written words	Med (7)	24	10.11 (3.68)	26	11 (3.82)	0.72
Taghavi et al., 2003	UK	ADIS	38	10-16	13.99 (2.39)	Written words	Med (9)	19	13.47 (3.23)	19	14.5 (1.01)	1.18

Note: *N = number; SD = standard deviation; SCARED = Screen for Child Anxiety Related Disorders; RCADS = Revised Children's Anxiety and Depression Scale; STAIC = State-Trait Anxiety Inventory; ADIS = Anxiety Disorders Interview Schedule*.

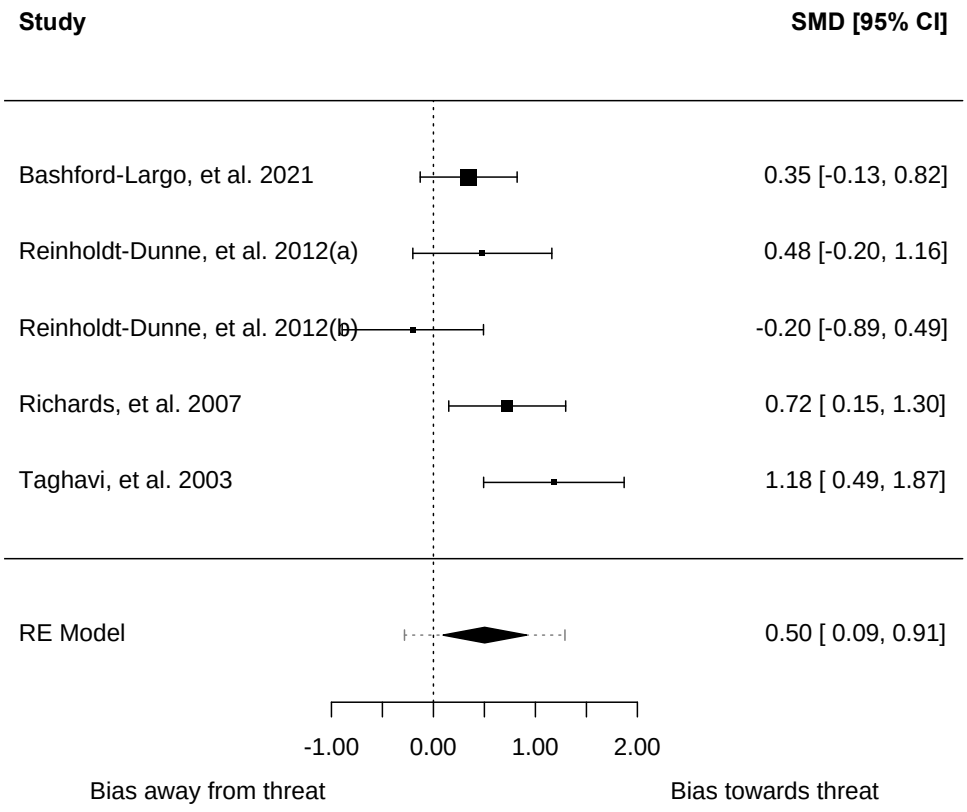
Attentional bias as measured by Emotional Stroop

Four separate studies assessed attention bias using an emotional Stroop task. Reinholdt-Dunne et al. (2012) reported data for two independent age groups, resulting in five sets of data. Three datasets involved emotionally valanced images (Bashford-Largo et al., 2021 and both Reinholdt-Dunne, 2012 datasets). The remaining two studies used visually presented threat- or anxiety-related words. Across these studies there were 109 anxious participants and 115 controls. The age range of participants was seven to 17 years. The characteristics of the included studies and effect size differences between the anxious and control groups are shown in Table 2.4.

The difference between the combined effect sizes showed significantly higher threat bias in anxious participants compared to that of controls ($k = 5$, $n = 224$, $g = 0.50$, $p = 0.02$). Figure 2.5 shows the forest plot of these effect sizes. The Q test was not significant ($Q = 8.7$, $df = 4$, $p = 0.07$), suggesting there was not significant heterogeneity in the effect sizes across studies ($I^2 = 54.85\%$).

Figure 2.5

Forest plot of effect sizes for emotional Stroop



Attentional bias summary

Table 2.5 presents a summary of the outcomes of the four meta-analyses exploring attention biases among anxious youth relative to controls. Overall, there was no evidence for an effect of attentional bias among anxious youth on dot probe tasks, but there was a significant attention bias on emotional Stroop tasks.

Table 2.5

Meta-analytic results of threat-related biases in attention, summarised by task

Task	*k*	*N*	*95% CI*	*Q*	*I2*	*Hedges' g*
Dot probe Congruent	11	633	-0.31 to 0.35	37.15	75.21%	0.02
Dot Probe Incongruent	11	633	-0.25 – 0.45	42.13	78.14%	0.1
Dot probe other	10	1234	-0.38 – 0.27	39.94	77.29%	-0.05
EmoStroop	5	224	0.09 to 0.91	8.7	54.85%	0.5

Publication Bias

Funnel plots were created for each meta-analysis (Appendix C). Inspection of these suggested no evidence of publication bias.

Memory bias

Only two studies investigating memory bias in anxious youth vs controls met inclusion criteria. The characteristics of these studies are summarised in Table 2.6. As there were insufficient studies to conduct a meta-analysis, a narrative synthesis is provided.

Ladoucer et al. (2005) explored the mechanisms underlying emotion regulation in affective disorders in youth, including measures of anxiety and working memory (an n-back task with distracting emotional information). Participants were 17 children with anxiety, 16 children with depression, 24 children with comorbid anxiety and depression and 18 controls, all aged between eight and 16 years old. No significant differences were found between RTs for emotive and neutral backgrounds for the anxious group, though the anxious group were slower to respond on trials with negative compared to neutral backgrounds, suggesting altered processing of emotional information among youth with anxiety.

Toffalini et al. (2015) used pictorial scripted material to explore the relationship between affective disorders, including anxiety and memory in 17 to 24 year olds. Thirty-four anxious and 34 control participants were recruited and asked to look at nine scripted episodes, each consisting of 14 pictures depicting an everyday event. Each episode depicted a cause-effect pattern with a single picture depicting a causal antecedent followed by three consequences: one positive, one negative and one neutral. The memory test consisted of a recognition task in which participants had to state whether they had seen the image in the encoding phase. Results showed an increase in negative, but not positive, false memories in anxious individuals (F (2, 130) = 5.91, $p < 0.01$), even after controlling for depression. They concluded that high trait anxiety enhances the elaboration of negative emotional material, leading to false memories of causal antecedents of negative events.

The results of these two studies contrast one another, with an effect found on a scripted recall task but not on an emotional n-back task. There may be an effect of anxiety on memory, though the findings presented here are not conclusive and, given the differing nature of the tasks, are difficult to synthesise.

Table 2.6

Characteristics of memory bias studies

Author, year	*Country*	*Anxiety measure(s)*	*Memory Task*	*Total N*	*Age range*	*Mean age (SD)*	*Stimuli*	*Risk of bias (/15)*	*Anxious Group*		*Control Group*	
									N	Mean age (SD)	N	Mean age (SD)
Ladoucer et al., 2005	USA	K-SADS SCARED	n back	75	8-16	12.69 (2.53)	Items, animals, scenes, people	Med (9)	17	11.68 (2.71)	18	11.94 (2.43)
Toffalini et al., 2015	Italy	QPAD	recognition	68	7-24	19.37 (-1.99)	Pictorially presented scripts	Med (6)	34	19.34 (2)	34	19.39 (1.99)

Note: *N = number; SD = standard deviation; K-SADS = Kiddie Schedule for Affective Disorders and Schizophrenia; SCARED = Screen for Child Anxiety Related Disorders; QPAD = Questionnaire on Palliative Care for Advanced Dementia.*

Discussion

This review sought to explore whether children and adolescents with anxiety show attentional and/or memory biases towards threat-related information. The first aim was to investigate whether an attentional bias towards threatening stimuli, as measured by emotional Stroop and dot probe tasks, was observed in anxious youth relative to controls. Building on an earlier meta-analytic review (Dudeney et al., 2015) by including more recent studies and reducing the heterogeneity of variables, our results indicate that anxious children and adolescents show a bias towards threat when measured by the emotional Stroop task, but not when measured by dot probe. The second aim was to explore whether anxious youth show biased recall for threat-related information compared to controls. Only two studies met the inclusion criteria, meaning a narrative review was conducted revealing conflicting results.

Attentional bias

Four meta-analyses were conducted, three for studies using dot probe tasks and one for those using emotional Stroop. The dot probe meta-analyses explored differences in RTs between young people with anxiety for congruent trials and incongruent trials separately. A third meta-analysis was conducted for studies that did not report RTs for the separate conditions; these reported bias scores.

For studies using the dot probe task, there was no evidence for an attentional bias towards threat in anxious young people compared to controls across congruent or incongruent trials, nor in studies reporting bias scores. This is consistent with Dudeney et al.'s (2015) earlier review of attentional bias in anxious youth. Symptoms of depression may prevent the manifestation of anxiety-related attentional biases in comorbid populations (Mogg et al., 1993; Bradley et al.,

1995). As the current review included children and adolescents with comorbid presentations, attentional biases may therefore have been masked.

This review explored biases *toward* threat (i.e., faster RTs to threatening stimuli in anxious youth). Studies included in these meta-analyses were highly heterogeneous; some studies showing a strong effect in the direction of threat-related material for the anxious group (e.g., Kallen et al., 2007; Hankin et al., 2010; Roy et al., 2008; Waters et al., 2010), others showing a strong effect in the opposite direction (e.g., Blicher et al., 2019; Brown et al., 2013; Sylvester et al., 2016). It is possible that these slow RTs reflect an attentional bias away from threat – an avoidance.

Consistent with this idea, one theoretical account of anxiety suggests that a logical response to threat is to take action to prevent a perceived negative outcome, which leads to a cognitive bias towards avoidant and escape behaviour (Salkovskis, 1991). Correspondingly, the time course of attentional allocation towards threatening stimuli is important in the maintenance of anxiety disorders, with a pattern of initial vigilance towards threat being followed by avoidance (Mogg & Bradley, 1998). Thus, while the current review found no evidence of an attentional bias toward threat, it is possible that pooling effects towards and away from threat to compare absolute differences between anxious children and adolescents, and controls meant that the effects balanced each other out, resulting in no significant group effect. It could be that anxious youth do show attentional biases, both towards and away from threat, reflecting both vigilance and avoidance. Alternatively, it could be that some anxious youth display avoidance of threat whilst others have a tendency for vigilance for threat-related material. Future meta-analyses could explore this by considering the direction of the group differences between anxious and non-anxious young people.

Research suggests that the varied effects of attentional bias reported across studies might be age-related, with younger children showing stronger biases towards threat as they lack the cognitive ability to inhibit the processing of threat-related material (Kindt, 1997). No such pattern was easily observable across the studies included in the current review and subgroup analyses of different age groups was not possible, due to insufficient data.

While there was no evidence of attentional bias toward threat in the dot probe meta-analyses, there was a significant medium-sized effect in the meta-analysis conducted on studies using the emotional Stroop task. Unlike the dot probe meta-analyses, many individual studies showed an effect in the same direction for the Stroop task, with anxious youth performing more poorly than controls when the task contained threat-related stimuli. In other words, they were less able to inhibit irrelevant information if it contained threat-related information, indicating an attentional bias toward threat.

Finding an effect for emotional Stroop but not dot probe aligns with Dudeney et al.'s (2015) results. They too found that attentional biases were only evident on the Stroop task in children, contrasting findings from adults that show differences between anxious and non-anxious people across both tasks (Bar-Haim et al., 2007). What does this mean for the presence of attentional bias in anxious youth? It is likely that anxious young people are biased toward and away from threat, and that the Stroop meta-analysis is detecting the former of these, while the dot probe is not able to differentiate between attentional biases towards or away from threat (Clarke et al., 2013), meaning it shows what looks like a null difference between anxious and control groups. Alternatively, the dot probe might not be sensitive enough to detect bias in children and adolescents, as it was developed for use with adults (McLeod et al., 1986).

Memory bias

There were not enough papers to complete a meta-analysis of memory bias in anxious youth. The two that met inclusion criteria were instead described in a narrative synthesis. Ladoucer et al.'s (2005) findings that anxious children were slower to respond on trials with a negative background than on trials with a neutral background did not reach significance. Toffalini et al., (2015) did find a significant difference, with anxious participants recalling significantly more negative false memories, suggesting they have a memory bias for negative information. This difference might reflect differences in the memory systems measured by the two tasks – while n-back taps into working memory, scripted recall tasks measure episodic/long-term memory. Thus, anxious youth might have memory biases for longer-term memory system, but not in short-term or working memory. Further studies are needed to test this speculative idea.

Another consideration is the ages of the participants in the two studies, with those in the Ladoucer et al. (2005) study being younger than those in in the Toffalini et al. (2015) study. As discussed above, age may play a role in the processing of threat-related material in anxious youth and further research is needed in this area.

A key finding of the systematic review of the literature in this field was a paucity of studies. Whilst there is extensive research into memory biases in depression (for a review, see Platt et al., 2017), there is comparatively little research available exploring the same in anxiety.

Strengths and limitations

A strength of this report was the robust methodology and strict inclusion criteria which resulted in a reduction of heterogeneity compared to previous reviews. This enabled greater confidence in the findings of each meta-analysis but resulted in a comparatively small number of

studies. Prior meta-analyses of attentional biases to threat (Bar-Haim et al., 2007; Dudeney et al., 2015) included a far greater number of studies as they had less strict inclusion criteria, which resulted in more heterogeneity in the study characteristics (e.g., samples and experimental variables). Whilst this methodological rigour enabled the exploration of biases in subgroups of tasks, it resulted in too small a pool to explore other areas of interest, such as developmental differences in biases.

Second, only searching for published papers in the English language may have restricted the search scope and missed the grey literature. However, this did result in a level of quality control and no publication bias was found. Also, most papers included in the meta-analyses reported only significant findings. While examination of the funnel plots for each meta-analysis suggested there was no publication bias, future studies may seek to include such data reporting nonsignificant effects, including in the grey literature.

Finally, it is important to note that only two tasks were examined in the meta-analyses: the dot probe and the emotional Stroop. Whilst both are robust and simple to administer, they do not provide information regarding underlying attentional processes. Reaction-time measures have also been criticised for only providing a snapshot of attentional processes in the moment participants respond. Different tasks may tap into different attentional processes, and it should be highlighted that only examining the dot probe and emotional Stroop may have impacted the results. A small number of articles in the initial search did utilise other tasks, such as a Go/No Go task that asks participants to respond by pressing a button when they see a "go" signal but not when they see a "no-go" signal. However, these tasks were very rarely used and studies including them were excluded due to other reasons, as outlined in figure 2.1.

Clinical implications

An attentional bias towards threat was most reliably indicated by the emotional Stroop task, which requires volitional control over attention. This is one element targeted in clinical interventions, such as cognitive behavioural therapy (CBT), which requires individuals, in part, to identify and work with attention. CBT has been shown to be effective for both preventing and treating childhood anxiety (Schwartz et al., 2019). A better understanding of the different roles attentional bias can play may help to better tailor the delivery and impact of such interventions for young people.

Future directions

The current study highlights the importance of investigating attentional biases towards *and* away from threat in young people. It suggests the dot probe task might not be sensitive to these differences, and therefore that future research should explore attentional bias with alternative paradigms, ideally with increased clinical relevance. The lack of studies on memory bias in anxious youth points to a gap in the literature that needs to be filled moving forward, especially as information processing theories regarding anxiety are highly prevalent. Finally, with a move towards transdiagnostic approaches to understanding mental ill health (Dalgleish et al., 2020), it would be interesting to explore attention and memory biases across groups with comorbid conditions, or to explore whether these information processing biases are transdiagnostic risk factors for specific symptoms.

Conclusion

This review suggests that young people with anxiety show an attentional bias towards threatening stimuli as measured by emotional Stroop tasks, but not when measured by the dot probe task. Attention bias is complicated though and may be better understood in terms of bias towards (vigilance) and bias away (avoidance) from threat. Future research should focus on better understanding this distinction to account for this heterogeneity.

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CHAPTER THREE

Bridging Chapter

Bridging Chapter

The broad aim of this thesis is to explore the relationship between cognition and mental health in children and adolescents. The meta-analysis presented in the previous chapter investigated whether young children and adolescents have biased information processing in two aspects of cognition, attention, and memory. The results revealed no significant evidence for an attentional bias towards threat in young people, although as previously discussed, it is important for future studies to disentangle biases both towards (vigilance) and away (avoidance) from threat. In terms of memory, there were too few studies to run a meta-analysis or conclude whether anxious young people show memory biases for affective information.

The aim of the empirical project presented in the next chapter is to extend the investigation into cognition and mental health in young people, with a particular focus on changes in mental health profiles from mid- to late-adolescence and their relationship to a range of cognitive abilities associated with self- and emotional-regulation.

CHAPTER FOUR

Empirical Research Paper

Prepared for submission to Developmental Science

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Mapping developmental transitions in mental health from mid- to late-adolescence: concurrent and longitudinal links to cognition

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Abstract

Background: Our current understanding of developmental changes in mental health largely focusses on changes between childhood and adolescence and symptom presentations at single time points. Here we focus on changes in mental health between mid- and late adolescence. We aimed to identify mental health profiles at both time points, map transitions across these profiles across development, and explore how changes in profile relate to cognitive function in mid-adolescence.

Method: We used data from 1,304 participants from the IMAGEN cohort, following them from mid- (age 14) to late (age 22) adolescence. We used k-means clustering on data from those with elevated mental health symptoms at both time points to identify common profiles of mental health symptoms. Those with no mental health symptoms formed their own cluster. We mapped transitions between the groups across time and explored how cognitive function at age 14 related to these changes.

Results: We identified three distinct mental health profiles, each with different levels of difficulties in externalising problems, internalising problems, or difficulties with social relationships. These profiles were similar in mid- and late adolescence. Externalising problems were more common in mid- than late adolescence. Persistent externalising and social problems were related to cognitive function in mid-adolescence but persisting internalising problems and problems that emerged or resolved in late adolescence were not.

Conclusion: Profiles of mental health change between mid- and late adolescence, and persistent externalising and social problems are related to earlier cognitive abilities. These data highlight the importance of understanding the developmental context in which mental health problems occur, and the factors linked to their persistence.

Introduction

Adolescence is a period of heightened biological, cognitive, and social change associated with increased risk for mental health difficulties (Blakemore & Mills 2014; Kessler et al., 2005; Tamnes et al., 2017). Worldwide, the prevalence of mental health disorders increases from childhood to adolescence, peaking during late adolescence as young people develop a sense of identity and transition into adulthood (Beauchamp et al., 2018; Costello et al., 2011; Dahl, 2004; Murphy & Fonagy, 2012). Despite this, approaches to understanding developmental changes in mental health typically focus on symptom presentations at a single time point or developmental stage, not accounting for the developmental course of psychopathology or the potentially adaptive nature of such presentations (Lewis & Rudolph, 2014; Willner et al., 2017). Alternatively, they focus on transitions from either childhood into adolescence or adulthood, from early- to mid-adolescence, or from mid-adolescence to adulthood, with little reference to late adolescence (Bartels et al., 2018; Bathelt, Vignoles & Astle, 2021; Benhamou & Astle, 2022; Copeland et al., 2014; Vaillancourt et al., 2013). This period, spanning the late teenage years into the mid-twenties is associated with an increased level of unmet mental health service need, increased vulnerability to substance abuse and reduced access to mental health services provided through schools (Blanco et al., 2008; Compton et al., 2007; Copeland et al., 2015; Kessler et al., 2005). To reduce the long term economic and social burden of mental ill-health (Knapp & Wong, 2020; Rehm & Shelf, 2016) and move towards a proactive model of intervention (Fenwick-Smith et al., 2018), it is necessary to understand how symptoms change in late adolescence, and what predicts these changes. This study adopted a transdiagnostic approach to mapping changes in mental health symptoms from mid- to late adolescence and explored their associations with cognition, concurrently and longitudinally.

The traditional approach to mapping developmental trajectories of mental ill-health relies on diagnostic systems to document prevalence at different ages (Copeland et al., 2014; Moffitt et al., 2015; Stringaris et al., 2018). Costello et al. (2011) documented rates of depression, panic disorder, agoraphobia and substance use disorders increase from childhood to adolescence, while separation anxiety and attention-deficit hyperactivity disorder (ADHD) decrease. Rates of panic disorder, agoraphobia and substance use disorders continue to increase into adulthood while social anxiety and other phobias, ADHD, and disruptive behaviours drop. The categorical diagnostic approach adopted by such studies, and endorsed by international classification systems such as the Diagnostic Statistical Manual (DSM-5; American Psychiatric Association, 2013), runs counter to a wealth of clinical and research evidence showing that mental health and neurodevelopmental disorders are highly comorbid, heterogeneous, variable across time, explained by multiple causes and not captured by a cardinal set of symptoms (Dalgleish et al., 2020; Astle et al., 2021). An alternative transdiagnostic approach emphasises the use of data-driven approaches to delineate more refined phenotypes along dimensions of interest (Astle et al., 2019; Caspi & Moffitt, 2018; Cuthbert & Insel, 2013; Holmes et al., 2021). These approaches allow tailoring of interventions to individual needs rather than single, potentially ill-fitting diagnostic labels (Newby, Mc-Kinnon, Kuyken, Gilbody, & Dalgleish, 2015; Weisz et al., 2012).

