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Conduct Problems and Head Injuries Across Development: Investigating Longitudinal Symptom Interplay and Common Neural Correlates

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Abstract

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Conduct problems and childhood head injuries are associated with a wide range of maladaptive outcomes. With emerging evidence suggesting a bidirectional association between the two, further investigation of their longitudinal interplay is warranted. In Paper 1, their linked developmental pathways were explored using latent class analysis on children enrolled in the Millennium Cohort Study (MCS). Results showed that known trajectories of conduct problems (i.e., childhood-limited, persistent, and adolescent-onset) appeared to have distinct linked pathways of head injury. Additionally, cumulative risk at the child, mother, and household levels as well as ADHD and negative maternal parenting were all strongly associated with membership to these clinically relevant linked pathways. Paper 2 elaborated from these findings to investigate whether their co-occurrence had a greater impact on adolescent delinquency compared to their isolated occurrence. Using MCS data, results from negative binomial regression models identified that, indeed, children with a history of co-occurring conduct problems and head injury until age 11 had significantly greater rates of adolescent delinquency at age 14 compared to children with a history of either in isolation or a history of neither. Paper 3 then explored whether neural mechanisms of reward processing were disrupted more so in children with co-occurring conduct disorder and mild traumatic brain injury (mTBI) compared to their isolated occurrence. From utilising data from the Adolescent Brain Cognitive Development study, results showed that their co-occurrence was associated with increased left amygdala and hippocampus activation during receipt of a monetary reward compared to those with either in isolation or typically developing controls. This suggests that children with co-occurring conduct disorder and a mTBI may have a stronger encoding of emotionally salient reward such as monetary gain, which could drive future goal-directed behaviour in pursuit of further reward.

Keywords: Conduct problems, delinquency, head injury, reward

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Research Thesis: Declaration of Authorship

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Definitions and Abbreviations

ABCD ..... Adolescent Brain Cognitive Development study

ACC ..... Anterior cingulate cortex

ACEs ..... Adverse childhood experiences

ADHD ..... Attention-Deficit/Hyperactivity Disorder

CBCL ..... Child Behaviour Checklist

CD ..... Conduct Disorder

CRI ..... Cumulative risk index

DBD ..... Disruptive Behaviour Disorder

DSM-5-TR ..... Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition Text Revision

fMRI ..... Functional magnetic resonance imaging

ICD-11 ..... International Classification of Diseases 11th Revision

K-SADS ..... The Kiddie Schedule for Affective Disorders and Schizophrenia

MCS ..... Millennium Cohort Study

MID ..... Monetary Incentive Delay task

mTBI ..... Mild traumatic brain injury

NAc ..... Nucleus accumbens

ODD ..... Oppositional Defiant Disorder

OFC ..... Orbital frontal cortex

ROI ..... Regions of interest

SDQ ..... Strengths and Difficulties Questionnaire

Chapter 1 An Introduction to Childhood Head Injury and Conduct Problems

1.1 Conduct Disorder: An Overview

Conduct disorder is a psychiatric disorder characterised by persistent disruptive or antisocial behaviour including aggression to people and animals, destruction of property, and deceitfulness or theft (American Psychiatric Association, 2022). The prevalence of conduct disorder is estimated globally between 2% and 4% (Ayano et al., 2024; Bachmann et al., 2024). It is the leading cause of global burden (i.e., condition with greatest years lived with a disability and years of life lost) from a mental health condition among children up to 14 year olds (GBD Mental Disorders Collaborators, 2022). Importantly, conduct disorder is one of the mental health disorder subtypes to show the most significant increase in global prevalence over the last three decades (Piao et al., 2022). However, one must consider whether this is due to more cases of conduct disorder occurring, or whether identification and correct diagnosis of conduct disorder has improved over the decades. Regardless, conduct disorder is not only highly prevalent, but has also been associated with an increased risk of maladaptive outcomes (see Section 1.1.6) extending from adolescence (Beaudry et al., 2021) into adulthood (Copeland et al., 2015). Taken together, the high prevalence and burden of conduct disorder, coupled with its association with long-term maladaptive outcomes justifies a need for continued research to enhance our understanding of this disorder. Such research will be useful for the subsequent development of effective preventive and therapeutic interventions.

1.1.1 Language

At this stage of the thesis, it is important to define key terms related to this psychiatric disorder. Behavioural phenomena are often hard to conceptualise in the social sciences. In fact, Gerring once observed that “the terminology of social science lacks the clarity and constancy of the natural science lexicon” (Gerring, 2001). In the natural sciences, terms such as "neuron" are universally understood and consistently applied to denote a neural nerve cell. However, a set of behavioural symptoms can be interpreted and labelled by one individual as conduct disorder, whilst another may label these as simply “disruptive behaviours”. As such, within this thesis I will aim to navigate these terminological ambiguities by selecting the most accurate and contextually appropriate terminology. This will be guided by the principle of selecting the correct level of abstraction, ensuring alignment with the population being examined and the methodological approaches employed. For instance, the term “conduct problems” will be selected when referring to

symptoms observed within a community sample, whilst “conduct disorder” will be selected when referring to cases where a diagnostic assessment has been conducted.

1.1.2 Epidemiology

1.1.2.1 Prevalence

The high global prevalence of conduct disorder is mirrored across countries. For example, the prevalence rate is approximately 4.6% among 5 to 19 year olds in the UK (5.8% for males and 3.4% for females; Sadler et al., 2018) and 1.1% in the US (1.47% for males and 1.10% for females), though this refers to only cases with an official diagnosis (Bachmann et al., 2024). Whilst this is a highly prevalent psychiatric disorder, it is also highly heterogeneous, with significant variation in both onset and symptom duration. The DSM-5-TR (American Psychiatric Association, 2022), and ICD-11 (World Health Organization, 2019), for example, categorise conduct disorder into three subtypes based on age of symptom onset:

1. Child-onset: symptomatic before age 10
2. Adolescent-onset: symptomatic after age 10
3. Unspecified onset: unable to determine age of onset

Whilst these manuals acknowledge both childhood and adolescent-onset subtypes, they do not account for the duration of symptom presentation. For example, child-onset conduct disorder can account for both childhood-limited or persist conduct disorder (Moffitt, 1993). Both forms present before the age of 10 but only persistent conduct disorder continues to present into adolescence. Importantly, these two types of conduct disorder differ significantly in the severity of their maladaptive outcomes (Bevilacqua et al., 2018). Therefore, although grouped under the same umbrella term within the DSM-5 and ICD-11, they should be regarded as separate presentations of conduct disorder.

In general, the prevalence of conduct disorder tends to increase with age (Maughan et al., 2004), with research suggesting that the adolescent-onset (often referred to as adolescent-limited) subtype is more common (4.6% for females and 51.% for males) than persistent conduct disorder (0.5% for females and 1.9% for males; Moore et al., 2017). Further, prevalence appears to be affected by a gender paradox. That is, whilst the overall prevalence of conduct disorder is greater in males, females appear to typically develop conduct disorder later (i.e., adolescent-onset) and appear to be more severely impacted by symptoms (Konrad et al., 2022). Nevertheless, conduct disorder, in general, is a highly prevalent disorder, which justifies the need for further research investigating its aetiology and pathophysiology in order to produce effective interventions.

1.1.2.2 Co-Morbidities

Conduct disorder is known to have both homotypic comorbidity (i.e., co-occurrence among other externalizing disorders) and heterotypic comorbidity (i.e., co-occurrence among internalizing disorders). Externalizing disorders such as conduct disorder project outwards (e.g., fighting and/or risk-taking) and are linked to poor impulse control and inattention. Internalizing conditions, on the other hand, refer to disorders that affect internal emotional states. The prevalence rate of having at least one other comorbid disorder alongside conduct disorder is estimated at around 46% in males and 36% in females in the UK (National Institute for Health Care Excellence, 2013). It is important to acknowledge possible comorbidities as presenting symptoms and outcomes may not necessarily be a result of conduct disorder aetiology and pathophysiology per se, but the result of a comorbid disorder or the overlap between the two. As such, it is important to be aware of and control for co-morbidities where possible when investigating the characteristics or outcomes of conduct disorder.

1.1.2.2.1 Homotopic Comorbidity

1.1.2.2.1.1 ADHD

Attention-deficit/hyperactivity disorder (ADHD) is one of the most common comorbidities in children with conduct disorder, with prevalence estimates thought to reach as high as 40% (Fairchild et al., 2019; National Institute for Health Care Excellence, 2013). ADHD is a neurodevelopmental disorder and is characterised by hyperactivity, impulsivity, and inattention (American Psychiatric Association, 2022; Epstein & Loren, 2013). Both ADHD and conduct disorder involve top-down dysregulation of information processing, and, whilst not a core symptom recognised by the DSM-5, have both been strongly associated with emotion dysregulation (Astenvald et al., 2022; Fairchild et al., 2019).

Notably, both conditions share significant overlap in their underlying aetiology and pathophysiology, including an impairment in sustained attention, cognitive switching, and inhibition (Rubia, 2011). These parallels can often make it difficult to differentiate between the two conditions and can create barriers in identifying their distinct mechanisms and outcomes. As such, it is often practical to control for ADHD symptoms in conduct disorder research. By doing so, it allows the researcher to investigate the effects of conduct disorder symptoms without the influence of ADHD. This can be more effective than excluding those with a co-morbid ADHD diagnosis, which we know could be as high as 40% of the conduct disorder population. Retaining these cases not only allows for a more comprehensive understanding of conduct disorder but by controlling for ADHD symptoms it further reduces its influence on the validity of research findings. This ultimately ensures that results accurately reflect the characteristics and mechanisms of conduct disorder independent of ADHD-related effects.

1.1.2.2.1.2 Oppositional Defiant Disorder

Oppositional defiant disorder (ODD) refers to persistent aggressive and irritable moods, argumentative and defiant behaviour, and high levels of vindictiveness (American Psychiatric Association, 2022). The comorbidity between conduct disorder and ODD is substantial, with children diagnosed with conduct disorder being 15 times more likely to also meet criteria for ODD (Copeland et al., 2013). This high comorbidity rate may be linked to their similar underlying characteristics and mechanisms. In fact, the ICD-11 groups conduct disorder and ODD under the umbrella term disruptive behaviour disorders (DBDs; World Health Organization, 2019), reflecting their similar ongoing patterns of disruptive behaviour (e.g., defiance and aggressive behaviour).

Historically, ODD has been thought to be a precursor to conduct disorder. Indeed, in the DSM-III, ODD was considered a subsyndrome of conduct disorder (American Psychiatric Association, 1987). However, recent evidence suggests that the transition from ODD to conduct disorder is far less common, supporting the preservation of separate diagnoses in the ICD-11 and DSM-5 (Rowe et al., 2010).

Despite this distinction, there is a recurrent trend in combining ODD and conduct disorder symptoms into a single measurement construct, often labelled “conduct problems”. For example, the Strengths and Difficulties Questionnaire (SDQ) includes a five-item conduct problems subscale, four of which arguably assess ODD symptoms (Ezpeleta et al., 2014; Hawes et al., 2023). This is discussed in more detail in Section 5.1.3. Consequently, one must take caution when using such measures to assess levels of conduct problems as they may inadvertently capture features of ODD, a distinct but commonly comorbid condition.

1.1.2.2.2 Heterotopic Comorbidity

Whilst conduct disorder is more commonly associated with homotopic comorbidities (i.e., other externalizing disorders), it can also occur alongside internalizing disorders including depression (McDonough-Caplan et al., 2018) and anxiety (Cunningham & Ollendick, 2010). In fact, in one study utilising the US census, 20.3% of those with diagnosed conduct problems had current depression and 36.6% had current anxiety (Ghandour et al., 2019). Such heterotopic comorbidity aligns with findings from the hierarchical model of psychopathology, which argues that there are significant correlations between internalizing and externalizing factors (Kotov et al., 2017; Krueger et al., 2018). In fact, the shared genetic underpinnings of these disorders are thought to contribute to their co-occurrence (Caserini et al., 2023).

Genetic influences may further explain sex differences in the observed co-morbidities. That is, whilst comorbid externalizing disorder are more frequently observed in males, comorbid

internalizing disorders are more often observed in females. This was demonstrated in one study where rates of comorbid ADHD were 44.7% for males and 30.4% in females whilst rates of comorbid depression were 11.2% and 18.7% respectively (Konrad et al., 2022). In particular, Konrad and colleagues found that females with conduct disorder reported a greater number of lifetime comorbidities including depression (Konrad et al., 2022), which provides yet further support for the gender paradox (see Section 1.1.2.1) proposed by Eme (Eme, 1992).

Although comorbid internalizing disorders in individuals with conduct disorder are less prevalent than externalizing comorbidities, acknowledging and statistically controlling for these can be beneficial. They are associated with overlapping challenges, including heightened antisocial behaviours and increased social difficulties with peers, for instance (Polier et al., 2012). As such, by statistically controlling for these disorders, it can offer a more nuanced understanding of conduct disorder and its broader psychosocial implications, irrespective of the influence of symptoms associated with comorbid internalizing disorders.

1.1.3 Aetiology

There have been many efforts to determine the causes of conduct disorder (Fairchild et al., 2019). Indeed, identification of possible causes could provide some assistance in the development of effective interventions. Whilst conduct disorder exhibits a moderate heritability rate (Fairchild et al., 2019; Wesseldijk et al., 2018), suggesting a partial genetic influence, this alone cannot account for its development. The moderate heritability underscores the importance of other contributing factors, such as environmental influences (Fairchild et al., 2019) and their interaction with genetic predispositions (Eilertsen et al., 2022). This creates a complex aetiology, prompting investigations into genetic, environmental, and gene-environment interplay within the literature.

1.1.3.1 Genes

Whilst genetic predispositions for conduct disorder are not the central focus of this thesis, a brief overview will be provided. This serves two purposes: first, to present a comprehensive overview of conduct disorder, and second, to acknowledge the potential interplay between genetic and environmental factors.

Conduct disorder is estimated to have a moderate heritability rate ranging between 5% and 74% (Fairchild et al., 2019; Wesseldijk et al., 2018), with twin studies refining this estimate to between 40% and 70% (Jaffee et al., 2005; Tesli et al., 2024). As with overall prevalence, heritability rates of conduct disorder appear to be higher in males (Fairchild et al., 2019; Gelhorn et al., 2006). There is not one specific gene that is associated with conduct disorder rather, it is thought that there

is an additive effect of many genetic variants making conduct disorder a polygenic disorder. Three notable gene candidates include:

- **Gamma-aminobutyric acid type A receptor subunit alpha2** (**GABRA2):** Thought to be associated with reward-related inhibition associated with conduct disorder (Dick et al., 2006; Salvatore & Dick, 2018).
- **Monoamine Oxidase A (MAOA):** One of the most well-documented genes associated with aggression and antisocial behaviour (Kolla & Bortolato, 2020). Low MAOA expression have been linked with adolescent conduct disorder (Salvatore & Dick, 2018).
- **Arginine Vasopressin Receptor 1A (AVPR1A):** Modulates social and aggressive behaviours, including territorial aggression (Charles et al., 2014).

Whilst all three genes are possible candidates, a meta-analysis tested 21 gene candidates, including the aforementioned, and found that only AVPR1A showed significant associations with childhood aggression (Pappa et al., 2016). It must be emphasised, however, that this meta-analysis focused specifically on aggression, which, whilst a core symptom, does not encapsulate the full symptom profile of conduct disorder. Further, a major caveat to the current literature is the issue of external reliability. That is, there is often a failure to replicate findings identifying a candidate gene for conduct disorder. For example, research investigating GABRA2 have yielded inconsistent results (Dick et al., 2013; Sakai et al., 2010; Salvatore & Dick, 2018). It may thus be more productive to investigate how genetic predispositions interact with environmental risk factors (e.g., harsh parenting or association with delinquent peers) to influence the development of conduct disorder. This gene-environment interplay may provide a more comprehensive understanding of the disorder's aetiology. Thus, while the genetic basis of conduct disorder remains an area of uncertainty, combining genetic and environmental perspectives may offer a more promising avenue for future research.

1.1.3.2 Environment

Though conduct disorder is considered to be a moderately heritable condition with potential influence from a range of genes, one cannot ignore the influence of the environment. In fact, research suggest that's around 50% of the variance in conduct disorder is attributable to environmental factors (Fairchild et al., 2019). These environmental factors are evident as early as the prenatal period but can continue to exert influence across development.

1.1.3.2.1 Prenatal Factors

Common prenatal factors that have been associated with the onset of conduct disorder include low birth weight (Reijneveld et al., 2006; Tosun et al., 2017; Whiteside-Mansell et al., 2009;

Wu et al., 2024) and premature birth (Reijneveld et al., 2006; Whiteside-Mansell et al., 2009), maternal smoking (Boden et al., 2010; Ruisch et al., 2018; Sellers et al., 2020; Van Adrichem et al., 2020), alcohol consumption (Easey et al., 2019; Ruisch et al., 2018; Van Adrichem et al., 2020) and drug taking during pregnancy (Daha et al., 2020; Van Adrichem et al., 2020), and prenatal maternal stress (MacKinnon et al., 2018). These adverse in utero exposures may influence conduct disorder through alterations to neurobiological systems. Specifically, disruptions to core neural pathways involved in key conduct problem symptoms (i.e., aggression and antisocial behaviour) have been linked to these prenatal risks (Knopik et al., 2019).

Whilst it is important to understand each risk factor's association with conduct disorder, it must be noted that these very rarely occur in isolation. For example, maternal smoking during pregnancy is strongly associated with preterm birth and low birth weight (Hamułka et al., 2018; Sellers et al., 2020). As such, it is plausible that the accumulation of prenatal risks is a more robust predictor of conduct disorder than any single risk factor. Consequently, research investigating conduct disorder must carefully balance the examination of specific prenatal risks with the broader impact of cumulative risk. This trade-off will be discussed in greater detail in the later sections of this thesis.

1.1.3.2.2 Early Life Psychosocial Adversity

The family environment in which a child is raised can have a significant impact on their risk for developing conduct disorder. An important aspect of the family environment, which is thought to be one of the most salient predictors of conduct disorder, is early life psychosocial adversity - often referred to as adverse childhood experiences (ACEs; Jones et al., 2024; Moffitt & Caspi, 2001; Zarei et al., 2021). Common ACEs include lower socioeconomic status (SES; Northerner et al., 2016; Trentacosta et al., 2008), maternal psychological distress (Ayano et al., 2021), poor maternal attachment (Curran et al., 2016), and a harsh or withdrawn parenting styles (Bauer et al., 2022; Hukkelberg & Ogden, 2021; Speyer et al., 2022).

The term ACEs can encompass a broad range of experiences that can vary greatly in severity. It can be hypothesised that more severe ACEs, such as physical abuse, will exert a greater risk of developing conduct disorder than less severe adversities, such as living in a single-parent household. With a host of experiences deemed adverse, a recent study conducted a latent class analysis to attempt to cluster certain types of ACEs and investigate their influence on conduct disorder (Oei et al., 2023). Their findings identified three distinct types of ACEs: indirect victimization (e.g., parental divorce or incarceration), abusive victimization (e.g., physical abuse), and polyvictimization (i.e., exposure to multiple ACE types). A significantly higher prevalence of conduct disorder was observed in all three groups of ACEs compared to children without conduct disorder. As expected, those who experienced polyvictimization (e.g., abuse) displayed the strongest association. Therefore, it appears

that whilst ACEs are associated with the development of conduct disorder, the strength of this association may be influenced by the severity of the ACEs.

Furthermore, Oei and colleagues' study (2023) demonstrate that, as with prenatal factors, an accumulation of adverse experiences can play a critical role in the development of conduct disorder. In fact, adverse experiences often co-occur, with individuals exposed to one form of adversity being more likely to experience others (Chartier et al., 2010). Research consistently links the accumulation of multiple ACEs to an increased risk of conduct disorder (Bevilacqua et al., 2021). Moreover, a recent study suggests that the presence of three or more ACEs significantly elevates the likelihood of conduct disorder (Turney, 2020). However, it is important to note that studies focusing on ACE accumulation often do not include severe adversities such as sexual abuse. Whilst such extreme adversities are less common, their profound impact underscores the importance of considering both severity and frequency of ACEs in understanding conduct disorder's aetiology. Nevertheless, the literature suggests that the accumulation of more commonly reported adversities (e.g., socioeconomic challenges or harsh parenting) is strongly associated with conduct disorder (Bevilacqua et al., 2021; Turney, 2020). As with prenatal factors, future research must weigh the merits of examining specific ACE types against their broader cumulative impact.

1.1.3.3 Gene X Environment Interplay

It is evident that conduct disorder is influenced by both genetic and environmental factors, yet neither alone fully explains its variance (Eilertsen et al., 2022). This is thus highly suggestive of a multifactorial aetiology. In fact, Eilertsen and colleagues (2022) argue that the heritability and environmental factors (in particular adversity) should not be investigated exclusively but rather simultaneously (Eilertsen et al., 2022). Nevertheless, it remains unclear whether genetic factors influence exposure to certain environments (a correlation) or whether genetic predispositions alter individual responses to environments (an interaction).

1.1.3.3.1 Gene + Environment Correlation

A gene + environment correlation (rGE) occurs when genetic predispositions influence the likelihood of exposure to particular environmental factors. Studies investigating conduct disorder often examine rGE via parenting behaviours, which offer support for both passive and evocative forms of rGE (Klahr & Burt, 2014).

A passive rGE can occur when parents pass on genetic variants which influence both the child's behaviour and their environment (shaped by parents' behaviour). For example, one study found a direct effect of parental maladaptive parenting on child DBDs and their antisocial behaviour was associated with increased conduct disorder symptoms in biological children compared to

adopted children (Bornovalova et al., 2014). This is suggestive of pleiotropy, where a single gene influences multiple traits. In fact, parenting itself is moderately heritable estimated at approximately 23%-40% (Klahr & Burt, 2014). Whilst it is not yet clear if this heritability is driven by the same gene, one could hypothesise that genetic variants associated with aggression in children might also influence parenting behaviours, creating a shared genetic basis for both traits.

Evocative rGE, on the other hand, occurs when a genetic predisposition elicits specific environmental responses. For example, a child's genetic predisposition for conduct disorder has been shown to elicit harsh parenting (Avinun & Knafo, 2014; Klahr & Burt, 2014). Adoption studies provide further evidence for evocative rGE, linking biological mothers' personality and antisocial traits to adoptive fathers' negative parenting (Hajal et al., 2015; Klahr et al., 2017). This suggests that inherited traits, even without a direct environmental influence from the biological parent, can still evoke a specific environmental response.

Active rGE occurs when a child's genetic predisposition actively shapes the environments they choose to engage with, such as seeking deviant peer groups (Kendler et al., 2008). This tendency to associate with delinquent peers could, in turn, contribute to the heightened risk of delinquent behaviours frequently observed in children with conduct disorder (Hammerton et al., 2019). As such, it is critical for the research community to deepen its understanding of the underlying mechanisms of active rGE, to create interventions aimed at mitigating the environmental risks that amplify delinquent behaviours in children with genetic predispositions for conduct disorder.

1.1.3.3.2 Gene x Environment Interaction

An interplay between genes and environment can also occur through a gene x environment interaction (GxE), wherein a genetic predisposition moderates the effects of environmental influences. That is, genes can influence how an individual reacts to certain environmental factors. One well-studied GxE involves the MAOA gene and child adversity. A study by Caspi and colleagues (2002) found that children with low levels of MAOA expression who were subsequently maltreated had a higher risk of developing later antisocial behaviour (Caspi et al., 2002). In fact, this GxE accounted for 65% of the variability in antisocial outcomes. Further studies examining this GxE have presented mixed findings (Foley et al., 2004; Huizinga et al., 2006) though the research typically focuses on male participants and therefore does not consider how this GxE may affect females. Regardless, when investigating GxE, the MAOA-adversity interaction remains one of very few GxE genotypes with somewhat consistent support across the literature (Fairchild et al., 2019; Nilsson et al., 2018).

Overall, whilst the aetiology of conduct disorder has been substantially investigated, inconsistent results highlight a need for further research to increase the external reliability. Future

research requires extremely large sample sizes and comprehensive information on both genetics and environmental factors to produce valid and reliable findings on conduct disorders aetiology via GxE interplay.

1.1.4 Pathophysiology

Conduct disorder is associated with pathophysiological changes at the neural level. In particular, these structural and functional neural alterations associated with conduct disorder have subsequent effects on a variety of neurocognitive domains.

1.1.4.1 Neuroanatomy

Reward-related neural pathways, integral to reward processing and motivation, play a significant role in neurocognitive functions associated with conduct disorder. These pathways include intricate neural systems within the mesocortical and mesolimbic dopamine systems. Both receive projections of dopamine, a neurotransmitter responsible for creating sensations of pleasure and motivation.

The mesocortical pathway projects to regions within the frontal cortex, including the orbitofrontal cortex (OFC) and anterior cingulate cortex (ACC) whilst the mesolimbic pathway projects to highly connected subcortical regions critical for reward processing and motivation, including the amygdala, hippocampus, and nucleus accumbens (NAc). The thalamus and insula are not directly part of these core dopaminergic pathways, but they have strong connections to these systems and play supporting roles in reward and emotional processing (Chen et al., 2022; Gogolla, 2017). Together, these regions form complex reward networks.

Notably, these key reward systems are known to show altered grey matter volume in those with conduct disorder (Fairchild et al., 2019). In particular, a meta-analysis revealed that those with conduct disorder exhibited decreased grey matter volume in the left amygdala, right insula, OFC, and ACC compared to healthy controls (Rogers & De Brito, 2016). Their sub-group meta-analysis further highlighted that the reduced volume of the left amygdala and right insula remained when including those with a childhood-onset conduct disorder only.

However, it remains unclear to what extent these structural alterations may be influenced by co-occurring factors such as sustaining a head injury. This is particularly relevant given that childhood head injuries can also lead to volumetric reductions and functional impairments in similar brain regions (see Section 1.2.4.1). Notably, head injury history was not consistently considered in the studies included in the above meta-analysis. Therefore, when interpreting neuroimaging findings in conduct disorder populations, it is important to consider the potential contribution of prior head injuries.

1.1.4.2 Neurocognition

Conduct disorder has been associated with structural and functional brain changes in regions associated with various cognitive processes including within the aforementioned dopamine pathways (i.e., mesocortical and mesolimbic systems). These pathways play a crucial role in the release of dopamine and are integral to higher-order executive functions, particularly decision-making and reward processing, both of which are linked to the maladaptive behaviours commonly observed in conduct disorder.

1.1.4.2.1 Decision Making & Risk-Taking

Decision-making refers to one's ability to select a course of action from multiple options, whilst risk-taking refers to one's proneness to engage in behaviour deemed to have a level of danger and/or risk to achieve a goal. For example, placing a high-stake bet where there is a high risk of losing that money but offers a slight potential to win more money. A recent scoping review has suggested that those with conduct disorder often show impaired quality decision-making and heightened risk-taking (Bentivegna et al., 2024). A further scoping meta-analysis has identified dysfunction in key brain regions related to such reward-based decision-making in individuals with conduct disorder, including the rostro-dorsomedial prefrontal cortex, fronto-cingulate cortex, and the ventral-striatum (Alegria et al., 2016). Dysfunction to such neural regions associated with decision-making are argued to increase the risk of frustration from undesirable outcomes and thus result in a reactive-based aggression and antisocial behaviour often observed in those with conduct disorder (Blair et al., 2018)

The decision-making impairments observed in individuals with conduct disorder can be broken down in terms of computational processes including reduced reward sensitivity (i.e., impairment in being motivated by a reward-relevant stimulus) and impaired avoidance response (i.e., an impairment in the ability to make a decision that prevents an adverse stimulus; Blair et al., 2018). Indeed, this poor, or rather biased, decision making observed in those with conduct disorder is thought to be the result of a greater influence from potential rewards and an insensitivity to potential punishment (Fairchild et al., 2019; Sonuga-Barke et al., 2016). Within this thesis, I will focus on exploring the role of reward processing.