Cluster analysis is an increasingly popular method for identifying data-driven subgroups with similar profiles of mental health, cognition, or behaviour (Archibald et al., 2013; Astle et al., 2019; Bathelt et al., 2018, 2021; Kushki et al., 2019; Mareva et al., 2019, 2022). These subgroups typically crosscut diagnostic boundaries and align better with underlying neurobiology than diagnostic groupings (Bathelt et al., 2018; Mareva et al., 2022). Few studies have used these approaches to track the developmental course of mental health. The exceptions

are Bathelt et al. (2021) who used a hierarchical clustering approach to identify profiles of behavioural problems associated with mental health disorders (e.g., hyperactivity, emotional problems) from childhood (10 years) to adolescence (16 years), and Benhamou et al. (in preparation) who used K-means clustering to identify profiles across similar measures at 5, 11 and 17 years. K-means clustering aims to partition a set of observations into clusters (k). In both studies, participants' transitions across the clusters (profiles) were tracked over development. Bathelt et al. (2021) showed that while externalising symptoms such as hyperactivity and conduct problems were common in childhood, decreasing into adolescence, internalising symptoms such as emotional problems and anxiety were more prominent in adolescence, compared to externalising behaviours. Similarly, Benhamou et al. (in preparation) showed behavioural problems reduced between childhood and adolescence, with more differentiated patterns of internalising and externalising symptoms emerging over time. In both studies, factors associated with better family resources and wellbeing (higher family income, education, better caregiver mental health) predicted improvements in mental health problems across development. Bathelt et al. (2021) additionally showed that higher cognitive performance in childhood was associated with a reduction in behavioural problems in adolescence.

The current study

This study used a data-driven clustering approach to identify subgroups of mental health profiles in a sample of 1,304 participants taken from the IMAGEN study (Schumann et al., 2014), – a large scale study examining factors that influence brain development and mental health in adolescence. We focussed on the transition between mid- and late adolescence, (ages 14 and 22 years), as this is an understudied period associated with heightened risk for mental health problems (Beauchamp et al., 2018). We identified clusters of mental health symptoms at each

timepoint using self-report measures from the well-validated Strengths & Difficulties Questionnaire (Goodman, 1997), capturing externalising and internalising symptoms. Transitions across these clusters were tracked from mid- to late adolescence, and associations between these changes and cognitive function were explored.

The developmental transition in late adolescence towards adulthood is marked by changes in social roles and responsibilities and adjustments to personal goals and motivations that require effortful cognitive control to attenuate and regulate behaviour and emotions (Crone & Dahl, 2012). We included measures of delay aversion and risk-taking because impulsive and risky decision-making increases in adolescence (Crone et al., 2016; Dekkers et al., 2022; Rosenbaum & Hartley, 2019), and problems both inhibiting impulsive responses and delaying gratification are associated with elevated externalising symptoms (Barkley, 1997; Chaarani et al., 2017; Nigg et al., 2006; Pollak et al., 2019; Schachar et al., 2011; Wright et al., 2014). The Cambridge Gambling Task was used to measure risk-taking because it provides a measure of delay aversion – a preference for smaller immediate rewards over larger-delayed rewards – alongside measures of the ability to tolerate risk and adjust risk-related behaviours. Dual-processing models posit that affective states have a greater impact on cognitive function in adolescence than in childhood or adulthood (Casey et al., 2016; Crone & Dahl, 2012; Schulman et al., 2016). Thus, an affective go/no go task was used to measure response inhibition to tap into the interaction between affective and cognitive processes. A spatial working memory task, with no affective component, was also included to explore whether cognitive function in the absence of emotional content predicted changes in mental health between mid- and late adolescence.

This was a data-driven, exploratory study so we did not formulate a hypothesis about the mental health profiles that would emerge, the concurrent cognitive features differentiating them,

the ways in which they would change over time, or the cognitive factors that would predict these changes. Instead, we designed the study as an exploratory investigation aiming to address four broad questions: (1) can we identify robust subgroups of adolescents presenting with distinct profiles of mental health at mid- and late adolescence within a large community sample; (2) do the subgroups differ in terms of cognitive function; (3) how do individuals transition across clusters over developmental time, and; (4) does baseline cognitive function differ between those with persisting, resolving or emerging mental health problems from mid- to late adolescence?

Method

Participants

A sample of n = 1,304 participants (males = 611, females = 693) was drawn from the IMAGEN cohort (Time point 1: *Mage* = 13.95 years, SD = 0.45; females, n = 693, *Mage* = 13.95, SD = 0.47; males, n = 611, *Mage* = 13.95, SD = 0.43; Timepoint 2: *Mage* = 22.1 years, SD = 0.71; females: *Mage* = 22.08, SD = 0.67; males: *Mage* = 22.11, SD = 0.75) at T2.

Materials and procedure

Authorisation to access the data was granted by the IMAGEN board (Appendices E, F and G). Data were drawn from the IMAGEN cohort (Schumann et al., 2014), a longitudinal study exploring the biological, psychological, and environmental factors that influence brain development and mental health during adolescence. Data were collected from eight sites across four European countries: London and Nottingham in the UK, Berlin, Hamburg, Mannheim and Dresden in Germany, Paris in France, and Dublin in Ireland. Ethical approval was obtained from the local research ethics committee at each site, and written consent from parents/carers or the

participants, or verbal assent from the participants, was obtained prior to testing. Participants received compensation of up to £100, depending on participation in follow-up assessments. Data were collected at four time points, when participants were aged 13 to 15, 16, 19 and 22.

Data from timepoint 1 (referred to hereafter as T1), when participants were aged 13 to 15 years, and the final assessment point, when participants were 22 years old (referred to hereafter as T2), were analysed in the current study. The data analysed include self-report measures of mental health at T1 and T2, and performance on three cognitive tasks at T1 and two at T2.

Mental health

Self-report versions of the Strengths and Difficulties Questionnaire (SDQ; Appendix H; Goodman, 1997) were administered at T1 and T2. At T1 the children and young people version was administered, with a separate version, S18+, administered at T2. The SDQ is comprised of 25 items measuring social and emotional functioning. Items are organised into five subscales: Emotional Problems, Hyperactivity, Conduct Problems, Peer Problems, and Prosocial behaviour. Age-uncorrected raw subscale scores were used in all analyses to allow for easier comparisons with other studies using the SDQ. Higher scores indicated more severe difficulties for Emotional Problems, Hyperactivity, Conduct Problems and Peer Problems. For the Prosocial subscale, high scores reflected more prosocial behaviour, indicative of fewer difficulties. The SDQ has been widely validated across countries and populations (Capron et al., 2007; Fonseca-Pedrero et al., 2011; Goodman, 1997; Klasen et al., 2000; Ortuño-Sierra et al., 2015), and has good internal consistency, with Cronbach's alpha values ranging from 0.63 to 0.85 (Deighton et al., 2014; Haywood et al., 2014).

Cognition

Cognitive measures from the Cambridge Neuropsychological Test Automated Battery (CANTAB https://www.cambridgecognition.com/cantab; Sandberg, 2011) were administered. At T1, three tasks were completed: the Cambridge Gambling Task (CGT), the Affective Go/No-Go task (AGN) and the Spatial Working Memory task (SWM). The CGT and SWM tasks were repeated at T2.

Cambridge Gambling Task (CGT). The CGT was used to measure risk taking and delay aversion outside of a learning context (all relevant information was presented within each trial). On each trial, participants were presented with a row of ten boxes across the top of the screen, some red and some blue. The ratio of red to blue boxes could range from 1 red: 9 blue, through to 1 blue: 9 red. Participants were first required to guess whether a yellow token was hidden in one of the boxes by clicking on a blue or red rectangle presented on screen. They started with a set number of points and were required to bet a proportion of these on the confidence of their judgement. The bet proportions were fixed across trials at 5%, 25%, 50%, 75%, or 95%, and presented on screen sequentially with a fixed delay between each proportion, requiring participants to delay their responses to select their preferred bet. The presentation order (ascending or descending) of the bet proportions was varied across trials. Participants gained additional points for correct guesses, and lost points for incorrect guesses. Multiple indices captured different aspects of risk-taking. In this study we used the measures of delay aversion/impulsivity, risk taking, and risk adjustment as they reflect most closely the aspects of cognitive function linked to risky behaviour and mental health problems in adolescence (Crone et al., 2016; Chaarani et al., 2017; Nigg et al., 2006; Pollak et al., 2019). Impulsivity/delay aversion was calculated as the difference in average betting ratios chosen across ascending and descending conditions for optimal trials (those where the participant chose the colour with the

most boxes). Larger negative values (lower values) correspond to impulsive betting (e.g., choosing the bets that appear on screen sooner). Risk taking was measured as an average of the proportion of points participants were willing to bet on optimal trials. Higher values corresponded to betting a higher proportion of points, indicating someone was better able to tolerate risks (e.g., they were less risk averse/more willing to take risks). Risk adjustment was included to capture participants' tendencies to bet more when the odds were in their favour, with lower scores representing poorer risk adjustment (e.g., being less likely to switch the choice of coloured box when the rules or ratio of blue: red boxes changed).

Spatial Working Memory (SWM). The SWM task was a self-ordered, serial search task, in which participants were presented with a set of boxes on screen and told to search for a token that was hidden beneath one of them. Participants searched the boxes by clicking on them one at a time. When the token had been found, participants were shown the same set of boxes and instructed to find the next token. They were told that once a token had been found under a particular box, it would not appear under the same box again within that block of trials. Thus, to perform the task well, participants had to remember which boxes the token had already been hidden under in any block of trials. The number of boxes on screen increased within a set of trials from 4 to 6 to 8, to increase the memory load. A new block of trials began once a participant had found the token under each box. The change in block was marked by a change in position and colour of the boxes. A higher score indicated more errors, suggesting poorer working memory. Each memory load condition (i.e., number of boxes on the screen) was presented four times resulting in 72 tokens in total that had to be located across 12 search sets. Between trial errors were recorded, representing the number of times a participant searched a

box in which a token had been found in an earlier trial within a block. The higher the score, the greater the number of errors, indicating poorer working memory.

Affective Go/No-Go (AGN). The AGN task indexed response inhibition for affective words. Participants were presented with single words on screen that were affectively valanced (happy or sad). Eight blocks of trials, each containing 18 words (nine positive, e.g., 'happy', and nine negative, e.g., 'useless'') were presented. Each word was presented on screen for 300ms, with a 900ms inter stimulus interval. Participants were instructed to press the space bar in response to positive words but not negative words in the first two blocks, but to switch to pressing the space bar in response to negative and not positive words in the next two blocks. The instructions (conditions) continued to alter every two blocks: positive, positive, negative, negative, positive, positive, etc. A measure of response bias for negative words was calculated as the mean difference between the response times (latency) for positive vs negative target words. Higher values indicated faster response times to negative than positive words (affective bias towards negative stimuli).

Analysis Plan

A data-driven K-means clustering algorithm was applied to the person-by-person associations across the SDQ subscales at T1 and T2 for children with elevated mental health problems to identify subgroups with similar profiles of mental health strengths and difficulties. SDQ ratings and cognitive performance were then compared between each of the derived subgroups and a group of adolescents with no mental health difficulties (non-clinical group) at T1 and T2. The number of participants who moved across the derived clusters from T1 to T2 was then calculated, and the cognitive function of individuals with persisting, emerging, or resolving mental health problems, and stable no difficulties (non-clinical) was explored. All analyses were

completed in R-version 4.2.0, using the individual packages described and psych_2.2.3 (Revelle, in preparation).

Data screening

Participants assessed during the first wave of IMAGEN testing, when they were aged 13–15 years, who had SDQ data at both timepoints were included in the current analyses. T1 SDQ profiles were compared between participants who had SDQ data at T2 and those who did not. There were significant group differences in T1 ratings of prosocial behaviour, conduct problems, and hyperactivity/inattention (all *p*s<.05, see Table S1 in supplementary materials). Those without follow-up data had elevated conduct problems and hyperactivity/inattention, and lower levels of prosocial behaviour at T1, but the effect sizes were small (Cohen's d=.24, .21 and .16 respectively).

Clustering

SDQ subscale scores were used to identify subgroups of adolescents with similar profiles of mental health at T1 and at T2. The same procedure was followed at both times points. In the first step, non-clinical participants without mental health problems were allocated to a 'no difficulties' (ND) group on the basis that they had scores in the 'close to average range' according to the SDQ scoring protocol (see Supplementary Materials, Figure S2). At T1, 520 (40%) participants were assigned to the ND group, leaving 784 participants with elevated difficulties who were included in the next step of clustering. At T2, 649 (49.76%) were identified as having ND, leaving 655 with elevated difficulties for further clustering. To optimise clustering performance (Dalmijer et al., 2020), the data for those with elevated difficulties, was reduced using uniform manifold approximation and projection (UMAP; McInnes et al., 2018). UMAP initially builds a topological representation of the original data, before minimising the cross-

entropy between the new lower-dimensional space and the original higher-dimensional space to optimise the lower-dimensional embedding. This method was favoured due its ability to preserve the local and global structure of the original data, its flexibility regarding choice of distance metrics, and its computational efficiency. UMAP parameters number of neighbours was set at 20 and a minimum distance at 0.0001 to allow for denser clusters and cleaner separations. K-means clustering (k=2-15) was then applied to the UMAP-reduced space using R-package NbClust 3.0 (Charrad, et al., 2014). The optimal number of clusters was chosen based on silhouette scores above 0.5 (Dalmaijer et al., 2020; Bathelt et al., 2021).

Cluster characterisation. The clusters derived at T1 and T2 were characterised in the same way. First, chi-square tests were used to compare the proportion of males and females in each cluster to the proportion of males and females in the whole sample. Planned comparison, pairwise t-tests were used to compare the SDQ ratings and cognitive test performance between each cluster and the non-clinical ND group.

Cluster transitions. The number of participants whose cluster membership changed across time was quantified by counting the number of adolescents who moved between any of the derived clusters and the ND group between T1 and T2. A series of planned comparison pairwise t-tests were used to characterise the T1 cognitive functioning of three types of transitions. These were: 1) persisting individuals who had difficulties across T1 and T2; 2) resolving – those who had difficulties at T1 but who transitioned to the ND group at T2; 3) emerging – those who were in the ND group at T1 but had difficulties at T2. The classification of persisting, resolving and emerging difficulties was completed for simple transitions and for cluster-specific transitions. For simple transitions, cluster membership was not used to differentiate the specific type of mental health difficulties. For cluster-specific transitions

changes in the type of mental health profile were considered. The planned comparisons conducted are detailed in Table 4.1 for transparency. To pre-empt the results, a three cluster solution was optimal at both time points, so for ease of interpretation, we report the planned comparisons based on a 3-cluster solution at both T1 and T2 in Table 4.1.

Table 4.1

Planned comparisons to explore cognitive function in relation to persisting, resolving, or emerging mental health problems

Cluster-specific transitions	***Transition***	***Compared to***
Emerging	T1 ND to cluster 1	ND at T1 and T2
	T1 ND to cluster 2	ND at T1 and T2
	T1 ND to cluster 3	ND at T1 and T2
Persisting	Stays in cluster 1 T1 to T2	ND at T1 and T2
	Stays in cluster 2 T1 to T2	ND at T1 and T2
	Stays in cluster 3 T1 to T2	ND at T1 and T2
Resolving	T1 cluster 1 to T2 ND	Stays in cluster 1 (soc) T1 to T2
	T1 cluster 2 to T2 ND	Stays in cluster 2 (int) T1 to T2
	T1 cluster 3 to T2 ND	Stays in cluster 2 (ext) T1 to T2
Simple transitions		
Emerging	T1 ND to T2 clusters 1, 2 or 3	ND at T1 and T2
Persisting	Stays in cluster 1, 2 or 3 T1 to T2	ND at T1 and T2
Resolving	T1 cluster 1,2 or 3 to T2 ND	ND at T1 and T2

Results

Clustering

UMAP data reduction combined with K-means clustering was applied to the SDQ data at T1, and separately to the SDQ data at T2, for all participants with scores outside the average range. Those with scores in the average range formed a no difficulties cluster and were used as a comparison group.

T1 cluster identification

The results of K-means (k = 2-15) clustering applied to the dimensionally-reduced dataset at T1 are presented in Figures 4.1 and 4.2.

Figure 4.1

Silhouette scores of K=2-15 cluster solutions at T1.

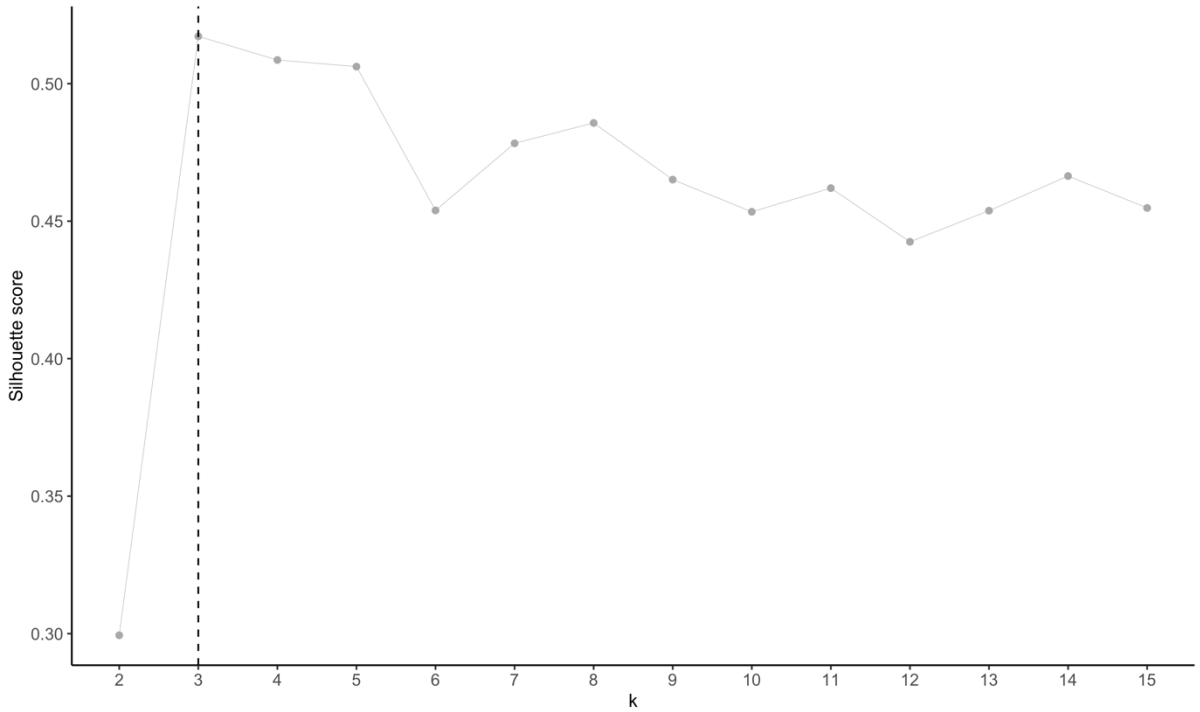
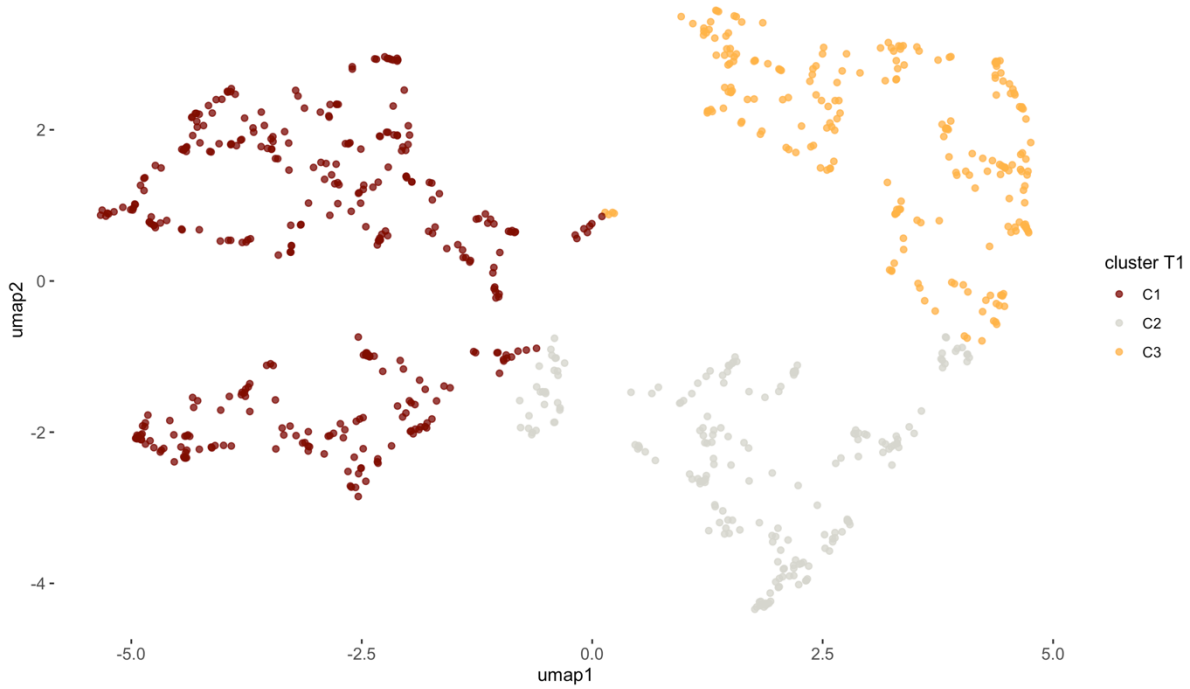


Figure 4.1 shows the average silhouette for different numbers of cluster solutions. Inspection of the silhouette coefficients indicated that a three-cluster solution was optimal (Figure 4.1). The reduced 2D UMAP space on which each participant's SDQ derived variable was projected is presented in Figure 4.2, with clusters coded in different colours.

Figure 4.2

UMAP space showing a 2D projection of each participant's SDQ score at T1.



T1 Cluster characterisation

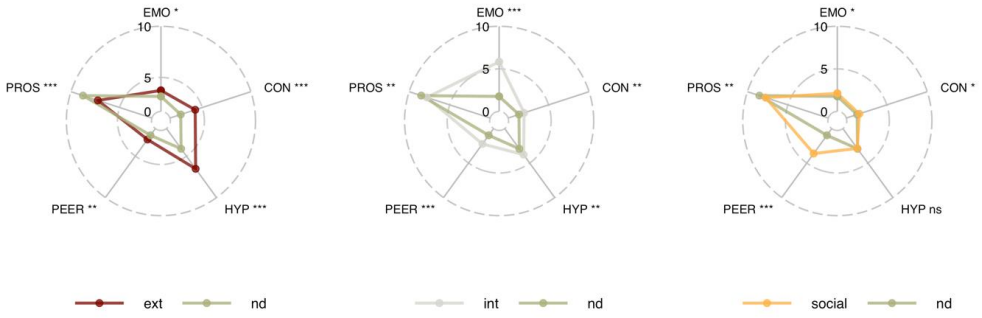
The SDQ profiles of the three clusters derived at T1 are shown as radar plots in Figure 4.3. SDQ scores are compared to the no difficulties (ND) group in each case and represented as

effect sizes for ease of interpretation (see Supplementary Table S3 for the full comparison of SDQ scores across clusters). Examination of these plots revealed significant difficulties across most subscales of the SDQ for each cluster relative to the ND group, with specific areas of more severe problems distinguishing them from one another.