1.1.4.2.2 Reward Processing

Reward processing refers to one's response to rewarding stimuli, an ability to learn from this reward, to anticipate future rewards, and to engage in goal-directed behaviour towards future reward. It has been closely linked to executive functioning (Salehinejad et al., 2021), and is thought to be a computational process which underlies reinforcement-based decision-making (Chan et al.,

2022; Fairchild et al., 2019). That is, one's ability to continuously adapt behaviour based on previous experiences to improve the chance of receiving a reward.

Conduct disorder has been associated with impairments in many aspects of reward processing including a decreased neural response to rewarding stimuli including monetary gains during passive avoidance tasks (Fairchild et al., 2019; White et al., 2013), a reduced reward sensitivity (Blair et al., 2018), and changes in responsiveness to reward cues (Zhang et al., 2023). In particular, those with conduct disorder appear to be more likely to make choices which are less informed by expectations of reward or punishment, likely due to alterations in key cognitive processes. For instance, impairments in stimulus-reinforcement learning and reversal learning (Blair, 2010). Due to such impairments, choices made can be impulsive. Such impulsive choices, which are not led by appropriate reasoning, can lead to an undesirable outcome and result in frustration (Blair, 2010). Blair and colleagues have argued that such increases in frustration can lead to reactive aggression—a common symptom of conduct disorder (Blair, 2010).

Recent fMRI findings have highlighted distinct neural patterns associated with these reward-processing deficits in conduct disorder and other DBDs. Namely, lower neural response to reward outcomes in the ventral striatum has been observed alongside increased neural response in the amygdala during loss outcomes (Cohn et al., 2015; Hawes et al., 2021). In particular, Hawes and colleagues (2021), who utilised national cohort data from the Adolescent Brain Cognitive Development (ABCD) Study (Casey et al., 2018), identified reduced activation of the dorsal ACC and thalamus during the anticipation of a monetary reward in youths with DBD. Conversely, following the receipt of a reward, they found that these youth showed increased cortical (e.g., OFC) and subcortical (e.g., NAc) activation. These alterations may indicate that there are different neural mechanisms for both reward anticipation and receipt.

Further regions associated with reward processing deficits in conduct disorder include the hippocampus, crucial for memory and contextual processing, and the insula, involved in interoceptive awareness and emotional processing. Diminished activity in these regions could impair the ability to use past experiences to guide future behaviour and appropriately assess risks and rewards. Indeed, structural alterations in both the hippocampus and insula have been linked to DBDs (Waller et al., 2020). Additionally, the caudate, a component of the dorsal striatum and integral to reward expectancy (Blair, 2013), exhibits altered activity in conduct disorder (Alegria et al., 2016; Grahn et al., 2008), potentially contributing to deficits in reward anticipation and motivation.

Together, these findings illustrate a pattern of neural dysfunction across multiple regions involved in reward processing and executive function, including the amygdala, hippocampus, NAc, medial OFC, ACC, insula, and thalamus. This distributed dysfunction likely contributes to the maladaptive decision-making and the heightened frustration associated with conduct disorder,

further supporting the hypothesis that impaired reward processing is a core mechanism underlying its behavioural manifestations.

1.1.5 Theoretical Perspectives of Conduct Disorder

Theoretical frameworks in mental health (i.e., biological, cognitive, and behavioural perspectives) offer various explanations for the development and presentation of disorders. Applying these frameworks to conduct disorder provides a comprehensive view of its psychopathology. In this section of the thesis, I turn to a selection of theories, which aim to explain the mechanisms driving aggressive and antisocial behaviours commonly associated with conduct disorder.

1.1.5.1 Coercive Parenting Theory

Coercive parenting theory focuses on the reciprocal adverse interactions between parents and children (Patterson, 1992). This theory argues that there is a mutual reinforcement during early childhood, whereby child problem behaviours reinforce coercive parenting and vice versa. The principal mechanism to this theory is negative reinforcement, which explains how both child and parent are conditioned to behave in ways which escalate conflict. That is, during this cycle of coercive behaviour whereby a child may be having a tantrum, and a parent may be shouting at them, if a child stops their tantrum to stop the parent's shouting, the coercive parenting is reinforced, whilst if a parent stops their shouting to stop the child's tantrum, then the child's coercive behaviour is reinforced. Over time, this leads to a biased response evaluation in the child. Specifically, children may develop a reliance on these maladaptive responses, reinforcing the aggressive tendencies that are symptomatic of conduct disorder. Coercive parenting theory thus places emphasis on parent-child exchanges as a primary mechanism underlying the development of conduct disorder and related antisocial behaviours.

Whilst this theory highlights how parenting (e.g., shouting at the child) can be associated with the development of conduct disorder, it could also be exasperated by the presence of a head injury. That is, children who experience a head injury may be more prone to tantrums or irritability, increasing the risk of coercive cycles with caregivers. This suggests that head injuries could indirectly exacerbate conduct disorder symptoms by heightening the risk of coercive interactions. Due to the possible influence of parenting techniques (e.g., shouting at the child) on conduct disorder and possibly head injury, they will be considered where possible in the analyses of this thesis and discussed with relevance to potential intervention strategies.

1.1.5.2 Dual Taxonomy Theory

Dual taxonomy theory focuses on neurophysiological and developmental factors which can lead to a persistent trajectory of conduct disorder (Moffitt, 1993). This taxonomy distinguishes between two primary trajectories of antisocial behaviour: adolescent-limited and life-course persistent antisocial behaviour. Most children belong to the adolescent-limited group. They will exhibit some form of antisocial behaviour during adolescence, but this is temporary and will desist by adulthood. However, children with conduct disorder are more likely to belong to the life-course persistent antisocial behaviour group, which is characterised by a chronic and pervasive pattern of antisocial behaviour that persist across the lifespan. Moffitt's theory suggests that membership to this group is caused by a cumulative interaction between neurophysiological deficits and environmental factors, which jointly disrupt development and behaviour regulation.

The life-course persistent trajectory is strongly associated with neurophysiological deficits that likely originate in the prenatal or early developmental period. For instance, maternal prenatal behaviours, such as smoking or alcohol consumption have been linked to foetal brain abnormalities (Hamułka et al., 2018). Such prenatal factors are thought to impair the development of the frontal lobes, a brain region crucial for executive functions such as impulse control, decision-making, and planning. Deficits in these functions contribute to increased risk-taking behaviours (Icenogle & Cauffman, 2021). This increased propensity for risk-taking can then be reflected via antisocial or criminal behaviours (e.g., stealing).

Moreover, the neurophysiological impairments associated with life-course persistent antisocial behaviour can interact with environmental factors, such as exposure to early adversity or poor parenting, to exacerbate the development of conduct disorder symptoms. For example, children with executive dysfunction may struggle to adapt to structured environments, leading to oppositional and defiant behaviours. Over time, these solidify into stable patterns of antisocial behaviour.

Whilst Moffitt's dual taxonomy offers a framework for understanding the pathways leading to antisocial behaviour (namely life-course persistent conduct disorder), Fairchild and colleagues have argued that this theory is in need of a reformulation (Fairchild et al., 2013). That is, they argue that additional subgroups of individuals exhibit antisocial behaviour with similar psychiatric (or neurodevelopmental as they refer to in their paper) origins. In particular, they acknowledge childhood-limited antisocial behaviour as a distinct group and challenge the idea that adolescent-onset antisocial behaviour is transient. Rather, they argue that adolescent-onset antisocial behaviour can also persist into adulthood. They argue that the differences in time-of-onset could be related to the timing and severity of environmental adversities. For example, evidence suggest that children with child-onset antisocial behaviour tend to have more severe or increased rates of adversity and

environmental risk factors (Moffitt & Caspi, 2001). Therefore, Fairchild and colleagues argue that this taxonomy is extremely useful in understanding clinically relevant antisocial behaviour but argue this needs to be expanded to consider the various ages of onset.

Overall, Moffitt's dual taxonomy, and proposed reformation by Fairchild and colleagues, highlights the various psychiatric pathways of antisocial behaviour that contribute to the emergence of conduct disorder. Importantly, this theory also highlights the interplay of neurophysiological deficits and environmental influences, which can influence the onset of these various pathways. This thesis will explore these pathways of antisocial behaviour in detail whilst also accounting for the role of sustaining a head injury on their trajectory and outcomes. Further, relevant prenatal and environmental factors acknowledge by this theory will be considered throughout the analyses of this thesis to enhance our understanding of co-occurring conduct disorder and head injuries .

1.1.5.3 Dual Systems Theory

Akin to Moffitt's theory is the dual systems theory (Steinberg et al., 2008). Whilst Moffitt arguably focuses on explaining persistent conduct disorder, it acknowledges a general increase in antisocial behaviour during adolescent. The dual systems theory elaborates on this by attempting to explain the mechanisms which drive adolescent antisocial behaviour. According to the dual systems theory there are two key systems: a socioemotional system and a cognitive control system (Steinberg et al., 2008). During adolescence, the socioemotional system, which drives sensitivity to rewards and emotional reactivity, matures and becomes highly active whilst the cognitive control system, responsible for regulating impulses and decision-making, is still developing. This imbalance in maturity between the two systems results in greater bottom-up reward-driven behaviour motivated by the socioemotional system with little top-down regulation from the cognitive control system. This leads to more risk-taking during adolescence in aim of frequent and great reward. Whilst this theory was not originally designed to explain adolescent antisocial behaviour, it has been argued to be more aptly defined as a developmental psychopathology model (Murray et al., 2021) and as such relevant to understanding conduct disorder. Sustaining a head injury could be a significant factor relating to the disruption of these systems maturation, which could further exasperate adolescent antisocial behaviour and is considered further in Paper 2 (Chapter 3).

1.1.6 Outcomes

Conduct disorder is associated with a range of maladaptive outcomes across the lifespan. These have been known to impact multiple facets including personal, educational, social, and familial domains. During adolescence, conduct disorder is associated with a greater risk of teen pregnancy (Bardone et al., 1998), poor education outcomes (Bevilacqua et al., 2018), substance use (Hopfer et al., 2013), and is highly prevalent amongst service settings including juvenile criminal settings

(Beaudry et al., 2021). By early adulthood, conduct disorder predicts a higher likelihood of numerous adverse outcomes including an increased risk of criminal behaviour (Hammerton et al., 2019), a poorer quality of life (Szentiványi & Balázs, 2018), and unemployment and poor academic outcomes (Erskine et al., 2016). One study demonstrated that childhood conduct disorder but not depression, anxiety, ADHD, ODD, or substance use disorder was predictive of two or more adverse outcomes in early adulthood (Copeland et al., 2015), highlighting the specificity of the long-term impacts of conduct disorder.

Further, different trajectories of conduct disorder are associated with nuanced risk patterns. In particular, whilst childhood-limited, persistent, and adolescent-onset trajectories of conduct disorder have been associated with worse outcomes compared to a "low level" trajectory, individuals in the persistent subgroup experience the most severe long-term outcomes (Bevilacqua et al., 2018). For example, the persistent trajectory displayed the largest effect sizes in reference to poor mental health outcomes, alcohol use, self-reported aggression, criminal behaviour, poor education, and poor occupational outcome (or poor employment outcome). Further, the adolescent-onset trajectory displayed a greater risk for cannabis use and general health outcomes. In contrast, those from a childhood-limited trajectory of conduct disorder showed only significantly greater risks for self-reported aggression and poor education outcomes compared to a "low level" trajectory. This suggests that poor outcomes in early adulthood are most strongly associated with conduct disorder symptoms present during key developmental periods between middle childhood and adolescence.

Notably, negative outcomes appear to persist as late as middle adulthood, particularly for those within a persistent trajectory of conduct problems. These include fewer years of education completed, increased probability of incarceration, lower levels of life satisfaction and family support and adult antisocial behaviour disorder (Olino et al., 2010). By mid-adulthood, those with a history of persistent conduct disorder have been shown to utilise more government resources in criminal justice, healthcare, and social welfare systems compared to those with low-level, childhood-limited, or adolescent-onset conduct problems (Rivenbark et al., 2018). This highlights the long-term societal and economic burden posed by persistent conduct disorder and emphasises a need for early intervention.

Not only is conduct disorder associated with negative outcomes directed at the self, but it also appears to pose a risk for poor intergenerational relationships. That is, adolescents with conduct disorder appear to have a greater risk of developing coercive styles of parenting in adulthood, which may serve as a catalyst for future generations of conduct disorder (Byford et al., 2014). Therefore, the potential burden of conduct disorder is not limited to the individual and highlights a critical need for preventative interventions to prevent future generations of conduct disorder and a repeat of unfavourable outcomes.

Given the extensive and far-reaching consequences of conduct disorder, from adolescence to middle adulthood and across generations, it is important that ongoing research continues to refine our understanding of its epidemiology, aetiology, and pathophysiology. Addressing these factors may help to develop effective interventions and breaking the cycle of maladaptive outcomes associated with this disorder.

1.2 Head Injury: An Overview

A head injury is defined as an injury to the brain, skull, or scalp and can range in severity from a bang on the head to a severe traumatic brain injury (TBI; National Institute for Health and Care Excellence, 2014). Head injuries are highly prevalent, with over 1.4 million people attending emergency departments annually in England and Wales (National Institute for Health and Care Excellence, 2014) and 2.5 million people in the US (Taylor et al., 2017). Whilst head injuries are highly prevalent, they can also be highly heterogeneous. For instance, they can range considerably in severity, which can lead to a wide range of outcomes. A common measure used to differentiate head injury severity is the Glasgow Coma Scale (GCS; Teasdale & Jennett, 1974). The GCS creates a sum score based on one's ability to open their eyes, move, and speak. It is used to distinguish between mild (GCS $\geq$ 13), moderate (GCS 9–12), and severe TBI (GCS $\leq$ 8). Whilst this trichotomy was not necessarily proposed by Teasdale and Jennett (1974), it has become increasingly popular in both clinical and research settings to distinguish head injury severity (Manley & Maas, 2024).

Whilst a GCS score is a standardised measure to differentiate between the different types of head injury, they can also be categorised based post-injury loss of consciousness and amnesia duration:

- Mild TBI (mTBI; also known as a mild head injury, minor head injury, or concussion): absence of a loss of consciousness or amnesia post-injury, or their presence for no longer than 30 minutes or 24 hours post-injury, respectively.
- Moderate TBI: a loss of consciousness between 30 minutes and 24 hours post-injury and amnesia post-injury lasting between 24 hours and 7 days.
- Severe TBI: a loss of consciousness for more than 24 hours post-injury and amnesia lasting greater than 7 days.

As one would expect, outcome are typically less favourable following a moderate to severe TBI and this includes a greater mortality risk (Nelson et al., 2023). However, whilst outcomes are less favourable following more severe head injuries, mTBIs (or head injuries) more commonly occur in the general population (National Institute for Health and Care Excellence, 2014), have been linked to increased rates of delinquency compared to when no head injury occurs (Mongilio, 2022; Schwartz et

al., 2017; Schwartz et al., 2018), and greater contact with the criminal justice system (Kennedy, Heron, et al., 2017). Taken together, the greater prevalence of head injuries (compared to moderate and severe TBI), coupled with their association with adverse outcomes highlights the critical need for continued research to enhance our understanding of head injuries. Such efforts are critical for the subsequent development of effective preventive and therapeutic interventions aimed at reducing their prevalence and mitigating their impact on behaviour and cognition.

1.2.1 Language

There is a wide range of head injury terminology and different terms are often used interchangeably within the research. Given the heterogeneity of head injuries, it is important to use accurate terminology when describing specific head injuries where possible whilst being mindful of ongoing philosophical debates concerning their naming, classification, and abstraction, similar to that surrounding conduct disorder. For the purpose of this thesis, I will use the term "head injury" to specifically refer to:

a) a bang to the head with or without a loss of consciousness, which has required some form of medical attention and/or

b) a mTBI – defined as a head injury with a loss of consciousness no greater than 30 minutes and amnesia no greater than 24 hours postinjury (i.e., a GCS $\geq$13).

Whilst I will often use the term "head injury" as an umbrella term to encompass both outlined above, I will also use more specific terminology to describe the type of head injury measured within the datasets analysed. That is, in Papers 1 and 2, I will use the term "head injury" (corresponding to the definition a above) as there is limited information on the nature of the head injuries within the dataset. In Paper 3, I will use the term "mTBI" (corresponding to definition b above), as this dataset uses a formal measure of TBI severity thus making "mTBI" the most accurate terminology.

1.2.2 Epidemiology (Prevalence)

Those forms of head injuries, as defined in Section 1.2.1, account for approximately 75% of all head injury cases in the US (National Center for Injury Prevention and Control, 2003; Taylor et al., 2017) and approximately 95% of head injury related presentations to UK hospitals (National Institute for Health and Care Excellence, 2014). Of the estimated 200,000 people formally admitted in UK hospitals with a head injury, around 80% are classed as a head injury rather than a TBI (National Institute for Health and Care Excellence, 2014). This demonstrates the importance of understanding

the broader implications of mild head injuries, which are more commonly sustained in the general population.

Importantly, children represent a significant proportion of head injury cases. Of the 1.4 million people who attend an emergency department in England or Wales annually with a head injury (who are not necessarily admitted), approximately 33%–50% of these cases involve children under 15 years old (National Institute for Health and Care Excellence, 2014). In the US, head injuries similarly account for around 18,000 hospitalisations and 640,000 emergency department visits annually in children under 15 years old (Taylor et al., 2017). It must be stressed that these figures likely severely underestimate the true prevalence of head injuries sustained as many go unreported or do not result in medical attention. However, it at least gives an estimate of the high prevalence rate of such head injuries and thus further justifies their investigation.

1.2.3 Aetiology and Risk Factors

Whilst the aetiology of conduct disorder can be partially explained by factors such as genetics, neurobiology, and cognition, the aetiology of head injury is exclusively external. That is, head injuries occur only by an external force to the head. Whilst some forms of brain injury can indeed be caused by internal factors including a stroke or aneurysm, these do not fall under the remit of the head injuries defined in this thesis.

The most common cause of such an external force to the head include falls, participating in sports activities, and motor vehicle accidents (Crowe et al., 2009). Whilst these incidents lead to an external force to the head (e.g., a ball hitting the head), it is possible to explore the indirect factors which can increase the likelihood of such events. For example, whilst one's neurocognition cannot directly cause a head injury, it can influence the behaviours that place a child in a situation with a greater risk of sustaining a head injury.

Therefore, to better understand the aetiology of head injuries, I will explore not only the immediate, external causes but also further factors that contribute to an increased risk of sustaining a head injury. This approach will provide a more comprehensive understanding of the pathways leading to head injuries and highlight potential areas for prevention and intervention.

1.2.3.1 Central Nervous System Disorders

Falls are one of the most common causes of a head injury. A fall can occur due to the symptoms of central nervous system disorders such as epilepsy including a seizure or blackout. In fact, a study found that seizure-related falls occurred in 83% of paediatric patients (Bajaj et al., 2022). Whilst this does not directly link to sustaining a head injury, one systematic review has indeed identified an increased risk of head injuries in children and adolescents with epilepsy (Jory et al.,

2019). This could be the result of the greater prevalence for seizure-related falls and thus further underscores the heightened vulnerability for head injury in children with a central nervous system disorder.

1.2.3.2 Environment

Specific environments and circumstances can also significantly increase the risk of sustaining a head injury. I will now address the different environments one can be exposed to which can increase their risk of sustaining a head injury.

1.2.3.2.1 Contact Sports

Participation in contact sports is a common cause for sustaining a head injury (Crowe et al., 2009). In particular, the risk for a sport-related head injury appears to be greatest during adolescence (Theadom et al., 2020). This increased risk may be attributed to the positive relationship between age and contact sport exposure. Specifically, exposure to contact sports tends to increase with age, beginning with limited or non-contact versions of sports during childhood (e.g., touch rugby), progressing to full-contact versions during adolescence (e.g., full-contact rugby). Therefore, limiting or preventing contact sport exposure to children and adolescents may be beneficial to the reduction in head injury cases.

1.2.3.2.2 Social Deprivation

Social deprivation has been associated with an increased risk for childhood head injury when measured by household income (Lopez et al., 2022) and geographical indicators such as postcode (Trefan et al., 2016). This association has been argued to be somewhat attributed to limited financial and temporal resources in low-income households, which may expose children to a wider range of hazards and less resources to protect themselves such as less parental supervision or less parental knowledge about preventing child injury (Kent et al., 2021; Laflamme et al., 2010; Schwebel & Gaines, 2007). Not only could social deprivation increase the risk of sustaining a head injury, but it could also influence the quality of care received following a head injury. For example, families in socially deprived areas may not have the resources to seek medical attention for their child following a head injury or to attend routine follow-up appointments, which can have a considerable impact on the child's outcomes (Ponsford et al., 2001).

However, the relationship between social deprivation and childhood head injury has not been consistently found when using alternative measures of deprivation. For example, this relationship was not found when measuring social deprivation via parent's occupational status or education level (McKinlay et al., 2010; Mongilio, 2022). These discrepancies may reflect the differing dimensions of deprivation captured by these various indicators. Whilst these measures are often

highly correlated, future research could clarify the specific role of social deprivation on influencing childhood head injury risk by employing more nuanced or multifaceted approaches to measuring social deprivation.

1.2.3.2.3 Early Life Psychosocial Adversity

Family adversity, particularly ACEs, has been identified as a significant risk factor for sustaining a childhood head injury. Consistent with conduct disorder findings discussed previously in this thesis, research has identified a dose-response relationship between ACEs and head injury risk in children aged 12–17 (Jackson, Posick, et al., 2022). That is, as number of ACEs increased, so did the likelihood of sustaining a head injury. Similarly, Saadi and colleagues (2024) reported a 140% increase in the odds of head injury among children with four or more ACEs (Saadi et al., 2024). As with conduct disorder, this thus highlights the important role adversity has on the risk for sustaining a head injury, particularly via the role of an accumulation of adversity.

Importantly, whilst these findings are commonly identified in adolescent populations, they do not appear to be specific to sport-related head injuries (Theadom et al., 2020). Jackson and colleagues found that the association between ACEs and head injuries was greater among children and adolescents aged 12 to 17 who were not involved in sport (Jackson, Posick, et al., 2022), a finding which has more recently extended to children under 12 years old (Riccardi & Hale, 2024). Together, these findings suggests that ACEs are linked to a specific subtype of child and adolescent head injury, namely those occurring outside of a sport-related context.

1.2.3.3 Neurocognition

Research has shown that poor impulse control and heightened impulsivity are both significant neurocognitive risk factors for sustaining a childhood head injury. Impulsivity refers to a tendency to act without thinking and impulse control refers to one's ability to resist urges, temptations, or impulsive behaviours. Studies have found that greater impulsivity is attributed to a greater likelihood of sustaining a head injury in childhood (Mosti & Coccaro, 2018) and adolescence (Schwartz et al., 2018). This suggests that children with poor impulse control struggle to inhibit impulsive behaviours (e.g., jumping off a wall), and instead execute such impulsive and potentially risky behaviours, which can increase their exposure to potentially injurious situations.

In addition to impulsivity, a history of conduct disorder has also been identified as a neurocognitive factor which can increase the risk of sustaining a head injury (Mongilio, 2022). That is, children with conduct problems often engage in high-risk behaviours and are more likely to be in environments that increase their exposure to injury. However, it is likely that this relationship is bidirectional. That is, conduct problems may predispose individuals to environments or behaviours

that increase the likelihood of injury whilst sustaining a head injury may exacerbate or contribute to later conduct problems (Brandt et al., 2022; Carr, Hall, Eisenbarth, et al., 2024). This will be discussed in more detail later in this chapter.

1.2.4 Pathophysiology

Head injury pathophysiology is linked to outcomes in neurocognition. However, such outcomes are highly heterogeneous due to the uniqueness of the injury itself and the individual. That is, behavioural and neural changes following a head injury can depend heavily on factors such as sex, age, and severity of injury, as well as the focal point of the injury (Ogolo & Ibe, 2021). Whilst each head injury will be unique, there are certain brain regions that are commonly associated with a head injury, which are attributed to common neurocognitive outcomes and these will be the focus of this thesis (McAllister, 2011).

1.2.4.1 Neuroanatomy

A head injury can alter the structural and functional physiology of the brain. For example, a head injury can result in oxidative stress (leading to cell and tissue damage), axonal transport deficits (leading to altered neuronal homeostasis, cargo aggregation, and neuron degeneration), and altered neurotransmission (transfer of information between neurons; Giza & Hovda, 2014; McAllister, 2011; McAllister et al., 2001). Additionally, macroscopic injuries such as a transcranial haemorrhage can further complicate such processes (Lumba-Brown et al., 2018).

The heterogeneity of head injuries makes it challenging to pinpoint general physiological outcomes as these are often specific to the context and severity of each injury. Nonetheless, there is evidence to suggest that brain abnormalities can occur following a childhood head injury including reduced cortical thickness (e.g., right rostral middle frontal gyrus) and subcortical volume (e.g., hippocampal volume) up to 4 months post-injury (Mayer et al., 2023). Interestingly, a childhood or adolescent head injury does not appear to have a long-term impact on white matter structures (Betz et al., 2024; Dégeilh et al., 2023). However, these findings are limited by a delay between participants sustaining a head injury and the imaging process. Therefore, it could be that structural effects are temporary (at least up to 4 months as Mayer and colleagues suggest) and diminish overtime. Alternatively, these changes may only occur in a subset of individuals and due to the heterogeneous nature of head injuries, group-level comparisons as conducted by Betz and colleagues (2024) and Dégeilh and colleagues (2023) may be insufficient to capture these individual differences.

1.2.4.2 Neurocognition

Whilst evidence for neuroanatomical changes can be somewhat mixed, findings of neurocognitive changes are often more consistent. This could be due to the intricate and highly interconnected neural networks which neurocognitive functions rely on. Therefore, deficits to a specific function could occur when any part of these interconnected regions are damaged and thus the heterogeneity in neuroanatomical changes will have a smaller impact on neurocognitive functioning.

One of the most well documented neurocognitive deficits following a head injury is impaired executive functioning including decision-making and self-regulation (Goh et al., 2021; Jones et al., 2021). Evidence suggests that children and adolescents who have sustained a head injury display higher levels of impulsivity (Khalaf et al., 2023) and impairments in response inhibition (Korgaonkar et al., 2021). Notably, these impairments can persist up to 3 years post-injury (Keenan et al., 2021). Such deficits can have detrimental effects to decision-making and reward processing, leading to broader challenges in social and cognitive functioning.

Much like the dual systems theory of conduct disorder, a childhood head injury can delay the maturation of specific brain regions and thus impair related neurocognitive domains. For example, whilst levels of impulsivity typically decline throughout development, evidence suggests that a childhood head injury can delay this decline in a dose-dependent manner (Fullerton et al., 2019). These developmental disruptions thus underscore the long-term consequences of childhood head injuries on neurocognitive functioning.

This thesis will not cover all forms of neurocognition which can be impacted by head injury. Rather, it aims to explore the impact of head injury on decision-making and reward processing, two interconnected neurocognitive domains that are particularly susceptible to disruption following a head injury. By examining these impairments, I aim to identify how they contribute to broader patterns of neurocognitive dysfunction and developmental challenges following a head injury.

1.2.4.2.1 Decision Making & Risk-Taking

Decision-making is a core executive function, which requires the utilisation of a range of intricate and interconnected neural networks. Decision-making impairments can be observed across multiple sub-domains including reward-based and socially moral decision making (Beauchamp et al., 2019). For example, whilst parents in one study reported enhanced global adaptive skills in adolescents with mTBI, these adolescents demonstrated poorer socially adaptive decision-making (Beauchamp et al., 2019). This highlights the potential nuanced impact of head injury on different

aspects of decision-making, although it must be noted that this is just one result from a single relatively small sample (*N*= 136) and thus further replication is required.