Relative to the ND group, the first cluster had significantly more difficulties across all SDQ subscales but showed the most pronounced problems with hyperactivity (d= 1.73), behavioural conduct (d = 1.41), and prosocial behaviour (d = -1.34). As these problems represent overt behavioural/mental health problems, and because the Hyperactivity and Conduct Problems subscales from the SDQ form an index of externalising problems (Goodman et al., 2010), this profile was labelled Externalising (abbreviated to Ext. in subsequent Tables and Figures).

Figure 4.3

SDQ profiles of each cluster relative to the no difficulties group at T1.



Note. Group differences are shown as effect sizes (* = small (>0.2 and <0.5), ** = medium (>.05 and <0.8), *** = large (>0.8)). Note. ext=externalising profile; int=internalising profile; soc=social profile; nd= no difficulties group.

The second cluster also had significantly more severe problems across all subscales of the SDQ compared to the ND group, with relatively more severe emotional problems (d = 3.10) and difficulties with peer relationships (d = 1.12). The sum of these two scales is widely used to index internalising problems (Goodman et al., 2010), so this cluster was labelled Internalising (abbreviated to Int. in Tables and Figures).

The third cluster had significantly more difficulties than the ND group on all SDQ subscales, except for Hyperactivity. The most pronounced difficulties for this cluster were in

making and sustaining friendships (Peer Relationships; d = 2.66) so it was labelled Social (abbreviated to Soc. on Tables and Figures).

The total number of participants and the numbers of males and females in each cluster at T1 is presented in Table 4.2. The largest group were those with no difficulties, followed by those with an externalising profile. A series of chi-square tests (see Supplementary Table S4) revealed that there were significantly more males than females in the externalising and social clusters (*p*s<.001), and significantly more females in the internalising cluster (*p*<.001).

Table 4.2

Number of participants in each cluster at T1.

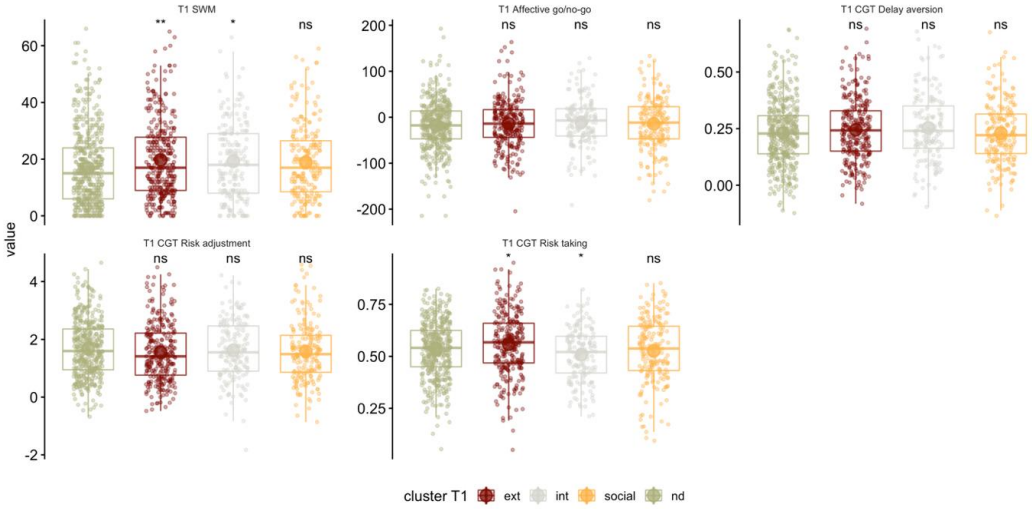
	Ext	*Int*	*Soc*	*ND*
n				
Female	153	151	92	297
Male	204	48	136	223
Total	357	199	228	520

Note. Ext=externalising profile; Int=internalising profile; Soc=social profile; ND= no difficulties group.

The cognitive profiles of the clusters derived at T1 are presented in Figure 4.4. The cognitive performance of each cluster was compared to the no difficulties group (see Supplementary Table S5). Those in the externalising cluster had significantly poorer spatial working memory scores (*p*=.003), and significantly higher risk-taking scores (*p*=.02) – indicating they were more prone to taking risks – than those with no difficulties.

Figure 4.4

Cognitive profiles at T1 by cluster.

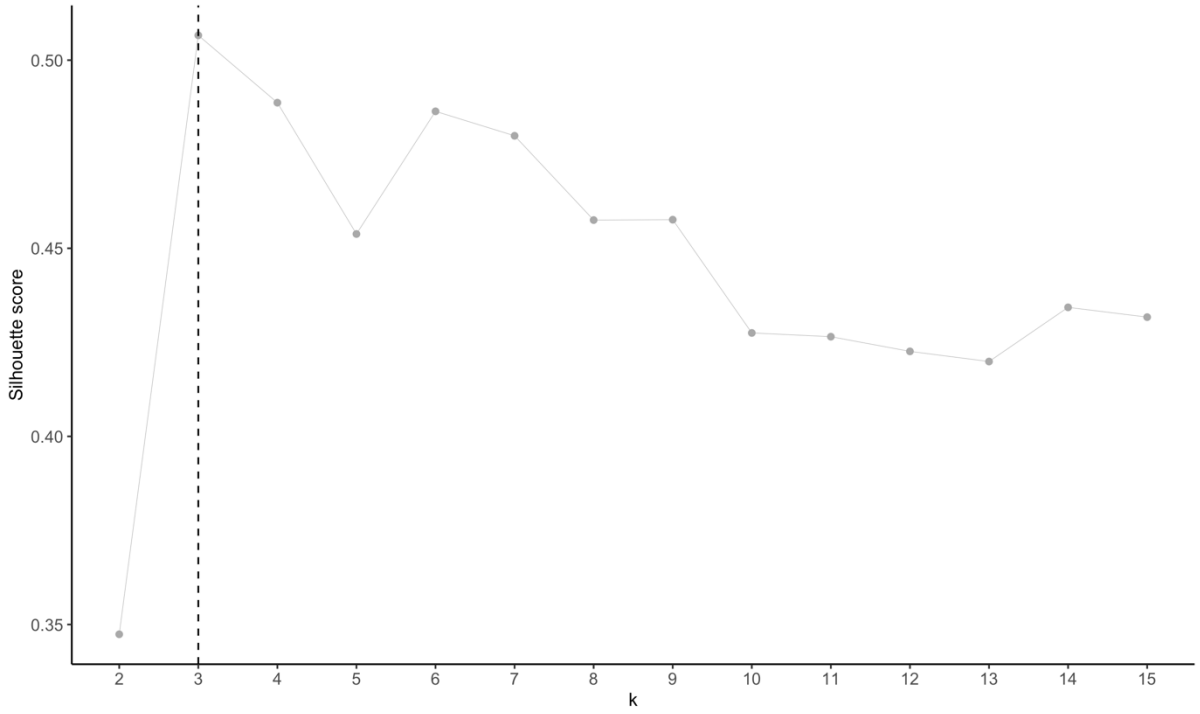


Note. Each cluster is compared to the no difficulties group. *=p<.05, **=p<.01. ext=externalising profile; int=internalising profile; soc=social profile; nd= no difficulties group.

Those in the internalising cluster also had significantly poorer working memory than the no difficulties group (p = 0.04) but were significantly less likely to take risks than the no difficulties group, as shown by significantly lower scores (p=.04). There were no significant differences in cognitive performance at T1 for those in the social cluster relative to the no difficulties group, and there were no significant group differences on the Affective Go/No-Go task.

Figure 4.5

Silhouette scores of K=2-15 cluster solutions at T2.

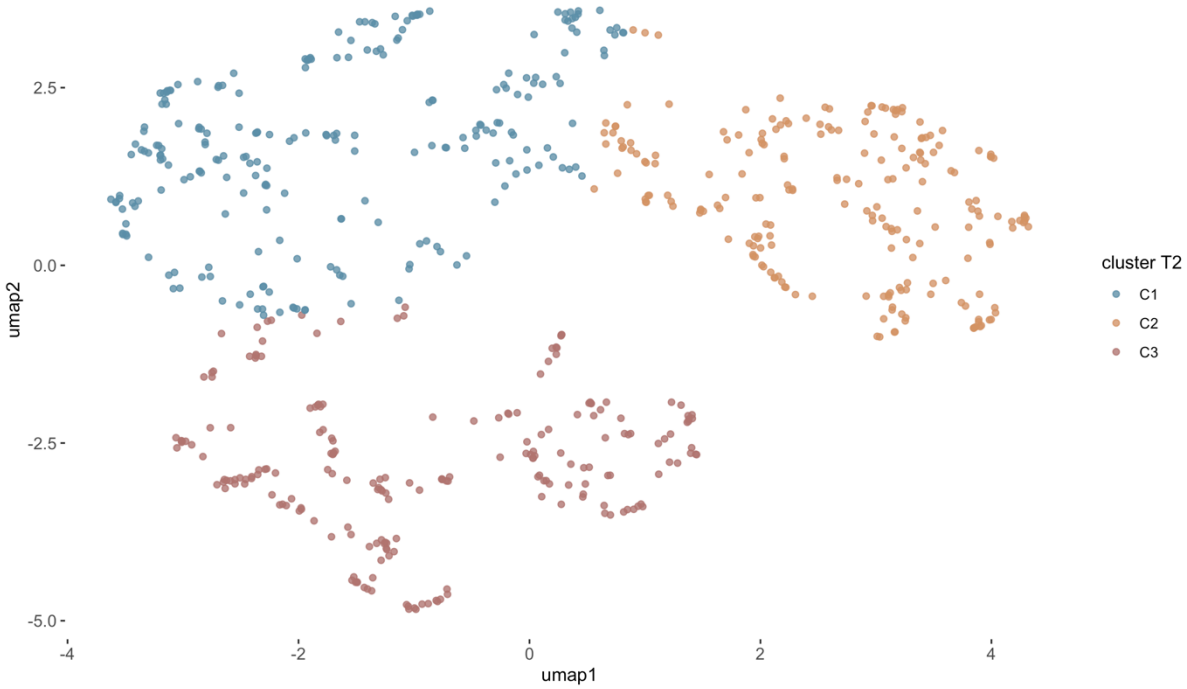


T2 cluster identification

K-means (k = 2-15) clustering was applied to the dimensionally-reduced dataset at T2. Figure 4.5 shows the average silhouette for cluster solutions ranging from 2 to 15, and as at T1, inspection of the silhouette coefficients indicated that a three-cluster solution was optimal as this is where the silhouette coefficient exceeded the .5 threshold (Figure 4.5). While a 3-cluster solution was optimal at T1 and T2, it is important to note that the same participants may not belong to the same clusters at T1 and T2 and that the profiles of the clusters changed subtly between time points. The 2D UMAP space on which each participant's SDQ derived variable was projected is presented in Figure 4.6, with clusters coded in different colours.

Figure 4.6

UMAP space showing a 2D projection of each participant's SDQ score at T2.

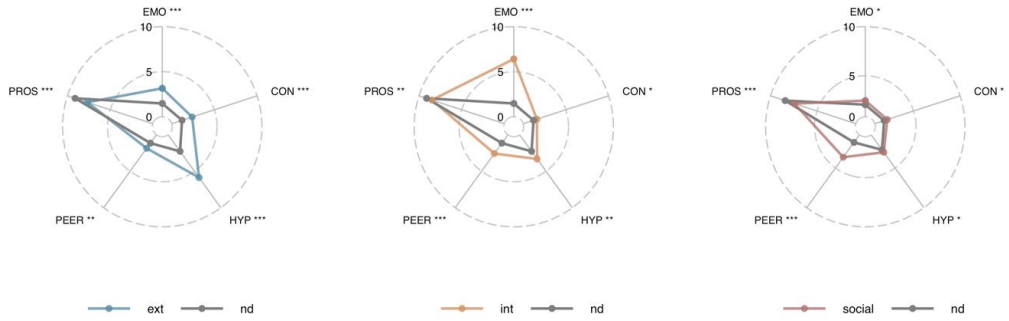


T2 cluster characterisation

The SDQ profiles of the three clusters derived at T2 are shown as radar plots in Figure 4.7. As at T1, SDQ scores are compared to the no difficulties (ND) group in each case and represented as effect sizes (see Supplementary Table S6 for means and SDs).

Figure 4.7

SDQ profiles of each cluster relative to the no difficulties group at T2



Note. Group differences are shown as effect sizes. (* = small (>0.2 and <0.5), ** = medium (>.05 and <0.8), *** = large (>0.8)). Ext=externalising profile; int=internalising profile; soc=social profile; nd= no difficulties group.

The first cluster had significant difficulties across all subscales of the SDQ relative to the no difficulties group at T2 but was characterised by relatively more pronounced problems with hyperactivity *(d* = 2.20*)*, conduct problems *(d* = 1.15*)* and prosocial behaviour (d=-1.13) as at T1, and emotional difficulties (*d* = 1.03). As two of these areas correspond to overt behaviours and form the externalising problems index of the SDQ (Goodman et al., 2010), this profile was labelled Externalising (abbreviated to Ext. in subsequent Tables and Figures), as at T1.

The second cluster also had significantly more severe problems across all subscales of the SDQ compared to the ND group, with relatively more severe emotional problems (d = 3.64) and

difficulties with peer relationships (d = 1.50). This profile matched that of the second cluster at T1, and so was similarly labelled Internalising (abbreviated to Int. in Tables and Figures).

The third cluster was also characterised by significantly more problems across all subscales of the SDQ relative to the no difficulties group, with the most pronounced areas of difficulty being in establishing and maintaining peer relationships (d=2.46) as at T1 and more pronounced difficulty exhibiting prosocial behaviour (d=-.97) than at T1. As at T1, this cluster was again labelled social (abbreviated to Soc. in figures and tables).

The distribution of participants and the numbers of males and females in each cluster derived at T2 is presented in Table 4.3. The largest cluster had no difficulties, and this was larger than at T1 (n=520 vs n=649). The discrepancies in the size of the internalising and externalising clusters were reduced at T2 (T1 n ext:int = 357:199, T2 n ext:int=232:213), mostly due to there being fewer people with externalising problems (T1 n=357, T2 n=232). As at T1, chi squared tests revealed there were significantly more males than females in the externalising clusters, and significantly more females than males in the internalising cluster (p<.001). There were no significant differences in the numbers of males and females in the social cluster (p=.05). See Supplementary Table S7 for the results. Overall, there were 50.23% of the population with difficulties at T2, a reduction from T1.

Table 4.3

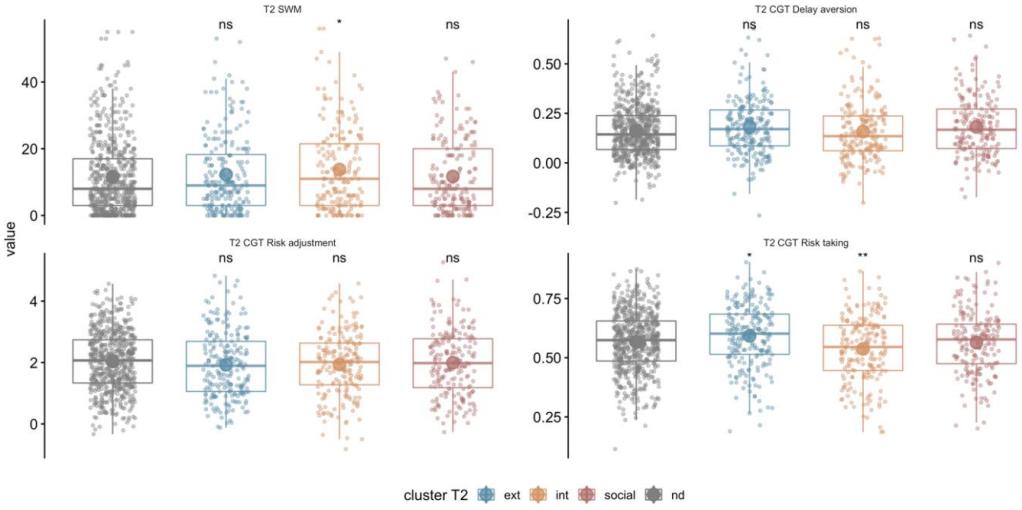
Number of participants in each cluster at T2.

n	*Externalising*	*Internalising*	*Social*	*No Difficulties*
Female	99	163	98	336
Male	133	50	112	313
Total	232	213	210	649

The cognitive profiles of the clusters derived at T2 are presented in Figure 4.8. Those in the externalising cluster were significantly more likely to take risks than those in the no difficulties group *(p* = 0.01), but there were no other significant group differences. Those in the internalising cluster were significantly less likely to take risks than the no difficulties group (*p* = 0.01) and had significantly poorer working memory performance *(p* = 0.03). This profile was identical to the internalising cluster at T1. As at T1, there were no significant group differences in cognitive performance between those in the social difficulties cluster and those in the no difficulties group.

Figure 4.8

Cognitive profiles at T2 by cluster.



Note. Each cluster is compared to the no difficulties group. *=p<.05, **=p<.01. ext=externalising profile; int=internalising profile; soc=social profile; nd= no difficulties group.

Transitions

Transitions in mental health profiles between T1 and T2 were mapped in two ways. First, cluster-specific transitions were considered (e.g., movement from a specific cluster at T1 to a different cluster at T2 or staying in the same cluster over time). Second, simple transitions were mapped (e.g., a change from mental health difficulties at T1, not split by cluster-type, to no difficulties at T2, persisting difficulties of any type, or having no problems at T1 and any type of difficulty at T2, irrespective of cluster membership).

Cluster-specific transitions

The numbers and percentages of adolescents transitioning across clusters between T1 and T2 is shown in Table 4.4. Most adolescents with no difficulties at T1 continued to have no difficulties at T2. Across the three clusters with different profiles of difficulties at T1, approximately 40% had transitioned to the no difficulties group by late adolescence. The remaining 60% had persistent problems, and for approximately half (30% of the cluster) their profiles of mental health problems did not change (i.e., they remained in the same cluster across time).

Table 4.4

Cluster-specific transitions between mid- (T1) and late- (T2) adolescence

Cluster at T1	Cluster at T2	N	%
ND	ND	333	64
	Ext	59	11
	Int	65	12
	Soc	63	12
Ext	ND	141	40
	Ext	113	32
	Int	54	15
	Soc	49	14
Int	ND	76	38
	Ext	32	16
	Int	63	32
	Soc	28	14
Soc	ND	99	43
	Ext	28	12
	Int	31	14
	Soc	70	31

Note. ext=externalising profile; int=internalising profile; soc=social profile; nd= no difficulties group.

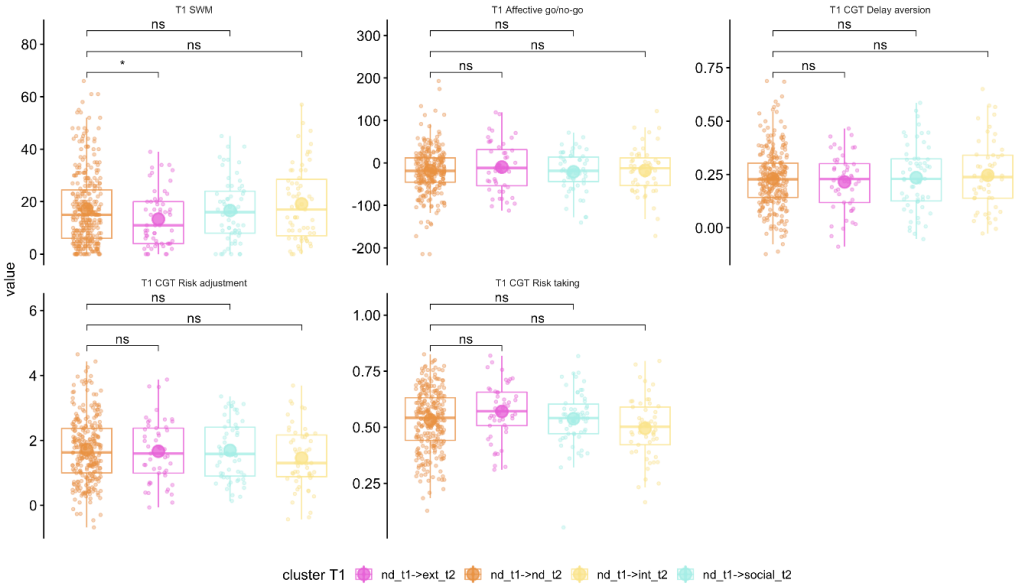
Cluster-specific transitions and cognitive function

To explore the relationship between changes in mental health over time and cognitive function, the cluster-specific transitions between T1 and T2 were classified as either persisting, emerging, or resolving. There were three groups with emerging difficulties: i) those with no difficulties at T1 and a profile of externalising problems at T2; ii) those with no difficulties at T1 and a profile of internalising problems at T2; iii) those with no difficulties at T1 and a profile of social difficulties at T2. The cognitive function of each of these groups at T1 was compared to the T1 cognitive function of the group of who had no difficulties across time in a series of

planned comparison pairwise t-tests (see Figure 4.9 and Table S8). The results revealed that those who developed externalising problems had significantly better T1 spatial working memory than those with no difficulties. There were no other significant group differences.

Figure 4.9

Differences in T1 cognitive performance for those with different profiles of emerging mental health problems.