The neural underpinnings of impaired decision-making following a head injury can involve damage to regions such as the medial OFC (Wood & Worthington, 2017), amygdala (Gupta et al., 2011), NAc (Sugam et al., 2012), and caudate (Zhang, 2022). These structures collectively support the evaluation of rewards, emotional regulation, and behavioural control, which are all critical components of effective decision-making.

Adolescence is a period particularly vulnerable to decision-making impairments following head injury. It is a period already marked by a general increase in risk-taking, attributed to reduced activation in neural regoins including the OFC and ACC compared to adults (Eshel et al., 2007). Sustaining a head injury during this critical developmental period can amplify these vulnerabilities by further disrupting said neural circuits involved in decision-making. Consequently, adolescents with head injuries may exhibit greater risk-taking behaviours and more pronounced decision-making deficits due to the combined effects of injury-related damage and age-related neural immaturity.

1.2.4.2.2 Reward Processing

A core component of decision-making is reward processing (Chan et al., 2022). Reward processing refers to the ability to learn associations between a stimulus and rewarding outcomes and adapt future behaviours based on these learned associations. Reward processing relies on the coordination of the brain's reward systems, including the mesocortical and mesolimbic pathways. As these systems have been discussed earlier in this thesis in connection with conduct disorder (see Section 1.1.4.2.2), I will not repeat that discussion but will instead focus on their specific associations with child and adolescent head injury.

Notably, head injuries appear to frequently disrupt neural activity within these key reward pathways. For example, a recent study utilising the ABCD dataset identified altered activation patterns during the reward anticipation phase of a monetary reward paradigm in children aged 9–10 with a mild TBI compared to well-matched controls (Hogeveen et al., 2024). Specifically, increased activation was observed in subcortical regions such as the NAc and caudate, reduced activation of the OFC, and alterations to the recruitment of the insula and caudal ACC. During the receipt of reward, there was increased activation of the OFC, NAc and putamen and deactivation of the insula and caudal ACC. On the other hand, in receipt of a loss, they found increased activation of the caudate and caudal ACC, and deactivation of the rostral ACC and OFC. These findings highlight the potential influence of head injuries on the neural mechanisms underlying reward processing in children. This is one of few studies which has investigated the association between childhood head

injury and reward-related activation patterns during different stages of reward-processing, and it emphasises the potential influence of childhood head injury on reward-related neural activation.

Whilst such findings have identified impairments to reward-related brain regions following a head injury, they are constrained by the diffuse nature of "natural" head injuries, which can vary in severity, location, and impact across individuals. Controlled animal studies offer a valuable alternative to identify the specific effects of head injuries on reward-related brain regions as these studies can meticulously target specific brain regions and replicate the same injury across a sample. For example, findings from mice studies have shown that an induced head injury consistently results in inflammation of reward-related brain regions and pathways, leading to heightened reward-seeking behaviours, including increased drug-seeking (Cannella et al., 2019). These studies help to clarify how a head injury can influence reward-related brain regions but also highlights the broader implications of this association, such as the subsequent development of maladaptive behaviours.

Overall, these findings emphasise the potential vulnerability of the mesocortical and mesolimbic systems to head injury, highlighting how the (direct or indirect) impact on these reward-related regions can disrupt reward processing. Such disruptions may not only affect one's ability to effectively process reward but can have the potential to exacerbate maladaptive outcomes such as drug-seeking behaviours. However, more research is needed to pinpoint how such changes in neural activity translate into observable reward-related behaviours.

1.2.5 Outcomes

Whilst sustaining a head injury at any stage of life can result in negative outcomes, those sustained during childhood and adolescence can delay the maturation of core developmental milestones. In fact, behaviour, cognitive functioning, and quality of life have been shown to remain impaired for up to 4 years post-injury (Jones et al., 2021; Jones et al., 2019). This disruption during critical periods of development has the potential to create a domino effect, influencing outcomes well into adulthood.

1.2.5.1 Cognitive and Behavioural Outcomes

Some of the most notable outcomes following a childhood head injury includes substance use, criminal behaviour, increased contact with the criminal justice system, as well as other forms of delinquency including antisocial behaviour (Kennedy, Cohen, et al., 2017; Kennedy, Heron, et al., 2017; Mongilio, 2022; Schwartz et al., 2017; Schwartz et al., 2018). For example, one study has shown that 80% of those in juvenile prison in Scotland had a reported history of childhood head injury, of which 84% were classified as mTBIs (McMillan et al., 2023). These outcomes may stem from head injury related impairments such as increased rates of reactive aggression and impulsivity

(Fullerton et al., 2019), poor impulse control (Schwartz et al., 2017; Schwartz et al., 2018), and differences in reward processing (Hogeveen et al., 2024).

Further impairments include behavioural, emotional, and social difficulties following a childhood head injury. For example, one study found considerably lower emotional functioning as well as peer relationship problems and social functioning difficulties in children up to 4 years post-injury (Jones et al., 2021). This suggests that head injuries can produce a multitude of psychosocial impairments across development and emphasise a need to prevent their occurrence.

Whilst there is a great deal of evidence supporting a link between childhood head injury and psychosocial outcomes, there appears to be at least some resilience to the long-term impacts of sustaining a head injury. Studies indicate that while temporary academic difficulties, such as impaired reading skills, may persist for up to 2 years post-injury (Kooper et al., 2024), educational attainment and employment in adulthood are generally unaffected (De Netto & McKinlay, 2020). Whilst this is a positive outcome, it does not distract from the multitude of unfavourable outcomes following a childhood head injury and thus there is still a critical need to prevent their occurrence.

1.2.5.2 Clinical Outcomes

Childhood head injuries have been associated with a wide range of psychiatric conditions across both internalizing and externalizing disorders (McCormick et al., 2021). As these conditions are independently associated with maladaptive outcomes (Retz et al., 2021), it is important to understand and account for these conditions when investigating the role of head injuries.

Among internalizing disorders, depression and anxiety have been frequently reported following a childhood head injury (McCormick et al., 2021; Sabir & Malhi, 2023). Prevalence rates of post-injury depression range between 5.3% to 36% in children and adolescents, dependent on factors such as the duration since the injury, levels of post-injury pain, and location of any brain lesions (Durish et al., 2018). Further, a head injury has been associated with higher levels of anxiety compared to control with an orthopaedic injury, particularly in the first 6 months post-injury, though they are less consistently reported after one year post-injury (Emery et al., 2016).

A further possible psychiatric outcome following a childhood head injury is substance use disorder. This refers to an inability to control one's use of substances such as alcohol, prescription drugs, and illegal substances. Whilst there is limited research investigating this relationship, it suggests that this relationship exists only for children hospitalised for a head injury (Emery et al., 2016; Kennedy, Cohen, et al., 2017; McKinlay et al., 2009). Therefore, it may be that this relationship exists for more severe head injuries.

Head injuries have also been associated with an increased risk of subsequent overall externalizing disorder (Kennedy, Cohen, et al., 2017; McCormick et al., 2021). Further, associations have been made between childhood head injury and specific externalizing disorders – namely, conduct disorder (Brandt et al., 2022; Jackson et al., 2017; Khalaf et al., 2023; Luukkainen et al., 2012), ODD (McKinlay et al., 2009), and ADHD (Adeyemo et al., 2014; Grigorian et al., 2019). A potential mechanism which could explain these relationships is impulsivity. In fact, impulsivity has been proposed as a possible mediating mechanism between head injury and later conduct problems (Khalaf et al., 2023). Whilst the exact temporal ordering of the relationship between externalizing disorders and head injuries remains unclear (e.g., whether preexisting behaviours increase risk *of* injury or result *from* the injury), the association is well-established and warrants further investigation. This will be discussed further in this thesis with specific attention made to conduct disorder.

1.2.5.3 Resilience to Outcomes

It is important to acknowledge that not all children experience significant or lasting impairments following a head injury – be that cognitive, behavioural, or clinical. Research suggests that this greater risk may be associated with multiple previous head injuries, preexisting health conditions, or a more severe head injury (i.e., requiring hospitalisation; Emery et al., 2016). Furthermore, emerging evidence highlights a potential genetic influence on outcomes. One study found that children with a head injury who do not possess the ApoE E4 allele tend to recover more favourably compared with those who carry the ε4 allele suggesting that genetic factors may modulate such negative outcomes following a head injury (McFadyen et al., 2019). Therefore, it is essential to recognize that maladaptive outcomes do not affect all children who sustain a head injury in the same manner. Instead, certain factors, such as injury severity, genetic predisposition, or prior health conditions, may exacerbate the risk and should be carefully considered in both research and clinical practice wherever possible.

1.3 The Challenge

1.3.1 Associations Between Conduct Problems and Head Injuries: What we Know so far

There is considerable scientific literature investigating the aetiology (or risk factors) and pathophysiology of conduct disorder and head injury separately (see Sections 1.1.3.2 and 1.2.3.2). Notably, both conditions appear to share overlapping underlying risk factors and pathophysiological mechanisms. Adversity, for example, significantly increases the likelihood of developing either condition (Jackson, Posick, et al., 2022; Jones et al., 2024; Moffitt & Caspi, 2001; Zarei et al., 2021). Furthermore, both are strongly associated with impairments in decision-making, heightened risk-

taking behaviours, and disruptions in reward-related neural functioning (see Sections 1.1.4 and 1.2.4). These shared characteristics underscore the importance of investigating their co-occurrence and the potential additive effects this co-occurrence may have on developmental trajectories and maladaptive outcomes.

1.3.1.1 Bidirectional Risk

Research continues to show support for a greater risk of conduct problem symptoms following a childhood head injury (Buckley & Chapman, 2017; Jackson et al., 2017; Khalaf et al., 2023; Luukkainen et al., 2012; Schwartz et al., 2017). Possible mechanisms explaining this association include alterations to brain areas involved in executive functioning and fear processing (Kramer et al., 2008), increased impulsivity (Khalaf et al., 2023), and changes to neural connectivity (Caeyenberghs et al., 2012).

In contrast, less research has investigated whether conduct disorder increases the risk of sustaining a head injury. Vassallo and colleagues (2007), for example, found that adolescent conduct disorder was associated with an increased likelihood of sustaining a head injury in adulthood (Vassallo et al., 2007). However, this study focused on US Vietnam war veterans and thus cannot infer whether there is a general or immediate increased risk for head injury during adolescence. Conversely, Dufour and colleagues (2020) found no association between conduct disorder and concussion in children aged 9–10 (Dufour et al., 2020). However, this study focused only on a subset of head injuries characterised by a loss of consciousness for 30 minutes or less. Further, the cross-sectional nature of this study prevents insight into the temporal ordering of conduct disorder and head injury. Nonetheless, whilst conduct problems have not consistently been directly associated with an increased risk for head injury, they have been associated with more severe post-concussion symptoms (Doan et al., 2023). Thus, while conduct disorder may not always directly contribute to the initial occurrence of head injury, it may, at the least, have an effect on the severity of head injury outcomes.

Taken together, the evidence suggests a potential bidirectional association between conduct problems and head injuries - though more research investigating the link between conduct problems and subsequent head injuries is required. In fact, recent research has identified mutual associations between the two and specifically identified a direct association between childhood head injuries and later adolescent conduct problems (Brandt et al., 2022). Brandt and colleagues (2022) utilised data from the Millennium Cohort Study, a UK-based national birth cohort, to identify the longitudinal relationships between conduct problems and head injuries in children from infancy to early adolescence. Not only did they find this direct effect of head injuries sustained between ages 5–7 on conduct problem levels at age 11 (as well as indirect effects on conduct problems at age 14), but an indirect effect of conduct problems at age 3 on sustaining a head injury between ages 7–11. This is

one of the first studies to allude to a potential bidirectional association between the two during development.

However, whilst these findings were promising, this study has limitations. Firstly, they excluded approximately 500 children with an ADHD diagnosis. ADHD has a high comorbidity rate with conduct problems (see Section 1.1.2.2.1.1) and their comorbidity has been associated with an earlier onset, more severe, and persistent symptoms (Fairchild et al., 2019). This exclusion this likely omitted a considerable proportion of children with high conduct problem symptoms from their sample, limiting the generalisability of their findings to conduct problems as a whole. In fact, this may partially account for the lack of direct effects from conduct problems to subsequent head injuries. Including children with ADHD and controlling for its effects would have provided a more comprehensive analysis of the association. Second, they did not control for salient risk factors of conduct problems and/or childhood head injury beyond sex and family income. Whilst these are important covariates, additional variables could be included to reduce this risk of confounded results. Granted, it is not feasible to account for every possible risk factor known of conduct problems or childhood head injuries, but the inclusion of further salient factors such as adversity (Jackson, Posick, et al., 2022; Jones et al., 2024; Moffitt & Caspi, 2001; Saadi et al., 2024; Zarei et al., 2021) or harsh parenting (Bauer et al., 2022; Hukkelberg & Ogden, 2021; Speyer et al., 2022) would have strengthened the analysis by accounting for their influence on the observed associations.

Following on from the work of Brandt and colleagues (Brandt et al., 2022), I continued to investigate the relationship between conduct problems and head injuries from ages 3–17 using the same UK-based dataset (Carr, Hall, Eisenbarth, et al., 2024). From conducting a similar cross-lagged path model whilst controlling for ADHD (rather than excluding those with ADHD) alongside various salient risk factors (e.g., sex and cumulative risk across multiple ecological levels), I indeed identified a bidirectional association between the two. Specifically, conduct problems at age 5 were associated with an increased risk of head injuries between ages 5–7 and head injuries sustained between ages 7–11 were associated with an increased risk of higher conduct problem levels at age 14. As such, it appears that the period between the ages of 5–11 (i.e., primary school age) may represent a sensitive developmental period during which conduct problems and head injuries mutually increase the risk of one another.

1.3.2 The Aim of This Thesis

Whilst research has begun to identify a bidirectional association between conduct problems and childhood head injuries (Brandt et al., 2022; Carr, Hall, Eisenbarth, et al., 2024), this research is still in its early stages. Current findings, while informative, lack depth in several critical areas. For example, as discussed previously (see Section 1.1.2.1), conduct disorder encompasses multiple

trajectories, including a persisting, adolescent-onset, and childhood-limited trajectory. Existing studies fail to account for these variations, making the broad claim of a bidirectional association between conduct problems and head injuries potentially misleading. Failing to distinguish between subtypes of conduct problems risks targeting all individuals with conduct problems, even those to whom interventions may be unnecessary and thus ineffective. For example, if the bidirectional association is only relevant to persistent conduct problems, then an intervention to prevent head injuries that targets all children with conduct problems would be ineffective for the children with other conduct problem subtypes. This could mean that effective interventions could be disregarded because they appear to not be effective due to the inclusion of children who the intervention will not be appropriate for in the first place. It is thus extremely important to tease apart this bidirectional association to identify which pathways of conduct problems has a co-occurrence with childhood head injuries.

Further, research must also investigate the longitudinal relationships between childhood head injuries and the subtypes of conduct problems. Even if all subtypes are associated with head injuries, the timing and nature of these associations are likely to vary. For example, one could hypothesise that adolescent-onset conduct problems may be more closely associated with later childhood and adolescent head injuries, whereas childhood-limited conduct problems may be associated with earlier patterns of head injury. By understanding these nuances, interventions can be tailored to address the heterogeneity of conduct problem subtypes, aligning strategies with specific trajectories and developmental timings. This approach is vital for designing effective preventative or therapeutic interventions to mitigate the co-occurrence of conduct problems and head injuries.

When there is a clearer picture of who this association is in fact relevant to, a pivotal research question that must be answered is "*what are the potential outcomes of their co-occurrence?*". Answering this question is important as it will highlight whether interventions to prevent their co-occurrence are essential. That is, if their co-occurrence does not have a significantly greater effect on maladaptive outcomes, then is there a need to prevent their co-occurrence in order to prevent maladaptive outcomes from occurring? Rather, it may be more resourceful to continue to address the prevention of conduct problems or head injuries in isolation in order to prevent their own associated maladaptive outcomes.

Importantly, this thesis has so far outlined that both conduct disorder and head injury are independently associated with a range of maladaptive outcomes across the lifespan, including antisocial behaviour, crime, and substance use (see Sections 1.1.6 and 1.2.5.1). Given the increased risk for their co-occurrence across development, it is important to determine whether this co-occurrence exacerbates the risk for such maladaptive outcomes. Notably, if evidence reveals that their co-occurrence significantly heightens the risk for maladaptive outcomes (particularly those

already associated with each condition individually, such as antisocial behaviour) it would provide a compelling rationale for further investigation.

A follow-up research question that needs to be addressed is *"what underlying mechanisms are characteristic of those with co-occurring conduct problems and head injury?".* Whilst numerous potential mechanisms warrant investigation, addressing all of them exceeds the scope of this thesis. As such, I have decided to focus on neural mechanisms related to reward processing. Both conduct problems and childhood head injuries are characterised by distinct neural pathophysiology involving reward-related pathways (see Sections 1.1.4.2 and 1.2.4.2). However, how changes to brain functioning may be influenced by their co-occurrence remains unexplored.

Understanding the neural mechanisms affected by the co-occurrence of conduct disorder and head injury could offer valuable insights into potential therapeutic strategies for those impacted. For example, both conditions independently are shown to have significant alterations in neural functioning of pathways involved in decision-making and reward processing (Hawes et al., 2021; Hogeveen et al., 2024). This raises a critical question of whether their co-occurrence exacerbates dysfunction in these pathways. If so, identifying and addressing these changes could help prevent subsequent maladaptive outcomes linked to such impaired reward-processing.

By answering these research questions, we could pave the way for the development of targeted interventions. Such interventions would aim to mitigate the neural dysfunction caused by the co-occurrence of conduct disorder and head injuries, potentially preventing the associated long-term maladaptive outcomes.

1.3.3 Methodological Approach

Whilst there are fundamental questions that need to be answered and are thus the aim of this thesis, there are further methodological challenges that need to be addressed. That is, investigating the co-occurrence of conduct problems and head injuries requires focusing on a small subpopulation, which presents two key challenges. First, identifying individuals who exhibit both conduct problems and a history of head injuries is inherently challenging, particularly when attempting to recruit participants for primary data collection. Second, even when such individuals can be identified, assembling a sample large enough sample to ensure adequate statistical power is exceptionally difficult, particularly within the time restraints of this thesis.

To overcome these difficulties, this thesis will utilise large national cohort datasets. These datasets provide access to extensive, representative samples of the general population, and enable the identification of individuals who meet the criteria for both conduct problems and head injuries. The large number of participants in national cohort studies facilitates the investigation of rare

exposures, such as the co-occurrence of these two conditions, which would otherwise be impractical to study using smaller-scale data.

National cohort studies also offer several other advantages which make them highly desirable to address the research questions previously set out. These datasets typically contain rich longitudinal data, allowing for the examination of the temporal relationship between conduct problems and head injuries across development. Additionally, they often include detailed demographic, behavioural, and health-related variables, which enables a comprehensive analysis that can control for numerous potential confounders. By leveraging these large-scale datasets, this thesis thus aims to provide robust and novel insights into the co-occurrence of conduct problems and head injuries, contributing to a deeper understanding of their interplay in general populations.

1.4 Thesis Overview

With key gaps in the literature identified, this thesis aims to address them through secondary analysis of national cohort datasets. Importantly, it was guided by a postpositivist approach and relied on previous evidence and theory to formulate key research questions and hypotheses, utilising advanced statistical techniques to create a more detailed picture of the association between conduct disorder and childhood head injury. The thesis was structured around three research papers.

1.4.1 Paper 1: Linked Head Injury and Conduct Problem Symptom Pathways From Early Childhood to Adolescence and Their Associated Risks: Evidence From the Millennium Cohort Study

The first paper aimed to identify whether the co-occurrence of conduct problems and head injuries is associated with specific subtypes of conduct problems. A secondary aim was to identify if salient risk factors could predict membership to linked pathways of conduct problems and head injury and thus identify potential targets for preventative interventions. To accomplish these aims, the following research questions were answered:

a. **Primary research question:** Are there distinct linked developmental pathways of conduct problems and head injury?
b. **Secondary research question:** What risk factors predict membership to these linked pathways of conduct problems and head injury?

To identify subgroups with linked conduct problems and head injury pathways across development, latent class analysis (LCA) was used. LCA is a statistical technique that identifies subgroups within a population based on observed variables. Whilst other statistical techniques, can

be useful for modelling longitudinal changes in variables, LCA was chosen due to its focus on identifying subgroups and not on identifying variations in behaviours across time.

A limitation of LCA is its probabilistic approach, as it estimates the likelihood of group membership and assigns individuals to the group with the highest probability. This means the resulting groups are latent (unobserved) rather than explicitly defined. Consequently, ambiguities in classification may arise, particularly when individuals have similar probabilities of belonging to multiple groups (Mori et al., 2020). Additionally, there is the risk of a naming fallacy, where the labels assigned to subgroups may not fully or accurately represent their characteristics (Weller et al., 2020).

To ensure the appropriate number of subgroups were identified and interpreted accurately, multiple statistical criteria were used to evaluate model fit. The statistical criteria included the Bayesian Information Criterion (BIC; Schwarz, 1978), Akaike information criterion (AIC; Akaike, 1987). Lower BIC and AIC indicate a better fitting model (Collins & Lanza, 2009; Connell et al., 2009). Further, the entropy, which is a summary statistic, was also used. This statistic identifies how accurately a model has identified its classes. This value (ranging 0–1) needs to be at least .80 or higher to be considered acceptable classification (Clark & Muthén, 2009). Whilst I was mainly guided by these fit indices, I also used my knowledge and understanding of the observed variables to ensure that the classes identified also made theoretical sense.

After identifying and appropriately naming the latent subgroups, the secondary aim of this paper was to examine risk factors which could predict or be associated with group membership. Variables measured prior to pathway onset were considered predictors, whilst those measured concurrently were regarded as associative factors. To account for the broad range of risk factors which could predict conduct problems and head injury pathways, CRIs were used. These allowed for a more streamlined approach by summarising risks at each ecological level (child, mother, and household), rather than focusing on individual, often highly correlated risk factors.

The models also accounted for associated factors, including negative maternal parenting styles, ADHD and epilepsy, measured between ages 3–14. These were not treated as predictors of group membership but as contextual influences. Whilst they cannot be directly targeted in preventative interventions, they can shape developmental pathways, with ADHD comorbidity, for example, being addressed within therapeutic interventions.

1.4.2 Paper 2: Adolescent Delinquency Following Co-Occurring Childhood Head Injuries and Conduct Problem Symptoms: Findings From a UK Longitudinal Birth Cohort

The LCA models in Paper 1 identified distinct linked pathways of conduct problems and head injuries across development. Importantly, these linked pathways highlighted that the co-occurrence

of conduct problems and head injuries was not confined to a specific subgroup. Instead, the co-occurrence was relevant across the known trajectories of conduct problems, with each trajectory having its own linked pathway of head injuries. This finding suggested that preventative interventions targeting co-occurring conduct problems and head injuries could be beneficial across a wide spectrum of individuals.

However, before creating such interventions, it was important to assess whether the co-occurrence of conduct problems and head injuries lead to negative outcomes that exceed the risks associated with either factor in isolation. If their co-occurrence did indeed result in worse outcomes, preventative interventions targeting the reduction of their co-occurrence would be warranted. Conversely, if no greater risks for outcomes were identified, recommendations would be made to continue to focus on interventions addressing conduct problems and head injuries independently.

A specific focus of this study was the risk for adolescent delinquency. Delinquent behaviours such as substance use, criminality, and antisocial behaviour have been associated with conduct problems (see Section 1.1.6) and head injuries (see Section 1.2.5.1) when considered separately. Further, they can be a catalyst for a cascade of subsequent negative outcomes including poor educational attainment (Kim, 2020), sleep deficiencies (Kim & Son, 2023), and poor physical and mental health in adulthood (Kim et al., 2020).

Thus, the primary aim of the second paper was to investigate rates of delinquency in children with co-occurring conduct problems and head injuries. As delinquency is associated with both conduct problems and head injuries in isolation, it was hypothesised that their co-occurrence would further amplify this risk due to a potential additive effect of their underlying mechanisms.

a. **Hypothesis:** Co-occurring conduct problems and head injury will have a heightened risk for adolescent delinquency.

I tested this hypothesis using negative binomial regression models. This statistical method allowed for the estimation of incidence rates of delinquency between those with a history of conduct problems, those who sustained a head injury, those with both, or those with neither. Delinquency was measured using a latent variable, which summed the number of delinquent behaviours self-reported across substance use, criminality, and antisocial behaviour. This produced a count outcome variable which had overdispersion (i.e., a large proportion of the sample reported few or no delinquent behaviours). Together, these characteristics made negative binomial regressions the most appropriate form of regression to use. Whilst it would have been possible to include delinquency as an associative factor in the LCA similar to ADHD, epilepsy, and negative parenting, the aim of this paper was to examine whether co-occurring conduct problems and head injuries increase the risk of delinquency at ages 14 and 17. Including delinquency in the LCA would have compromised this aim,

particularly for age 14 delinquency, because the LCA model incorporated conduct problem and head injury data beyond this timepoint. This would have introduced temporal overlap between the predictor (latent class membership) and the outcome, undermining the ability to establish a clear predictive relationship. Further, as conduct problems and head injuries appear to follow linked developmental pathways across all clinically relevant groups, it was appropriate to investigate the general impact of a history of both, regardless of specific pathway types (e.g., childhood-limited). Additionally, the more simplistic modelling approach used in Paper 2 allowed for a more detailed analysis by incorporating specific covariates such as sex rather than the broader CRIs used in the LCA model of Paper 1. This approach enabled a more precise interpretation of each variable's contribution to adolescent delinquency.

Compared to the LCA utilised in Paper 1, the negative binomial regression models in Paper 2 were less complex. As such, relevant risk factors were able to be included as separate covariates, which enabled the consideration of their individual contributions to the association between conduct problems, head injuries, and delinquent outcomes. The covariates included most of the risk factors that comprised the CRIs in Paper 1, although some were omitted to avoid overcomplicating the model. For instance, epilepsy was excluded because it was associated only with the adolescent-onset trajectory of conduct problems and head injuries in Paper 1 whilst this study accounted for conduct problem symptoms and reported head injuries up until ages 11 and 14. Further, there is limited evidence to suggest that epilepsy is associated with delinquent behaviours (Saleh et al., 2019). In contrast, variables such as ADHD were retained due to their broader and stronger associations with both conduct problems (Fairchild et al., 2019; National Institute for Health Care Excellence, 2013), head injuries (Adeyemo et al., 2014; Grigorian et al., 2019), and delinquency (Retz et al., 2021).

1.4.3 Paper 3: Reward-Related Neural Pathways in Children with Conduct Disorder and Mild Traumatic Brain Injury

Building on from the findings of Paper 2, which identified an increased risk for higher rates of early adolescent delinquency in children with co-occurring conduct problems and head injuries, a logical next step was to identify potential mechanisms driving this increased rate for delinquency. Whilst numerous mechanisms could contribute to this increased risk, Paper 3 focused specifically on reward processing and the neural pathways underlying this process.

Reward processing relies on an intricate network of neural systems including those within the mesocortical (e.g., prefrontal cortex and ACC) and mesolimbic pathways (e.g., amygdala and NAc). Previous research has shown disrupted functioning in these regions in children with conduct problems (Fairchild et al., 2019; Hawes et al., 2021; Rubia, 2011) and a history of head injury (Cannella et al., 2019; Huang et al., 2019; Mayer et al., 2015). Further, such disruptions in neural

reward pathways have been associated with an increased risk of delinquent behaviour (Hyde et al., 2013; Reyna et al., 2018).