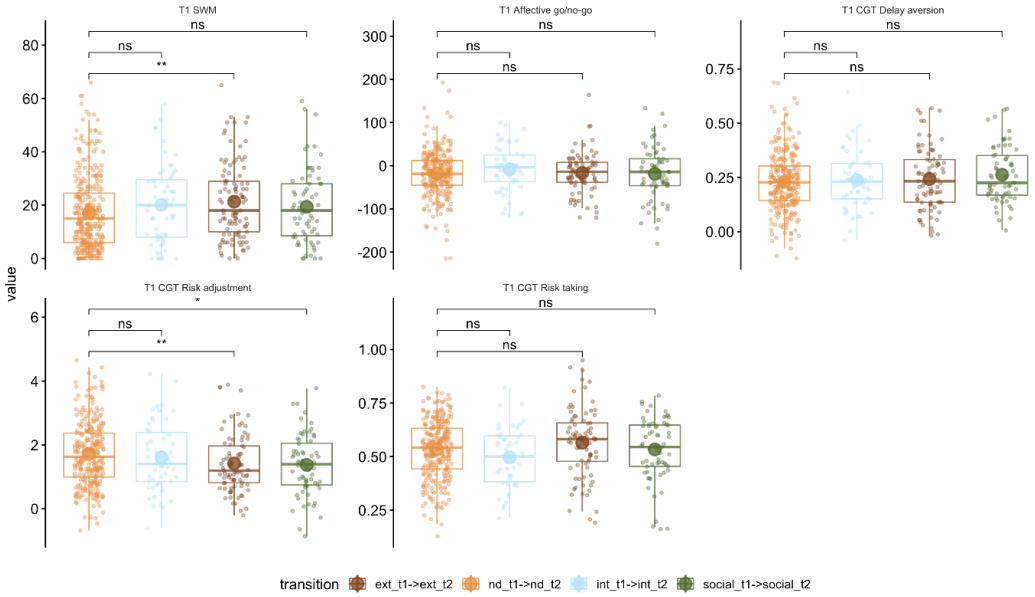
Note. ext=externalising profile; int=internalising profile; soc=social profile; nd= no difficulties group.

There were three groups with persisting difficulties longitudinally, classified as such because their profile of problems did not change between T1 and T2. There were: i) those with relatively more elevated externalising problems at T1 and T2, than any other problems; ii) those with relatively more elevated internalising problems at both time points, and iii) those with relatively more problems with social difficulties at T1 and T2. The T1 cognitive function of each

of these groups was compared to T1 cognitive function of whose had no difficulties at T1 and who continued to have no difficulties at T2 (see Figure 4.10, and Table S9). The results revealed that those with persistent problems with externalising symptoms had poorer spatial working memory and were less able to adjust their risk related behaviour than those who were in the stable no difficulties group. Those who had a profile of persistent difficulties with social difficulties were also significantly less able to adjust their risk related behaviour compared to those with a profile of no difficulties over time. There were no other significant group differences.

Figure 4.10

Differences in T1 cognitive performance for those with persisting mental health problems that do not change in profile over time.

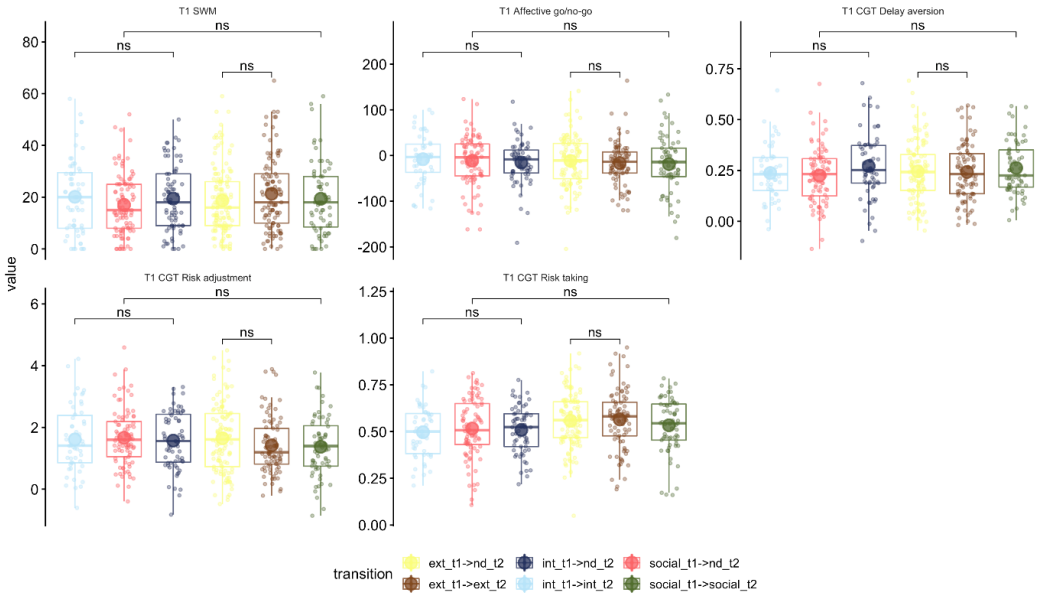


Note. ext=externalising profile; int=internalising profile; soc=social profile; nd= no difficulties group.

The third category of transitions, resolving, also had three groups. Each group's T1 cognitive function was compared to that of a group who had persisting difficulties in the area in which those with resolved problems had difficulties at T1. The comparisons were therefore: i) those with externalising problems at T1 who moved to the no difficulties group at T2 compared to those with persisting externalising problems at T1 and T2; ii) those with internalising problems who moved to the no difficulties group at T2 compared to those with persisting problems at T1 and T2; and iii) those with social difficulties at T1 who moved to the no difficulties group at T2 compared to those with persisting social problems at T2. The outcomes of these comparisons are shown in Figure 4.11 (see Table S10). There were no significant group differences.

Figure 4.11

Differences in T1 cognitive performance for those with resolving mental health problems compared to those with problems that persist and do not change in profile over time.



Note. ext=externalising profile; int=internalising profile; soc=social profile; nd= no difficulties group.

Simple transitions

To explore simple transitions in mental health longitudinally, adolescents were classified as having mental health problems if they were in any of the three clusters (internalising, externalising or social), and as not having mental health problems if they were in the no difficulties group. In other words, at each timepoint, the three 'difficulties' clusters were collapsed. This enabled us to explore three simple transitions: i) having mental health problems of any type at T1 that resolve by T2 (resolving); ii) having mental health problems of any type at T1 that persist in any form at T2 (persisting), and iii) having no mental health problems at T1,

but difficulties of any type at T2 (emerging). We also recorded the number of adolescents with no difficulties at T1 and T2. The number and percent of adolescents following each of these transitions is shown in Table 4.5.

Table 4.5

Simple transitions between mid- (T1) and late- (T2) adolescence

Simple Transition	N	%
No difficulties T1 and T2	333	26
Emerging difficulties T1 to T2	187	14
Persisting difficulties T1 to T2	468	36
Resolving difficulties T1 to T2	316	24

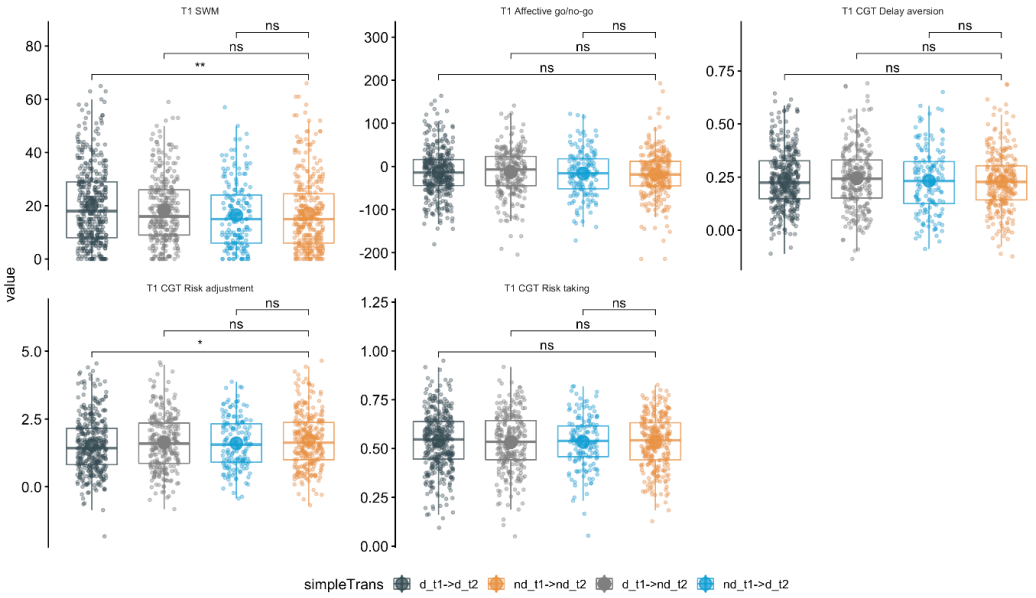
The largest proportion of adolescents had persisting difficulties from T1 to T2 (36%), with about a quarter of the sample either having a stable profile of no difficulties over time or problems that resolved. Mental health problems emerged over time for approximately 14% of the sample.

Simple transitions and cognitive function

The T1 cognitive function of each of the three transitioning groups (emerging, resolving and persisting) was compared to that of the group who had no difficulties across time in a series of planned comparisons. The results revealed that those who had persistent mental health problems had poorer spatial working memory and were less able to adjust their risk-related behaviours than those with a stable profile of no difficulties. There were no other significant group differences (see Figure 4.12, Table S11).

Figure 4.12

Differences in T1 cognitive performance for those with resolving, emerging or persisting mental health problems, irrespective of type or profile of mental health symptoms.



Note. ext=externalising profile; int=internalising profile; soc=social profile; nd= no difficulties group.

Discussion

This study used a data-driven approach to identify changes in mental health profiles between mid- and late adolescence, and associations between these transitions and cognitive function. Three distinct profiles of mental health difficulties were identified. One was characterised by relatively more severe externalising symptoms, another by relatively more severe internalising problems, and a third by difficulties with social relationships. The same three profiles emerged during mid- and late adolescence, with subtle differences in their composition between time points and some differences in the participants represented in each of them. An inability to adjust risk-taking behaviour in response to contextual information was linked to persistent externalising and social problems from mid- to late adolescence, and poor spatial working memory was linked to continuing externalising problems. These results are discussed below.

Mental health profiles

Three data-driven subgroups were identified among individuals with elevated scores on the SDQ (Goodman, 1997) during mid (age 14) and late adolescence (age 22). All three had broad ranging mental health problems relative to a subgroup of individuals classified as having no mental health problems, but were distinguished from one another by different profiles of relative difficulties: predominantly externalising, predominantly internalising or predominantly social problems. These cluster profiles align with three symptom dimensions identified in contemporary hierarchical models of psychopathology. These frameworks (e.g., the Hierarchical Taxonomy of Psychopathology, HiTOP, Kotov et al., 2017) include a general factor of psychopathology (p factor), which sits above spectra that align with broad internalising and externalising factors – dimensions that correspond to the profiles of the internalising and

externalising clusters found here. These spectra then become progressively more specific, breaking down into lower-order dimensions. One such dimension, social maladjustment, predicts peer relationship problems (Holmes et al., 2021), consistent with the profile of our social cluster. Our clustering approach therefore provides complementary information to dimensional models of psychopathology. It also goes beyond defining broad dimensions that differentiate individuals, enabling us to plot an individual's location in multidimensional space and their transition across developmental time. In doing so, our data reveals that individuals exist with profiles of elevated mental health problems in particular domains that map on to single dimensions of psychopathology, and that these profiles can change between mid- and late adolescence. In the following sections, the detailed profiles of the three clusters are considered.

Cluster 1 – Externalising

One cluster was characterised by relatively more severe externalising symptoms. In mid-adolescence, this profile was associated with relatively more severe conduct problems, elevated levels of hyperactivity, and more antisocial behaviour. By late adolescence, it also included elevated emotional problems. This suggests individuals with externalising symptoms that persist from mid-adolescence to late adolescence are likely to develop equally severe internalising problems, reflecting trends observed in other studies showing early externalising symptoms predict later internalising symptoms (Dugre et al., 2019; Kjeldsen et al., 2016). At both time points, this profile was associated with increased risk taking. This aligns with previous findings showing that difficulties inhibiting impulsive responses and delaying gratification in adolescence are associated with risk-taking (Dumontheil, 2016) and increased vulnerabilities to elevated externalising symptoms (Barkley, 1997; Chaarani et al., 2017; Nigg et al., 2006; Pollak et al., 2019; Schachar et al., 2010; Wright et al., 2014).

Cluster 2 – Internalising

A second subgroup had more pronounced difficulties with emotional problems and peer relationships. As the sum of these two subscales of the SDQ indexes internalising problems (Goodman et al., 2010), it was labelled internalising. The profile of this cluster did not change between mid- and late adolescence: at both time points individuals in this cluster had relatively more severe internalising problems, accompanied by poorer working memory and increased risk aversion relative to adolescents with no mental health difficulties. Associations between poor working memory and internalising symptoms in adolescence are well documented (Owens, Stevenson, Norgate, & Hadwin, 2008), and may reflect either the negative impact of anxious or depressive symptoms on the limited resources of working memory (Owens et al., 2014; Visu-Petra et al., 2013), or the impact of poor working memory on the ability to direct attention away from worrisome or negative thoughts (Koster et al., 2017; Rinsky & Hinshaw, 2011). Existing evidence for associations between altered risk-taking behaviour and internalising symptoms in adolescence is mixed, typically finding no links or positive correlations between increased risk taking and increased psychological distress (Prendergast et al., 2019; Spriggs and Halpern, 2008). Finding that risk taking was lower in adolescents with a predominantly internalising profile suggests they may exercise more caution and require more certainty when making decisions – something which is more typically seen in adulthood (Tymula et al., 2012) – and may reflect more general patterns of avoidant behaviour associated with internalising symptoms (Peris & Galvan, 2021).

Cluster 3 – Social

The third cluster was marked by difficulties in social functioning, with a profile of relatively more severe problems with peer relationships at both time points, accompanied by

elevated antisocial behaviour in late adolescence. There were no differences in cognitive function between adolescents with this profile and those with no mental health problems. The absence of an association between cognitive difficulties and elevated social difficulties could be genuine, with profiles of pronounced social problems arising through social or environmental factors. However, it might also reflect the limited range of cognitive tasks included in this study. Appropriate social interaction relies on pragmatic communication skills. In turn these skills rely on structural (formal) language knowledge (Redmond et al., 1998) and a range of executive functions (Tannock et al., 1996) to facilitate monitoring and maintaining appropriate topics of conversation and planning coherent and understandable speech. It is therefore possible that social difficulties are associated with cognitive skills, such as those related to communication problems, that were not assessed in the current study.

Prevalence

A large proportion of adolescents were assigned to the no difficulties group at both time points. There were fewer adolescents in this group in mid- compared to late adolescence, suggesting overall prevalence rates reduce over time. Consistent with this, our exploration of simple transitions – difficulties that either emerged, resolved, or persisted over time, irrespective of profile – revealed that mental health problems resolve for more adolescents than those for whom they emerge. This runs contrary to data suggesting mental health problems increase into late adolescence (Beauchamp et al., 2018). That said, our overall prevalence rates were much higher at both times points than current estimates suggest. Our clustering data suggest as many as 60% of adolescents experience impactful symptoms in mid adolescence, and 50% in late adolescence, compared to published estimates of 14%–25% (Global Health Data Exchange, 2019; Oksanen et al., 2017). Across both time points, males were overrepresented in the

externalising subgroup and females in the internalising subgroup, which is consistent with prevalence rates previously reported between gender groups (Boyd et al., 2015; Seedat et al., 2009).

Transitions

Transitions between clusters were remarkably similar for each of the three profiles. Mental health problems resolved for approximately 40% of adolescents with either an externalising, internalising, or social profile between 14 and 22 years of age. Approximately 30% of each cluster had a similar profile of mental health problems across time points. The remaining 30% transitioned to one of the other two profiles, in each case with a reasonably even split between the clusters they moved into.

There were more adolescents in the externalising cluster than the internalising or social clusters during mid-adolescence, but this distribution was more even in late adolescence due to a reduction in the number of adolescents with predominantly externalising problems. This reduction is consistent with Bathelt et al.'s (2021) study of transitions in mental health from childhood to adolescence showing that externalising symptoms such as hyperactivity and behavioural difficulties reduce with age. However, it is worth noting that those participants who did not have data at late adolescence, had elevated externalising difficulties at mid-adolescence, comparative to participants with data at both time points. Although the effect sizes were small, this may contribute to this reduction.

To explore the relationship between changes in mental health over time and cognitive function, transitions were classified as either emerging (mental health problems emerge in late adolescence), persisting (mental health difficulties are present in mid- and late adolescence), or resolving (mental health problems at age 14 are no longer evident at age 22). The relationship

between these patterns of transition was explored in relation to cognitive function at mid-adolescence.

Our data revealed that both spatial working memory and the ability to adjust risk-related behaviours were related to problems that persisted from mid- to late adolescence, but not to problems that resolved or emerged over time. Exploration of the cluster-specific transitions revealed that this effect was driven by persistent externalising problems, which were related to both poorer spatial working memory and risk adjustment problems at age 14, and by persistent social difficulties, which were related to poorer risk adjustment skills at 14 years.

Finding a specific link between working memory and persistent externalising problems is consistent with the outcomes of a recent study showing working memory deficits were uniquely associated with the severity of externalising disorders when controlling for the association between working memory and general psychopathology (Huang-Pollock et al., 2017). It also adds to evidence suggesting weaknesses in working memory contribute to the maintenance of externalising symptoms because they provide an index of executive functions – skills that play an important role in regulating and controlling behaviour (Barkley, 2012; Nigg, 2017). Links between externalising symptoms and poor executive control in adolescence (Kim-Spoon, Deater-Deckard, Calkins, King-Casas, & Bell, 2019) may arise as a result of the poor cognitive control of behaviour (Giancola & Mezzich, 2003), or through externalising behaviours (e.g., aggression, defiance) discouraging positive social interactions, thereby limiting opportunities to engage in adaptive regulation strategies (Brieant et al., 2022; Eisenberg et al., 2010; Farley & Kim-Spoon, 2014). While our data cannot speak directly to the direction of these effects, they do suggest that poorer cognitive control at 14 is associated with persistent externalising problems. It should be noted that while working memory was linked to continued externalising symptoms, our measure

of response inhibition was not. This was unexpected, but likely reflects the measure used to index performance on the Go/No-Go task possibly tapped into affective biases towards negative information rather than response inhibition per se.

Risk adjustment was linked to persistent externalising and socialising difficulties, but risk-taking was not. This runs counter to evidence suggesting risk taking increases vulnerability to mental health difficulties during adolescence (Dumontheil, 2016). It is, however, consistent with the notion that adolescent risk taking can be adaptive and useful in the transition to adulthood and in peer socialisation during adolescence (Jessor, 1992; Shedler & Block, 1990; Spear, 2007), and that it is only those who engage in risky behaviour without sufficient cognitive control (i.e., without the capacity to adjust risk-related behaviours) who are vulnerable to adverse outcomes (Romer et al., 2011).

There was no association between cognitive function at mid-adolescence and mental health problems that resolved over time. Several other factors might contribute to the reduction in mental health problems observed in late adolescence. Environmental factors, such as changes in personal relationships, leaving full-time education and moving into employment, may have helped adolescents overcome challenges, or they may have been able to compensate for their vulnerabilities. The absence of an association between cognitive skills at mid-adolescence and emerging mental health problems suggests that good cognitive function in mid- adolescence does not necessarily protect against later mental health problems, and likewise that poor cognitive function does not increase vulnerability to the onset of later mental health problems. This is an unexpected finding given the wealth of literature implicating cognitive impairments in the onset and maintenance of mental health difficulties (Carlson & Wang, 2007; Huang-Pollock et al., 2017; LeMoult & Gotlib, 2019; Millan et al., 2012; McTeague et al., 2016;) and the well-

documented interactions between cognition and mental health interact across development (Furhmann et al., 2020). One explanation for our finding is that the impact of cognitive variability on the onset of mental health problems between mid- and late adolescence is washed out by other more impactful factors, including increased stress as individuals take on adult roles and responsibilities, increases in substance abuse and reduced access to mental health services as adolescents move out of schools, (Blanco et al., 2008; Compton et al., 2007; Copeland et al., 2015; Kessler et al., 2005). A further explanation is that the cognitive tasks examined here do not measure the constructs which are most meaningful for this group.

Clinical implications

These findings suggest that mental health profiles do not align with the diagnostic framework, rather, mental health profiles seem to be broad ranging, with adolescents experiencing relative areas of more severe difficulties that can change over time. The data suggest that while individuals have relative areas of heightened need, they typically have multiple co-occurring mental health needs. This suggests that interventions should be tied to individual profiles of need rather than diagnostic labels, pointing toward a need for more individual approaches to mental health assessment and support.

It should also be noted that a portion of the participants in this study had difficulties at mid-adolescence that resolved by late adolescence, without any intervention. Clinicians should be cognisant of the balance between early identification and treatment of mental health symptoms without over-pathologizing transient difficulties."

Limitations

There are several limitations to the current study. First, the range of mental health symptoms and cognitive assessments was limited to those available across many participants at ages 14 and 22. This will have limited both the range of mental health profiles detectable and the depth with which we could explore links to cognition. Relatedly, cognition was measured by artificial tasks, raising the questions of how well these relate to real-world cognitive abilities. Also, the only measure of mental health symptoms available was the SDQ. We used the SDQ to identify internalising, externalising, and social patterns of difficulties but this may not align as well with diagnostic categories as other measures, such as the Revised Child Anxiety and Depression Scale (Chorpita, et al., 2000). Had a range of other such measures been available, this may have impacted the results. Second, the exclusion of participants receiving treatment for mental health problems and attrition between time points may have introduced a bias. Indeed, those who did not return for the follow-up assessment at age 22 had elevated conduct problems and hyperactivity at mid-adolescence, and were less prosocial, than those who did. As such, our analyses may have underestimated the prevalence of mental health problems detected in our sample in late adolescence. Third, our analyses were based on data from self-reported mental health problems. Obtaining data from other informants may have produced different clusters. Finally, there were multiple permutations for capturing transitions, so even though our sample size was large, we had to pre-plan which ones to map.