To investigate the potential role of these neural mechanisms those with co-occurring conduct problems and head injuries, Paper 3 employed a new dataset which provided neuroimaging data for a more in-depth analysis. The ABCD dataset used in this study offered several strengths over the dataset used in Papers 1 and 2. In particular, the measurement of conduct problems in the ABCD dataset allowed for the identification of individuals with a formal conduct disorder diagnosis, providing a more clinically relevant and stringent operationalisation. Further, the measurement of head injury in the ABCD dataset utilised standardised criteria that differentiated between the severity of head injuries. This allowed the term mTBI to be employed, increasing the precision and specificity of the findings.

The aim of the third paper was thus to investigate reward-related neural correlates associated with the co-occurrence of conduct disorder and mTBI. Using functional magnetic resonance imaging (fMRI) data from the ABCD dataset, this study examined neural activation within eight reward-related regions of interest (ROIs) during a reward processing paradigm in children aged 9 to 10. This investigation sought to identify potential reward-related neural characteristics of co-occurring conduct disorder and mTBI. Whilst its association with subsequent delinquency could not be tested, it would act as a first step to identify if this could be a potential mechanism to predict such outcomes.

a. Hypothesis: Co-occurring conduct disorder and mTBI will have a distinct pattern of reward-related neural activation.

To test this hypothesis, I ran multinomial logistic regression models to estimate neural activation within predefined reward-related ROIs. These ROIs included key areas of the mesocortical and mesolimbic systems, such as the ventral striatum, amygdala, and prefrontal cortex, which are known to be integral to reward processing. Neural activation was measured during a reward processing task designed to elicit responses within these regions.

In addition to the primary variables of interest (conduct disorder and mTBI), covariates were included in the models to control for potential confounding factors. Whilst these covariates were similar to those used in Paper 2, they were adapted based on the variables available in the ABCD dataset. These covariates included demographic (e.g., age, sex, socioeconomic status), clinical (e.g., ADHD diagnosis), and contextual variables (e.g., family environment).

1.5 Author Contributions

HC was the lead author and wrote all three papers submitted as part of this thesis. For Paper 1, co-authors VB and JH were involved in the development of research questions, supervised the analysis, the interpretation of findings, and editing the final manuscript. DG advised on the inclusion of supplementary analysis and was involved in editing the final manuscript. For Paper 2, co-authors VB and JH were involved in the interpretation of findings and editing the final manuscript. For Paper 3, VB and HE were involved in the development of research questions, interpretation of findings, and editing the final manuscript. Co-authors DG and RW were involved in editing the final manuscript.
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Chapter 2 Linked Head Injury and Conduct Problem Symptom Pathways From Early Childhood to Adolescence and Their Associated Risks: Evidence From the Millennium Cohort Study

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2.1 Abstract

Conduct problems and head injuries increase the risk of delinquency and share a bidirectional association. However, how they link across development is unknown. The present study aimed to identify their linked developmental pathways and associated risk factors. Latent class analysis was modelled from Millennium Cohort Study data (*N* = 8,600) to identify linked pathways of conduct problem symptoms and head injuries. Head injuries were parent-reported from ages 3–14 and conduct problems from ages 3–17 using the Strengths and Difficulties Questionnaire (SDQ). Multinomial logistic regression then identified various risk factors associated with pathway membership. Four distinct pathways were identified. Most participants displayed low-level conduct problem symptoms and head injuries (*n*=6,422 [74.7%]). Three groups were characterised by clinically relevant levels of conduct problem symptoms and high-risk head injuries in childhood (*n*=1,422 [16.5%]), adolescence (*n*=567 [6.6%]), or persistent across development (*n*=189 [2.2%]). These clinically relevant pathways were associated with negative maternal parenting styles. These findings demonstrate how pathways of conduct problem symptoms are uniquely linked with distinct head injury pathways. Suggestions for general preventative intervention targets include early maternal negative parenting styles. Pathway specific interventions are also required targeting cumulative risk at different ecological levels.

Keywords: birth cohort, conduct problems, head injury, latent class analysis

2.2 Introduction

Evidence suggests that conduct problems (i.e., violations of age-appropriate societal norms including fighting and threatening behaviours; Girard et al., 2019) are partially predicted by previous head injuries (a bang on the head with or without a loss of consciousness; Davis & Ings, 2015; Yates et al., 2006) and vice versa (Brandt et al., 2022; Carr, Hall, Eisenbarth, et al., 2024). However, despite the high prevalence of childhood head injuries (33–50% of the 1 million head injury admissions in the UK; National Institute for Health and Care Excellence, 2014), the link between conduct problems and head injuries over time and the risks associated with their co-occurrence are vastly under researched (McKee & Daneshvar, 2015) compared to the association between traumatic brain injuries (TBI) and conduct problems (Bellesi et al., 2019).

Research indicates that there are distinct developmental pathways to conduct problems (Gutman et al., 2019) and head injuries (Keenan et al., 2020). The DSM-5 describes two conduct disorder pathways: childhood-onset (presentation before age 10) and adolescent-onset (presentation after age 10; American Psychiatric Association, 2022). Whilst further research suggests an additional childhood-limited high conduct problems pathway (Gutman et al., 2019). Similarly, head injuries have developmental pathways based on their initial severity and impact on infant cognition (Keenan et al., 2020).

The consequences of both conduct problems and head injuries are well known and include increased likelihood of delinquency and criminal behaviour (Kennedy, Heron, et al., 2017; Mongilio, 2022). A better understanding of how their pathways link during development is therefore important for intervention and prevention practices aimed at jointly reducing both. To create effective intervention and prevention practices we need to not only understand how conduct problems and head injuries link but also the risk factors for these links (e.g., childhood maltreatment may increase the risk for developmentally stable high risk of both head injuries and conduct problems).

The bidirectional association between childhood head injuries and conduct problems has been previously linked to cumulative risk at the child, mother, and household levels, such as alcohol consumption during pregnancy, mother psychological distress, and a low income household (Carr, Hall, Eisenbarth, et al., 2024). In turn, cumulative risk indices (CRIs) are commonly used to inform interventions and prevention policies (Hogye et al., 2022). Negative parenting styles (i.e., harsh, avoidant, and abusive parenting) have been associated with increased conduct problems (Hukkelberg & Ogden, 2021; Speyer et al., 2022) and could create increased opportunities to sustain

a head injury (Schnitzer et al., 2015). These associations, however, are yet to be investigated in a model of both head injuries and conduct problems.

The current study thus investigates distinct development pathways linking conduct problem symptoms and head injuries between early childhood and adolescence. By drawing on secondary data from a longitudinal cohort study, it provides an in-depth perspective on the patterns of linked head injury and conduct problems symptoms across development that is not possible from a cross-sectional design. We utilised latent class modelling on this longitudinal dataset to reveal the different pathways linking head injury and conduct problem symptoms from ages 3–17 years. It further elaborates to identify if distinct developmental pathways are associated with accumulated risks at the child, mother, and household levels, such as alcohol consumption during pregnancy, mother psychological distress, and a low-income household, as well as negative parenting styles.

2.3 Methods

2.3.1 Participants

The Millennium Cohort Study (MCS; https://www.cls.ioe.ac.uk/mcs) is an ongoing longitudinal UK birth cohort of 18,786 individuals born in the UK, aged 9 months at the first measurement timepoint (T1) between 2000–2002 (Fitzsimons et al., 2020). Participants were studied at six further timepoints at the ages of 3 (T2), 5 (T3), 7 (T4), 11 (T5), 14 (T6), and 17 years (T7). For this study, we included participants who completed the last wave at age 17, who were first-born children, whose main respondent in the study was their biological mother, and who had complete CRI data (*N* = 8,600; 4,320 females [50.2%]; 7,136 [83%] “White British”). For more information and justifications for these exclusions and for the participant flow chart see Appendix A and B.

Written informed consent was provided to the MCS by the parent of each child. Ethical approval for this analysis was given by the University of Southampton Ethics Committee (ID = 62100). This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cohort studies.

2.3.2 Measures

2.3.2.1 Conduct Problem Symptoms

Conduct problem symptoms were parent-reported at T2 (age 3) to T7 (age 17), using the five items from the Strength and Difficulties Questionnaire (SDQ) Conduct Problem Subscale

(Goodman, 2001). This subscale is widely used as a reliable and valid measure of conduct problems and externalizing behaviour (Patalay & Hardman, 2019; Zendarski et al., 2021). The items were coded from 0 (*not true*) to 2 (*certainly true*) and were summed to create a total score at each timepoint (possible range: 0–10). Based on the newer 4-band categorisation (see www.sdqinfo.org), scores reflect the following levels of conduct problems: *close to average* (0-2), *slightly raised* (3), *high* (4-5), or *very high* (6-10).

Whilst the SDQ (and many of the measures describe below) were parent-reported within the MCS, they have been labelled as so for accuracy. However, as the analytical sample included children whose main respondent was their biological mother, it can be assumed that in the context of this study, these measures were mother-reported.

2.3.2.2 Head Injuries

Head injuries were parent-reported from T2 (age 3) to T6 (age 14). Parents reported their child sustaining a "*bang to the head*" or "*loss of consciousness after bang to the head*". Uniting both responses regarding head injury was a replication of the head injury variables created in previous published MCS analyses (Brandt et al., 2022; Carr, Hall, Eisenbarth, et al., 2024; Mongilio, 2022).

Though head injuries were reported at T1 these were not included due to the temporal ordering of the risk factors below.

2.3.2.3 Potential Risk Factors

Risk factors were distinguished across three levels (child, mother, and household) and were assessed via the creation of CRIs (Bronfenbrenner, 1977). CRIs refer to the summation of risk factors. That is, each risk factor is dichotomised and then summed to emphasise volume of risk rather than individual relationships of risk factors (Hall et al., 2010; Rutter, 1979). The factors included in the CRIs replicate those used previously in the modelling of the bidirectional association between conduct problems and head injuries (Carr, Hall, Eisenbarth, et al., 2024).

At each ecological level, five potential risks for conduct problems and/or head injuries were identified and labelled as either "*present"* or "*high risk"* (1), as compared to "*absent"* or "*low risk"* (0). The high-risk thresholds were informed by previous literature (see below). These risks were summed to create the three CRIs (score ranging from 0–5 at each level):

2.3.2.3.1 Child-level Risks

Potential risks included: low birth weight (< 2.5 kg) and premature birth (<= 252 days gestation; Reijneveld et al., 2006; Whiteside-Mansell et al., 2009), male sex (Fullerton et al., 2019; McKinlay et al., 2010), and whether the child's biological mother smoked or drank alcohol during pregnancy (Van Adrichem et al., 2020). These were all measured at T1. Unfortunately, further child-level risk factors such as drug use during pregnancy were not available in the MCS and thus could not be accounted for.

2.3.2.3.2 Mother-level Risks

Potential risks included: unemployment (Van Adrichem et al., 2020), no high-school qualification (Greitemeyer & Sagioglou, 2016; Trentacosta et al., 2008; Van Adrichem et al., 2020), pregnancy before age 18 (McKinlay et al., 2010; Trentacosta et al., 2008), low attachment with child (<= 22 on the Condon Maternal Attachment Scale; six 5-point items ranging from 1 [*almost all the time*] to 5 [*never*] summed; Condon & Corkindale, 1998; Curran et al., 2016), and high maternal psychological distress (>= 4 on Rutter Malaise Inventory; nine binary items [0 [*no*], 1 [*yes*]] summed; McKinlay et al., 2010; Rutter et al., 1970). These were all measured at T1.

2.3.2.3.3 Household-level Risks

Potential risks included: low household occupational status (semi-skilled or lower; Greitemeyer & Sagioglou, 2016), low household income (< 60% of median household income; Northerner et al., 2016; Trentacosta et al., 2008), single parent household (Northerner et al., 2016; Trentacosta et al., 2008), household overcrowding (fewer rooms than people; Northerner et al., 2016; Trentacosta et al., 2008), and low-quality home learning environment (bottom quartile of the [early] Home Learning Environment scale [HLE]; Sylva et al., 2004). The (early) HLE scale was comprised of six items that assessed the frequency of child engagement in early learning activities such as being read to. The items were scored from 0 (*not at all*) to 7 (*every day*) and summed (possible range: 0–42). A higher score indicated a higher quality home learning environment. All were measured at T1 except for the (early) HLE, which was measured at T2.

2.3.2.3.4 ADHD

ADHD is a risk factor due to its comorbidity with conduct problems (Gnanavel et al., 2019) and sustaining a head injury (Ramos Olazagasti et al., 2013). ADHD was measured by parents reporting if their child had received an ADHD diagnosis between T3–T6 (age 5–14). A binary variable was created (0 [*no diagnosis*], 1 [*diagnosis of ADHD*]).

2.3.2.3.5 Epilepsy

Epilepsy is a risk factor due to its comorbidity with conduct problems (Lin et al., 2012) and sustaining a head injury (Annegers & Coan, 2000). Epilepsy was measured by parents reporting if their child had received an epilepsy diagnosis between T2–T6 (ages 3–14). A binary variable was created (0 [*no diagnosis*], 1 [*diagnosis of epilepsy*]).

2.3.2.3.6 Negative Parenting Styles

Negative parenting styles were measured at T3 (age 5) using the Parent-Child Conflict Tactic Scale (Straus et al., 1998). This measures how often the mother engages in harsh parenting (smacking, shouting at, or telling off) and withdrawal tactics (ignoring, sending to room, or taking away toys). Mothers were asked to report the frequency of these behaviours on a 5-point Likert scale ranging from 1 (*never*) to 5 (*daily*). The three items for each parenting style were summed to create a score (possible range: 3–15). A higher score indicated harsher parenting or greater levels of withdrawal.

2.3.3 Statistical Analysis

Analyses were conducted using Mplus v7.4 (Muthén & Muthén, 2017). Latent class analysis was used to identify distinct development pathways linking conduct problem symptoms and head injuries from 3–17 years. The first step was to identify the optimum number of classes starting with a two-class model and increasing the number of classes until the solution that best fitted the data was found. This was established by comparing model fit indices between competing potential solutions (Weller et al., 2020) and interpretability (see Appendix C).

Missing data from T2–T6 were accounted for by using Full Information Maximum Likelihood (FIML).

MCS sample weights from T7 were included (accounting for stratification, nonresponse bias, and attrition) to facilitate generalization of findings to the UK population. ADHD, epilepsy, and three CRIs at the child, mother, and household level were included in the analysis and were tested for their association with an individual's distinct developmental pathway via multinomial logistic regression. Post hoc analyses further probed if negative parenting styles (harsh parenting or withdrawal tactics) at T3 were associated with class membership (see Appendix D). Though exclusions were applied to the sample (refer to

and B), additional analysis without these exclusions was completed on the final class solution to ensure the exclusions did not alter the interpretability of the linked pathways identified.

2.3.4 Data Availability

The MCS data that support the findings of this study are openly available at the UK Data Service (https://discover.ukdataservice.ac.uk/series/?sn=2000031). To access the data, one must register to the UK Data Service and submit a data request.

2.4 Results

2.4.1 Participants and Demographics

Sample characteristics, variable differences between the analytical and excluded sample, and information on missing data can be seen in Table 1. Though there were significant differences between the included and excluded samples these effects were typically small (*d* = -.02–.18; V = .03–.10).

Table 1

Sample Characteristics and Differences Between the Analytical and Excluded Samples

Variable	Analytical Sample (*N*=8,600)		Excluded Sample (*N*=10,186)				
	n(%)	*SD*	*n(%)*	*SD*	$\chi^2(df)$	*p*	V
Sex					14.68 (1)	<.001	.03
Male	4,280 (49.8)	..	5,355 (52.6)	..	..	..	..
Female	4,320 (50.2)	..	4,831 (47.4)	..	..	..	..
Ethnicity					15.90 (5)	.007	.03
White	7,136 (83.0)	..	8,346 (80.8)	..	..	..	..
Mixed	246 (2.9)	..	316 (3.2)	..	..	..	..
Black	265 (3.1)	..	413 (4.2)	..	..	..	..
Indian	222 (2.6)	..	247 (2.6)	..	..	..	..
Pakistani	600 (7.0)	..	663 (7.3)	..	..	..	..
Other	117 (1.4)	..	147 (1.6)	..	..	..	..
Conduct problems [c]							
Wave 2	7,645 (88.9)	2.69 (2.00)	6,713 (64.1)	2.95 (2.12)	7.61 (14,356)[a]	<.001	.13[b]
Wave 3	7,692 (89.4)	1.42 (1.46)	6,431 (66)	1.61 (1.56)	7.46 (14,391)[a]	<.001	.13[b]
Wave 4	7,809 (90.8)	1.29 (1.48)	5,341 (56.4)	1.52 (1.63)	8.36 (13,148)[a]	<.001	.15[b]
Wave 5	7,968 (92.7)	1.28 (1.49)	4,433 (50)	1.56 (1.68)	9.55 (12,399)[a]	<.001	.18[b]
Wave 6	7,796 (90.1)	1.33 (1.57)	3,261 (39.5)	1.57 (1.72)	7.14 (11,055)[a]	<.001	.15[b]

Wave 7	8,600 (100)	1.17 (1.48)	452 (17.7)	1.14 (1.41)	-.378 (9,050)[a]	.705	-.02[b]
Head injuries [d]							
Wave 2	1,018 (11.8)	..	868 (8.5)	..	55.42 (1)	<.001	.05
Wave 3	768 (8.9)	..	636 (6.8)	..	47.89 (1)	<.001	.05
Wave 4	579 (6.7)	..	383 (4.2)	..	84.54 (1)	<.001	.07
Wave 5	503 (5.8)	..	274 (3.1)	..	115.75 (1)	<.001	.08
Wave 6	392 (4.6)	..	119 (1.5)	..	200.54 (1)	<.001	.10

Note. If *n* totals less than 8,600 or 10,186 respectively this indicates missing data.

[a] Independent t-test

[b] Cohen's *d*

[c] As measured by the Parent-version of the Strengths and Difficulties Questionnaire Conduct Problem Subscale

[d] As measured by parent reports of accidents resulting in a bang to the head with or without a loss of consciousness

2.4.2 Identification of Distinct Linked Developmental Pathways

Upon comparison of latent class models with two to five classes, a 4–class solution appeared to best fit the MCS data based on model fit (see Table 2) and interpretability (see Appendix E).

The 4-class solution identified four distinct and interpretable classes of linked conduct problem symptoms (Figure 1a) and head injuries (Figure 1b). The first class (*n* = 6,422 [74.7%]) was labelled *stable low-level conduct problem symptoms and head injuries*. Members of this class were characterised by consistent "close to average" levels of conduct problem symptoms as well as low levels of head injuries at all waves. The second class (*n* = 1,422 [16.5%]) was labelled *childhood-only high conduct problem symptoms and head injuries*. Members of this class presented with "high" levels of conduct problem symptoms at age 3, which declined into the lower range by age 7. Similarly, levels of head injury were highest at age 3, declining until age 14. The third class (*n* = 567 [6.6%]) was labelled *high adolescent conduct problem symptoms and childhood onward head injuries*. Members of this class showed high levels of conduct problem symptoms from age 14–17 as well as an increase in head injuries from age 11–14. The fourth class (*n* = 189 [2.2%]) was labelled *persistent high conduct problem symptoms and childhood-limited head injuries*. Members of this class showed persistently "slightly raised" to "very high" levels of conduct problem symptoms and the highest level of head injuries from ages 3–17 with a particular increase in head injuries during ages 7–11.

Classes two to four indicated distinct developmental pathways that were deemed to be "clinically relevant" due to the levels of conduct problem symptoms shown by their members in accordance with the SDQ categorisations (see Methods).

Supplementary analysis identified a similar 4-class solution when no exclusions were applied to the sample (see Appendix F).

Table 2

Model Fit Indices of a Latent Class Analysis of conduct Problems and Head Injuries

k	AIC	BIC	Entropy	Smallest class (%)
2	162,544.69	162,754.30	.93	9.5
3	160,846.61	161,437.83	.84	4.7
4	**159,485.75**	**160,106.99**	**.86**	**2.7**
5	158,602.55	159,343.80	.86	2.1

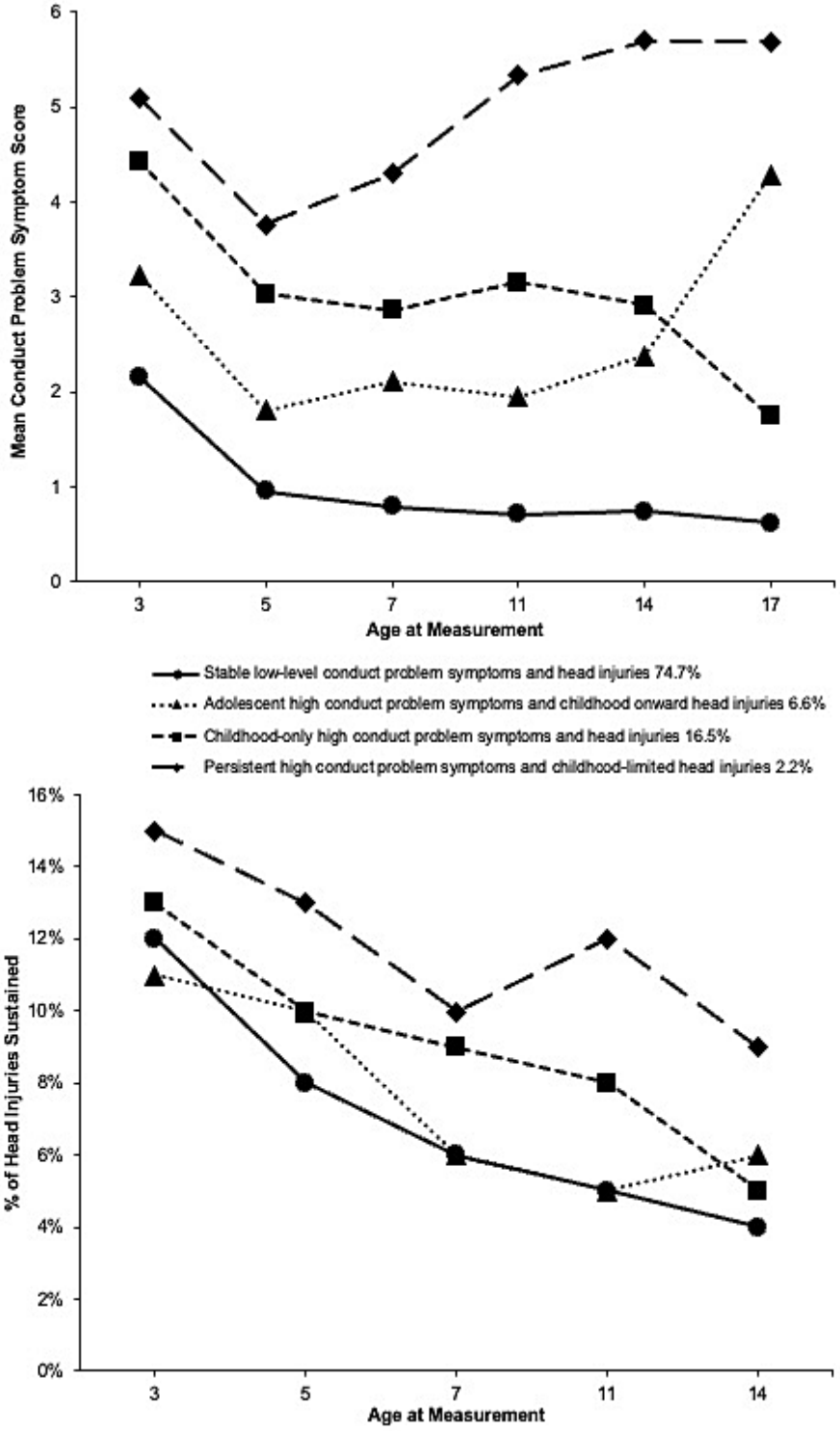
Note. Bold typeset indicates final class solution. k = classes; AIC = Akaike's Information Criterion; BIC = Bayesian Information Criterion.

Figure 1

A Figure of the Linked Pathways of Mean Conduct Problem Symptoms and Head Injuries at Each Timepoint for the 4-Class Solution

a)

b)



Note. This figure shows the linked pathways of (a) mean conduct problem symptoms and (b) frequency of head injuries within the 4-class solution where conduct problem symptoms were measured using the Conduct Problem Subscale of the SDQ and head injuries were parent-reported based on a history of a bang on the head with or without a loss of consciousness. The circles represent the "typically developing" group with low

levels of conduct problem symptoms and sustained head injuries. The squares represent those with higher early levels of conduct problems symptoms and head injuries, which decline during development. The triangles represent those with low early levels of conduct problem symptoms and head injuries which both begin to rise from late childhood to adolescence. The diamonds represent persistently higher levels of head injuries and conduct problem symptoms.

2.4.3 Association between Distinct Linked Developmental Pathways and potential Risk Factors

Multinomial logistic regression showed that higher scores on all three CRIs were generally associated with a greater likelihood of a child belonging to a clinically relevant developmental pathway compared to the stable low-level conduct problem symptoms and head injuries pathway (see Table 3). The only exception being the mother-level, which showed no evidence of an association with the adolescent-onset pathway (class 3).

Compared to the stable low-level conduct problem symptoms and head injuries pathway, ADHD had a strong association with all the clinically relevant classes (see Table 3) whilst epilepsy was only significantly associated with the adolescent-onset class (see Table 3).

Table 3

Multinomial Logistic Regression of the Associations With Class Membership

	Childhood-only high conduct problem symptoms and head injuries (class 2)[a]	High adolescent conduct problem symptoms and childhood onward head injuries (class 3)[a]	Persistent high conduct problem symptoms and childhood-limited head injuries (class 4)[a]
Covariates	*OR* [95% CI]	*OR* [95% CI]	*OR* [95% CI]
Child CRI	**1.28* [1.10–1.49]**	**1.20* [1.01–1.43]**	**1.58* [1.05–2.40]**
Mother CRI	**1.51** [1.27–1.78]**	1.31 [0.99–1.74]	**2.21* [1.40–3.49]**
Household CRI	**1.55** [1.37–1.76]**	**1.41** [1.18–1.70]**	**1.53* [1.12–2.08]**
ADHD	**10.43** [5.94–18.31]**	**5.06* [2.00–12.81]**	**122** [53.14–280.07]**
Epilepsy	1.44 [0.90–2.31]	**2.35** [1.51–3.65]**	1.42 [0.60–3.38]

Note. OR = odds ratio; CRI = cumulative risk index.

[a] Versus stable low-level conduct problem symptoms and head injuries (class 1)

* $p<.05$

** $p<.001$

2.4.4 Association between Distinct Linked Developmental Pathways and Maternal Negative Parenting Styles

Post-hoc multinomial logistic regression revealed that both greater use of maternal withdrawal tactics and harsh parenting at age 5 was significantly associated with a child's membership to all three clinically relevant developmental pathways compared to the stable low-level conduct problem symptoms and head injuries pathway. Maternal withdrawal tactics and harsh parenting were most strongly associated with the persistent pathway (*OR* = 1.33, 95% CI [1.14, 1.54]; *OR* = 1.38, 95% CI [1.22, 1.56], respectively) followed by the child-limited pathway (*OR* = 1.28, 95% CI [1.20, 1.35]; *OR* = 1.26, 95% CI [1.19, 1.34], respectively) and most weakly associated with the adolescent-onset pathway (*OR* = 1.09, 95% CI [1.01, 1.17]; *OR* = 1.16, 95% CI [1.09, 1.24], respectively).