Conclusion

We used a data-driven clustering approach to identify homogenous profiles of mental health problems in mid- and late adolescence, map transitions across these profiles over time, and related these transitions to cognitive function in mid-adolescence. Three profiles of relative

difficulties emerged, which were remarkably similar at both time points. One was characterised by predominantly externalising problems and elevated risk taking, with an over-representation of males. The second had relatively more severe internalising problems, accompanied by poor working memory and an aversion to risk, and was more common in females. The third had difficulties with social relationships and no cognitive problems and was more common in males. The number of adolescents with a predominantly externalising profile declined between mid- and late adolescence. Those with persistent difficulties in this area were characterised by poorer working memory and a reduced ability to adjust risky behaviours, as measured by the CGT at age 14. The rates of persistent difficulties were similar for each of the profiles. Persistent social difficulties were linked to poorer risk adjustment behaviours at age 14. There were no associations between cognitive function at mid-adolescence and emerging or resolving mental health problems in late adolescence, or between persistent internalising problem and cognitive ability in mid-adolescence. This is the first study of its kind to map transitions in mental health profiles between mid- and late adolescence. Moving towards proactive models of mental health support will depend on recognising the reproducibility of these shifts.

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CHAPTER FIVE

Overall Discussion and Critical Evaluation

Chapter Five. Overall Discussion and Critical Appraisal

Chapter overview

This Chapter recaps the main goals of the thesis, and summarises the key findings of both the systematic review and meta-analysis and the empirical paper. The theoretical and clinical implications of both projects are considered, and a critical appraisal of the methods is provided. The Chapter concludes with a section on self-reflection and directions for future research.

Thesis goals

Adolescence is often described as a period of 'storm and stress', epitomised by accelerated cognitive development, hormonal fluctuations, changes in brain structure and marked alterations in an individuals' environment and social relationships (Dahl et al., 2018). Mental health difficulties are highly prevalent across adolescence, with approximately 14% of 10- to 19-year olds experiencing diagnosed mental health conditions globally (Global Health Data Exchange, 2019). These difficulties change across the course of adolescent development (e.g. Costello et al., 2011), and have been linked to the many biological, cognitive, social, and environmental changes that occur during this period. If left untreated, these difficulties can significantly impact an individual's health, income, and interpersonal relationships later in life and create an enormous burden on social, healthcare, and economic systems (Goodman et al., 2011; Green et al, 2005; Kowalenko & Culjak, 2018). The development of timely, effective treatments relies on a deeper understanding of the factors increasing vulnerability to mental health difficulties, and the relationship between these factors and changes in mental health profiles across development.

The factors implicated in the onset and maintenance of mental health problems are wide ranging (see Chapter One for a brief introduction). This thesis focussed on cognitive factors due to their importance in regulating emotions and behaviour (e.g., Barkley, 2012; Nigg, 2017). Chapter Two involved a meta-analysis and systematic review of memory and attention biases in anxious children and adolescents. Chapter Four was an empirical research project using secondary data analysis to explore changes in mental health profiles between mid- and late adolescence and their links to cognitive function, as measured by working memory, response inhibition and risk-taking tasks, in mid-adolescence. Evidence suggests that many adolescents who experience psychological distress and seek mental health support do not have a formal DSM-IV diagnosis (e.g., Jorg et al., 2015; Wang et al., 2007). For this reason, a transdiagnostic approach was adopted across both studies to explore the relationships between cognitive function and elevated symptoms of mental health difficulties, rather than diagnosed mental health problems.

Summary of findings

Systematic review and meta-analyses

Four separate meta-analyses were conducted to explore attentional biases towards threat in children and adolescents, in Chapter Two. The data revealed that young people with elevated symptoms of anxiety showed an attentional bias towards threatening stimuli when it was measured by an emotional Stroop task, but not when it was measured by a dot probe task. The measure of attentional bias indexed by the dot probe task could signal biases towards threat (vigilance) in the form of faster response times, and biases away from (avoidance) threat in the form of slower response times. The analyses conducted in Chapter Two adopted the conventional

approach of testing for biases towards threatening material and revealed no significant effect. However, exploration of the pattern of results across individual studies included in the meta-analysis revealed biases both towards and away from threat. The differences in direction of these effects may have therefore resulted in them cancelling each other out when they were combined into a single meta-analysis. Considering these results together, it seems possible that anxious young people are biased both towards and away from threat, and that the meta-analysis conducted using the Stroop task detected the latter of these, while the dot probe analyses were not able to differentiate between attentional biases towards or away from threat (Clarke, McLeod & Gustella, 2013).

A key finding from the systematic review on memory and anxiety in youth was the finding that only two studies met the inclusion criteria, meaning a meta-analysis could not be conducted. A narrative review of these two studies revealed one finding that anxious youth may have a memory bias for negative information, with an anxious group recalling significantly more negative false memories than a non-anxious group (Toffalini et al., 2015). However, the second paper revealed working memory was related to depression and not anxiety in young people (Ladoucer et al., 2005). Speculatively, these two studies suggest anxious youth might have biases for longer-term memories, but not for short-term information that is held in short-term or working memory.

Empirical research paper

A data-driven approach was used on secondary data from the IMAGEN cohort in Chapter Four to explore changes in mental health profiles between mid- and late adolescence and their association with response inhibition, risk-taking and working memory tasks in mid-adolescence.

Overall, 60% of participants experienced symptoms of mental ill-health in mid-adolescence and 50% in late adolescence. These estimates are higher than previous estimates (e.g. Global Health Data Exchange, 2019; Oksanen et al., 2017) suggesting there is likely to be a high level of unmet service need during this developmental stage.

Three distinct profiles of mental health symptoms were identified at each time point. These corresponded to: i) pronounced internalising symptoms; ii) relatively more severe externalising symptoms, and iii) relatively more severe difficulties with social relationships. These profiles were largely stable between mid- and late adolescence, with some subtle differences in symptom-levels between time points and differences in the adolescents presenting with each profile. Exploration of adolescents' transitions revealed that mental health difficulties had resolved in late adolescence for approximately 40% of those with any mental health symptoms in mid-adolescence. Approximately 30% continued to experience similar mental health symptoms at both time points. The remaining 30% transitioned between profile clusters: for example, they transitioned from experiencing relatively more severe problems with social relationships during mid-adolescence to experiencing relatively more severe internalising symptoms by late adolescence. An impaired ability to adjust risk-taking behaviours in response to contextual information was linked to profiles of persistent externalising symptoms and social difficulties. Poor spatial working memory was associated with persisting externalising problems. These findings suggest that mental health profiles resolve or stay consistent for approximately 70% of adolescents as they move into late adolescence, and that persistent profiles of externalising or social difficulties are linked with cognitive control abilities in mid-adolescence.

Combined results

Together, the studies conducted in this thesis show that certain aspects of cognitive function are related to youth mental health difficulties. In childhood and adolescence, those with elevated levels of anxiety may have attentional biases both towards and away from threat, and greater symptomology may be linked with biases towards recalling negative information over the long-term but not the short-term. Memory function was also related to elevated mental health problems in adolescence, and in particular to having profiles of predominantly externalising symptoms or social difficulties that persisted into late adolescence. However, this was for working memory - longer-term aspects of memory were not measured. Together these data suggest that mental health and cognition interact across development; anxiety can impact on the cognitive processing of information, and cognitive control in mid-adolescence contributes to persistent patterns of mental health difficulties.

Theoretical implications

The data presented across the meta-analyses and empirical work are consistent with theories describing mutual interactions between cognition and mental health across childhood and adolescence. In the meta-analysis, anxiety biased attention towards threat as measured by the affective Stroop task. Individual papers included in the dot probe meta-analyses found biases both towards and away from threat. This is consistent with the interference hypothesis, which suggests psychological distress disrupts cognitive processing by shifting cognitive resources (e.g. attention) away from task-relevant information (Llewellyn et al., 2008; Stawski et al., 2006). The empirical project suggested that cognitive function during mid-adolescence was associated with persisting mental health difficulties. This is consistent with the cognitive reserve hypothesis,

which suggests poor cognitive function impairs the downregulation of negative emotional responses, such as worry, fear or sadness, leading to elevated and persistent mental health difficulties (LeMoult & Gotlib, 2019; Millan et al., 2012). Together then, these data indicate that psychological distress can impact on cognitive function, and that cognitive function can increase vulnerability for mental health difficulties. These bidirectional effects are consistent with the theory of mutualism – a complex system approach that conceptualises development in terms of dynamic processes in which different domains interact over time (Borsboom, 2017; Furhmann et al., 2020; Mareva & Holmes, 2021; Van Der Maas et al., 2006). According to these accounts, cognition and mental health are complex systems that interact with one another, sometimes in different ways for different individuals, at different points during development (e.g., Furhmann et al., 2021).

The outcomes of the meta-analyses revealed some evidence for attentional biases both towards and away from threat in children and adolescents with elevated anxiety. Capacity limitations in our processing systems, particularly our visual system and working memory, require us to be selective in the information we attend to in our environments. Information is prioritised for processing through both top-down, voluntary, goal-directed processes, and bottom-up, automatic, attentional processes (Weierich et al., 2008). Similarly, attentional filtering can be either overt (e.g., directional eye-movements), or covert (e.g., internal attention). In overt filtering, visual sensitivity is primed for a sought after stimulus (e.g., searching for a particular object in the environment). However, a visually salient object can capture attention in a bottom-up manner. For example, if a person is fearful of spiders, they might be distracted by a dirty smudge on the wall, mistaken for a spider (covert), while actively searching for their phone (overt). Similarly, a person might use overt attentional control to avoid stimuli that causes them

distress. Typically, attentional selection is weighted in favour of bottom-up processing, especially for threat-related stimuli, in anxious compared to non-anxious people (Eysenck et al., 2007) as found with the meta-analysis of emotional Stroop tasks. However, contemporary research suggests that volitional attention can be used to prevent distraction by emotionally salient stimuli, shifting attention towards or away from threat (Cisler & Koster, 2010). Exploration of the direction of effects of the individual studies included in these meta-analyses suggest both top-down and bottom-up pathways of attention may be at play, with some studies showing clear patterns of threat avoidance, and others showing heightened attention to threat, in anxious youth. It is possible that these two pathways account for individual differences in the presentation of vigilance towards and avoidance of threat in people with anxiety symptoms.

The empirical paper identified three distinct profiles of mental health in mid- adolescence and a similar set during late adolescence. Each of these cluster profiles maps on to a dimension of difficulty described in contemporary hierarchical models of mental health (e.g., the Hierarchical Taxonomy of Psychopathology, HiTOP, Kotov et al., 2017): internalising and externalising to the two main spectra sitting below the p factor and social difficulties to the social maladjustment factor. Each of the cluster profiles was characterised by broad-ranging mental health difficulties, with relatively more elevated internalising or externalising symptoms or relatively more pronounced difficulties with social relationships. Thus, individuals with each presentation did not have selective difficulties that would correspond to a particular DSM diagnosis. Rather they had difficulties across a spectrum of mental health dimensions, with relative difficulties in particular areas. This is consistent with predictions from dimensional models of psychopathology that emphasise the importance of continuous factors that span the full range of functioning, from adaptive to maladaptive, that can cut across traditional categories

of mental ill health (e.g., Caspi & Moffitt, 2018; Holmes et al., 2021). It is also consistent with transdiagnostic approaches (upon which dimensional models are founded that focus on identifying the causes of everyday symptoms irrespective of diagnostic boundaries (e.g., Cuthbert & Insel, 2013).

The patterns of association between cognitive function and mental health in adolescence were broadly consistent with existing theories linking poor cognitive control to an increased vulnerability to, and maintenance of, mental health difficulties. A profile of externalising symptoms in mid or late adolescence was linked to concurrently elevated risk-taking relative to individuals without mental health problems, and persistent externalising symptoms were linked to difficulties adjusting risk-related behaviours. Both externalising symptoms and risk-taking are linked to problems inhibiting impulsive responses (e.g., Dumontheil, 2016), which might explain their concurrent association. Risk-adjustment skills, but not risk-taking per se, was linked to a persistent profile of externalising symptoms. This is consistent with the idea that it is only those who engage in risky behaviour without sufficient cognitive control (i.e., without the capacity to adjust risk-related behaviours) who are vulnerable to adverse outcomes (e.g., Romer et al., 2011). Corroborating this, poorer working memory (a marker of cognitive control) during mid-adolescence, was also associated with a persistent profile of externalizing problems. A profile of pronounced internalising symptoms was linked to concurrently poor working memory and increased risk aversion, but there were no links between the cognitive skills measured and persistent problems in this area. This finding is consistent with the idea that poorer cognitive control limits the ability to direct attention away from worrisome or negative thoughts (e.g., Koster et al., 2017; Rinsky & Hinshaw, 2011), which may increase risk aversion as individuals are unable to focus on decision-making. Finally, a profile of persistent social relationship

problems was associated with reduced risk-adjustment skills in mid-adolescence. The absence of strong links between cognitive function and social relationship problems was unexpected, and discussed in Chapter Four, likely reflects the limited number of cognitive skills measured in study rather than an absence of a link between cognitive function and social functioning.

Clinical implications

Together the findings from the meta-analyses and the empirical project point toward a need for more individual approaches to mental health assessment and support. The meta-analyses suggest links between attention and anxiety may be mediated by individual differences, with some people being biased towards threat and others away. This raises the question of whether services should be adopting a ‘one-size-fits-all' approach or moving towards a ‘My size fits me’ framework (for a review see Schaeuffele et al., 2020). Similarly, the empirical project revealed that mental health profiles do not align with the diagnostic framework. Rather, mental health profiles seem to be broad ranging, with adolescents experiencing relative areas of more severe difficulties that can change over time. The diagnostic framework, with the DSM and ICD at its centre, has become a self-perpetuating system that defines both how we conceptualise and treat mental health difficulties (Dalgleish et al., 2020). It provides the framework for core texts in psychiatry and clinical psychology training, which in turn define how we assess and treat mental health difficulties. This thesis, along with a growing body of literature, highlights that mental health difficulties may not be so easily slotted into neat, diagnostic boxes and that we need to consider alternative methods for identifying and supporting mental health needs.

Evidence-based interventions must remain at the centre of clinical practice, but given the diversity of biological, psychological, and social pathways associated with the onset and

maintenance of mental health difficulties, and the broad range of individual differences in these and other areas, a more individualised approach to therapy, such as stratified medicine may be beneficial (Lester and Eley, 2013). As an example of the need for tailored assessment and intervention, consider the evaluation of the dot probe data in Chapter Two. These data show that anxiety can manifest as either an avoidance of threat-related material or vigilance towards threat. These different manifestations might explain why the relationship between attentional-biases and pre- and post-treatment outcomes differ across studies (for a review, see Barry et al., 2015); one treatment approach will not address difficulties that operate in opposing directions. This example highlights the need to fully understand, at an individual level, what the specific profile of an individual's symptoms are. In this case, an assessment of attentional bias could determine whether intervention should focus on vigilance towards, or avoidance of, threat. Likewise, the data from the empirical project suggest that while individuals have relative areas of heightened need, they typically have multiple co-occurring mental health needs. For example, an externalising profile in mid-adolescence was associated with equally severe emotional problems in late adolescence for some individuals, while others had a predominantly internalising profile linked to emotional problems in the absence of severe externalising problems. This suggests that interventions should be tied to individual profiles of need rather than diagnostic labels.

Of course, individual assessment and tailored intervention is resource and time costly, but in practice clinicians often eschew disorder-specific intervention programs for more eclectic approaches that address individual or multiple difficulties. There are a few emergent programs that are comprised of therapeutic packages to address symptoms commonly experienced by individuals irrespective of their official diagnostic status (e.g., Weisz et al., 2012) – they adopt a more transdiagnostic and individual approach to intervention. One example comes from The

Healthy and Resilient Mind Programme (HARMONIC; Black et al., 2018), which developed a transdiagnostic intervention called Shaping Health Minds. This approach draws on several evidence-based treatment approaches to better address the needs of people with comorbid symptoms. The intervention is modular, allowing psychologists and skilled clinicians to deliver treatment modules based on the formulation of client's presenting difficulties rather than a single diagnosis. While the results of this trial are not yet available, this model offers one way to combine individual, client-focussed therapy in a flexible way that does not require retraining clinicians or lengthy individualised assessment because it draws on formulation and existing treatment tools.

A similar initiative is the harmonised transdiagnostic assessment protocol for outlined by Boulton et al. (2021). This is one of the first attempts to incorporate a transdiagnostic framework within services and clinics. It was formulated in consultation with a large group of clinicians, researchers, and community groups across Australia. A national research committee surveyed stakeholders and organised national summits to reach a consensus on a set of diverse and feasible measurement areas to include in the harmonised protocol. The identified assessment instruments span several domains of needs, such as child functioning and wellbeing, child mental health, caregiver mental health, and family background. The goal of the initiative is to achieve impact at both the clinical and research level: firstly, to enable transdiagnostic clinical assessments for children with neurodevelopmental needs; and secondly, to facilitate harmonised large-scale data collection that has the potential to inform research, policy, and practice. The outputs of this transdiagnostic protocol will enable one of the first empirical evaluations of whether the examination of transdiagnostic needs beyond primary diagnoses could enable more integrated care and improve child outcomes. In the long-term, this approach could facilitate a departure

from categorical approaches and subsequently feed into the design of interventions in which enrolment is based on individual needs and strengths across domains, as opposed to primary diagnoses (Finlay-Jones et al., 2019).

A major benefit of modular interventions, such as Shaping Healthy Minds, lies in offering people interventions targeting the most impactful elements of their presentations, before then offering tools to help with future difficulties that might develop. As the data from the empirical project show, we can now use existing large datasets to predict what these difficulties might be, and indeed what the predictors of such changes are. Adopting an approach that addresses immediate need using a modular transdiagnostic intervention model, but is informed by what we know from longitudinal studies, has the potential to equip people with the tools needed to manage later mental health difficulties rather than asking them to re-engage with services at a later point in time. Of course, short 'top-up' interventions may be required to consolidate previous learning and support individuals if this model were adopted.

The data from the empirical paper provide one example of how longitudinal studies can inform prospective treatment approaches. Identifying factors that predict later mental health difficulties, and changes in the profile of these difficulties, provides useful targets for intervention. In this case, tools targeting working memory and decision-making in mid-adolescence might reduce the persistence of externalising symptoms and difficulties with social relationships. One such example is working memory training, which has been shown to reduce symptoms of anxiety and depression in adolescents (e.g., Beloe & Derakshan, 2020). Moving from reactive approaches, which offer professional intervention only when difficulties have escalated, to proactive models that reduce psychological distress by offering helpful tools before symptoms become functionally impairing, are likely to be cost-effective and helpful in reducing

the burden on mental health services. In sum, the data in this thesis adds to the growing evidence-base suggesting that interventions need to be tailored to individual needs rather than single and potentially ill-fitting diagnostic labels (e.g., Newby, Mc-Kinnon, Kuyken, Gilbody, & Dalgleish, 2015; Weisz et al., 2012).

A key strength of clinical psychology lies in developing individual formulations, summarising and integrating a broad range of biopsychosocial factors. Such formulations are constructed collaboratively with individuals, taking into account personal meanings, psychological theory and research. Using this process clinical psychologists can and do develop individualised approaches to support individuals to create meaningful change. However, with an ever-growing demand on mental health systems, we must look to ways to provide such modular approaches as outlined above, which can be delivered at the point of identification of need, by a range of mental health workers, under the supervision of qualified clinical psychologists who can draw on formulation skills.

Critical evaluation

This section provides a critical evaluation of the meta-analysis and systematic review presented in Chapter Two and the empirical project presented in Chapter Four.

The systematic review and meta-analysis were well designed. The Preferred Reporting Items for Systematic Review and Meta-Analyses guidelines (Moher, et al., 2009) were closely followed to ensure the quality of the review. The choice to set strict inclusion criteria ensured homogeneity of the tasks in each meta-analysis. In contrast to existing meta-analyses of anxiety and memory and attention in youth, (Dudeney, et al., 2015), the present study separated congruent and incongruent trials. Previous research has suggested that there is low test-retest

reliability among inference scores (e.g., scores calculated by subtracting performance in one condition from performance in another).

I made the decision to exclude studies concerned with anxieties with a specific focus, such as social anxiety and other phobias. I also excluded studies that examined symptoms of anxiety within a specific diagnostic group, for example anxiety symptoms in those with autism or with asthma. These decisions were made to offer a broad target population and a focus on general anxiety. However, there is large overlap of symptoms across the different types of anxiety, and a high prevalence of symptoms of anxiety experienced comorbidly with other disorders (Palitz, et al., 2018). With this in mind, broadening the inclusion criteria for studies in the literature search may have offered a more representative population, offering better insights into how cognition is related to anxiety in a broader range of experiences. The inclusion of only a specific number of presentations of anxiety in the meta-analyses limited the interpretation of the results.

A major strength of the empirical project was the use of a large secondary dataset that followed a large cohort of individuals through adolescence, with multiple measures of cognition and mental health. It provided a novel investigation into the changes in mental health between mid- and late adolescence. Many scientific studies define adolescence as the second decade of life, or as ending at eighteen years. The current study is unique in exploring changes in mental health up to 22 years of age, a significant contribution to the literature. It included participants from a range of sites across Europe, providing a more diverse population than other large cohort studies that typically recruit from within a country. It would not have been possible to collect such rich data within the financial and temporal constraints of a clinical doctoral thesis.

Accessing these data and using an advanced data-driven approach enabled me to capture the complex nature of mental health symptoms, and how they change over time.

Large longitudinal datasets, such as the IMAGEN data used in the empirical project, have revolutionised our ability to study developmental patterns across hundreds, even thousands of participants. They offer the opportunity to expand research questions in ways which are not often possible in experimental designs, and particularly well suited to the exploration of developmental processes (Zyphur et al., 2020). They also increase statistical power by including large numbers of participants, protecting against the misestimation of effect sizes in a manner that would be prohibitively costly and time-consuming for most individual researchers or research groups (Gelman & Carlin, 2014).

While secondary data analysis has many benefits, it is not without its challenges. Datasets can differ substantially in the quality and richness of their data (Kievit et al., 2021), constraining the questions that can be asked and the interpretations that can be made. Indeed, the empirical project reported in Chapter Four was limited by the data available at the two timepoints studied. Ideally a broader range of cognitive and mental health assessments would have been included. It would have been particularly valuable to have cognitive tasks tapping into verbal abilities to further explore the relationship between social difficulties and cognitive function (see Chapter One for a fuller discussion of this point). It would also have been useful to include mental health measures capturing a wider set of symptoms of psychological distress to obtain potentially more nuanced profiles. Additional data on childhood experiences or socioeconomic status, which were not available in the IMAGEN data, would have enriched the study, enabling us to explore the effects of deprivation and threat – two key facets of adverse childhood experiences (ACES) that are highly related to later cognitive function and mental health (e.g., Carozza et al., 2022).

Further, the lack of ecological validity of the cognitive tasks available may have limited the real-life application of these findings.

The participants recruited and selected also limits investigations that can be conducted with secondary data. In this case, a major drawback was the exclusion of young people seeking professional help for mental health problems. While a substantial proportion of the sample had symptoms of mental health difficulties above what would be expected, a proportion of adolescents with mental health difficulties were not represented. It is not possible to say whether these individuals had more severe problems than those detected in the sample worked with here, but we can say the results are only generalisable to those with mental health symptoms among people not currently receiving support. It is possible other mental health profiles may have emerged if participants receiving support were included. A related problem is attrition, particularly for longitudinal studies spanning multiple years. In this case, those who did not return for the follow-up assessment at age 22 had elevated mental health problems at age 14 compared to those who did return at age 22, suggesting the analyses may not be fully representative of the range of mental health problems in late adolescence.

Other general concerns with secondary data analyses include many researchers accessing the same data sets, possibly with overlapping questions, using different analytic approaches. This issue may lead to inflated Type I error rates (Thompson et al., 2020). Further, while longitudinal investigations are increasingly adopted to address developmental research questions, they typically span only a few years limiting what is known about temporal stability over longer timeframes (Taylor et al., 2020). In this case, data were only available from age 14 upwards. Having data spanning childhood through to late adolescence would have enhanced the richness of the understanding of changes in mental health profiles across development.

The aim of the empirical paper was to identify subgroups of individuals with similar profiles of mental health difficulties without labelling the groups apriori. The most suitable method for doing this was cluster analysis, a method of identifying subgroups based on their relationships across multiple measures with no prior assumptions about who should or should not group together (e.g., there are no assumptions that all people with depression should form a single subgroup based on their symptoms, people are instead 'grouped' based on the structure of the data). Cluster analysis is typically applied to spatial representations of the relationships between variables to determine how many subgroups exist in that space (i.e., how close variables are together in space based on their similarity to one another). In this case, the spatial representation depicted the similarity of the adolescents to one another based on their scores on the self-report SDQ: those with more similar profiles were positioned closer together in space. As there were multiple measures on the SDQ (the data were multidimensional), it was necessary to carry out dimensionality reduction. There are multiple methods for reducing dimensionality (e.g., multi-dimensional scaling, uniform manifold approximation and projection). I chose to use Uniform manifold approximation and projection (UMAP) as it has been shown to improve cluster separation, increasing the chances of identifying distinct clusters (Dalmaijer et al., 2020). Different clustering algorithms can be applied to dimensionality-reduced data, with community detection, k-means, and c-means being most widely applied (Dalmaijer et al., 2020). There are no firm guidelines as to which method should be chosen, but because the aim was to identify discrete subgroups, c-means clustering was discounted. C-means clustering is more suited to identifying overlapping groups (Dalmaijer et al., 2022). Community-detection methods are easy to apply, but the application of these methods to psychological data has not been studied as extensively as it has for other data types (Lancichinetti & Fortunato, 2009, Gates et al., 2019,

Gates et al., 2014), relative to other clustering methods (Depaoli, 2013, Grimm et al., 2017, Harring et al., 2016). For this reason, k-means clustering was selected, a method that offers the benefit of not demanding a priori assumptions about the data or tuning of the parameters, and which makes no pre-determined assumptions about the number of clusters. The optimal number of clusters is determined by the silhouette coefficient (see Chapter Four), meaning the data themselves determine the outcomes.

The analytic decisions made were based on the goal of the study – to identify subgroups with distinct profiles of mental health. It could be argued that community detection would have been a better approach as it can distinguish between 'flat' profiles more easily than k-means clustering. Flat profiles can include people with consistently low scores across a set of measures (no peaks or troughs across the measures), and someone with consistently high scores. It is vital to distinguish these profiles, particularly in a clinical context. In situations where there is not enough variance in the data, k-means is less likely to categorise people with flat profiles of high scores and people with flat profiles of low scores into separate clusters (i.e., it is less likely to distinguish clusters based on severity). This was not relevant to our study for two reasons: first, those with 'average range' scores were not entered into the clustering, reducing the chance of detecting only 'high' and 'low' groups, and secondly, there was sufficient variance in the data for the k-means clustering to perform well in distinguishing groups with different 'spikey' profiles. For this reason, using k-means, which has been better validated on psychological data than community detection, seemed more appropriate (Dalmaijer et al., 2020). It could also be argued that a better way to capture the complexity of mental health symptoms would be to identify overlapping clusters, or people who sit on the boundary of two clusters, as a c-means clustering algorithm would do. While this might be more in line with a transdiagnostic approach,

it would not map across to pragmatic interpretations of the data that would be useful for clinical practice. Subgrouping individuals allows for simpler clinical interpretation of profiles, something that is needed in clinical services to provide time efficient and affordable assessment and support.

Future directions

The empirical project revealed that working memory was potentially a strong indicator of concurrent and persistent mental health problems, yet in the meta-analysis very few experimental studies had been conducted to explore the relationship between anxiety and memory. Given many longitudinal and secondary data analytic studies reveal prospective associations between working memory and child and adolescent mental health outcomes, a clear next step will involve developing hypotheses to test experimentally how the two are related, and in which contexts. Understanding more about the mechanistic links between the two (e.g., do memory impairments increase vulnerability to mental health problems, do mental health problems impair memory function, or are there other variables influencing both?) will be important for designing interventions.

It will also be important to lengthen the developmental timeframe when studying links between cognition and mental health in future studies. A strength of the meta-analysis was the inclusion of young people aged up to 25 years, yet the age range in included studies did not go beyond 18 years. Similarly, a strength of the empirical paper was that it spanned into late adolescence, unlike many previous longitudinal studies using similar approaches that stop in mid-adolescence (e.g., Bathelt et al., 2021). As it is now widely accepted that adolescence spans into the mid- early to mid-twenties (Mills et al., 2014; Raznahan et al., 2012), it is vital the field

conducts further experimental and longitudinal work when studying youth mental health that includes the late adolescence period. This is relevant not only for research, but also for clinical practice. Understanding whether mental health profiles and their correlates in late adolescence are more similar to those seen in mid-adolescence or those seen in adulthood can inform clinical practice and service models (i.e., should people in their late adolescent years be included in youth rather adult services?). Related to this, future work exploring changes in mental health profiles, as in Chapter Four, would benefit from the inclusion of earlier time points. Including data spanning early childhood through to late adolescence would facilitate investigations into the stability of individual profiles, developmental cascades, bidirectional cross-domain couplings, and sensitive periods. Studying patterns of desistence and persistence over this broader timeframe could help identify potential modifiable factors that can promote positive outcomes. The focus of this thesis was on cognitive factors. While these are an important source of variance in mental health among children and adolescents, other factors that are highly related to mental health outcomes (e.g., socioeconomic disadvantage, adverse childhood experiences) need to be considered. In short, future longitudinal investigations would benefit from the inclusion of multiple levels of assessment (brain, cognition, environment, behaviour, mental health) across broader timeframes.

The meta-analysis exploring biased information processing in anxious youth revealed one potentially large confound in the field: researchers typically focus on biases toward affective stimuli and do not account for the potentially clinically significant nature of biases away from threat. Future work should consider this issue and distinguish between these two effects, both in their experimental paradigms and in analyses that combine effects across studies.

A final key point relates to the clinical relevance of the outcomes from this thesis, which support the transdiagnostic movement. Rather than persisting with diagnostics approaches, future research should focus on data-driven transdiagnostic approaches, such as the Power Threat Meaning Framework (Johnstone & Boyle, 2018) or the HiTop model (Kotov et al., 2017), to understand mental health difficulties as they present in real-life, rather than attempting to fit people's experiences into ill-fitting diagnostic boxes. Using such frameworks to identify the mechanisms that give rise to common and complex profiles of symptoms will inform intervention development. Related to this, further research is needed to explore both the clinical effectiveness and utility of modular interventions that build on transdiagnostic approaches.

Personal reflections

A challenge in selecting a line of research was in identifying an area that could add meaningful information to the field. I decided to explore youth mental health and how it was associated with cognitive abilities because, having worked in this field prior to beginning doctoral training, I am keen to support young people and improve their chances of better wellbeing. For the empirical paper, there were multiple ways I could have approached the data to answer different questions. One was to use a latent variable approach to identify dimensions (latent factors) of mental health and explore how they changed over time. While this would have been informative, I felt it would be more clinically interesting to explore changes in individual mental health presentations over developmental time. This led to learning about clustering methods and how they can be used to answer questions about profiles and subgroups.

It has been interesting to explore how different questions can be explored using different methods, but it has also been incredibly challenging. Using secondary data to answer questions

about developmental change involved the use of advanced analytic tools; analyses that were more complex than might have been applied if a simpler experimental study had been conducted (King et al., 2018). The methods sections of papers reporting cluster analysis and other similar analyses were advanced and highly condensed. For a novice in the field, they were hard to understand, and it was a steep learning curve. Attempting this analysis required the support of statistical experts, which underscores the importance of collaborative work in science.

I have developed several new skills that I can use in my career as a Clinical Psychologist, through my thesis journey. I can critically evaluate research papers, which will be invaluable in evaluating new ideas about the causes of mental health difficulties or new therapeutic approaches. I have developed a wide-ranging set of skills that will enable me to engage in clinical science research. Completing a meta-analysis facilitated my understanding of a particular field and enabled me to consolidate findings and present them in a manner fit for publication, and my empirical paper has given me a greater understanding of the importance of developmental context when trying to understand a young person's difficulties.

Completing the thesis in the context of a global pandemic, while home schooling two children, tested me and my passion for research. My commitment to this area of research has driven me to complete the work, even in the most challenging of circumstances. I have learnt that, with the right support in place, I am more capable than I had perhaps previously believed. To the point of support, this thesis has cemented in me the belief that collaboration is key for exploring ideas and enabling a broad range of analytic approaches which may not be possible in isolation.

Overall conclusion

This thesis portfolio has demonstrated: i) that youth anxiety is associated with some forms of biased attentional processing, but that there are too few studies to determine whether it is also related to biased memory recall; ii) that there are complex profiles of mental health difficulties in adolescence that do not correspond to specific diagnoses; iii) profiles of mental health difficulties are similar in mid- and late adolescence; iv) adolescents' mental health profiles change between 14 and 22 years, with 40% of mental health symptoms resolving, 30% persisting and 30% changing in presentation; v) mental health profiles associated with relatively more severe externalising problems or relatively more difficulties with social relationships that persist from mid- to late adolescence are associated with cognitive control abilities during mid-adolescence. Together these findings highlight the bidirectional nature of the relationship between mental health and cognitive function in young people and demonstrate that developmental context should be considered when exploring young mental health and its correlates. Developing evidence-based therapeutic approaches for alleviating current, and preventing later, psychological distress should be one of the central motivations for mental health research. The transdiagnostic approach adopted here can help us achieve this. If our samples are representative of the full spectrum of young people we are trying to help, and not just those with diagnosed conditions, and our methods better suited to capture the dynamics of development, then our theories will likely have greater practical significance.

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Appendix A

Author guidelines for British Journal of Developmental Psychology

British Journal of Developmental Psychology — the british psychological society

BJDP AUTHOR GUIDELINES

Sections

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Authors should kindly note that submission implies that the content has not been published or submitted for publication elsewhere except as a brief abstract in the proceedings of a scientific meeting or symposium.

Once the submission materials have been prepared in accordance with the Author Guidelines, manuscripts should be submitted online at http://www.editorialmanager.com/bjdp

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The *British Journal of Developmental Psychology* publishes full-length, empirical, conceptual, review and discussion papers, as well as brief reports, and Registered Reports, in all of the following areas:

- motor, perceptual, cognitive, social and emotional development in infancy;
- social, emotional and personality development in childhood, adolescence and adulthood;
- cognitive and socio-cognitive development in childhood, adolescence and adulthood, including the development of language, mathematics, theory of mind, drawings, spatial cognition, biological and societal understanding;
- atypical development, including developmental disorders, learning difficulties/disabilities and sensory impairments;
- the impact of genetic, biological, familial, interpersonal, educational, societal and cultural factors upon human psychological development;
- comparative approaches to behavioural development that help to elucidate developmental processes in humans;
- theoretical approaches to development, including neo-Piagetian, information processing, naïve theory, dynamic systems, ecological and sociocultural approaches.

3. MANUSCRIPT CATEGORIES AND REQUIREMENTS

The following types of paper are invited:

- papers reporting original empirical investigations;
- theoretical papers which may be analyses of, or commentaries on, established theories in developmental psychology, or presentations of theoretical innovations

› How to boost your CPD profile
› Journal access in developing countries
› Publish Open Access
› Why publish in the BPS Journals?
› Podcasts
› Registered Reports Guidelines
› Legacy files
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Associated titles

› British Journal of Psychology
› British Journal of Clinical Psychology
› British Journal of Educational Psychology
› British Journal of Health Psychology
› British Journal of Social Psychology
› British Journal of Mathematical and Statistical Psychology
› Journal of Neuropsychology
› Journal of Occupational and Organizational Psychology
› Legal and Criminological Psychology
› Psychology and Psychotherapy: Theory, Research and Practice

psychology, or presentations of theoretical innovations, extensions or integrations;
- methodological papers dealing with any methodological issues of particular relevance to developmental psychologists;
- review papers, which should aim to provide systematic overviews, analyses, evaluations or interpretations of research in a given field of developmental psychology, and identify issues requiring further research. All systematic reviews must be pre-registered.

In those cases deemed appropriate, peer commentaries on key papers/reviews will be solicited from other researchers in the relevant field. These peer commentaries will be published immediately after the target article, with the authors(s) of the article being invited to write a response to the commentaries.

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- A short informative title containing the major key words. The title should not contain abbreviations (see Wiley's

The title should not contain abbreviations (see Wiley's best practice SEO tips);
- A short running title of less than 40 characters;
- The full names of the authors;
- The author's institutional affiliations where the work was conducted, with a footnote for the author's present address if different from where the work was conducted;
- Abstract;
- Keywords;
- Data availability statement (see Data Sharing and Data Accessibility Policy);
- Acknowledgments.

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Please provide an abstract of between 100 and 150 words, giving a concise statement of the intention, results or conclusions of the article and brief information regarding the ages and background and distinctive characteristics of any sample. The abstract should not include any sub-headings.

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Acknowledgments

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Authors are required to provide a Statement of Contribution that identifies existing knowledge in the area and summarises the new knowledge added by the submitted paper. It should include two subheadings with 2 or 3 bullet points of no more than 100 characters under each, outlining (i) what is already known on this subject, and (ii) what the present study adds. The Statement of Contribution is submitted as a separate file.

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Review Board (IRB), including adherence to the legal requirements of the study county.

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Author Guidelines updated April 2019

Appendix B

Risk of Bias Tool

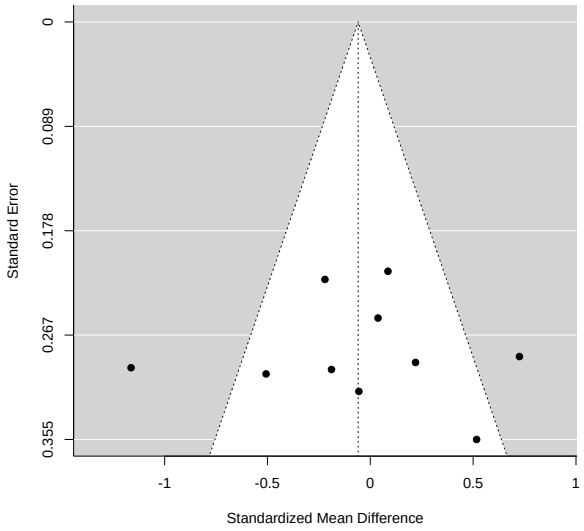
	Yes	No	Can't say	Does not apply
Study Design				
Did the study address an appropriate and clearly focused question?				
Was the study well-designed with age and sex-matched groups (for the anxious and non-anxious groups)?				
Participants				
Were participants recruited in an acceptable way?				
Was the study population clearly specified and defined?				
Were participant attrition rates and exclusion criteria clearly reported?				
Measurement and Analysis				
Was the measure of anxiety a standardised, reliable and well-known tool?				
The measure was not subject to reseacher bias (e.g. researchers did not administer the interviews / complete questionnaires on behalf of the participants).				
Was the measure of attention bias and/or memory bias a standardised, reliable and well-known task?				
Evidence from other sources is presented to show that measurements are reliable (reliability estimates provided in the paper)?				
Have authors accounted for important confounding factors in the design, analysis and/or discussion?				
Have confidence intervals been provided?				
Are effect sizes reported?				
Study Outcomes				
Taking into account the methods, statistical power, and analysis, do you believe the study outcomes?				
Were the results clear and precise?				
Are the results representative/can they be directly applied to the group (anxious people) targetted by this research?				
	High quality	**Acceptable**	**Unacceptable**	
Overall Assessment	**10 to 15**	**5 to 9**	**0 to 4**	
Score				

Sources: The Critical Appraisal Skills Programme (CASP) checklist for cohort study; The Scottish Intercollegiate Guidelines Network (SIGN) Methodology checklist: cohort study; The Cochrane Collaboration's tool for assessing risk of bias

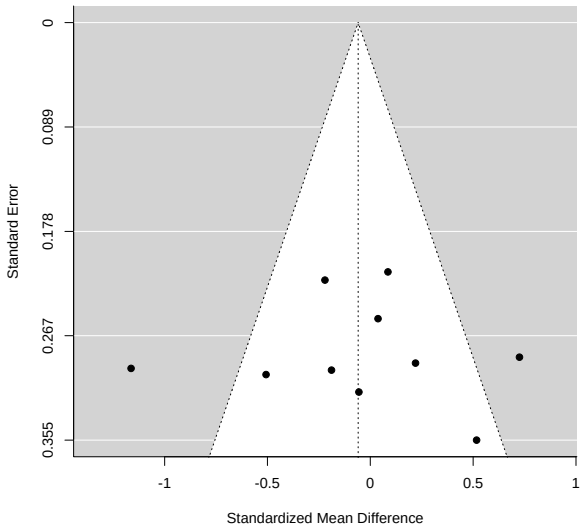
Appendix C

Funnel plots for attention bias meta-analyses

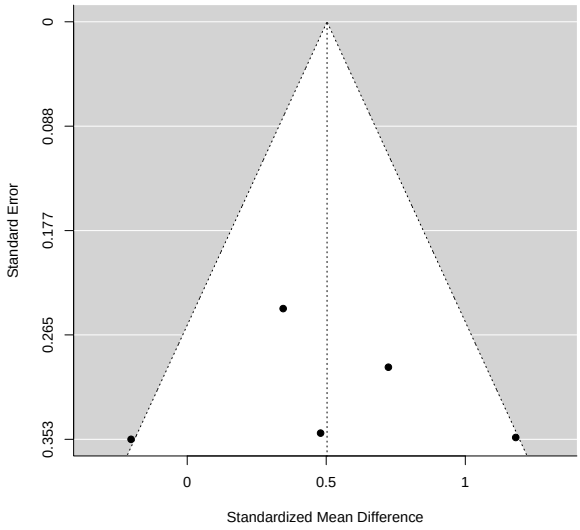
Funnel plot of publications using dot-probe tasks – congruent/incongruent



Funnel plot of publications using dot-probe tasks – other



Funnel plot of publications using Emotional Stroop tasks



Appendix D

Author guidelines for Developmental Science

Developmental Science

Author Guidelines

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change, or work that specifically attempts to elucidate mechanisms of developmental change at one level. We do not consider submissions on aging, although studies on the effects of early experience on later development (especially those from a biological perspective) are welcome. Manuscripts judged to fall outside this remit may be rejected without full refereeing.

All papers published in *Developmental Science* are eligible for Panel A: Psychology, Psychiatry and Neuroscience in the Research Excellence Framework (REF).

All manuscripts (whether Short Reports or Papers) will initially be assessed rapidly for relevance to the aims of the journal, breadth of interest, and potential impact. *Developmental Science*looks for submissions that will have general significance for a broad spectrum of developmentalists, reporting findings that can be considered as more breakthrough than incremental, with a focus on mechanism, and with a developmental theme. Please see our full notes on the Rapid Internal Review process.