2.5 Discussion

This study identified four distinct developmental pathways linking conduct problem symptoms and head injuries between early childhood and adolescence (between 3–17 years). As expected, the majority of the sample (75%) displayed low levels of conduct problem symptoms and a low likelihood for head injuries from 3–17 years (class 1). However, three clinically relevant pathways were identified. Seventeen percent displayed clinically relevant levels of conduct problem symptoms and an elevated risk for head injuries in childhood, but both declined after childhood (child-only; class 2). A further 6% developed clinically relevant levels of conduct problem symptoms in adolescence and showed an elevated risk of head injuries from ages 11–14 (adolescent-onset; class 3). The final 2% displayed consistently high levels of conduct problem symptoms across development and displayed the highest rates of head injury with a particular sharp increase during ages 7–11 (persistent; class 4). The three developmental pathways show patterns of clinically relevant conduct problem symptoms that are consistent with the DSM-5's conduct disorder classifications (American Psychiatric Association, 2022) and conduct disorder pathways previously identified within the MCS dataset (Gutman et al., 2019). These results, however, provide new insight into how such developmental pathways of conduct problem symptoms link with pathways of head injuries. It teases apart the previously identified bidirectional association between conduct problems and head injuries (Carr, Hall, Eisenbarth, et al., 2024) and suggests that this bidirectional association may not be relevant to all individuals but to specific subsets of individuals at different periods from early childhood to adolescence.

Though three clinically relevant pathways were identified, emphasis should be placed on the linked pathways of classes 3 (adolescent-onset) and 4 (persistent). These are the only two classes to display increasing levels of conduct problem symptoms in adolescence and increasing levels of head injuries during development. These characteristics are associated with an increased risk for

adolescent delinquency (Kennedy, Heron, et al., 2017; Mongilio, 2022) and greater odds of problematic behaviours in adulthood (Bevilacqua et al., 2018). Taken together, these features, thus, suggest the need for prevention work to stop individuals from entering these clinically relevant developmental pathways.

Such interventions may target risk factors associated with membership of these pathways. ADHD was highly associated with all clinically relevant pathways and most strongly with the class displaying persistent conduct problem symptoms (class 4). This finding is unsurprising due to ADHD's strong association with conduct problems (particularly persistent or child-onset conduct problems; Fairchild et al., 2019; Silberg et al., 2015) and head injuries (Ramos Olazagasti et al., 2013), as well as interactions between ADHD and harsh parenting (Golm & Brandt, 2024). The strength of the association provides further support for the relevance of interventions to manage conduct disorder with comorbid ADHD, e.g., psychosocial intervention for the conduct disorder symptoms and stimulant medication for the ADHD symptoms (Fairchild et al., 2019). By doing so, such interventions may also inadvertently reduce the risk of sustaining a head injury during development and the associated implications of this.

It must be noted that whilst ADHD was strongly associated with group membership it is important to acknowledge potential sex differences. That is, males have a stronger association with both conduct disorder and co-morbid ADHD (Fairchild et al., 2019; Konrad et al., 2022). These sex differences could play a role in the associations that ADHD shares with these linked developmental pathways and the development of the pathways themselves. Whilst for the purpose of this research, we aimed to provide a novel understanding of how head injuries and conduct problem symptoms co-occur across development irrespective of sex (and other potential confounders), future research may wish to look at how the identified linked developmental pathways differ between males and females and how sex may influence potential risk factors associated with pathway membership (particularly with reference to the role of ADHD). This could provide important findings that will further aid the development of such interventions as those proposed above and their appropriate target population.

Our findings further suggest that early (by age 3) accumulation of risk at the child, mother, and household-level (Carr, Hall, Eisenbarth, et al., 2024) are associated with membership to the clinically relevant classes, again replicating that of previous literature (Gutman et al., 2019). For the persistent pathway (class 4), the strongest association of cumulative risk was at the mother-level. This supports previous literature, which identifies mother-level risk as strongly associated with a risk for both persistent conduct problems (Gutman et al., 2019) and head injuries (McKinlay et al., 2010). Thus, preventions that might reduce the likelihood of individuals entering this development pathway might aim to primarily reduce undesired maternal unemployment, (potential future) mothers leaving high school with no qualifications, pregnancies before 18 years, low mother attachment with child, and

high maternal psychological distress. Future research might determine which of these risk factors are particularly important, in order to develop targeted interventions, such as early support for mother-child attachment for mothers experiencing mental health difficulties.

Whilst the mother-level was the strongest accumulated risk for the persistent pathway, there was no evidence for an association between the mother-level and the adolescent-onset pathway (class 3). This is not in line with previously identified association between mother-level factors (e.g., maternal depression) and an increased risk of head injury by adolescence (McKinlay et al., 2010). However, only early mother-level risk factors (by age 3) were taken into account in our study, and it is possible that mother-level risk later in development is more relevant to this adolescent-onset pathway that links head injury and conduct problem symptoms. The adolescent-onset pathway was instead most strongly associated with household risk factors, i.e., low household income, single parent household, household overcrowding, and low-quality home learning environment. This continues to support previous literature, which has shown this pathway of conduct problems to be most strongly associated with SES (Gutman et al., 2019). This also provides further support for the hypothesis that there are potential latency effects from child and household accumulative risk to later emerging conduct problem symptoms (Gutman et al., 2019; Schoon et al., 2003) and its associated higher levels of late childhood head injuries. Thus, preventative measures might aim to primarily reduce household risk factors, or provide effective interventions that are appropriate for families from a low SES background (Leijten et al., 2017). It could further provide interventions to improve the early home learning environment, such as improving the interaction between pre-school staff and parents particular those with a low SES (Kuger et al., 2019).

Our findings identify a further opportunity for preventions to reduce the likelihood of a child entering these developmental pathways of conduct problems and head injuries via provision of greater support to mothers to prevent the emergence of negative parenting styles with children through to age 5. Mother's negative parenting styles were associated with all clinically relevant pathways. It must be noted that whilst the mother-level cumulative risk was not associated with the adolescent-onset pathway, mother's negative parenting styles were. Though this effect was small for this pathway, adolescent head injuries have been previously associated with negative parenting styles (McKinlay et al., 2010). Efforts to prevent the emergence of maternal withdrawal tactics and harsh parenting (Speyer et al., 2022) should therefore be addressed to reduce both conduct problem symptoms and head injuries in all clinically relevant pathways. Such interventions could include parent feedback and coaching (McConnell et al., 2020) and/or parental wellbeing courses (Tapp et al., 2018).

2.5.1 Strengths and Limitations

A key strength of this study is that it is the first to reveal multiple distinct pathways linking conduct problems and head injuries from 3–17 years of age. This will have important implications for when interventions should be administered and to whom. This study benefits from its analysis of data belonging to a large population representative national cohort study, which aids statistical power and generalizability.

The study, however, also has limitations. Note that we refer to "clinically relevant" levels of conduct problems symptoms. The SDQ is not a diagnostic measure of conduct problems. Therefore, the described developmental pathways can only infer clinically relevant symptoms. Such use of parent-report measures may also lead to social desirability bias in the reporting of both key variables (Bornstein et al., 2015). Future research may use health and clinical records, for example, to remove such potential bias from the results. Further, the measure of harsh parenting used in the MCS omits the severe harsh parenting items included in the original scale. This may explain why only a small effect is evident. Further research may wish to investigate this association further outside of the MCS where the more severe harsh parenting items can be explored. Finally, we encourage follow-up of this epidemiological research with smaller-scale neurological investigation to uncover possible neurological mechanisms at play between the distinct developmental pathways found in this paper.

2.5.2 Conclusions

This study identifies four distinct developmental pathways that link conduct problems and head injuries between 3–17 years of age. Two of these pathways showed a tendency towards clinically relevant levels of conduct problem symptoms and increasing levels of head injuries at some point during this period. Children were more likely to exhibit one of these pathways in the presence of negative parenting styles through to age 5 years or alongside diagnosed ADHD. Cumulative risk at various ecological levels had unique associations with these pathways and should also be utilised in early interventions to prevent membership to clinically relevant pathways of linked head injuries and conduct problems. Such interventions are necessary to prevent subsequent outcomes associated with these pathways including delinquency and criminality.

Chapter 3 Adolescent Delinquency Following Co-occurring Childhood Head Injuries and Conduct Problem Symptoms: Findings from a UK Longitudinal Birth Cohort

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3.1 Abstract

Childhood conduct problems and head injuries share a bidirectional association but how this affects the risk of adolescent delinquency is unknown. Due to their similar underlying mechanisms (i.e., increased impulsivity) this study aims to identify whether their co-occurrence increases the risk of adolescent delinquency. Data was obtained from 11,272 children at age 14 and 10,244 at age 17 enrolled in the UK Millennium Cohort Study. Conduct problem symptoms (via the Strengths and Difficulties Questionnaire) and head injuries were parent-reported from ages 3–14. Delinquency was self-reported at ages 14 and 17 including substance use, criminality, and antisocial behaviour. Incident rate ratios (IRR) were estimated for delinquency at ages 14 and 17 by childhood conduct problem and head injury status. Co-occurring head injuries and high conduct problem symptoms presented the greatest risk for overall delinquency and substance use at age 14 compared to those with the presence of one or neither (IRRs from 1.20–1.60). At age 17, conduct problems (with or without co-occurring head injuries) presented the greatest risk for overall delinquency, substance use, and antisocial behaviour. There was no evidence for an increased risk of delinquency at ages 14 or 17 following a head injury only. Whilst these findings suggest childhood head injuries alone do not increase the risk of adolescent delinquency, when co-occurring alongside high conduct problem symptoms there is a heightened earlier risk. These results provide further insight into adolescent delinquency and the outcomes of co-occurring childhood head injury and conduct problem symptoms.

Keywords: adolescence, conduct problems, delinquency, head injury

3.2 Introduction

The adolescent stage of development is a crucial milestone for the maturation of social, emotional, and cognitive abilities. Adolescent delinquency can disrupt this critical phase of development leaving an individual vulnerable to a plethora of negative outcomes. Adolescent delinquency can include criminality, substance use, and antisocial behaviour. These behaviours often share similar underlying mechanisms (i.e., impulsivity; Defoe et al., 2022; Loeber, 1990) and as such, predict similar negative outcomes including a disruption to educational attainment (Kim, 2020), poor physical (Kim et al., 2020) and mental health (Moffitt et al., 2002), and criminality persisting into adulthood (Moffitt, 1993). Due to the cascade of negative outcomes associated with adolescent delinquency, identifying associated risk factors is crucial.

Of the many risk factors for adolescent delinquency, two are postulated to have a complex combined effect: childhood conduct problems and head injuries. Childhood conduct problems refer to violations of age-appropriate societal norms (Girard et al., 2019) and are associated with delinquent behaviour in adolescence (Hammerton et al., 2019; Hopfer et al., 2013; Picoito et al., 2021) and adulthood (Bevilacqua et al., 2018; Erskine et al., 2016). Furthermore, head injuries may similarly be associated with later delinquent behaviour (Kennedy, Cohen, et al., 2017; Kennedy, Heron, et al., 2017; Mongilio, 2022; Schwartz et al., 2017). Here, we refer to general head injuries which may result in seeking medical attention but do not result in ongoing impairment (i.e., a traumatic brain injury). However, evidence investigating the role of head injury on delinquency is limited and must be interpreted with caution. Notably, Mongilio and colleagues did not control for the potential influence disorders such as conduct disorder (McCormick et al., 2021) could have on this association (Mongilio, 2022) whilst Schwartz and colleagues suggested that the association between head injury and delinquency may be mediated by a relevant symptom of conduct disorder: impulse control (Schwartz et al., 2017). Thus, whilst the literature alludes to an association between head injury and later delinquency, further evidence is required.

Head injuries and conduct problems may also share a bidirectional relationship that poses an additional risk for adolescent delinquency (Carr, Hall, Eisenbarth, et al., 2024). That is, childhood conduct problems are associated with an increased risk of head injuries and vice versa (Carr, Hall, Eisenbarth, et al., 2024). We hypothesize that when both conditions co-occur some of their underlying mechanisms (i.e., increased impulsivity; Fairchild et al., 2019; Fullerton et al., 2019) may create an additive effect, which will subsequently lead to an even greater risk for delinquency. However, no study has yet investigated the potential for a heightened risk of delinquent behaviour as a consequence of head injuries and conduct disorder occurring

separately as well as in addition to one another. In response, this study analysed data from a large UK population-based birth cohort study to identify if the co-occurrence of childhood high levels of conduct problem symptoms and sustained head injuries posed a greater risk factor for adolescent delinquent behaviour at ages 14 and 17.

3.3 Method

3.3.1 Study design and participants

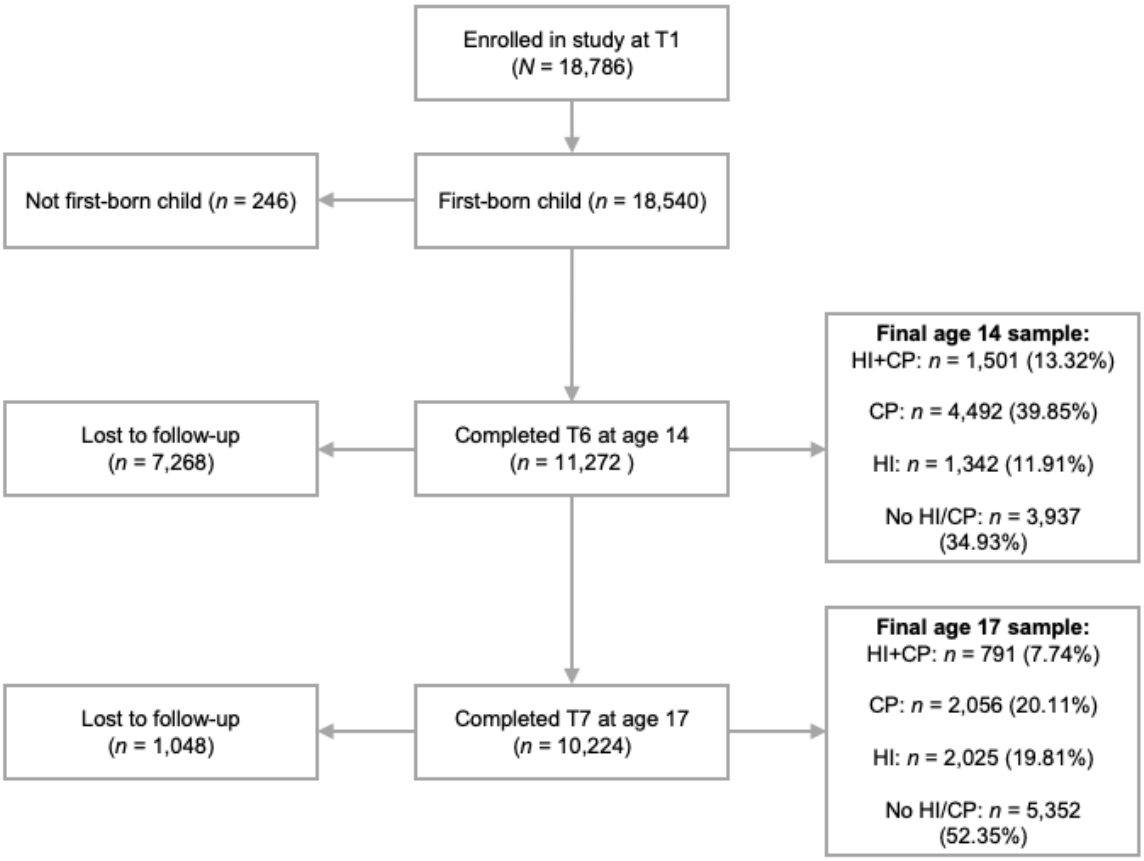
Participants were enrolled in the UK Millennium Cohort Study, a longitudinal birth cohort study following 18,786 individuals born between 2000 and 2002. They were measured at seven timepoints from timepoint 1 (T1) at age 9 months to timepoint 7 (T7) at age 17 (Fitzsimons et al., 2020). All data is freely accessible to researchers via the UK Data Archive (beta.ukdataservice.ac.uk/datacatalogue/series/series?id=2000031).

Two analytic samples were defined as participants enrolled at T1 and still enrolled at either age 14 or 17. Figure 2 presents an overview of sample selection. Only first-born children were included to allow independence of observation (Grawitch & Munz, 2004) and due to different levels of aggression and head injury risk between siblings (Honda et al., 2020).

Participants gave written consent for their data to be shared for secondary analysis. Ethical approval for this analysis was given by the University of Southampton Ethics Committee (ID = 62100.A1). The current study follows the appropriate Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines

Figure 2

A Flow Chart of Sample Acquisition



Note. This figure shows the exclusions made to reach the analytical samples and the breakdown of their groups. HI+CP refers to the group with a history of both high conduct problem symptoms and reported head injuries. CP refers to the group with a history of high conduct problem symptoms but no reported head injuries. HI refers to the group with a history of reported head injury but no high levels of conduct problem symptoms. No HI/CP refers to the group without a history of either high conduct problems symptoms or reported head injuries. HI+CP = combined head injury and conduct problems; CP = conduct problems only; HI = history of head injury only; No HI/CP = history of neither.

3.3.2 Measures

3.3.2.1 Conduct Problem (CP) Symptoms

Conduct problem symptoms were measured using the Strength and Difficulties Questionnaire (SDQ) conduct problem subscale (Goodman, 2001), a validated measure of conduct problems (Becker et al., 2004; Goodman et al., 2000) shown to be invariant across timepoints (Sosu & Schmidt, 2017). This subscale includes five items measured from 0 (*not true*) to 2 (*certainly true*), which are summed to produce a conduct problem symptom score (maximum score of 10). High conduct problem symptoms were determined by a score greater than 3 (see https://www.sdqinfo.org/).

3.3.2.2 Head Injuries (HI)

Head injuries were parent-reported during parent interviews. At each timepoint parents were asked if, since the last wave, their child had encountered an accident or injury which resulted in seeking a health professional. Those injuries coded as a bang to the head with or without a loss of consciousness were grouped to create a binary head injury variable (0 [*absent*], 1 [*present*]) mirroring the classification used within the relevant literature (Mongilio, 2022).

3.3.2.3 Group Classification

Four groups were created in each of the two analytic samples (estimating delinquency at ages 14 and 17) based on participant's history of conduct problem symptoms and/or reported head injury.

The head injury and high conduct problem symptom (HI+CP) group had a history of high conduct problem symptoms (SDQ score > 3) and at least one reported head injury. The conduct problem (CP) group reported high conduct problem symptoms (SDQ score > 3) but not head injuries. The head injury (HI) group reported at least one head injury but not high conduct problem symptoms. The fourth group reported no history of head injuries or high conduct problem symptoms (no HI/CP).

For age 14 delinquency, groups were determined by head injury and conduct problem data measured from T2 (age 3) to T5 (age 11). For age 17 delinquency, they were determined by head injury data measured from T2–T6 (age 14) and by conduct problem data measured from T5–T6. For further details on these groups and details of supplementary group classifications see Appendix G. In short, two separate samples were used in order to investigate both age 14 and age 17 delinquency. Due to the temporal ordering of variables, if a single sample was used then

conduct problems could not be measured past age 11, which was important for the investigation of age 17 delinquency.

Figure 2 displays the breakdown of groups for the age 14 and 17 analytical samples.

3.3.2.4 Adolescent Delinquency

Adolescent delinquency was measured at ages 14 and 17 from nine items across substance use, criminality, and antisocial behaviour (see Appendix H). An overall delinquency score at each age summed the nine delinquent behaviours (range 0–9) as is often created in the literature (Kim & Son, 2023; Mongilio, 2022). A higher score indicated greater cumulative delinquency. Delinquency was further measured at each sub-level by summing relevant items, all of which had been recoded into binary (1 [*yes*], 0 [*no*]) variables.

Substance use. Participants self-reported smoking, binge drinking (>= five alcoholic drinks in one sitting), or using cannabis in the last 12 months. Substance use ranged from 0–3.

Criminality. Participants self-reported ever being stopped or given a caution or formal warning by the police. At age 17, new variables were created to account for criminality reported since the last wave (age 14). Criminality scores ranged from 0–2.

Antisocial behaviour. Participants self-reported spray painting, damaging property, shoplifting, or stealing from someone else in the last 12 months. Antisocial behaviour scores ranged from 0–4.

3.3.2.5 Covariates

Study covariates included prenatal and SES risk factors all parent-reported at T1. We further included child sex, negative parenting styles, and ADHD (see Appendix I). These covariates are commonly controlled for in delinquency research (Picoito et al., 2021; Retz et al., 2021), are associated with conduct problems (Trentacosta et al., 2008; Van Adrichem et al., 2020), or sustaining a head injury (McKinlay et al., 2010).

3.3.3 Statistical Analysis

All analyses were conducted in Stata, version 16.1 (StataCorp, 2019). Missing data were present across various predictor and outcomes variables and was accounted for using multiple imputation with chained equations (Stata's MICE command), using 30 imputations. MCS survey weights at age 14 (T6) and 17 (T7) respectively were included in the imputations and in all subsequent analyses to account for attrition, nonresponse bias, and stratification (more

information on MCS weights can be found here: https://cls.ucl.ac.uk/wp-content/uploads/2017/07/User-Guide-to-Analysing-MCS-Data-using-Stata.pdf).

First, we tested the associations between childhood conduct problem symptoms and head injury status with age 14 and 17 delinquency (overall, substance use, criminality, and antisocial behaviour) using negative binomial regression models. All regression models included the aforementioned covariates. Supplementary regression models included conduct problem symptoms irrespective of head injury status and vice versa including head injuries which incurred a loss of consciousness only compared to those without a history of head injury.

3.4 Results

Of 18,786 original participants, 11,272 were included in the age 14 analysis (5,631 [50%] female and 9,326 [82.7%] White) and 10,224 in the age 17 analysis (5,107 [50%] female and 8,349 [81.7%] White). Characteristics of the study populations and comparisons to the excluded samples are shown in Table 4. Though there were significant differences between some exposure and outcome variables these were weak ($d < .23$ or $V < .11$).

Figure 3 displays the levels of (a) overall delinquency, (b) substance use, (c) criminality, and (d) antisocial behaviour reported by each group. Levels of delinquency generally increased from ages 14 to 17 with the exception of criminality. At ages 14 and 17, mean levels of conduct problem symptoms between the HI+CP and CP groups ($t(4,399) = -1.55$, $p = .12$; $t(1,438) = -1.09$, $p = .279$, respectively) and mean rates of head injury between the HI+CP and HI groups ($t(2,842) = -0.06$, $p = .52$; $t(2,815) = -0.26$, $p = .80$, respectively) did not significantly differ.

Table 4

Sample Characteristics and Differences Between the Analytical and Excluded Sample

	Age 14 analytical sample		Age 14 excluded sample					Age 17 analytical sample		Age 17 excluded sample				
Characteristics	*n(%)*	*M(SD)*	*n(%)*	*M(SD)*	χ^2 (*df*)	*p*	V	*n(%)*	*M(SD)*	*n(%)*	*M(SD)*	χ^2 (*df*)	*p*	V
Sex					17.45 (1)	<.001	.03					13.79 (1)	<.001	.03
Male	5,641 (50)	NA	3,994 (53.2)	NA	NA	NA	NA	5,117 (49.8)	NA	4,518 (52.8)	NA	NA	NA	NA
Female	5,631 (50)	NA	3,520 (46.8)	NA	NA	NA	NA	5,107 (50.2)	NA	4,044 (47.2)	NA	NA	NA	NA
Ethnicity					43.27 (5)	<.001	.05					45.98 (5)	<.001	.05
White	9,326 (82.7)	NA	6,165 (82)	NA	NA	NA	NA	8,349 (81.7)	NA	7,142 (83.4)	NA	NA	NA	NA
Mixed	307 (2.7)	NA	255 (3.4)	NA	NA	NA	NA	297 (3.0)	NA	265 (3.1)	NA	NA	NA	NA
Black	353 (3.1)	NA	325 (4.3)	NA	NA	NA	NA	348 (3.1)	NA	330 (3.9)	NA	NA	NA	NA
Indian	292 (2.6)	NA	178 (2.4)	NA	NA	NA	NA	282 (2.6)	NA	188 (2.2)	NA	NA	NA	NA

Pakistani	836 (7.4)	NA	435 (5.8)	NA	NA	NA	NA	796 (7)	NA	475 (5.5)	NA	NA	NA	NA
Other	158 (1.4)	NA	108 (1.4)	NA	NA	NA	NA	152 (1.4)	NA	114 (1.3)	NA	NA	NA	NA
Conduct problems														
Age 3	9,866 (87.5)	2.75 (2.03)	4,492 (59.8)	2.95 (2.13)	5.25 (14,356)[a]	<.001	.10[b]	8,926 (87.3)	2.72 (2.02)	5,432 (63.4)	2.96 (2.12)	6.70 (14,356)[a]	<.001	.12[b]
Age 5	10,324 (91.6)	1.45 (1.47)	4,069 (54.2)	1.64 (1.60)	6.64 (14,391)[a]	<.001	.12[b]	9,354 (91.5)	1.44 (1.47)	5,039 (58.9)	1.63 (1.58)	7.13 (14,391)[a]	<.001	.13[b]
Age 7	10,115 (89.7)	1.33 (1.51)	3,035 (40.4)	1.58 (1.66)	7.89 (13,148)[a]	<.001	.16[b]	9,167 (89.7)	1.31 (1.49)	3,983 (46.5)	1.56 (1.66)	8.70 (13,148)[a]	<.001	.17[b]
Age 11	10,366 (92.0)	1.34 (1.54)	2,035 (27.1)	1.61 (1.70)	7.26 (12,399)[a]	<.001	.18[b]	9,341 (91.4)	1.30 (1.51)	3,060 (35.7)	1.63 (1.72)	10.30 (12,399)[a]	<.001	.22[b]
Age 14	NA	NA	NA	NA	NA	NA	NA	9,113 (89.1)	1.35 (1.59)	1,944 (22.7)	1.63 (1.74)	6.84 (11,055)[a]	<.001	.17[b]
Head injuries														
9 months-3 years	1,289 (11.4)	NA	596 (7.9)	NA	60.90 (1)	<.001	.06	929 (9.1)	NA	576 (6.7)	NA	35.19 (1)	<.001	.04

3-5 years	952 (8.4)	NA	452 (6.0)	NA	38.23 (1)	<.001	.05	701 (6.9)	NA	422 (4.9)	NA	30.81 (1)	<.001	.04
5-7 years	720 (6.4)	NA	243 (3.2)	NA	91.85 (1)	<.001	.07	515 (5.0)	NA	264 (3.1)	NA	44.76 (1)	<.001	.05
7-11 years	616 (5.5)	NA	160 (2.1)	NA	126.32 (1)	<.001	.08	444 (4.3)	NA	176 (2.1)	NA	76.37 (1)	<.001	.06
11-14 years	NA	NA	NA	NA	NA	NA	NA	359 (3.5)	NA	56 (0.1)	NA	176.10 (1)	<.001	.10
Delinquency [c]														
Binge drinking	940 (8.3)	NA	9 (0.1)	NA	.25 (1)	.62	.02	4,648 (48.8)	NA	166 (1.9)	NA	.19 (1)	.67	.01
Smoking	387 (3.4)	NA	4 (0.1)	NA	.48 (1)	.49	.01	1,863 (18.2)	NA	63 (0.7)	NA	.01 (1)	.93	.001
Cannabis use	470 (4.2)	NA	3 (<.01)	NA	2.25 (1)	.13	.01	2,356 (23.0)	NA	85 (1.0)	NA	.31 (1)	.58	.01
Stopped by police	1,479 (13.1)	NA	18 (0.2)	NA	.63 (1)	.43	.01	1,124 (11.0)	NA	10 (0.1)	NA	1.71 (1)	.19	.02
Cautioned	790 (7.0)	NA	10 (0.1)	NA	.20 (1)	.66	.004	108 (1.1)	NA	3 (<.01)	NA	10.85 (1)	<.001	.03
Spray paint	284 (2.5)	NA	5 (.1)	NA	.19 (1)	.66	.004	276 (2.7)	NA	11 (0.1)	NA	.32 (1)	.57	.01

Property damage	333 (3.0)	NA	5 (0.1)	NA	.01 (1)	.94	.001	302 (3.0)	NA	7 (0.1)	NA	1.02 (1)	.31	.01
Shoplifting	357 (3.2)	NA	3 (<.01)	NA	.94 (1)	.33	.01	536 (5.2)	NA	18 (0.2)	NA	<.001 (1)	.99	<.001
Stealing	121 (1.1)	NA	3 (<.01)	NA	.87 (1)	.35	.01	149 (1.5)	NA	6 (0.1)	NA	0.19 (1)	.67	.004

Note. If (*n*) is less than the n included, this refers to missing data within the variable.

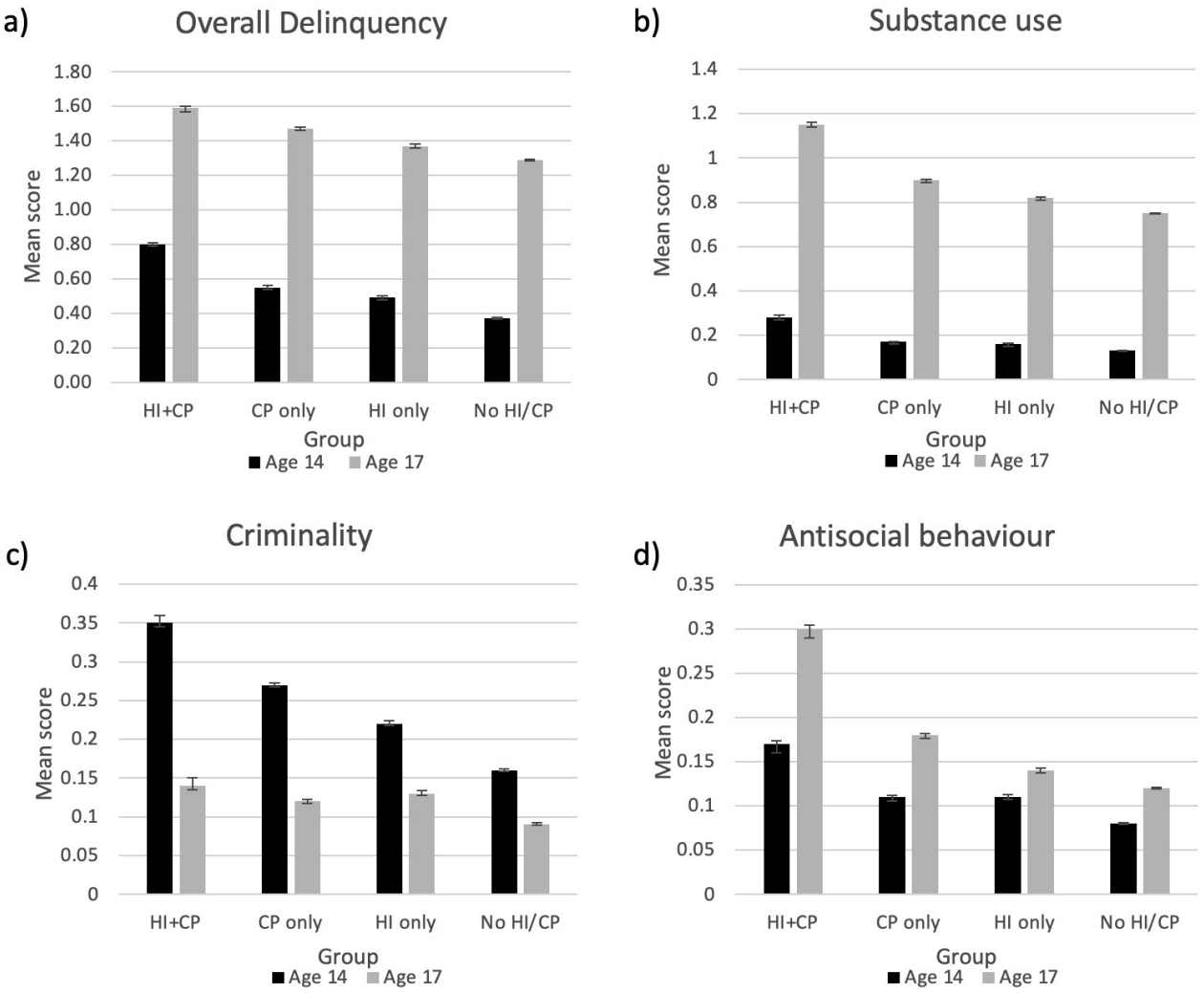
[a] Independent samples t-test

[b] Cohen's *d*

[c] For age 14 and 17 analytical samples, delinquency as measured at age 14 and 17, respectively.

Figure 3

The Mean Delinquency Scores of Groups Defined by Childhood Conduct Problem Symptom and Head Injury Status



Note. This figure shows the mean rates of a) overall delinquency, b) substance use, c) criminality, and d) antisocial behaviour at ages 14 (black) and 17 (grey). These scores are displayed for 1) those with no history of high conduct problem symptoms or head injuries (HI+CP), 2) those with a history only of high conduct problem symptoms and not head injury (CP only), 3) those with a history of sustaining a head injury but no high levels of conduct problem symptoms (HI only), and 4) those without a history of both high conduct problems and sustaining a head injury (no HI/CP). This figure shows mean scores typically increasing from ages 14 to 17 with the exception of criminality.

3.4.1 Age 14 Delinquency

At age 14, 2,489 (22.08%) participants reported at least one delinquent behaviour. A summary of the regression models is shown in Table 5. The HI+CP and CP groups were associated with a significantly greater risk of reporting overall delinquency, substance use, criminality, and antisocial behaviour compared to the no HI/CP group. The HI+CP group was also associated with a significantly greater risk of overall delinquency and substance use when compared to the CP and HI groups.

We found no evidence of an association between the HI group and any delinquent behaviour (Table 5). However, post-hoc analyses identified a significant association between a history of head injuries (irrespective of conduct problem symptoms) with overall delinquency and substance use compared to a group with no history of head injury (see Appendix J). This association remained significant but became stronger when a loss of consciousness was compared to those without a history of head injury (see Appendix J). Further associations were identified between conduct problems (irrespective of head injury) with overall delinquency, substance use, and crime compared to a group without a history of conduct problems (see Appendix J).

3.4.2 Age 17 Delinquency

At age 17, 5,461 (53.41%) participants reported at least one delinquent behaviour. A complete summary of the regression models is shown in Table 6. Compared to the no HI/CP group, the HI+CP and CP groups showed an increased rate of overall delinquency whilst the HI+CP group also showed further increased rates of substance use. Both the HI+CP and CP groups also showed significantly increased rates of antisocial behaviour compared to the no HI/CP and HI groups. There was no evidence for increased rates of criminality in any of the groups nor any significant differences between the HI+CP and CP groups.

Post-hoc analyses found further evidence for a significant association between a history of conduct problems (irrespective of head injury status) with overall delinquency and substance use compared to those without a history of conduct problem symptoms (see Appendix K). There was no evidence for an increased rate of delinquency in those with a head injury (irrespective of conduct problem symptom status) even when considering those head injuries with a loss of consciousness only (see Appendix K).

Table 5

Adolescent Cumulative Delinquency at Age 14 Predicted by Childhood Conduct Problems and Head Injury during ages 3 to 11

	Overall delinquency	Substance use	Crime	Antisocial behaviour
	IRR [95% CI]	*IRR* [95% CI]	*IRR* [95% CI]	*IRR* [95% CI]
HI+CP vs no HI/CP	**1.60** [1.34–1.91]**	**1.80** [1.40–2.31]**	**1.56** [1.29–1.90]**	**1.41* [1.04–1.91]**
HI+CP vs CP	**1.20* [1.01–1.43]**	**1.38* [1.08–1.77]**	1.12 [0.94–1.33]	1.13 [0.85–1.51]
HI+CP vs HI	**1.39* [1.13–1.72]**	**1.48* [1.11–1.98]**	**1.52** [1.21–1.92]**	1.11 [0.78–1.59]
CP vs no HI/CP	**1.33* [1.13 – 1.56]**	**1.30* [1.05–1.62]**	**1.40** [1.17–1.25]**	1.24 [0.94–1.64]
CP vs HI	1.16 [0.96–1.39]	1.07 [0.83–1.38]	**1.36* [1.12–1.66]**	0.98 [0.71–1.36]
HI vs no HI/CP	1.15 [0.96–1.37]	1.21 [0.97–1.52]	1.03 [0.84–1.25]	1.27 [0.95–1.69]
Sex	**1.22** [1.09–1.36]**	**0.78* [0.67–0.90]**	**1.54** [1.37–1.74]**	**1.47** [1.21–1.78]**
ADHD	0.95 [0.69–1.30]	0.74 [0.48–1.16]	0.96 [0.70–1.32]	1.20 [0.76–1.92]
Low birth weight	0.76 [0.59–0.99]	**0.58* [0.38–0.86]**	0.98 [0.73–1.32]	0.74 [0.47–1.17]
Premature birth	0.98 [0.74–1.28]	1.09 [0.72–1.65]	0.90 [0.65–1.24]	0.81 [0.51–1.27]
Smoking during pregnancy	**1.84** [1.62–2.08]**	**2.15** [1.81–2.57]**	**1.79** [1.57–2.03]**	**1.44* [1.16–1.78]**
Alcohol during pregnancy	**1.14* [1.02–1.29]**	**1.35** [1.16–1.58]**	1.01 [0.89–1.14]	1.08 [0.88–1.33]

Teenage pregnancy	1.34 [0.97–1.85]	1.37 [0.87–2.14]	1.33 [0.99–1.77]	1.07 [0.63–1.80]
Low parental education	0.92 [0.77–1.09]	0.87 [0.68–1.12]	0.95 [0.80–1.13]	0.89 [0.65–1.22]
Low parent occupation	**1.18* [1.03–1.36]**	1.02 [0.84–1.24]	**1.32** [1.13–1.54]**	1.20 [0.96–1.51]
Low household income	1.14 [0.99–1.32]	1.07 [0.88–1.30]	**1.23* [1.05–1.43]**	1.08 [0.83–1.39]
Single parent household	0.87 [0.74–1.02]	0.89 [0.70–1.13]	0.91 [0.77–1.07]	0.80 [0.61–1.06]
Harsh parenting	1.02 [0.99–1.06]	1.04 [1.00–1.09]	1.00 [0.97–1.03]	1.05 [1.00–1.10]
Parental withdrawal tactics	1.00 [0.98–1.03]	0.99 [0.95–1.02]	1.01 [0.99–1.04]	0.99 [0.95–1.03]

Note. X vs Y, Y is the reference group. IRR = incidence rate ratio; HI = head injury; CP = conduct problem symptoms.

*p<.05

**p<.001

Table 6

Adolescent Cumulative Delinquency at Age 17 Predicted by Childhood Conduct Problems at ages 11 and 14 and Head Injury during ages 3 to 14

	Overall delinquency	Substance use	Criminality	Antisocial behaviour
	IRR [95% CI]	*IRR* [95% CI]	*IRR* [95% CI]	*IRR* [95% CI]
HI+CP vs no HI/CP	**1.33* [1.08–1.65]**	**1.32* [1.07–1.64]**	1.11 [0.63–1.93]	**1.55* [1.01–2.36]**
HI+CP vs CP	1.08 [0.83–1.41]	1.14 [0.87–1.48]	0.93 [0.46–1.86]	0.92 [0.52–1.62]
HI+CP vs HI	1.27 [1.00–1.60]	**1.27* [1.01–1.60]**	0.87 [0.49–1.53]	**1.58* [1.00–2.47]**
CP vs no HI/CP	**1.23* [1.02–1.49]**	1.16 [0.97–1.40]	1.19 [0.68–2.07]	**1.69* [1.02–2.79]**
CP vs HI	1.17 [0.96–1.43]	1.12 [0.92–1.35]	0.93 [0.56–1.55]	**1.72* [1.07–2.77]**
HI vs no HI/CP	1.05 [0.95–1.17]	1.04 [0.94–1.15]	1.28 [0.97–1.67]	0.98 [0.76–1.27]
Sex	**1.21** [1.10–1.33]**	**1.11* [1.01–1.21]**	**1.37* [1.04–1.81]**	**2.01** [1.54–2.62]**
ADHD	1.08 [0.84–1.40]	1.05 [0.80–1.38]	1.27 [0.65–2.49]	1.11 [0.68–1.81]
Low birth weight	0.89 [0.66–1.21]	0.88 [0.61–1.27]	0.95 [0.57–1.60]	0.92 [0.51–1.66]
Premature birth	1.00 [0.76–1.30]	1.10 [0.81–1.47]	0.62 [0.34–1.14]	0.75 [0.41–1.38]
Smoking during pregnancy	**1.30** [1.15–1.47]**	**1.34** [1.19–1.51]**	1.01 [0.71–1.44]	1.28 [0.91–1.80]
Alcohol during pregnancy	**1.24** [1.14–1.35]**	**1.30** [1.19–1.42]**	0.96 [0.75–1.24]	1.07 [0.85–1.35]
Teenage pregnancy	0.99 [0.69–1.43]	1.16 [0.79–1.71]	0.61 [0.26–1.48]	0.37 [0.14–1.03]
Low parental education	0.82 [0.67–1.02]	**0.80* [0.65–0.99]**	0.97 [0.54–1.77]	0.93 [0.52–1.67]
Low parental occupation	0.89 [0.78–1.01]	**0.86* [0.76–0.98]**	1.06 [0.77–1.45]	0.95 [0.69–1.31]
Low household income	**0.85* [0.73–0.98]**	**0.83* [0.72–0.95]**	1.27 [0.90–1.80]	0.69 [0.46–1.03]
Single parent household	0.96 [0.80–1.14]	1.00 [0.83–1.19]	1.12 [0.70–1.77]	0.70 [0.44–1.10]
Harsh parenting	1.03 [1.00–1.05]	1.02 [0.99–1.05]	**1.09* [1.01–1.19]**	1.02 [0.94–1.11]
Parental withdrawal tactics	1.01 [0.99–1.04]	1.02 [0.99–1.04]	1.00 [0.94–1.07]	1.00 [0.94–1.08]

Note. X vs Y, Y is the reference group. IRR = incidence rate ratio; HI = head injury; CP = conduct problem symptoms

*p<.05

**p<.001

3.5 Discussion

This large, prospective cohort study provides novel evidence for a greater risk of early delinquency following the co-occurrence of childhood head injuries and high conduct problem symptoms compared to a history of one or neither, when controlling for common risk factors. This is the first study to show that this co-occurrence is associated with an earlier increased risk of delinquency by age 14 compared to all other groups.

In line with previous studies (Hammerton et al., 2019; Hopfer et al., 2013; Picoito et al., 2021), childhood conduct problems were associated with an increased risk of earlier delinquency compared to those without the presence of either at age 14, and this was significantly greater when accompanied by co-occurring head injuries. This may be explained by the bidirectional association between childhood conduct problems and head injuries across development (Carr, Hall, Eisenbarth, et al., 2024), which may exacerbate one another's characteristics associated with subsequent delinquency (i.e., increased impulsivity). That is, causal models of conduct disorder argue that environmental factors, such as childhood adversity, can result in altered cognitive and neural functioning (i.e., poor executive functioning or hypervigilance to aggressive cues) and this can increase the risk of conduct problem symptoms (Krol et al., 2004) and engagement in delinquent behaviours (Defoe et al., 2022). Similarly, common cognitive impairments following head injuries relating to emotional, behavioural, and social difficulties (Jones et al., 2021), including impulsivity (Fullerton et al., 2019) may further increase such engagement in delinquent behaviours (Schwartz et al., 2017). When head injuries and high conduct problem symptoms co-occur in middle childhood, these respective impairments may thus add up or interact to result in a significantly greater risk of early adolescent delinquency.

In contrast, our findings show that childhood head injuries without co-occurring high conduct problem symptoms do not predict adolescent delinquency. This suggests that the neural and cognitive impairments associated with childhood head injury may be modestly associated with adolescent delinquency. Only when they present alongside co-occurring high conduct problem symptoms and generate an accumulative or additive effect do the impairments then create a significantly increased risk of adolescent delinquency. This contradicts the findings reported in the literature, which suggest head injury is associated with various forms of delinquency (Kennedy, Cohen, et al., 2017; Kennedy, Heron, et al., 2017; Mongilio, 2022; Schwartz et al., 2017). The disparity may arise from our investigating head injuries whilst excluding co-occurring conduct problem symptoms from ages 3 - 11. Only when we considered a history of head injury regardless of (as was done in the previous literature) or explicitly alongside high conduct problem symptoms, did we identify an association with early overall delinquency and substance use. Although some of the previous studies accounted for factors such as conduct problems at age 3 (Mongilio, 2022),

psychopathy (Schwartz et al., 2017), or early behavioural problems at ages 1–5 (McKinlay et al., 2014), none fully addressed the impact of sustained conduct problems over time. Consequently, prior findings may have been confounded by unaccounted-for, elevated levels of conduct problems across development.

In alignment with previous research (Bevilacqua et al., 2018; Hammerton et al., 2019; Hopfer et al., 2013; Picoito et al., 2021), we found evidence for an increased rate of age 17 delinquency (overall, substance use, and antisocial behaviour) following conduct problem symptoms regardless of head injury history. That is, childhood head injuries did not exacerbate the association above and beyond when later conduct problem symptoms were present without a history of head injury. With rates of reported head injuries decreasing throughout development, we argue that their additive effect alongside co-occurring conduct problem symptoms may dissipate overtime leaving only later conduct problem symptoms (as measured at ages 11 and 14) to drive continued delinquency.

Notably, the findings showed no evidence for an association between conduct problem symptoms and later criminality at age 17. This could be due to a general decrease in criminality across all groups. Such a decrease in criminality may be explained by delayed maturation of the cognitive control systems as described by the dual systems theory (Steinberg et al., 2008). An early mismatch in the maturation of the cognitive control system and the socioemotional system may make adolescents vulnerable to delinquent behaviour. By late adolescence, the systems converge allowing the cognitive control system to effectively provide top-down control to override illegal behaviours.

3.5.1 Strength and limitations

This study used a prospective birth cohort study and therefore the results are generalisable to children born in the UK between 2000–2002. Its longitudinal design is a further strength. By analysing such data, this is the first study to identify the longitudinal nature of the associations between childhood conduct problems and head injuries and subsequent adolescent delinquency.

This study does present with limitations, however. Conduct problems were measured using the SDQ, which is not a diagnostic measure. As such, we note the continued reference to “conduct problem symptoms” throughout. The groups created in this study also homogenise head injury. That is, it includes those with a history of a single or “one-off” head injury as well as those with multiple head injuries. Further analysis on larger datasets that can differentiate between the number of head injuries is required to identify how this may impact on delinquency. In addition, we cannot infer causation because the criminality measures were not temporally limited to after the reporting of conduct problem symptoms and head injury. We endeavoured to minimise this by creating variables at age 17 which accounted only for criminality reported after age 14. However, the age 14 criminality

variables remain problematic with the potential of reverse causation. This must be taken into consideration when interpreting the results.

3.5.2 Conclusions

This study provides novel findings which add to our understanding of how early adolescent delinquency may occur. Importantly, it suggests that sustaining a mild head injury during childhood without exhibiting conduct problem symptoms may not increase one's risk of adolescent delinquency. Nonetheless, if they co-occur alongside higher levels of conduct problem symptoms, there appears to be an increased risk on early adolescent delinquency above and beyond when they occur separately or not at all. These novel findings are important in furthering our understanding of adolescent delinquency whilst highlighting the potential negative implications of childhood co-occurring head injuries and high conduct problem symptoms.

Chapter 4 Neural Reward Processing Among Children With Conduct Disorder and Mild Traumatic Brain Injury in the ABCD Study

4.1 Abstract

Conduct disorder and childhood head injuries frequently co-occur and are linked to a higher risk of later delinquency. While both are known to disrupt reward-related neural circuits, this study investigated whether their combined presence leads to a unique disruption in these pathways, potentially accounting for the increased risk of delinquency. Using neuroimaging data from the baseline (age 9–10) assessment from the Adolescent Brain and Cognitive Development (ABCD) study, four groups were compared: children with conduct disorder (CD, *n* = 588), a mild traumatic brain injury (mTBI, *n* = 1,216), both (mTBI+CD, *n* = 252), and typically developing controls (TD, *n* = 705). Neural activation in eight regions of interest (amygdala, hippocampus, nucleus accumbens, caudal anterior cingulate cortex, rostral anterior cingulate cortex, medial orbitofrontal cortex, thalamus, and insula) during reward anticipation and receipt were assessed during the monetary incentive delay task. After controlling for several covariates including sex, ADHD, and internalizing problems**,** the mTBI+CD group displayed greater left amygdala and hippocampal activation during reward receipt compared to all other groups. While they displayed increased activation in the right hippocampus and thalamus compared to TD controls and right hippocampus compared to the mTBI group, they did not differ from the CD group. No group differences emerged during reward anticipation. Increased left amygdala and hippocampus activation in children with conduct disorder and a history of mild traumatic brain injury may reflect robust encoding of emotionally charged reward experiences, potentially reinforcing memory-guided, reward-seeking behaviours.

4.2 Introduction

Conduct disorder (CD) is a prevalent psychiatric disorder associated with numerous maladaptive outcomes (Fairchild et al., 2019), including adolescent delinquency such as criminality, substance use, and antisocial behaviour (Hammerton et al., 2019). Interestingly, similar adverse outcomes are associated with a history of childhood mild traumatic brain injury (mTBI; Mongilio, 2022). Defined as an impact to the head often accompanied by a loss of consciousness or amnesia lasting up to 30 minutes post-injury, this is distinguishable from moderate to severe TBI, which typically involves prolonged post-injury deficits (i.e., a loss of consciousness for greater than 24 hours) and can result in persistent health problems (Mostert et al., 2022). Given that mTBI accounts for roughly 75% of reported head injuries in the US (National Center for Injury Prevention and Control, 2003), continued research is critical to further understand its consequences and long-term effects.

Importantly, CD and childhood mTBI may not be entirely independent constructs. In fact, the literature suggests that CD may increases the risk of childhood mTBI (Vassallo et al., 2007) and conversely mTBI may increase the risk for CD (Delmonico et al., 2024), indicative of a bidirectional relationship (Carr, Hall, Eisenbarth, et al., 2024). Moreover, their co-occurrence has been associated with an increased risk of later maladaptive outcomes, particularly a greater rate of early adolescent delinquency compared to either condition alone (Carr, Hall, & Brandt, 2024). It is therefore paramount that their co-occurrence is explored further, highlighting potential characteristics that may jointly contribute to such a greater risk for delinquency.

One possible explanation for this elevated risk could relate to disruptions to underlying neural mechanisms of reward processing. The brain's reward system involves intricate dopaminergic pathways including those within the mesolimbic (e.g., amygdala, nucleus accumbens [NAc], and hippocampus) and mesocortical systems (e.g., medial orbitofrontal cortex [OFC] and anterior cingulate cortex [ACC]), which receive dopamine inputs from the ventral tegmental area ((Cao et al., 2019; Dixon & Dweck, 2022; Rosenberg et al., 2024; Silverman et al., 2015). Although the thalamus and insula are not direct components of this mesocorticolimbic circuit, they are critical for facilitating communication within them (e.g., between the NAc and PFC), and modulate dopamine release from the ventral tegmental area (Haber & Knutson, 2010). Disruptions in these regions during reward processing have in fact been linked with both CD (Fairchild et al., 2019; Hawes et al., 2021; Rubia, 2011), mTBI (Cannella et al., 2019; Huang

et al., 2019; Mayer et al., 2015) and, consequently, with an increased risk of subsequent antisocial behaviour (Hyde et al., 2013; Reyna et al., 2018). As their co-occurrence increases the risk for maladaptive outcomes such as adolescent delinquency above and beyond when they occur in isolation (Carr, Hall, & Brandt, 2024), one may hypothesize that co-occurring CD and childhood mTBI may also be associated with even greater disrupted functioning of reward-related brain regions above and beyond their disrupted functioning in isolation.

However, to date, studies investigating reward-related neural patterns in CD have produced conflicting results (Alegria et al., 2016; Noordermeer et al., 2016). For example, recent meta-analyses have reported both increased (Noordermeer et al., 2016) and decreased (Alegria et al., 2016) caudate activation during reward processing. These discrepancies likely arise from using different reward-related paradigms, which target different reward mechanisms. That is, some studies have utilised the reward reversal learning task, which focuses on reward learning and cognitive flexibility while others have used the monetary incentive delay task (MID) task, which focuses on reward anticipation, motivation, and response to reward. It is thus essential to recognise the different reward paradigms and the specific reward mechanisms they engage to be consistent with the interpretation of results.

A further critical consideration that must be made is to the distinction between reward anticipation and outcome. Reward anticipation refers to incentive motivation - the willingness to expend effort based on learned cues signalling potential reward (Hawes et al., 2021; Swartz et al., 2020). Reward receipt, on the other hand, refers to the hedonic processing related to the outcome of a reward (Hawes et al., 2021). Recent meta-analyses have identified distinct brain regions associated with these phases including the striatum for reward anticipation and the medial OFC and caudal ACC for reward receipt (Chen et al., 2022; Oldham et al., 2018; Wilson et al., 2018). Subsequently, emerging evidence suggests that CD is uniquely linked to these distinct phases of reward processing (Hawes et al., 2021). For example, a study using baseline data from the Adolescent Brain Cognition Development (ABCD) study at ages 9–10 found that children with Disruptive Behaviour Disorders (DBDs, including CD) displayed hypoactivation in the dorsal ACC during reward anticipation and significantly increased activation in cortical (e.g., dorsal ACC) and subcortical (e.g., NAc) regions during reward receipt. These findings stress the need to investigate reward anticipation and receipt independently among children with CD while considering the potential impact of childhood mTBI.

The neural mechanisms underlying reward anticipation and receipt in childhood mTBI remain less well understood. While resting-state fMRI and MEG studies have identified differences in reward-

related neural activation in the medial prefrontal, anterior cingulate and anterior insula following a childhood mTBI (Healey et al., 2022; Huang et al., 2020), only one study has directly investigated reward-related activation during a reward-based task (Hogeveen et al., 2024). Using baseline (age 9–10) and 2 year follow-up (age 11–13) data from the ABCD study, this research found hyperactivation of the medial prefrontal and orbitofrontal cortex (OFC) as well as hypoactivation of the ACC and anterior insula during reward anticipation and observed no changes in neural activation during reward receipt (Hogeveen et al., 2024). As this is the first study, to our knowledge, which has investigated the neural mechanisms of reward anticipation and receipt in childhood mTBI, further investigation is needed to clarify the relationship between mTBI and these distinct reward processing phases while also accounting for the influence of CD.

To date, no published studies have investigated the effects of co-occurring CD and childhood mTBI on neural activation during reward anticipation and receipt. Considering their potential risk for co-occurring and a subsequent heightened risk for delinquency, it is paramount that this avenue is explored further. Utilising baseline data from the ABCD study, the present study aims to identify the neural mechanisms underlying reward processing in children with both CD and mTBI. Specifically, this study aims to identify if disrupted reward-related activation is more pronounced in children with CD and mTBI compared to typically developing youth, and importantly, those with mTBI or CD only. Therefore, our hypothesis was: co-occurring CD and mTBI will have a distinct pattern of reward-related neural activation compared to mTBI or CD only or TD controls.