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(ii) Research highlights;
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(iv) Main
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Sampathkumar Ranganathan, Editorial Assistant

E-mail: devsciedo" ce@wiley.com

Author Guidelines updated 2 September 2021

Appendix E

Application to access IMAGEN data

IMAGEN Proposal Form

1. General Information

Project Title: Developmental trajectories of symptoms of internalising and externalising disorders in young people, and their relationship with cognitive functions.	Lead Investigator: Dr. Joni Holmes
Email: Joni.Holmes@mrc-cbu.cam.ac.uk	IMAGEN PI:
Email: j.parker2@uea.ac.uk	Centre Institution: University of Cambridge
Type of Project (e.g., PhD, post-doc): Doctorate of Clinical Psychology	Starting Date: September 2019
Finishing Date (If known): September 2022	

2. Behavioural *or* Biochemical

2.1 Clinical Characterisation

☒ DAWBA	☒ Strength and Difficulties Questionnaire
☐ CAPE-42	☐ MINI
☐ BSI-53	☐ EDEQ
☒ CES-D	☐ ADRS
☐ TFEQ	☐ BIS-11
☐ CES-D	☐ PANAS

☐ PHQ-8	☐ K6+

☐ **Biochemistry**

2.2 General Characterisation

☐ HRQOL	☐ BSI-53
☐ WHO-5	

2.3 Neuropsychology Measures: CANTAB

☒ PRT / SMRT [memory]	☐ AGNG [emotional bias]
☐ CGT [risk taking / decision making]	☒ RVP [attention]
☒ IED [attention shifting/flexibility]	

2.4 Cognitive / Behavioural Performance

☐ Face Recognition [Morphed Faces]	☐ Emotional Dot-Probe
☐ Delayed Discounting [KIRBY]	☒ Verbal / Non-verbal IQ [WISC, 14]
	☒ Verbal / Non-verbal IQ [WAIS, 22]
☐ Passive Avoidance Learning Paradigm [PALP]	☐ Paradigm [Numbers Task]

2.5 Personality / Temperament

☐ Personality [NEO-FFI, TCI, SURPS]	☐ Physical Development [PDS]
☐ Handedness [Pegboard]	
☐ Child Alcohol / drug use [AUDIT, DAST, MAST, ESPAD, TLFB]	☐ Parent Alcohol / drug use [AUDIT, DAST, MAST, ESPAD, TLFB]

2.6 Family / Environment

☐ Family History ☐ Life Events Questionnaire

☐ Urbanicity ☐ Pregnancy / Birth Questionnaire

☐ Conflict Tactic Scale ☐ Childhood Trauma Questionnaire

☐ Bullying Questionnaire

2.7 Demographic Variables

Age, sex, parental education, socio-economic status, recruitment centre

3. Neuroimaging

3.1 fMRI

☐ Faces Task ☐ Stop Signal Task

☐ Monetary Incentive Delay Task ☐ Global Cognition Task

☐ Breath Hold Task

3.2 Structural MRI

☐ MPRAGE T1 ☐ DTI

4. Genetic Database (-omics)

Do you require access to the genetic database?

☐ Yes ☐ No

5. Puberty

☒ **Puberty Development Scale**

6. Details of Planned Analyses

Main Analyses

Other / additional models / contrasts, *please specify* (e.g. DCM, vector support machines, etc):

1. Factor analysis to determine latent variables for measures of psychopathology (internalising and externalising factors derived from subscales of SDQ, DAWBA and NEO)
2. Group-based trajectory models to determine patterns of developmental change in psychopathology
3. Regression models to identify cognitive predictors of the different trajectories

Subject inclusion / exclusion criteria:

All participants to be included.

Approximate timeframe:

Analyses: October 2020 – December 2021

7. Project Proposal

Please include goals / objectives and methods. Please be specific in what you plan to investigate and how you plant to investigate it. *A proposal should correspond to one publication.*

Background:

Mental health difficulties have a higher prevalence in young people compared to any other stage of life (Gulliver, Griffiths & Christensen, 2010), with roughly 25% of young people experiencing psychological distress (Oksanen et a./, 2017). Over half of all mental ill health starts by the age of 14 (Murphy & Fonagy, 2012) and, left untreated, can have a significant impact on an individual's health, income and relationships in later life (Goodman, Joyce & Smith, 2011; Green et al, 2005; Kowalenko & Culjak, 2018). Understanding the development and progression of mental health difficulties is of paramount importance to aid the development of tailored interventions to reduce both individual distress and demands on health and social care systems.

Little is known about how mental health problems change and develop over time. A recent study identified six developmental trajectories of internalising and externalising symptoms and found that particular childhood experiences predicted which trajectory a young person followed (Dugre et al., 2019). This study was conducted with data collected at two time points from 10-18year olds in the Longitudinal Studies of Child Abuse and Neglect (LONGSCAN) Consortium.

Aim:

The primary aim of the current study is to replicate the trajectory-based modelling in Dugre et al. (2019) in the IMAGEN dataset to test whether the same six trajectories emerge. The IMAGEN dataset has similar time points to LONGSCAN, so may be comparable in it's sensitvity to subtle changes in the time course of externalising and internalising symptoms. A second aim is to extend Dugre et al.'s (2019) study by exploring whether baseline cognitive abilities predict developmental trajectories of psychopathology. Cognitive impairments are implicated in the onset and maintenance of mental health difficulties (e.g. Carlson & Wang, 2007; Huang-Pollock et al., 2017; McTeague et al. 2016; Ochsner & Gross, 2005). It is therefore prudent to test whether different profiles of cognitive impairment differentially predict the time course of symptoms of psychopathology. Understanding more about how cognitive and mental health problems co-occur across adolescence will provide important insights into risk and resilience factors and may inform the development of tailored therapies.

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8. Terms & Conditions

☒ I have read and agree to the IMAGEN Data Access Policy.

☒ I agree that I will comply with the EU General Data Protection Regulation in the use of the data provided by IMAGEN.

☐ (If requesting access to -omics data) I agree to only use the data for the stated research purposes.

Appendix F

Approval to access IMAGEN data

Sunday, June 12, 2022 at 15:30:57 British Summer Time

Subject: Proposal update
Date: Wednesday, 17 February 2021 at 12:19:16 Greenwich Mean Time
From: Robert Whelan
To: Joni Holmes
CC: Jenna Parker (MED - Postgraduate Researcher), Marc Bennett

Warning: This email is from outside the UEA system. Do not click on links or attachments unless you expect them from the sender and know the content is safe.

Hi Joni et al.,

Sorry for the delayed notification about the IMAGEN proposal; there was a bit of staff turnover in IMAGEN. The proposal has been approved, happy to catch up at some point about this,

All the best,
Rob

Robert Whelan, PhD
http://www.whelanlabtcd.org/meet-the-team/robert-whelan/

Emails are being monitored, however I will be slow to reply in February I would be grateful if you could please allow additional time for a reply.

Begin forwarded message:

From: "Quinlan, Erin" <erin.quinlan@kcl.ac.uk>
Subject: Re: A New Year! (with a new transition and gratitude)
Date: 16 February 2021 at 18:58:31 GMT
To: Robert Whelan <whelanrob@gmail.com>

Hi Rob,

I was talking to Lauren Robinson and she mentioned you asked about the status of your proposals circulated just before the holidays.

I didn't receive any comments so indeed they're approved. Apologies for not sending the confirmation sooner!!

Best wishes,
Erin

_____
Erin Burke, PhD
Lecturer / IMAGEN Project Coordinator
Social, Genetic and Developmental Psychiatry Centre
Centre for Population Neuroscience and Precision Medicine (PONS)

Appendix G

Amendment to approval access IMAGEN data

From: "Joni Holmes (PSY - Staff)" <Joni.Holmes@uea.ac.uk>
Subject: RE: [ext] RE: Written approval of permission required
Date: 9 May 2022 at 15:16:06 BST
To: "Schumann, Gunter" <gunter.schumann@charite.de>, Arun Bokde <BOKDEA@tcd.ie>, "Jenna Parker (MED - Postgraduate Researcher)" <J.Parker2@uea.ac.uk>, ponscentre <ponscentre@charite.de>
Cc: "imagendatabase@cea.fr" <imagendatabase@cea.fr>, Robert Whelan <Robert.Whelan@tcd.ie>

Many thanks Gunter and Arun

From: Schumann, Gunter <gunter.schumann@charite.de> **Sent:** 09 May 2022 13:59 **To:** Arun Bokde <BOKDEA@tcd.ie>; Joni Holmes (PSY - Staff) <Joni.Holmes@uea.ac.uk>; Jenna Parker (MED - Postgraduate Researcher) <J.Parker2@uea.ac.uk>; ponscentre <ponscentre@charite.de> **Cc:** imagendatabase@cea.fr; Robert Whelan <Robert.Whelan@tcd.ie> **Subject:** Re: [ext] RE: Written approval of permission required

Dear Joni,

on behalf of the IMAGEN consortium I approve of the requested changes.

Best wishes,

Gunter Schumann

- IMAGEN coordinator-

Professor Gunter Schumann, MD PhD; Chair and Director, Centre for Population Neuroscience and Stratified Medicine (PONS), ISTBI, Fudan University Shanghai and Dept. of Psychiatry and Neuroscience, Charité University Medicine, Berlin.

From: Arun Bokde <BOKDEA@tcd.ie>**Sent:** 09 May 2022 10:53**To:** Joni Holmes (PSY - Staff); Jenna Parker (MED - Postgraduate Researcher); ponscentre; Schumann, Gunter**Cc:** imagendatabase@cea.fr; Robert Whelan**Subject:** [ext] RE: Written approval of permission required

Dear Gunter,

Please see email below from Joni Holmes in regards using IMAGEN data – requesting a formal approval for using the data.

Best wishes,

Arun

Arun Bokde, PhD

Associate Professor

Discipline of Psychiatry, School of Medicine

and

Trinity College Institute of Neuroscience

Trinity College Dublin

Dublin, IRELAND

Post address:

Lloyd Institute

TCIN room 305

Trinity College Dublin

Dublin 2 IRELAND

Email: bokdea@tcd.ie

From: Joni Holmes (PSY - Staff) <Joni.Holmes@uea.ac.uk> **Sent:** Sunday 8 May 2022 11:45 **To:** Jenna Parker (MED - Postgraduate Researcher) <J.Parker2@uea.ac.uk>; ponscentre@charite.de **Cc:** imagendatabase@cea.fr; Arun Bokde <BOKDEA@tcd.ie>; Robert Whelan <Robert.Whelan@tcd.ie> **Subject:** Written approval of permission required

Dear Arun et al.,

Further to the correspondence below, I am writing to request written permission for us to use the Affective Go/ No Go and Cambridge Gambling task data from baseline and Time 3 in our analyses, in addition to the other cognitive data we already have permission to use. We received informal approval a few months back, but need an email confirming this approval because Jenna, the clinical psychology doctoral student using these data, needs to submit her thesis on 24th May with proof that the request was approved. I am sure you can appreciate the time pressure Jenna is under to put her thesis together alongside her clinical practice work, so I would very grateful if you could send the approval as soon as possible.

We look forward to sharing our analyses with you soon, With many thanks,

Joni

Professor Joni Holmes

Professor of Psychology and Deputy Research Director, University of East Anglia

Senior Affiliated Scientist, MRC Cognition & Brain Sciences Unit, University of Cambridge

www.joniholmeslab.com

School of Psychology

Faculty of Social Sciences

University of East Anglia (UEA)

Norwich Research Park

Norwich, Norfolk, NR4 7TJ

***I work flexibly and do not expect you to respond outside your normal working hours.**

From: Jenna Parker (MED - Postgraduate Researcher) <J.Parker2@uea.ac.uk>
Sent: 29 April 2022 10:27 **To:** ponscentre@charite.de **Cc:** imagendatabase@cea.fr; arun.bokde@tcd.ie; Robert Whelan <whelanr3@tcd.ie>; Joni Holmes (PSY - Staff) <Joni.Holmes@uea.ac.uk> **Subject:** Re: [Imagen database] Database account **Importance:** High

Dear all,

I wondered if there had been any progress regarding my request below. I already have access to the data, as provided previously, but require a simple e-mail confirming that I have approval to use data not included in my original request.

With best wishes,

Jenna

From: Jenna Parker (MED - Postgraduate Researcher) <J.Parker2@uea.ac.uk>**Date:** Friday, 22 April 2022 at 10:16**To:** ponscentre@charite.de <ponscentre@charite.de>**Cc:** imagendatabase@cea.fr <imagendatabase@cea.fr>, arun.bokde@tcd.ie <arun.bokde@tcd.ie>, Robert Whelan <whelanr3@tcd.ie>, Joni Holmes (PSY - Staff) <Joni.Holmes@uea.ac.uk>**Subject:** Re: [Imagen database] Database account

Dear all,

Further to my e-mail below, I wondered if you have had chance to consider my request to use the AGNG and CGT data from the IMAGEN study as an extension to previously granted permission?

This is for a paper to be submitted as part of a doctorate in clinical psychology, and so there is time pressure as my submission date approaches.

With very many thanks,

Jenna

From: Jenna Parker (MED - Postgraduate Researcher) <J.Parker2@uea.ac.uk>**Date:** Wednesday, 23 March 2022 at 15:52**To:** ponscentre@charite.de <ponscentre@charite.de>**Cc:** imagendatabase@cea.fr <imagendatabase@cea.fr>, arun.bokde@tcd.ie <arun.bokde@tcd.ie>, Robert Whelan <whelanr3@tcd.ie>, Joni Holmes (PSY - Staff) <Joni.Holmes@uea.ac.uk>**Subject:** FW: [Imagen database] Database account

Hello,

Further to our conversation with Dimitri, below, I am contacting you to request permission to use the AGNG and CGT data from the IMAGEN study as an extension to previously granted permission (see attached for original application).

We initially asked for permission to use data from some of the CANTAB tasks, but having looked at the available data we feel that the inclusion of the AGNG and CGT task data would be beneficial to our analysis.

I would be very grateful if you could inform me how best to proceed with this request, or if it is something you could answer directly?

With many thanks,

Jenna Parker

Appendix H

Strengths and difficulties questionnaire

Strengths and Difficulties Questionnaire

For each item, please mark the box for Not True, Somewhat True or Certainly True. It would help us if you answered all items as best you can even if you are not absolutely certain or the item seems daft! Please give your answers on the basis of the child's behaviour over the last six months or this school year.

Child's Name ..... Male/Female

Date of Birth.....

	Not True	Somewhat True	Certainly True
Considerate of other people's feelings	☐	☐	☐
Restless, overactive, cannot stay still for long	☐	☐	☐
Often complains of headaches, stomach-aches or sickness	☐	☐	☐
Shares readily with other children (treats, toys, pencils etc.)	☐	☐	☐
Often has temper tantrums or hot tempers	☐	☐	☐
Rather solitary, tends to play alone	☐	☐	☐
Generally obedient, usually does what adults request	☐	☐	☐
Many worries, often seems worried	☐	☐	☐
Helpful if someone is hurt, upset or feeling ill	☐	☐	☐
Constantly fidgeting or squirming	☐	☐	☐
Has at least one good friend	☐	☐	☐
Often fights with other children or bullies them	☐	☐	☐
Often unhappy, down-hearted or tearful	☐	☐	☐
Generally liked by other children	☐	☐	☐
Easily distracted, concentration wanders	☐	☐	☐
Nervous or clingy in new situations, easily loses confidence	☐	☐	☐
Kind to younger children	☐	☐	☐
Often lies or cheats	☐	☐	☐
Picked on or bullied by other children	☐	☐	☐
Often volunteers to help others (parents, teachers, other children)	☐	☐	☐
Thinks things out before acting	☐	☐	☐
Steals from home, school or elsewhere	☐	☐	☐
Gets on better with adults than with other children	☐	☐	☐
Many fears, easily scared	☐	☐	☐
Sees tasks through to the end, good attention span	☐	☐	☐

Signature ..... Date .....

Parent/Teacher/Other (please specify:)

Thank you very much for your help

Appendix I

ERP supplementary materials

Table S1.

Comparison of SDQ data at T1 for participants with and without T2 data.

SDQ subscale	N no Follow up	M no Follow up	SD no Follow up	N follow up	M follow up	SD follow up	t	df	p	d
Emotion	1,225	2.64	2.05	79	2.70	2.20	-0.20	86.95	0.84	0.03
Conduct	1,225	1.97	1.44	79	1.96	1.40	0.07	88.94	0.95	-0.01
Hyper	1,225	3.86	2.12	79	3.62	1.96	1.04	90.10	0.30	-0.11
Peer	1,225	1.79	1.57	79	1.81	1.73	-0.10	86.52	0.92	0.01
Prosoc	1,225	7.78	1.64	79	7.82	1.52	-0.26	90.09	0.79	0.03

Figure S2.

SDQ Scoring Protocol

Scoring the Strengths & Difficulties Questionnaire for age 4-17

The 25 items in the SDQ comprise 5 scales of 5 items each. It is usually easiest to score all 5 scales first before working out the total difficulties score. 'Somewhat True' is always scored as 1, but the scoring of 'Not True' and 'Certainly True' varies with the item, as shown below scale by scale. For each of the 5 scales the score can range from 0 to 10 if all items were completed. These scores can be scaled up pro-rata if at least 3 items were completed, e.g. a score of 4 based on 3 completed items can be scaled up to a score of 7 (6.67 rounded up) for 5 items.

Table 1: Scoring symptom scores on the SDQ for 4-17 year olds

	Not True	Somewhat True	Certainly True
Emotional problems scale			
Often complains of headaches... *(I get a lot of headaches…)*	0	1	**2**
Many worries... *(I worry a lot)*	0	1	**2**
Often unhappy, downhearted... *(I am often unhappy….)*	0	1	**2**
Nervous or clingy in new situations... *(I am nervous in new situations…)*	0	1	**2**
Many fears, easily scared *(I have many fears…)*	0	1	**2**
Conduct problems Scale			
Often has temper tantrums or hot tempers *(I get very angry)*	0	1	**2**
Generally obedient... *(I usually do as I am told)*	**2**	1	0
Often fights with other children... *(I fight a lot)*	0	1	**2**
Often lies or cheats *(I am often accused of lying or cheating)*	0	1	**2**
Steals from home, school or elsewhere *(I take things that are not mine)*	0	1	**2**
Hyperactivity scale			
Restless, overactive... *(I am restless…)*	0	1	**2**
Constantly fidgeting or squirming *(I am constantly fidgeting….)*	0	1	**2**
Easily distracted, concentration wanders *(I am easily distracted)*	0	1	**2**
Thinks things out before acting *(I think before I do things)*	**2**	1	0
Sees tasks through to the end... *(I finish the work I am doing)*	**2**	1	0
Peer problems scale			
Rather solitary, tends to play alone *(I am usually on my own)*	0	1	**2**
Has at least one good friend *(I have one goof friend or more)*	**2**	1	0
Generally liked by other children *(Other people my age generally like me)*	**2**	1	0
Picked on or bullied... *(Other children or young people pick on me)*	0	1	**2**
Gets on better with adults than with other children *(I get on better with adults than with people my age)*	0	1	**2**
Prosocial scale			
Considerate of other people's feelings *(I try to be nice to other people)*	0	1	**2**
Shares readily with other children... *(I usually share with others)*	0	1	**2**
Helpful if someone is hurt... *(I am helpful is someone is hurt…)*	0	1	**2**
Kind to younger children *(I am kind to younger children)*	0	1	**2**
Often volunteers to help others... *(I often volunteer to help others)*	0	1	**2**

Total difficulties score: This is generated by summing scores from all the scales except the prosocial scale. The resultant score ranges from 0 to 40, and is counted as missing of one of the 4 component scores is missing.

'Externalising' and 'internalising' scores: The externalising score ranges from 0 to 20 and is the sum of the conduct and hyperactivity scales. The internalising score ranges from 0 to 20 and is the sum of the emotional and peer problems scales. Using these two amalgamated scales

may be preferable to using the four separate scales in community samples, whereas using the four separate scales may add more value in high-risk samples *(see Goodman & Goodman. 2009 Strengths and difficulties questionnaire as a dimensional measure of child mental health. J Am Acad Child Adolesc Psychiatry 48(4), 400-403).*

Generating impact scores

When using a version of the SDQ that includes an 'impact supplement', the items on overall distress and impairment can be summed to generate an impact score that ranges from 0 to 10 for parent- and self-report, and from 0 to 6 for teacher-report.

Table 2: Scoring the SDQ impact supplement

	Not at all	Only a little	A medium amount	A great deal
Parent report:				
Difficulties upset or distress child	0	0	1	2
Interfere with HOME LIFE	0	0	1	2
Interfere with FRIENDSHIPS	0	0	1	2
Interfere with CLASSROOM LEARNING	0	0	1	2
Interfere with LEISURE ACTIVITIES	0	0	1	2
Teacher report:				
Difficulties upset or distress child	0	0	1	2
Interfere with PEER RELATIONS	0	0	1	2
Interfere with CLASSROOM LEARNING	0	0	1	2
Self-report report:				
Difficulties upset or distress child	0	0	1	2
Interfere with HOME LIFE	0	0	1	2
Interfere with FRIENDSHIPS	0	0	1	2
Interfere with CLASSROOM LEARNING	0	0	1	2
Interfere with LEISURE ACTIVITIES	0	0	1	2

Responses to the questions on chronicity and burden to others are not included in the impact score. When respondents have answered 'no' to the first question on the impact supplement (i.e. when they do not perceive themselves as having any emotional or behavioural difficulties), they are not asked to complete the questions on resultant distress or impairment; the impact score is automatically scored zero in these circumstances.

Cut-points for SDQ scores: original three-band solution and newer four-band solution

Although SDQ scores can be used as continuous variables, it is sometimes convenient to categorise scores. The initial bandings presented for the SDQ scores were 'normal', 'borderline' and 'abnormal'. These bandings were defined based on a population-based UK survey, attempting to choose cutpoints such that 80% of children scored 'normal', 10% 'borderline' and 10% 'abnormal'.

More recently a four-fold classification has been created based on an even larger UK community sample. This four-fold classification differs from the original in that it (1) divided the top 'abnormal' category into two groups, each containing around 5% of the population, (2) renamed the four categories (80% 'close to average', 10% 'slightly raised, 5% 'high' and 5% 'very high' for all scales except prosocial, which is 80% 'close to average', 10% 'slightly lowered', 5% 'low' and 5% 'very low'), and (3) changed the cut-points for some scales, to better reflect the proportion of children in each category in the larger dataset.