4.3 Method

4.3.1 Participants

Data was obtained from the ABCD study, which recruited 11,874 healthy children aged 9–11 at 21 research sites across the US. The data used in this study came from the ABCD 4.0 data release (https://nda.nih.gov/study.html?id=1299). Participants were recruited from various primary schools via probability sampling within the 21 catchment areas (Garavan et al., 2018). Institutional review boards at the 21 participating universities had approved all study procedures. Written consent was provided by both study participants (assent) and their legal parent or guardian (consent). Ethical approval to conduct this secondary analysis was provided by the University of Southampton Ethics Committee (ID 62100).

We adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Exclusion criteria included inadequate performance on the MID task (indicated by a performance flag), incomplete data for the CD and head injury variables, and not meeting the criteria for one of four analytical groups (having CD, a mTBI, both, or typically developing, as described below). The final sample consisted of *N* = 2,761 participants (see Table 7 for demographic information and further in the Results section).

Table 7

Demographic and Clinical Characteristics by Analytical Group

	Groups							
	mTBI+CD (*n* = 252)		CD (*n* = 588)		mTBI (*n* = 1,216)		TD (*n* = 705)	
Demographics	*M(SD)*	*n(%)*	*M(SD)*	*n(%)*	*M(SD)*	*n(%)*	*M(SD)*	*n(%)*
Age	9.95 (0.61)[a]	—	9.92 (0.63)[a]	—	9.97 (0.62)[a]	—	9.95 (0.62)[a]	—
Male Sex	—	179 (71.0)[a]	—	342 (58.2)[b]	—	680 (55.9)[b]	—	315 (44.7)[c]
Ethnicity								
Asian	—	4 (1.6)[a]	—	2 (.30)[a]	—	18 (1.5)[a]	—	31 (4.4)[b]
Black	—	48 (19.0)[a]	—	168 (28.6)[b]	—	80 (6.6)[c]	—	182 (25.8)[a,b]
Hispanic	—	44 (17.5)[a,b]	—	87 (14.8)[a]	—	198 (16.3)[a,b]	—	143 (20.3)[b]
White	—	114 (45.2)[a]	—	257 (43.7)[a]	—	810 (66.6)[b]	—	290 (41.1)[a]
Other	—	42 (16.7)[a]	—	74 (12.6)[a,b]	—	110 (9.0)[b]	—	59 (8.4)[b]
Conduct Disorder								
CBCL CP Scale (T-score)	68.29 (6.05)[a]	—	67.73 (5.96)[a]	—	50.0 (0)[b]	—	50.0 (0)[b]	—
K-SADS CD	—	103 (40.9)[a]	—	253 (43.0)[a]	—	0[b]	—	0[b]

Diagnosis								
TBI								
Improbable TBI	—	189 (75.0)[a]	—	0[c]	—	1,001 (82.3)[b]	—	0[c]
Possible mild TBI	—	43 (17.1)[a]	—	0[b]	—	165 (13.6)[a]	—	0[b]
Mild TBI	—	20 (7.9)[a]	—	0[b]	—	50 (4.1)[c]	—	0[b]
Covariates								
Low birth weight	—	55 (21.9)[a,b]	—	135 (23.0)[a]	—	206 (16.9)[b]	—	160 (22.7)[a]
Premature birth	—	46 (18.3)[a]	—	112 (19.0)[a]	—	199 (16.4)[a]	—	111 (15.7)[a]
Smoking	—	83 (32.8)[a]	—	186 (31.7)[a]	—	134 (11.0)[b]	—	53 (7.5)[b]
Alcohol	—	95 (37.6)[a]	—	175 (29.7)[a]	—	360 (29.6)[a]	—	103 (14.6)[b]
ADHD (CBCL T-score)	63.09 (8.97)[a]	—	60.97 (8.20)[b]	—	51.67 (3.72)[c]	—	50 (0)[d]	—
Internalizing problems (CBCL T-score)	61.28 (10.22)[a]	—	58.12 (10.77)[b]	—	46.92 (9.46)[c]	—	33.97 (1.73)[d]	—
Low parental education	—	38 (15.1)[a]	—	140 (23.8)[b]	—	94 (7.7)[c]	—	154 (21.9)[d]
Low household income	—	116 (45.9)[a]	—	318 (54.0)[a]	—	214 (17.6)[b]	—	222 (31.5)[c]

Family conflict	3.08 (2.33)[a]		2.85 (2.16)[a]		1.76 (1.82)[b]		1.77 (1.80)[b]	
MID Performance								
Total earnings ($)	19.90 (13.22)[a]	—	17.71 (17.87)[b]	—	20.77 (13.29)[a]	—	19.76 (15.51)[a,b]	—
Mean reaction time (ms)	313.83 (58.79)[a]	—	331.44 (67.83)[b]	—	313.69 (55.77)[a]	—	322.40 (64.64)[a,b]	—

Notes. [a,b,c,d] For each row, non-matching superscript indicates significant differences between groups (p<.05). mTBI+CD = co-occurring mild traumatic brain injury and conduct disorder; CD = conduct disorder only; mTBI = mild traumatic brain injury only; TD = typically developing youth; CP = conduct problem; CBCL = Child Behaviour Checklist; K-SADS = The Kiddie Schedule for Affective Disorders and Schizophrenia.

4.3.2 Measures

4.3.2.1 Conduct Disorder

CD was assessed using the computerized versions of the Child Behaviour Checklist (CBCL) DSM-orientated Conduct Problems Scale(Achenbach & Ruffle, 2000) and The Kiddie Schedule for Affective Disorders and Schizophrenia for school-aged children (K-SADS-PL DSM-5; Kaufman et al., 2017). The CBCL consists of 17 items rated from 0 (*not true*) to 2 (*very true* or *often true*), which together produce a T-score ranging from 50–100. A T-score >= 65 indicates borderline and clinical ranges of CD. K-SADS-PL DSM-5 generates a CD diagnosis based on DSM-5 diagnostic criteria. CD was evident if participants had a T-score >= 65 or a CD diagnosis as ascertained by K-SADS-PL DSM-5.

4.3.2.2 Mild Traumatic Brain Injury

Head injury status was determined by the Modified Ohio State Traumatic Brain Injury (TBI) Screen (short version; Corrigan & Bogner, 2007). Parents reported if their child had ever sustained a TBI. These were classified as an improbable (without loss of consciousness or memory loss), possible mild (memory loss but no loss of consciousness), mild (loss of consciousness less than 30 minutes), moderate (loss of consciousness from 30 minutes to 24 hours), or a severe TBI (loss of consciousness greater than 24 hours). A binary variable was created (1 = *mTBI*, 0 = *no head injury*) where a mTBI included an improbable to mild TBI (i.e., a TBI with a loss of consciousness $<$ 30 minutes). Those with a reported moderate or severe TBI (*n* = 7) were excluded from analysis as the focus of this study was to investigate mTBI, which are more common in the general population and a comparison with the small number of participants with a moderate to severe TBI would not be appropriate due to low statistical power.

4.3.2.3 Group Classification

Participants were assigned to one of four groups based on their CD and mTBI history reported at baseline (age 9–10). The CD group consisted of children with a diagnosis or clinical levels of CD (CBCL T-score >= 65) but no reported history of head injury (*n* = 588). The mTBI group consisted of children with a reported history of mTBI but no diagnosis or clinical levels of CD (CBCL T-score = 50, mTBI, *n* = 1,216). The co-occurring group consisted of children with a reported history of mTBI and a diagnosis or clinical levels of CD (mTBI+CD, *n* = 252). Lastly, a group of typically developing (TD) controls was created based on that used in the previous literature (Hawes et al., 2021) and included those with a CBCL T-score = 50 across eight syndrome and six DSM-5 oriented scales and no reported history of sustaining a head injury (TD, *n* = 705).

4.3.2.4 Covariates

Several prenatal, child-level, and family-level covariates were controlled for in the statistical analysis due to their association with CD (Fairchild et al., 2019; Van Adrichem et al., 2020), head injuries (McKinlay et al., 2010), or reward processing (Blair et al., 2022). These included male sex, ethnicity, participant age, ADHD (as measured by the CBCL ADHD DSM-orientated Scale), internalizing problems (as measured by the CBCL Internalizing Syndrome Scale), low birth weight (< 5lbs), premature birth (< 37 weeks' gestation), smoking or alcohol consumption during pregnancy, low parental education, low household income (< $50,000), and family conflict. Family conflict was measured by the Youth Family Environment Scale family conflict subscale, which was modified from PhenX (Moos & Moos, 1994). Nine items including "we fight a lot in our family," were measured on a binary scale (1 = *true*, 0 = *false*) and summed to create a family conflict score (possible range 0–9) with higher scores indicating higher levels of family conflict. Further analyses with the addition of IQ proxies were also conducted and included in the Appendix (see Appendix L)

4.3.2.5 Monetary Incentive Delay Task

A version of the MID task (Knutson et al., 2000) was used to measure neural activation during reward anticipation and reward receipt (Figure 4; Casey et al., 2018). The task includes three trial conditions with five trial types: win (+$0.20 or +$5), loss (-$0.20 or -$5), or neutral (+/-$0). Each is associated with a specific incentive cue (a pink circle, yellow square, or blue triangle, respectively). For each trial, participants saw one of these cues on the screen for 2,000 ms followed by 1,500–4,000 ms of jittered anticipatory delay (a fixation cross). A black target the same shape as the cue then appeared on the screen for 150–500 ms and participants had to respond as quickly as possible to the target by pressing a button. Successfully pressing the button when the target was on the screen resulted in either winning money (win trial), avoiding losing money (loss trial), or neither winning nor losing money (neutral trial). If participants responded too fast or slow (i.e., before or after the target appeared on the screen) they did not win money (win trial), they lost money (loss trial), or they neither won nor lost money (neutral trial). This feedback was presented to participants after each trial. To ensure all participants maintained a 60% accuracy rate on this paradigm, the MID task individualizes the difficulty by adjusting target duration based on the overall accuracy rate of the six previous trials. If participants accuracy was below 60%, the target duration was increased, if their accuracy was above 60%, the target duration was shortened. Participants completed two runs of the task each consisting of 50 contiguous trials (20 reward trials, 20 loss trials, and 10 neutral trials) presented in pseudorandom order and lasting approximately 5.5 minutes.

Figure 4

Outline of the Monetary Incentive Delay Task for Each of the Five Trial Types

Note. This figure highlights the timeline of the monetary incentive delay task as utilized within the ABCD study, broken down by the five trial types.

4.3.3 Image Preprocessing

Functional magnetic resonance imaging data from the 21 study sites was harmonized across three 3T scanner platforms (Siemens Prisma, Philips, General Electric 750; Casey et al., 2018). Centralized processing, quality control, and analysis of the raw imaging data were performed by the ABCD Data Analysis Informatics and Resource Centre (DAIRC; Hagler et al., 2019). FreeSurfer v5.3 (Fischl, 2012) was used to create cortical surface reconstruction and subcortical segmentation for the regions of interest. We used beta coefficients available in the ABCD data release (version 4.0) for task-related Blood Oxygen Level Dependent (BOLD) activation during the MID task. These beta coefficients were derived from estimates for the task-related BOLD activation strength computed at the subject level using a general linear model (GLM). They represent the average of the beta coefficients for each of the two MID task runs. We focused on two specific contrasts available in the data release and used in the previous literature (Hawes et al., 2021) a) reward anticipation: anticipation of large reward ($5) versus no incentive ($0), and b) reward receipt: positive feedback (won money) versus negative feedback (did not win money).

4.3.4 Regions of Interest

Eight regions of interest (ROIs) were selected from the brain regions available within the ABCD dataset. These ROIs were selected due to their known associations with reward processing (Cao et al., 2019; Chen et al., 2022; Oldham et al., 2018; Wilson et al., 2018), and specifically associated with reward processing in either CD or mTBI (Alegria et al., 2016; Cannella et al., 2019; Hawes et al., 2021). In particular, when considering regions associated with CD and reflecting on the results of Hawes et al. (2021), we were interested in those regions found significant during reward processing for the DBD overall or DBD plus callous unemotional (CU) traits groups. Whilst other reward-related regions could be included based on possible theoretical reasoning, a targeted ROI approach was used to reduce the number of statistical comparisons, thereby aiming to balance the risk of Type I (i.e. a false-positive) and Type II error (i.e. a false-negative) after applying a false discovery rate (FDR) correction. By only including reward-related ROIs consistently found to be associated with CD or TBI, this approach enhances statistical power while maintaining interpretability.

These ROIs included: amygdala, NAc, hippocampus, medial OFC, caudal ACC, rostral ACC, thalamus, and insula (Figure 5).

Figure 5

The Eight Regions of Interest Used to Investigate Reward Anticipation and Reward Receipt in Children With a History of Conduct Disorder and/or Mild Traumatic Brain Injury

Note. This figure shows the anatomical locations of the eight regions of interest (ROI's) as viewed from a) sagittal (left), b) superior, c) inferior, d) anterior, and e) posterior viewpoints.

4.3.5 Statistical Analysis

Multinomial logistic regression was used to identify activation differences in eight ROIs for reward anticipation and receipt during the MID task (as measured by the beta coefficients) between the following groups: 1) mTBI+CD versus TD controls, 2) CD versus TD controls, 3) mTBI versus TD controls, 4) mTBI+CD versus CD, 5) mTBI+CD versus mTBI, and 6) CD versus mTBI. All models controlled for the following covariates: low birth weight, premature birth, smoking or alcohol consumption during pregnancy, male sex, ethnicity, ADHD, internalizing problems, age, family low SES, and family conflict.

Any missing data for the covariates were accounted for using maximum likelihood estimation with robust standard errors (MLR) and a Monte Carlo numerical integration algorithm. Complex sampling of the dataset was accounted for by using a cluster correction for sibling pairs and stratification of study site in Mplus (TYPE = COMPLEX).

The statistical significance for all regression models was set at an alpha level of .05 after applying an FDR correction for multiple comparison using the Benjamini-Hochberg procedure (Benjamini & Hochberg, 1995). All analyses were conducted in Mplus, version 7.4 (Muthén & Muthén, 2017) with the exception of the FDR-correction, which was conducted in *R* statistical software version 4.4.1.

4.4 Results

The study included 2,761 children at baseline (1,245 female [45.1%] and 1,471 [53.3%] White). Descriptive statistics including demographic information can be seen in Table 7. As expected, there were some significant group differences on most covariates controlled for in the regression models (e.g., a significantly greater proportion of boys in the mTBI+CD group compared to all other groups; see Table 7). Children in the mTBI+CD group reported significantly milder TBI's and fewer instances of improbable TBI's compared to children in the mTBI group. There were no significant differences in CD (either K-SADS diagnosis or CBCL T-score) between the CD and mTBI+CD groups. Children in the CD group displayed significantly lower total earnings and a slower mean reaction time on the MID task compared to children in the mTBI and mTBI+CD groups.

4.4.1 Reward Anticipation

The results of the multinomial logistic regression models for reward anticipation can be seen in Table 8. No significant differences in activations across ROIs during reward anticipation across the four groups were found.

4.4.2 Reward Receipt

The results from the multinomial logistic regression models for reward receipt are presented in Table 9. Children in the mTBI+CD group showed greater activation of the left amygdala and hippocampus compared to all other groups. While the mTBI+CD group showed differences in activation compared to all other groups in the left insula, right caudal ACC, thalamus, and hippocampus, only activation in the right hippocampus (compared to TD and mTBI groups) and right thalamus (compared to TD group) survived the FDR-correction. Further findings, which did not survive the FDR-correction were an increased activation of the bilateral medial OFC, left caudal ACC and right rostral ACC compared to TD youth and the right amygdala compared to mTBI youth as well as greater activation in the left insula and right rostral ACC and medial OFC in the CD group compared to TD (see Table 9).

Table 8

Multinomial Regression Model Results Comparing Activation During Reward Anticipation across Groups

	Group comparisons					
	CD vs TD	mTBI vs TD	mTBI+CD vs TD	mTBI+CD vs CD	mTBI+CD vs mTBI	CD vs mTBI
ROI	*OR* [95% CI]	*OR* [95% CI]	*OR* [95% CI]	*OR* [95% CI]	*OR* [95% CI]	*OR* [95% CI]
Left hemisphere						
Amygdala	1.11 [0.70–1.76]	1.35 [0.90–2.01]	0.97 [0.58–1.65]	0.88 [0.55–1.39]	0.72 [0.45–1.16]	0.83 [0.55–1.24]
NAc	1.03 [0.67–1.59]	1.26 [0.90–1.76]	1.84 [1.05–3.22]	1.78 [1.06–2.99]	1.47 [0.87–2.48]	0.82 [0.57–1.20]
Caudal ACC	1.26 [0.72–2.22]	1.52 [0.98–2.37]	2.30 [1.18–4.49]	1.82 [1.03–3.24]	1.51 [0.81–2.82]	0.83 [0.50–1.38]
Rostral ACC	1.36 [0.76–2.44]	1.36 [0.96–1.93]	2.24 [1.23–4.07]	1.65 [0.92–2.95]	1.64 [0.94–2.85]	1.00 [0.60–1.66]
Medial OFC	1.00 [0.77–1.29]	0.98 [0.82–1.16]	1.38 [0.99–1.91]	1.38 [1.01–1.88]	1.41 [1.02–1.94]	1.02 [0.81–1.30]
Hippocampus	1.11 [0.57–2.14]	1.46 [0.85–2.49]	1.11 [0.49–2.52]	1.00 [0.47–2.15]	0.76 [0.36–1.63]	0.76 [0.42–1.38]
Thalamus	1.36 [0.70–2.63]	1.70 [0.99–2.92]	1.84 [0.81–4.18]	1.35 [0.63–2.90]	1.08 [0.50–2.34]	0.80 [0.44–1.45]
Insula	1.16 [0.54–2.50]	1.40 [0.81–2.44]	1.79 [0.72–4.47]	1.54 [0.67–3.55]	1.27 [0.54–3.02]	0.83 [0.42–1.65]
Right hemisphere						
Amygdala	1.11 [0.68–1.82]	1.35 [0.89–2.03]	1.02 [0.57–1.83]	0.92 [0.54–1.57]	0.76 [0.45–1.29]	0.82 [0.54–1.27]

NAc	1.01 [0.65–1.58]	1.14 [0.84–1.56]	1.73 [0.99–3.02]	1.71 [1.01–2.87]	1.51 [0.90–2.54]	0.89 [0.60–1.31]
Caudal ACC	1.06 [0.59–1.92]	1.13 [0.72–1.77]	1.68 [0.83–3.39]	1.58 [0.81–3.07]	1.49 [0.77–2.88]	0.94 [0.55–1.61]
Rostral ACC	1.12 [0.66–1.88]	1.03 [0.70–1.52]	2.06 [1.08–3.91]	1.85 [1.00–3.41]	1.99 [1.09–3.66]	1.08 [0.68–1.73]
Medial OFC	0.87 [0.67–1.12]	0.93 [0.78–1.12]	1.24 [0.87–1.77]	1.42 [1.03–1.98]	1.33 [0.94–1.88]	0.93 [0.75–1.17]
Hippocampus	0.92 [0.45–1.88]	1.59 [0.95–2.65]	1.09 [0.46–2.58]	1.19 [0.53–2.67]	0.69 [0.31–1.54]	0.58 [0.31–1.09]
Thalamus	1.24 [0.61–2.50]	1.62 [0.97–2.72]	1.86 [0.76–4.53]	1.50 [0.65–3.45]	1.15 [0.50–2.64]	0.76 [0.41–1.42]
Insula	0.94 [0.47–1.90]	1.24 [0.74–2.06]	1.76 [0.74–4.18]	1.87 [0.84–4.16]	1.42 [0.63–3.21]	0.76 [0.41–1.42]

Note. CD = conduct disorder only; TD = typically developing youth; mTBI = mild traumatic brain injury only; mTBI+CD = co-occurring mild traumatic brain injury and conduct disorder; OR = odds ratio; NAc = nucleus accumbens; ACC = anterior cingulate cortex; OFC = orbitofrontal cortex.

Table 9

Multinomial Regression Model Results Comparing Activation During Reward Receipt across Groups

	Group comparisons					
	CD vs TD	mTBI vs TD	mTBI+CD vs TD	mTBI+CD vs CD	mTBI+CD vs mTBI	CD vs mTBI
ROI	*OR* [95% CI]	*OR* [95% CI]	*OR* [95% CI]	*OR* [95% CI]	*OR* [95% CI]	*OR* [95% CI]
Left hemisphere						
Amygdala	1.03 [0.69–1.54]	0.87 [0.62–1.20]	2.18* [1.29–3.66]	2.12* [1.28–3.49]	2.51* [1.50–4.21]	1.19 [0.80–1.77]
NAc	1.22 [0.86–1.72]	1.07 [0.80–1.42]	1.51 [0.94–2.43]	1.24 [0.81–1.91]	1.42 [0.89–2.24]	1.14 [0.83–1.56]
Caudal ACC	1.32 [0.81–2.15]	1.25 [0.85–1.85]	2.35 [1.20–4.62]	1.78 [0.95–3.34]	1.88 [0.96–3.69]	1.05 [0.66–1.68]
Rostral ACC	1.32 [0.87–2.00]	1.17 [0.83–1.65]	1.66 [0.99–2.79]	1.26 [0.79–2.03]	1.42 [0.87–2.33]	1.13 [0.76–1.66]
Medial OFC	1.27 [0.99–1.62]	1.19 [0.98–1.43]	1.44 [1.07–1.93]	1.13 [0.88–1.46]	1.21 [0.92–1.59]	1.07 [0.86–1.33]
Hippocampus	1.66 [0.95–2.88]	1.12 [0.72–1.74]	4.20* [2.09–8.47]	2.54* [1.36–4.72]	3.76* [1.91–7.41]	1.48 [0.88–2.49]
Thalamus	1.27 [0.72–2.25]	1.13 [0.73–1.73]	2.14 [0.91–5.06]	1.68 [0.76–3.73]	1.90 [0.83–4.39]	1.13 [0.67–1.90]
Insula	1.22 [0.68–2.19]	1.06 [0.66–1.69]	2.50 [1.17–5.33]	2.04 [1.00–4.18]	2.36 [1.15–4.85]	1.16 [0.68–1.96]
Right hemisphere						
Amygdala	1.22 [0.83–1.78]	0.89 [0.64–1.22]	1.55 [0.96–2.50]	1.27 [0.80–2.02]	1.75 [1.06–2.89]	1.38 [0.93–2.05]

NAc	1.12 [0.80–1.58]	0.89 [0.66–1.20]	1.34 [0.79–2.28]	1.19 [0.74–1.92]	1.51 [0.89–2.54]	1.26 [0.90–1.77]
Caudal ACC	1.27 [0.78–2.08]	1.09 [0.74–1.62]	2.32 [1.25–4.32]	1.83 [1.03–3.26]	2.12 [1.15–3.90]	1.16 [0.72–1.86]
Rostral ACC	1.56 [1.03–2.39]	1.34 [0.95–1.89]	1.67 [1.01–2.76]	1.07 [0.68–1.67]	1.25 [0.76–2.05]	1.17 [0.78–1.76]
Medial OFC	1.32 [1.02–1.70]	1.19 [.97–1.45]	1.47 [1.07–2.00]	1.11 [0.86–1.44]	1.24 [0.92–1.66]	1.11 [0.89–1.39]
Hippocampus	1.69 [0.95–3.01]	1.26 [0.78–2.03]	3.19* [1.65–6.19]	1.89 [1.10–3.25]	2.53* [1.38–4.63]	1.34 [0.80–2.24]
Thalamus	1.43 [0.85–2.41]	1.35 [0.89–2.04]	2.98* [1.46–6.07]	2.08 [1.06–4.08]	2.22 [1.09–4.49]	1.06 [0.64–1.76]
Insula	1.11 [0.61–2.02]	1.09 [0.69–1.71]	1.60 [0.71–3.59]	1.44 [0.69–3.04]	1.47 [0.67–3.22]	1.02 [0.58–1.77]

Note. CD = conduct disorder only; TD = typically developing youth; mTBI = mild traumatic brain injury only; mTBI+CD = co-occurring mild traumatic brain injury and conduct disorder; OR = odds ratio; NAc = nucleus accumbens; ACC = anterior cingulate cortex; OFC = orbitofrontal cortex.

*p <.05 (FDR-corrected)

4.5 Discussion

In this study, we investigated whether co-occurring CD and childhood mTBI were associated with greater changes in neural activation during reward processing compared to their effects in isolation (i.e., CD only or a mTBI only). While there were no significant group differences during reward anticipation, significantly higher subcortical neural activation was identified during reward receipt in children with both CD and a history of mTBI

Consistent with our hypothesis, and expanding upon previous research (Hawes et al., 2021; Oldham et al., 2018), this study identified increased activation in reward-related mesolimbic structures (i.e., left amygdala and hippocampus) during reward receipt in children with CD but only when co-occurring alongside mTBI (mTBI+CD group) compared to all other groups. The left amygdala is associated with emotion processing and assessing the salience (Costanzo et al., 2015) and emotional value of stimuli (Šimić et al., 2021) while the hippocampus is associated with encoding reward experiences (Knierim, 2015). These findings align with previous work suggesting that the hippocampus integrates emotional information from the amygdala during the encoding of episodic memory (Shigemune et al., 2010). Thus, this specific pattern of increased activation observed in the hippocampus and the amygdala may indicate that children with co-occurring CD and mTBI likely encode both contextual and emotional aspects of reward events more intensely. Such enhanced encoding may drive future memory-guided reward seeking behaviours in the pursuit of similar rewards. These findings were only identified when CD co-occurred alongside mTBI suggestive of an interplay between the two, which should be considered in future CD research investigating neural activation patterns during reward receipt.

Our findings regarding reward receipt further align with previous mTBI work highlighting no significant activation differences during reward receipt in children with mTBI alone (Hogeveen et al., 2024). However, we expand upon these findings by highlighting increased neural activation during reward receipt in children with mTBI only when co-occurring alongside CD. This thus suggests that heightened neural activity patterns during reward receipt may be specific to a subset of children with co-occurring mTBI and CD. Notably, there were significantly more severe forms of mTBI (i.e., mTBI compared to improbable or probable mTBI) in the mTBI+CD group compared to the mTBI group suggesting that mTBI often co-occurs alongside CD. This may thus further highlight why research should consider their association when investigating mTBI. As such, and similarly to CD research, we thus recommend further exploration of the role of reward processing in children with a mTBI both when co-occurring alongside CD, or when controlling for the influence of CD.

We found no significant differences in neural activation during reward anticipation across clinical groups. This contrasts with the previous literature in children with DBDs (Hawes et al., 2021) and mTBI (Hogeveen et al., 2024). These discrepancies may stem from differences in sample characteristics. For instance, Hawes et al. (2021) identified significant alterations in reward anticipation in children with DBDs, but their sample included both children with CD and oppositional defiant disorder (Hawes et al., 2021), suggesting that reward anticipation deficits may be more characteristic of other DBDs rather than CD alone. Similarly, our mTBI group included all children at baseline with a history of sustaining any form of mild head injury from an improbable TBI to a mTBI whereas Hogeveen and colleagues (2024) focused on those with a mTBI with a loss of consciousness. This suggests that changes to neural activation patterns during reward anticipation may be more pronounced in those with more severe mTBI. Additionally, Hogeveen et al.'s (2024) mTBI sample included children who sustained head injuries between study visits, reducing the delay between sustaining the reported mTBI and completing the reward-based paradigm. The longer delay in our study may have diminished the observable effects of mTBI on neural activation patterns during reward anticipation.