Table 3: Categorising SDQ scores for 4-17 year olds

	Original three-band categorisation			Newer four-band categorisation			
	Normal	Borderline	Abnormal	Close to average	Slightly raised (/slightly lowered)	High (/Low)	Very high (very low)
Parent completed SDQ							
Total difficulties score	0-13	14-16	17-40	0-13	14-16	17-19	20-40
Emotional problems score	0-3	4	5-10	0-3	4	5-6	7-10
Conduct problems score	0-2	3	4-10	0-2	3	4-5	6-10
Hyperactivity score	0-5	6	7-10	0-5	6-7	8	9-10
Peer problems score	0-2	3	4-10	0-2	3	4	5-10
Prosocial score	6-10	5	0-4	8-10	7	6	0-5
Impact score	0	1	2-10	0	1	2	3-10
Teacher completed SDQ							
Total difficulties score	0-11	12-15	16-40	0-11	12-15	16-18	19-40
Emotional problems score	0-4	5	6-10	0-3	4	5	6-10
Conduct problems score	0-2	3	4-10	0-2	3	4	5-10
Hyperactivity score	0-5	6	7-10	0-5	6-7	8	9-10
Peer problems score	0-3	4	5-10	0-2	3-4	5	6-10
Prosocial score	6-10	5	0-4	6-10	5	4	0-3
Impact score	0	1	2-10	0	1	2	3-10
Self-completed SDQ							
Total difficulties score	0-15	16-19	20-40	0-14	15-17	18-19	20-40
Emotional problems score	0-5	6	7-10	0-4	5	6	7-10
Conduct problems score	0-3	4	5-10	0-3	4	5	6-10
Hyperactivity score	0-5	6	7-10	0-5	6	7	8-10
Peer problems score	0-3	4-5	6-10	0-2	3	4	5-10
Prosocial score	6-10	5	0-4	7-10	6	5	0-4
Impact score	0	1	2-10	0	1	2	3-10

Note that both these systems only provide a rough-and-ready way of screening for disorders; combining information from SDQ symptom and impact scores from multiple informants is better, but still far from perfect.

Table S3.

Comparison of SDQ scores across clusters at T1

SDQ subscale	N	M	SD	N nd	M nd	SD nd	t	df	p	d	dStars	Cluster Name
Cluster 1												
Emotion	357	2.48	1.91	520	1.77	1.28	-6.11	572.5	0	0.45	*	ext_t1
Conduct	357	3.13	1.68	520	1.34	0.89	-18.42	495.11	0	1.41	* * *	ext_t1
Hyperactivity	357	5.83	1.82	520	2.93	1.57	-24.47	687.31	0	1.73	* * *	ext_t1
Peer problems	357	1.58	1.48	520	0.97	0.78	-7.12	494.83	0	0.54	* *	ext_t1
Prosocial	357	6.69	1.77	520	8.52	0.99	17.67	508.88	0	-1.34	* * *	ext_t1
Cluster 2												
Emotion	199	5.83	1.39	520	1.77	1.28	-35.87	334.22	0	3.1	* * *	int_t1
Conduct	199	1.98	1.26	520	1.34	0.89	-6.48	276.65	0	0.63	* *	int_t1
Hyperactivity	199	3.78	1.85	520	2.93	1.57	-5.76	313.02	0	0.52	* *	int_t1
Peer problems	199	2.23	1.73	520	0.97	0.78	-9.88	229.95	0	1.12	* * *	int_t1
Prosocial	199	7.83	1.6	520	8.52	0.99	5.66	258.14	0	-0.58	* *	int_t1
Cluster 3												
Emotion	228	2.13	1.46	520	1.77	1.28	-3.22	385.77	0.001	0.27	*	social_t1
Conduct	228	1.6	1.02	520	1.34	0.89	-3.38	384.19	0.001	0.28	*	social_t1
Hyperactivity	228	2.87	1.62	520	2.93	1.57	0.5	421.07	0.61	-0.04	ns	social_t1
Peer problems	228	3.62	1.36	520	0.97	0.78	-27.48	295.35	0	2.66	* * *	social_t1
Prosocial	228	7.76	1.63	520	8.52	0.99	6.52	303	0	-0.62	* *	social_t1

Table S4.

Chi square results for males and females at T1

Cluster identity at T1	Boys	Girls	Chi-square	p.value
Internalising	48	151	41.31	>0.001
Externalising	204	153	15.17	>0.001
Social difficulties	136	92	14.99	>0.001
No difficulties	223	297	3.29	0.07

Table S5.

Cognitive profiles of SDQ clusters at T1

	N	M	SD	N nd	M nd	SD nd	t	df	p	d	p.fdr	Sig. level
SWM Between errors Ext	338	19.76	13.76	505	16.87	13.35	-3.03	707.68	0.003	0.21	0.04	* *
SWM Between errors Cext												
AGN Affective response bias Mean ext	270	-13.99	52.56	427	-17.5	53.17	-0.86	577.19	0.39	0.07	0.53	ns
AGN Affective response bias Mean Cext												
CGT Delay aversion Ext	280	0.24	0.14	435	0.23	0.14	-1.26	606.25	0.21	0.1	0.35	ns
CGT Delay aversion Cext												
CGT Risk adjustment Ext	281	1.55	1.01	439	1.68	0.98	1.65	580.13	0.1	-0.13	0.22	ns
CGT Risk adjustment Cext												
CGT Risk taking Ext	281	0.56	0.15	439	0.53	0.13	-2.27	549.15	0.02	0.18	0.16	*
CGT Risk taking Cext												
SWM Between errors Int	186	19.22	13.67	505	16.87	13.35	-2.02	323.28	0.04	0.17	0.16	*
SWM Between errors Cint												
AGN Affective response bias Mean Int	160	-10.81	51.46	427	-17.5	53.17	-1.4	294.12	0.16	0.13	0.31	ns
AGN Affective response bias Mean Cint												
CGT Delay aversion Int	163	0.25	0.15	435	0.23	0.14	-1.63	276.68	0.1	0.15	0.22	ns
CGT Delay aversion Cint												

CGT Risk adjustment Int	163	1.62	1.03	439	1.68	0.98	0.65	277.4	0.52	-0.06	0.62	ns
CGT Risk adjustment Cint												
CGT Risk taking Int	163	0.51	0.13	439	0.53	0.13	2.1	299.61	0.04	-0.19	0.16	*
CGT Risk taking Cint												
SWM Between errors Social	219	18.94	13.17	505	16.87	13.35	-1.94	419.56	0.05	0.16	0.16	ns
SWM Between errors Csocial												
AGN Affective response bias Mean Social	189	-14.47	57.72	427	-17.5	53.17	-0.62	334.9	0.53	0.06	0.62	ns
AGN Affective_response_bias_Mean_Csocial												
CGT Delay aversion Social	196	0.23	0.14	435	0.23	0.14	0.04	385.54	0.97	-0	0.97	ns
CGT Delay aversion Csocial												
CGT Risk adjustment Social	196	1.58	1.03	439	1.68	0.98	1.11	355.96	0.27	-0.1	0.4	ns
CGT Risk adjustment Csocial												
CGT Risk taking Social	196	0.53	0.15	439	0.53	0.13	0.52	329.71	0.6	-0.05	0.64	ns
CGT Risk taking Csocial												

Note. SWM = Spatial working memory; AGN = Affective Go/No-go; CGT = Cambridge Gambling Task.

Table S6.

Comparison of SDQ scores across clusters at T1

SDQ subscale	N	M	SD	N nd	M nd	SD nd	t	df	p	d	dStars	Cluster Name
Cluster 1												
Emotion	232	3.16	2.25	649	1.48	1.34	-10.74	291.87	0	1.03	* * *	ext_t2
Conduct	232	2.39	1.5	649	1.21	0.81	-11.43	279.93	0	1.15	* * *	ext_t2
Hyperactivity	232	5.86	1.77	649	2.27	1.59	-27.22	371.16	0	2.2	* * *	ext_t2
Peer problems	232	1.85	1.39	649	1.14	0.77	-7.38	283.32	0	0.73	* *	ext_t2
Prosocial	232	7.68	1.8	649	9.11	1.03	11.54	286.8	0	-1.13	* * *	ext_t2
Cluster 2												
Emotion	213	6.41	1.39	649	1.48	1.34	-45.25	350.26	0	3.64	* * *	int_t2
Conduct	213	1.6	1.27	649	1.21	0.81	-4.25	270.35	0	0.42	*	int_t2
Hyperactivity	213	3.32	1.61	649	2.27	1.59	-8.3	356.18	0	0.66	* *	int_t2
Peer problems	213	2.57	1.36	649	1.14	0.77	-14.54	257.77	0	1.5	* * *	int_t2
Prosocial	213	8.49	1.59	649	9.11	1.03	5.35	272.45	0	-0.52	* *	int_t2
Cluster 3												
Emotion	210	1.98	1.52	649	1.48	1.34	-4.27	320.74	0	0.36	*	social_t2
Conduct	210	1.62	1.12	649	1.21	0.81	-4.93	282.54	0	0.46	*	social_t2
Hyperactivity	210	2.63	1.6	649	2.27	1.59	-2.91	351.86	0	0.23	*	social_t2
Peer problems	210	3.38	1.26	649	1.14	0.77	-24.35	261.38	0	2.46	* * *	social_t2
Prosocial	210	7.91	1.75	649	9.11	1.03	9.41	256.97	0	-0.97	* * *	social_t2

Table S7.

Chi square results for males and females at T2

Cluster identity at T2	Boys	Girls	Chi-square	p.value
Internalising	50	163	45.88	0.001
Externalising	133	99	10.68	0.001
Social difficulties	112	98	3.8	0.05
No difficulties	313	336	0.67	0.41

Table S8.

Comparisons of cognitive function of participants with emerging mental health symptoms at T2 to those with stable no difficulties.

Task	Group1	Group2	p	p.adj	p.format	Sig level
SWM	nd_t1-> nd_t2	nd_t1-> ext_t2	0.02	0.09	0.01869	*
Affective go/no-go	nd_t1-> nd_t2	nd_t1-> ext_t2	0.36	0.58	0.35953	ns
CGT Delay aversion	nd_t1-> nd_t2	nd_t1-> ext_t2	0.47	0.58	0.46736	ns
CGT Risk adjustment	nd_t1-> nd_t2	nd_t1-> ext_t2	0.72	0.72	0.72478	ns
CGT Risk taking	nd_t1-> nd_t2	nd_t1-> ext_t2	0.06	0.16	0.06392	ns
SWM	nd_t1-> nd_t2	nd_t1-> int_t2	0.3	0.49	0.29611	ns
Affective go/no-go	nd_t1-> nd_t2	nd_t1-> int_t2	0.94	0.94	0.93937	ns
CGT Delay aversion	nd_t1-> nd_t2	nd_t1-> int_t2	0.51	0.64	0.50975	ns
CGT Risk adjustment	nd_t1-> nd_t2	nd_t1-> int_t2	0.07	0.18	0.07352	ns
CGT Risk taking	nd_t1-> nd_t2	nd_t1-> int_t2	0.06	0.18	0.06156	ns
SWM	nd_t1-> nd_t2	nd_t1-> social_t2	0.78	0.84	0.77808	ns
Affective go/no-go	nd_t1-> nd_t2	nd_t1-> social_t2	0.69	0.84	0.69074	ns
CGT Delay aversion	nd_t1-> nd_t2	nd_t1-> social_t2	0.83	0.84	0.83082	ns
CGT Risk adjustment	nd_t1-> nd_t2	nd_t1-> social_t2	0.84	0.84	0.84199	ns
CGT Risk taking	nd_t1-> nd_t2	nd_t1-> social_t2	0.8	0.84	0.80042	ns

Note. SWM = Spatial working memory; CGT = Cambridge Gambling Task; nd = no difficulties; ext = externalising; int = internalising; ns = not significant.

Table S9.

Comparisons of cognitive function of participants with persisting mental health symptoms at T2 to those with stable no difficulties.

Task	group1	group2	p	p.adj	p.format	Sig level
SWM	nd_t1-> nd_t2	ext_t1-> ext_t2	0.01	0.02	0.00886	* *
Affective go/no-go	nd_t1-> nd_t2	ext_t1-> ext_t2	0.78	0.78	0.7849	ns
CGT Delay aversion	nd_t1-> nd_t2	ext_t1-> ext_t2	0.47	0.59	0.47144	ns
CGT Risk adjustment	nd_t1-> nd_t2	ext_t1-> ext_t2	0.01	0.02	0.0099	* *
CGT Risk taking	nd_t1-> nd_t2	ext_t1-> ext_t2	0.1	0.17	0.10211	ns
SWM	nd_t1-> nd_t2	int_t1-> int_t2	0.15	0.37	0.14887	ns
Affective go/no-go	nd_t1-> nd_t2	int_t1-> int_t2	0.24	0.4	0.24127	ns
CGT Delay aversion	nd_t1-> nd_t2	int_t1-> int_t2	0.73	0.73	0.72725	ns
CGT Risk adjustment	nd_t1-> nd_t2	int_t1-> int_t2	0.52	0.65	0.51788	ns
CGT Risk taking	nd_t1-> nd_t2	int_t1-> int_t2	0.09	0.37	0.08859	ns
SWM	nd_t1-> nd_t2	social_t1-> social_t2	0.23	0.39	0.23343	ns
Affective go/no-go	nd_t1-> nd_t2	social_t1-> social_t2	0.93	1	0.93051	ns
CGT Delay aversion	nd_t1-> nd_t2	social_t1-> social_t2	0.08	0.19	0.07615	ns
CGT Risk adjustment	nd_t1-> nd_t2	social_t1-> social_t2	0.01	0.06	0.01187	*
CGT Risk taking	nd_t1-> nd_t2	social_t1-> social_t2	1	1	0.99502	ns

Note. SWM = Spatial working memory; CGT = Cambridge Gambling Task; nd = no difficulties; ext = externalising; int = internalising; ns = not significant.

Table S10.

Comparisons of cognitive function of participants with resolving mental health symptoms at T2 to those with stable no difficulties.

Task	group1	group2	p	p.adj	p.format	Sig level
SWM	nd_t1-> nd_t2	ext_t1-> ext_t2	0.01	0.02	0.00886	**
Affective go/no-go	nd_t1-> nd_t2	ext_t1-> ext_t2	0.78	0.78	0.7849	ns
CGT Delay aversion	nd_t1-> nd_t2	ext_t1-> ext_t2	0.47	0.59	0.47144	ns
CGT Risk adjustment	nd_t1-> nd_t2	ext_t1-> ext_t2	0.01	0.02	0.0099	**
CGT Risk taking	nd_t1-> nd_t2	ext_t1-> ext_t2	0.1	0.17	0.10211	ns
SWM	nd_t1-> nd_t2	int_t1-> int_t2	0.15	0.37	0.14887	ns
Affective go/no-go	nd_t1-> nd_t2	int_t1-> int_t2	0.24	0.4	0.24127	ns
CGT Delay aversion	nd_t1-> nd_t2	int_t1-> int_t2	0.73	0.73	0.72725	ns
CGT Risk adjustment	nd_t1-> nd_t2	int_t1-> int_t2	0.52	0.65	0.51788	ns
CGT Risk taking	nd_t1-> nd_t2	int_t1-> int_t2	0.09	0.37	0.08859	ns
SWM	nd_t1-> nd_t2	social_t1-> social_t2	0.23	0.39	0.23343	ns
Affective go/no-go	nd_t1-> nd_t2	social_t1-> social_t2	0.93	1	0.93051	ns
CGT Delay aversion	nd_t1-> nd_t2	social_t1-> social_t2	0.08	0.19	0.07615	ns
CGT Risk adjustment	nd_t1-> nd_t2	social_t1-> social_t2	0.01	0.06	0.01187	*
CGT Risk taking	nd_t1-> nd_t2	social_t1-> social_t2	1	1	0.99502	ns

Note. SWM = Spatial working memory; CGT = Cambridge Gambling Task; nd = no difficulties; ext = externalising; int = internalising; ns = not significant.

Table S11.

Comparisons of cognitive function of participants with any mental health symptoms at T2 to those with stable no difficulties.

Task	group1	group2	p	p.adj	p.format	p.signif
T1						
SWM	nd_t1-> nd_t2	d_t1-> d_t2	0.0036883	0.0037	0.0037	* *
SWM	nd_t1-> nd_t2	d_t1-> nd_t2	0.23824267	0.24	0.2382	ns
SWM	nd_t1-> nd_t2	nd_t1-> d_t2	0.58349232	0.58	0.5835	ns
Affective go/no-go	nd_t1-> nd_t2	d_t1-> d_t2	0.30567098	0.31	0.3057	ns
Affective go/no-go	nd_t1-> nd_t2	d_t1-> nd_t2	0.23512169	0.24	0.2351	ns
Affective go/no-go	nd_t1-> nd_t2	nd_t1-> d_t2	0.73948113	0.74	0.7395	ns
CGT Delay aversion	nd_t1-> nd_t2	d_t1-> d_t2	0.3291771	0.33	0.3292	ns
CGT Delay aversion	nd_t1-> nd_t2	d_t1-> nd_t2	0.22696227	0.23	0.227	ns
CGT Delay aversion	nd_t1-> nd_t2	nd_t1-> d_t2	0.87230088	0.87	0.8723	ns
CGT Risk adjustment	nd_t1-> nd_t2	d_t1-> d_t2	0.0223089	0.022	0.0223	*
CGT Risk adjustment	nd_t1-> nd_t2	d_t1-> nd_t2	0.350109	0.35	0.3501	ns
CGT Risk adjustment	nd_t1-> nd_t2	nd_t1-> d_t2	0.23866833	0.24	0.2387	ns
CGT Risk taking	nd_t1-> nd_t2	d_t1-> d_t2	0.6547972	0.65	0.6548	ns
CGT Risk taking	nd_t1-> nd_t2	d_t1-> nd_t2	0.93955949	0.94	0.9396	ns
CGT Risk taking	nd_t1-> nd_t2	nd_t1-> d_t2	0.9846222	0.98	0.9846	ns
T2						
SWM	nd_t1-> nd_t2	d_t1-> d_t2	0.01169453	0.012	0.0117	*
SWM	nd_t1-> nd_t2	d_t1-> nd_t2	0.23576427	0.24	0.2358	ns
SWM	nd_t1-> nd_t2	nd_t1-> d_t2	0.92425247	0.92	0.9243	ns
CGT Delay aversion	nd_t1-> nd_t2	d_t1-> d_t2	0.059331	0.059	0.0593	ns
CGT Delay aversion	nd_t1-> nd_t2	d_t1-> nd_t2	0.15418886	0.15	0.1542	ns
CGT Delay aversion	nd_t1-> nd_t2	nd_t1-> d_t2	0.25211891	0.25	0.2521	ns
CGT Risk adjustment	nd_t1-> nd_t2	d_t1-> d_t2	0.07734672	0.077	0.0773	ns

CGT Risk adjustment	nd_t1-> nd_t2	d_t1-> nd_t2	0.74100097	0.74	0.741	ns
CGT Risk adjustment	nd_t1-> nd_t2	nd_t1-> d_t2	0.88567009	0.89	0.8857	ns
CGT Risk taking	nd_t1-> nd_t2	d_t1-> d_t2	0.790209	0.79	0.7902	ns
CGT Risk taking	nd_t1-> nd_t2	d_t1-> nd_t2	0.44903995	0.45	0.449	ns
CGT Risk taking	nd_t1-> nd_t2	nd_t1-> d_t2	0.23422191	0.23	0.2342	ns

Note. SWM = Spatial working memory; CGT = Cambridge Gambling Task; nd = no difficulties; d = difficulties; ns = not significant.

Appendix J

University of East Anglia ethical approval

University of East Anglia
Norwich Research Park
Norwich. NR4 7TJ

Email: ethicsapproval@uea.ac.uk
Web: www.uea.ac.uk

Study title: Developmental trajectories of internalising and externalising symptoms of mental health in young people and their cognitive predictors.

Application ID: ETH2122-1528

Dear Jenna,

Your application was considered on 17th March 2022 by the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee).

The decision is: **approved**.

You are therefore able to start your project subject to any other necessary approvals being given.

This approval will expire on **20th May 2022**.

Please note that your project is granted ethics approval only for the length of time identified above. Any extension to a project must obtain ethics approval by the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) before continuing.

It is a requirement of this ethics approval that you should report any adverse events which occur during your project to the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) as soon as possible. An adverse event is one which was not anticipated in the research design, and which could potentially cause risk or harm to the participants or the researcher, or which reveals potential risks in the treatment under evaluation. For research involving animals, it may be the unintended death of an animal after trapping or carrying out a procedure.

Any amendments to your submitted project in terms of design, sample, data collection, focus etc. should be notified to the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) in advance to ensure ethical compliance. If the amendments are substantial a new application may be required.

Approval by the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) should not be taken as evidence that your study is compliant with the UK General Data Protection Regulation (UK GDPR) and the Data Protection Act 2018. If you need guidance on how to make your study UK GDPR compliant, please contact the UEA Data Protection Officer (dataprotection@uea.ac.uk).

Please can you send your report once your project is completed to the FMH S-REC (fmh.ethics@uea.ac.uk).

I would like to wish you every success with your project.

On behalf of the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee)

Yours sincerely,

Paul Linsley

Appendix K

University of East Anglia ethical approval amendment

University of East Anglia
Norwich Research Park
Norwich. NR4 7TJ

Email: ethicsapproval@uea.ac.uk
Web: www.uea.ac.uk

Study title: Developmental trajectories of internalising and externalising symptoms of mental health in young people and their cognitive predictors.

Application ID: ETH2122-1831 (significant amendments)

Dear Jenna,

Your amendment to your study was considered on 27th April 2022 by the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee).

The decision is: **approved**.

This approval will expire on **31st October 2022**.

Please note that your project is granted ethics approval only for the length of time identified above. Any extension to a project must obtain ethics approval by the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) before continuing.

It is a requirement of this ethics approval that you should report any adverse events which occur during your project to the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) as soon as possible. An adverse event is one which was not anticipated in the research design, and which could potentially cause risk or harm to the participants or the researcher, or which reveals potential risks in the treatment under evaluation. For research involving animals, it may be the unintended death of an animal after trapping or carrying out a procedure.

Any amendments to your submitted project in terms of design, sample, data collection, focus etc. should be notified to the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) in advance to ensure ethical compliance. If the amendments are substantial a new application may be required.

Approval by the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) should not be taken as evidence that your study is compliant with the UK General Data Protection Regulation (UK GDPR) and the Data Protection Act 2018. If you need guidance on how to make your study UK GDPR compliant, please contact the UEA Data Protection Officer (dataprotection@uea.ac.uk).

Please can you send your report once your project is completed to the FMH S-REC (fmh.ethics@uea.ac.uk).

I would like to wish you every success with your project.

On behalf of the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee)

Yours sincerely,

Paul Linsley