Children with co-occurring mTBI and CD (mTBI+CD group) exhibited moderate increases in neural activation in the right caudal ACC, hippocampus, and thalamus compared to all other groups, though not all findings survived the FDR-correction. These activation patterns were not observed in the CD or mTBI groups compared to TD controls (even prior to FDR-correction) suggesting that these heightened activation patterns may be somewhat unique to the co-occurrence of mTBI and CD compared to children with CD or mTBI alone or typically developing youth. The thalamus plays a crucial role in relaying sensory and emotional information to the striatum (Wolff et al., 2021). As such, increased thalamic activation in the mTBI+CD group may reflect heightened emotional and sensory processing of reward-related stimuli. Additionally, the caudal ACC, which integrates inputs from the thalamus as well as the amygdala, and hippocampus, is involved in evaluating whether received rewards meet expectations, monitoring errors, and adjusting motivation (Umemoto et al., 2017). Together, the heightened activity in these interconnected regions could suggest a unique neural profile in children with mTBI+CD, characterised by an amplified sensitivity to the emotional and sensory aspects of monetary reward, as well as an increased arousal to reward expectations and motivation. However, we stress that not all findings survived FDR-correction and should be interpreted with caution. Further research is thus necessary to expand upon these findings and hypotheses further.

4.5.1 Strengths and limitations

We note that the large sample and the analysis design, which controls for ADHD alongside several relevant covariates across the child and family levels are strengths of our research. However,

we note several limitations of the current study. A cross-sectional methodology can allow us to only assume correlational relationships from our findings and cannot identify developmental changes in reward-related neurocircuitry related to CD or mTBI. Future research could utilise further waves of ABCD data, which will also enable the inclusion of children with adolescent-onset CD, older than our current sample. Finally, the MID task restricts our findings to monetary reward. To identify if these neurological pathways are similar across various reward subtypes, a comparable research framework should be applied to other paradigms, for example, social reward.

4.5.2 Conclusions

Overall, we found novel evidence that furthers our understanding of the neural pathways associated with children with co-occurring mTBI and CD. That is, this group was characterised by significantly greater activation in the left amygdala and hippocampus during reward receipt compared to typically developing children and, importantly, children with CD or mTBI alone. The increased amygdala activation may suggest an emotional hyperresponsivity to positive reward outcomes in children with co-occurring CD and mTBI, while the increased hippocampal activation may indicate more robust encoding of such emotionally charged reward experiences, potentially reinforcing memory-guided, reward-seeking behaviour. Together, these finding could be an important first step in understanding the stronger drive toward reward-seeking behaviours in this population, which may contribute to the higher risk of maladaptive outcomes, such as delinquency previously observed in those with co-occurring CD and mTBI (Carr, Hall, & Brandt, 2024).

Chapter 5 Overall Discussion

The primary aim of the research presented in this thesis was to produce a comprehensive understanding of the association between childhood head injuries and conduct problems, including their developmental pathways, risk factors, outcomes, and neurobiological underpinnings. Whilst recent evidence has suggested potential bidirectional links between conduct problems and childhood head injuries (Brandt et al., 2022; Carr, Hall, Eisenbarth, et al., 2024), there are still gaps in the literature that need to be addressed. Addressing these gaps is beneficial to further our understanding of the associations between conduct problems and childhood head injuries and to guide future research. Ultimately, aiming to inform effective intervention strategies to reduce their co-occurrence. The following key gaps were explored in this thesis:

1. **Identifying Subgroups:** Whilst research has identified a bidirectional association between conduct problems and childhood head injuries (Brandt et al., 2022; Carr, Hall, Eisenbarth, et al., 2024), it is important to identify which subgroups this association applies to. Notably, there are distinct trajectories of conduct disorder characterised by variations in onset and duration (American Psychiatric Association, 2022; Fairchild et al., 2019; Gutman et al., 2019). Identifying the specific conduct problem trajectories relevant to this association is important to improve the effectiveness of prevention and treatment interventions. By narrowing the focus to only affected subgroups, future research can more accurately investigate this relationship and develop more accurate targeted interventions.
2. **Identifying Relevant Risk Factors:** Identifying risk factors linked with co-occurring conduct problems and head injury (whether as predictors or associations) could assist in the development of effective prevention and treatment interventions.
3. **Understanding the Outcomes of This Association:** Conduct disorder and childhood head injuries can increase the risk for subsequent maladaptive outcomes including delinquency (Connolly & McCormick, 2019; Hammerton et al., 2019; Mongilio, 2022; Schwartz et al., 2017; Schwartz et al., 2018). However, little is known about how their co-occurrence can influence these outcomes. That is, whether their co-occurrence poses an even greater risk for subsequent maladaptive outcomes compared to their isolated occurrence. By addressing this gap, it can highlight a further need for preventing their co-occurrence in order to reduce subsequent negative outcomes.
4. **Understanding Underlying Mechanisms:** Investigating the co-occurrence between conduct problems and childhood head injuries provides an opportunity to identify key underlying mechanisms. These will not only help to further our understanding of their

co-occurrence but may begin to explain why their co-occurrence leads to specific maladaptive outcomes such as delinquency. Understanding these mechanisms could highlight potential targets for future interventions aimed at mitigating the negative outcomes associated with their co-occurrence.

This chapter provides an in-depth discussion of the research findings presented in this thesis and their implications. The first two papers contribute to understanding the associations between childhood head injuries and conduct problems by exploring how they co-occur across development and their combined impact on future maladaptive outcomes. The final paper provides a deeper insight into the underlying neural mechanisms associated with their co-occurrence.

5.1 Co-occurring Conduct Problems and Childhood Head Injuries are not Limited to a Single Subgroup

First and foremost, it was important to identify who co-occurring conduct problems and childhood head injuries were relevant to. The findings from Paper 1 revealed that the known pathways of conduct problems (i.e., childhood-limited, persistent, and adolescent-onset) were all uniquely linked to distinct head injury pathways. Specifically, spikes in head injury rates appeared to align closely with periods of elevated conduct problem symptoms. This synchronisation between the conduct problem and head injury pathways may highlight the dynamic, reciprocal nature of their association across development.

The persistent pathway was characterised by increasing conduct problem symptom from age 5, which maintained at a “high” level (SDQ score >3) throughout development. These children also displayed increased head injury rates between ages 7–11 but also consistently the highest rates of head injuries compared to all other identified pathways. This aligns with previous findings using the MCS sample, whereby early conduct problems were associated with subsequent head injuries, which were then associated with greater conduct problems symptoms (Carr, Hall, Eisenbarth, et al., 2024). These findings suggest that the bidirectional association between conduct problems and head injury identified in the previous study may at the very least reflect a continuous, reciprocal relationship between persistent conduct problems and head injuries across development.

However, the identified adolescent-onset pathway may highlight another group to whom the previous association may be relevant to. The adolescent-onset pathway was characterised by increased head injury rates between ages 11–14 and increasing levels of conduct problems from age 11, reaching a high level by age 17. In Carr and colleagues’ study (2024), childhood head injuries were associated with later adolescent conduct problems, suggesting that their findings may also encapsulate the adolescent-onset pathway identified here. However, our understanding of the reciprocal relationship between late conduct problems and head injuries is limited by the omission of

head injury measurement between ages 14–17. This is something that warrants further investigation and is considered in greater detail below. Further, whilst this pathway appears to highlight a group of adolescents characterised by adolescent-onset conduct problems, symptoms (i.e., reflected by high SDQ scores) are thought to typically emerge earlier in adolescence. This delay in reported high conduct problem symptoms may indicate that this pathway does not completely capture adolescent-onset conduct disorder. Environmental factors, such as increased exposure to deviant peers or antisocial behaviour later in adolescence, may contribute to this presentation but further investigation is warranted to understand this further. Nonetheless, these findings do reflect an adolescent-onset subtype of conduct problems and further support the association between childhood head injuries and later adolescent conduct problems (Carr, Hall, Eisenbarth, et al., 2024).

The childhood-only (or childhood-limited) pathway exhibited high conduct problem symptoms at age 3, which declined to "close to average" (SDQ score < 3) levels by adolescence. Head injury rates mirrored this pattern, peaking at age 3 and declining until rates were similar to those observed in the stable group. Whilst this decline would initially suggest a limited need for interventions, childhood-limited conduct problems are associated with high levels of aggression and poor educational outcomes in young adulthood (Bevilacqua et al., 2018). Additionally, early childhood injuries are associated with poorer cognitive and behavioural outcomes (Séguin et al., 2022). Whilst it is important to create effective interventions targeting other pathways (i.e., persistent and adolescent-onset), which are associated with greater persistent negative outcomes into adulthood (Bevilacqua et al., 2018), mitigating risks associated with all linked pathways could still be beneficial.

5.1.1 The Relevant Risk Factors for Linked Pathways of Conduct Problems and Childhood Head Injuries

Whilst it was important to identify groups whom the association between conduct problems and childhood head injuries was relevant to, identifying these groups alone provides limited insight for the research and clinical community in understanding and addressing their co-occurrence. Therefore, a secondary aim of this research was to identify factors that either predicted or were associated with membership to these linked pathways of conduct problems and head injuries. Identifying such factors could be useful in guiding accurate and effective intervention strategies.

The findings revealed that early cumulative risk (by age 3) at the child and household levels significantly predicted membership to all "clinically relevant" linked pathways, whilst mother-level cumulative risk predicted membership to the childhood-only and persistent pathways only. These results emphasise a need for timely targeted interventions to reduce early cumulative risk exposure during infancy at various ecological levels. Such interventions to reduce the exposure to cumulative

risk could include smoking cessation interventions for pregnant women. These have been shown to not only reduce smoking in expectant mothers but also reduce the risk of low birth weight and premature birth (Koivu et al., 2023) and could thus considerably reduce the cumulation of child-level risk exposure. Interventions at the mother-level could include improving mother-child attachment via administering attachment-based programmes such as the Attachment and Biobehavioural Catch-up programme (O'Byrne et al., 2023) to mothers who show early signs of poor attachment. The primary aim of this programme is to help parents to become more nurturing, follow their child's lead, and reduce negative or frightening behaviours (Berlin et al., 2016) and has been found to produce a small to medium effect on parental sensitivity and attachment-related parent outcomes (O'Byrne et al., 2023). At the household-level, interventions could be aimed at improving family SES such as low household income and low occupation status. To reduce the number of risks at this ecological level, policy rather than psychological or behavioural interventions may be more appropriate. Such policy implications are considered later in this discussion (see Section 5.5.2).

Further, maternal maladaptive parenting behaviours (i.e., harsh and withdrawn parenting) at age 5 were also associated with membership to all three clinically relevant pathways. However, whilst those exposed to negative maternal parenting in the childhood-only or persistent pathway had a 26%–38% greater odds of being part of a clinically relevant pathway, the significantly increased odds for the adolescent-onset pathway were lower at 9%–16%. These weaker odds could be a result of the delay between the measurements of maternal maladaptive parenting (at age 5), and the observed increased rates of head injury and high conduct problem symptoms from age 11 onwards. Therefore, there may be a temporal effect of early maternal maladaptive parenting on conduct problem and head injury pathways, which is reflected in the stronger association with those linked pathways emerging early in childhood and increasing from age 5. This appears to be in line with Fairchild and colleagues' suggested reformulation of the dual taxonomy theory (Fairchild et al., 2013; Moffitt, 1993). That is, they argue that the timing (as well as severity) of adversity is associated with age-of-onset. Therefore, this could explain why we see here a stronger association between early harsh parenting and early-onset conduct disorder pathways. Regardless of the strength of the association, early interventions targeting maternal maladaptive parenting by age 5 could mitigate children's membership to linked conduct problem and head injury pathways across development and thus could serve as a promising "universal" intervention target.

Interventions for conduct problems specifically have already been created which utilise attachment and social learning theories to address coercive parenting cycles such maternal maladaptive parenting (i.e., harsh parenting; see Section 1.1.5.2). These interventions typically guide parent's attention away from negative behaviours which induce coercive interactions and towards more positive child behaviours thus increasing positive parent-child interactions. Examples include the Incredible Years (IY) parenting programme and Video-feedback Intervention to promote Positive

Parenting and Sensitive Discipline (VIPP-SD). IY is a 14-week group-based intervention, which teaches parents relationship building, positive reinforcement, and non-violent discipline techniques and has been shown to reduce parent-reported harsh parenting (Creasey et al., 2024) and reduce conduct problem symptoms (Leijten et al., 2018; Leijten et al., 2020; Morpeth et al., 2017; Overbeek et al., 2021). VIPP-SD, on the other hand, involves six sessions including video feedback on parent-child interactions, focusing on sensitive discipline (e.g., sensitive timeout) and sensitive parenting (e.g., sharing emotions). Unlike IY, findings on the effectiveness of VIPP-SD for externalizing behaviours are mixed (van IJzendoorn et al., 2023). However, studies have reported significant reductions specifically in conduct problem symptoms (Juffer et al., 2017; O'Farrelly et al., 2021) and harsh parenting (Juffer et al., 2017). Overall, there have been many efforts to create effective interventions aimed at reducing conduct problems via the improvement of parenting behaviours such as the harsh and/or coercive parenting factors associated with the linked pathways of conduct problems and head injuries in this study.

Whilst these parent-targeted interventions may be effective in reducing conduct problems and, thus with the reduction of conduct problems could indirectly reduce the risk of subsequent head injuries (though this is yet to be tested), they do not directly address the links between conduct problems and childhood head injuries. Adaptions could be made to the above interventions to more directly mitigate the risk of future head injuries. That is, within these parenting programmes, modules on the awareness of head injury risk, injury prevention (e.g., identifying and encouraging safe play, risk evaluation, and promoting close monitoring and clear physical boundaries) as well as positive reinforcement for safe choices (e.g., praise safe behaviours) could be implemented and tested to identify their efficacy in reducing both conduct problems and childhood head injuries.

Notably, reducing the level of cumulative risk in infancy as well as improving maternal maladaptive parenting by age 5 may all aid in the prevention or withdrawal of membership to the clinically relevant pathways. It could therefore be beneficial to combine interventions in a way that could mirror the temporal ordering of the factors investigated here. In fact, parenting programmes to address coercive or harsh parenting have been found to be more effective in mother's with lower maternal distress (one of the mother-level cumulative indices; Kjøbli et al., 2014). As such, combining interventions sequentially such as addressing maternal distress (e.g., via cognitive behavioural therapy; Matvienko-Sikar et al., 2023) alongside other CRI-related interventions mentioned previously before implementing parenting programs such as IY or VIDD-SP could potentially enhance their overall effectiveness. Whilst current multicomponent interventions addressing both do not appear to improve parental mental health (Al Sager et al., 2024), more research is needed to improve the efficacy of such multicomponent programmes and to investigate their effectiveness at reducing both childhood conduct problems and head injuries with the further inclusion of head injury related modules as suggested above.

An additional factor which was strongly associated with all clinically relevant pathways was ADHD. This finding aligns with prior research highlighting its strong comorbidity with conduct disorder (Fairchild et al., 2019; Silberg et al., 2015). However, as ADHD was measured throughout development until age 14, it cannot be concluded that ADHD predicted group membership but rather was an associated factor. Consequently, interventions should focus on managing the comorbidity between conduct problems and ADHD such as pharmacological therapies (Fairchild et al., 2019) and various psychosocial (Villodas et al., 2012) and cognitive behavioural therapy interventions (Battagliese et al., 2015). Whilst interventions to target comorbid ADHD and conduct disorder have been trialled in the literature, it must be noted that ADHD was associated not only with conduct problems but its linked head injury pathways in the current study. Awareness of head injuries could thus also be incorporated into ADHD interventions alongside those targeting conduct problem comorbidity. For example, greater efforts to target the impulsive behaviours in ADHD which could lead to an accident or injury resulting in a head injury, as well as continuing to address aggressive behaviours associated with comorbid conduct disorder could help to prevent continuation of membership to these linked pathways.

Finally, epilepsy was associated only with the adolescent-onset pathway, potentially due to the progressive nature of seizures, which can escalate over time if untreated, leading to severe blackouts, falls, and head injuries (Jory et al., 2019), and behavioural problems (Kuzman et al., 2020). Another potential explanation for the delayed emergence of conduct problems in this pathway is the adverse behavioural effects of antiepileptic drugs, with aggression being one of the most common psychiatric side effects (Kawai et al., 2022; Steinhoff et al., 2021). Therefore, epilepsy may be a relevant factor to consider when addressing adolescent conduct problems and head injuries. Awareness campaigns around the risk of head injuries and conduct problems could be beneficial in reducing the risk of being a apart of this linked pathway as well as careful consideration of appropriate antiepileptic medication (Kawai et al., 2022; Steinhoff et al., 2021) and routine screening for conduct problem symptoms in children with epilepsy.

Whilst the identification of factors which either predicted or were associated with group membership was important to this study, a consideration of their strengths and limitations must be considered, particularly when considering the inclusion of CRIs. That is, the use of CRIs in this study presents a methodological trade-off that warrants careful consideration. On one hand, CRIs can simplify complex models such as the latent class models used here by reducing the number of variables entered into the analysis. On the other hand, CRIs limit the depth of insight into the impact of each individual risk factor on pathway membership. For example, whilst cumulative risk at the mother-level predicted membership to the persistent pathway, it could not clarify whether maternal distress or teenage pregnancy was the stronger predictor of pathway membership. Whilst this

limitation is inherent to the use of CRIs, their utility lies in capturing the broader patterns of risk without overcomplicating already complex analyses.

5.2 An Increased Risk for Adolescent Delinquency

Building on the findings from Paper 1, which identified linked pathways of conduct problems and head injury across development, the next step was to explore the outcomes of their co-occurrence – specifically, delinquency. Both conduct problems (Hammerton et al., 2019; Hopfer et al., 2013; Picoito et al., 2021) and childhood head injuries (Kennedy, Cohen, et al., 2017; Kennedy, Heron, et al., 2017; Mongilio, 2022; Schwartz et al., 2017) have been shown to increase the risk for subsequent delinquency compared to children without. Paper 2 thus sought to identify whether co-occurring conduct problems and childhood head injuries further amplify the risk of delinquency above and beyond the effects of each occurring in isolation.

A key finding in this paper was the significantly increased risk of delinquency at age 14. That is, adolescents who experienced both conduct problems and head injuries by age 11 exhibited a 60% increase in overall rates of delinquency compared to those with a history of neither, a 20% increase compared to those with conduct problems only, and a 39% increase compared to those who had a history of sustaining a head injury only. These increased rates highlight the combined impact of co-occurring conduct problems and head injuries on early adolescent delinquent behaviour and demonstrates a critical need to prevent their co-occurrence during childhood.

When looking at specific types of delinquency, co-occurring conduct problems and childhood head injury were associated only with a greater risk of substance use. This finding suggests that the heightened risk for overall delinquency may be largely driven by this significantly increased rate of early substance use. This could relate to a greater dysregulation of the brain's reward system in children with co-occurring conduct problems and head injuries, which could potentially drive sensation-seeking behaviours such as substance use. Additionally, environmental factors such as affiliations with deviant peers who normalise substance use, parental substance use, poor parent-child relationships, and low parental monitoring could all contribute to the increased rate of early substance use in this group (Rusby et al., 2018). However, further research is needed to clarify these hypotheses. Nonetheless, this is an important finding as early substance use is associated with a cascade of negative outcomes, including sleep deficiency (Kim & Son, 2023), which is associated with poor educational attainment (Curcio et al., 2006) and increased cardiometabolic risk (Park & Kim, 2022). As such, preventing the co-occurrence of conduct problems and head injuries is important to mitigate the greater risk of subsequent negative outcomes. Possible preventative interventions for their co-occurrence have been addressed previously in this chapter (see Section 5.1.2).

By age 17, adolescents with high levels of conduct problems reported between ages 11–14 had a 55%–69% increased rate of antisocial behaviour. This suggests that conduct problems may play a more influential role in predicting antisocial behaviour during later adolescence. This aligns with the dual systems theory (Steinberg et al., 2008), which argues that individuals with conduct disorder experience a delay in the maturation of the cognitive control system. As a result, their behaviour is driven predominantly by the socioemotional system, leading to heightened emotional reactivity and increased engagement in antisocial behaviours, such as physical aggression. This association underscores the importance of early identification and interventions for conduct problems (Fairchild et al., 2019; Fairchild et al., 2013).

Interestingly, the lack of increased risk for delinquency at age 17 following co-occurring conduct problems and head injuries beyond conduct problems alone may be partially attributed to the timing of the sustained head injuries. In this study, 78% of head injuries were reported by age 7. These early head injuries combined with high conduct problem symptoms may disrupt cognitive and emotional functioning, leading to early delinquency. However, as time progresses, neurodevelopment processes, such as neuroplasticity may support recovery, potentially mitigating the long-term impact of the head injuries. These findings emphasise the importance of examining how the timing and interplay of head injuries and conduct problems affect long-term outcomes, particularly delinquency.

Notably, childhood head injuries alone did not significantly predict an increased rate of delinquency at either age 14 or 17, contrasting previous research (Kennedy, Cohen, et al., 2017; Kennedy, Heron, et al., 2017; Mongilio, 2022; Schwartz et al., 2017). Given the strong association between conduct problems and delinquency, it is possible that the previous findings linking childhood head injury to an increased risk of delinquency may have been confounded by externalizing behaviours, such as conduct problems, which can present alongside a childhood head injury (Carr, Brandt, et al., 2024). In Paper 2, conduct problems were excluded from the head injury group to reduce such confounding effects, leading to the observation that head injuries, in isolation, may not predict delinquency. In fact, supplementary analysis identified an association between head injury and age 14 delinquency only when levels of conduct problems were not accounted for. This further suggests that there may be an element of confound from pre-existing conduct problems which should be considered in future head injury research.

A key limitation of the study was the reliance on self-reported delinquency data, which may be subject to biases such as underreporting or desirability bias. Underreporting may have been more pronounced at age 14 compared to age 17, as certain delinquent behaviours, such as alcohol use, become more socially acceptable at age 17 when participants approach the UK legal drinking age. Further, participants may have underreported more serious delinquent behaviours, such as antisocial

acts, to avoid self-incrimination. Such biases have been identified in individuals with ADHD (Sibley et al., 2010) and, whilst it remains unexplored in the context of conduct problems, it certainly warrants caution and further exploration. Due to the substantial bias inherent in self-reported delinquency data, previous research has recommended corroborating such reports with multiple sources such as parent-reports and external records, such as those from police or healthcare services (van Batenburg-Eddes et al., 2012). Future studies should integrate these sources to improve the reliability of delinquency assessments.

5.3 Strengths and Limitations of the MCS

Although I have thus far critiqued the use of the MCS in the context of Paper's 1 and 2, before moving on to discussing the third paper of this thesis, which utilises a different dataset, it seems appropriate to firstly provide an overall critique of the MCS dataset.

A major strength of the MCS is its large, UK-based national cohort, which ensures the findings from Papers 1 and 2 are robust, representative, and generalisable to the broader UK child population. The substantial sample size allows for the application of complex analytical methods, such as latent class analysis, to uncover smaller subgroups. For example, the persistent pathway of conduct problems and head injury in Paper 1 accounted for only 2.2% of participants; a subgroup that might have been overlooked in a smaller dataset. The application of sample weights further enhances representativeness by correcting for underrepresentation in specific demographic groups (i.e., specific geographical areas or ethnicities). Together, these attributes make the MCS dataset highly representative and suitable for generalisation to the UK child population.

An additional strength of the MCS is its capacity to identify hard-to-reach populations, such as those who have sustained a mild head injury, or those children with co-occurring conduct problems and head injuries. Direct recruitment opportunities for such populations (e.g., schools, A&E departments, or mild injuries units) would require a highly complex, multi-collaborative strategy across the UK, which is logistically challenging, time-consuming, and potentially impractical for a thesis. The MCS dataset thus provides a time-efficient and effective alternative, facilitating secondary analysis of these groups without the need for direct recruitment.

Further, the longitudinal design of the MCS is another valuable feature. It enables researchers to examine relationships and associations across time, providing opportunities to infer causal links. For example, in Paper 1, this allowed a deeper understanding of how conduct problems and head injury pathways link across development, whilst in Paper 2, this allowed the investigation of how conduct problems and head injuries increase the risk for delinquency. Therefore, the use of such longitudinal data was extremely valuable in answering the key research questions of this thesis.

Despite its strengths, the use of secondary data creates certain limitations, particularly regarding control over available measures. For example, conduct problems were assessed using the SDQ. Whilst this is considered a valid measure of conduct problems (Kersten et al., 2016) and appropriate for longitudinal analysis (Sosu & Schmidt, 2017), some of its items overlap with ODD symptoms (Hawes et al., 2023). For example, items such as “often fights with other children” and “steals from home, school or elsewhere” relates to DSM-5 symptoms of conduct disorder, whilst items such as “generally obedient” and “often has temper tantrums or hot tempers” are more relevant to ODD symptoms. This overlap introduces ambiguity and necessitates caution when interpreting findings related to conduct problems based on the SDQ.

Additionally, the SDQ does not provide a diagnostic measure of conduct disorder. Whilst this allows the inclusion of individuals with high conduct problem symptoms who may not yet have received a formal diagnosis, it also means that the conduct disorder group may include individuals with subclinical symptoms. Consequently, the term "conduct problems" is used here to reflect the broader, less specific nature of this measure compared to diagnostic tools.

Similarly, the measurement of head injuries in the MCS also has limitations. It relies on parent-reported data, which lacks detailed insight into injury severity. Whilst it was possible to differentiate between head injuries with or without a loss of consciousness, the dataset did not provide information on the duration of unconsciousness, which would have been a valuable piece of information to distinguish between mild (loss of consciousness less than 30 minutes) and moderate-to-severe (loss of consciousness longer than 30 minutes) head injuries. This limitation restricts the ability to explore the distinct impacts of varying severities of childhood head injuries.

Another limitation relates to the temporal inconsistency in the measurement of head injuries. That is, they were parent-reported at most time points, except at wave 7 (ages 14–17). Consequently, within Paper 1, I could not investigate the longitudinal trajectory of linked conduct problems (measured at age 14) and head injuries during adolescence. This gap limits the ability to determine whether the rising conduct problems observed in the adolescent-onset pathway were accompanied by increased rates of head injuries during this developmental period. Future research could address this gap by leveraging later MCS waves, if available, or by using alternative datasets that extend into adolescence.

5.4 Unique Reward-Related Neural Profile

The final paper of this thesis aimed to build a more in-depth picture of the characteristics associated with the co-occurrence between conduct problems and childhood head injuries. Following on from Paper 2, which identified a heightened risk of early adolescent delinquency in children with co-occurring conduct problems and head injuries by age 11, the third and final paper of this thesis

aimed to identifying potential neural mechanisms associated with their co-occurrence, which could potentially underly such maladaptive outcomes. Identification of these mechanisms are highly beneficial as they not only further our understanding of the characteristics of their co-occurrence but could potentially inform the creation of effective interventions to prevent future maladaptive outcomes from occurring.

The mechanism of interest in this thesis was reward processing, which has been implicated in child and adolescent delinquency. That is, delinquent youths have been shown to demonstrate a greater sensitivity to reward outcomes and are more reward-driven (Duell et al., 2023). Further, disruptions to reward-related brain regions during reward processing has been linked with both conduct disorder (Fairchild et al., 2019; Hawes et al., 2021; Rubia, 2011), mTBI (Cannella et al., 2019; Huang et al., 2019; Mayer et al., 2015), and antisocial behaviour (Hyde et al., 2013; Reyna et al., 2018).

The study found that children with a history of both mTBI and conduct disorder displayed significantly greater activation of the left amygdala and hippocampus during reward receipt compared to children with conduct disorder or mTBI only and typically developing youth. These brain regions are key structures within the mesolimbic dopamine pathway, which plays a central role in reward processing. This heightened activation suggests an increased sensitivity to receiving rewards and greater encoding of their emotional salience in this group. This could predispose these individuals to reward-seeking and goal-directed behaviours that stimulate further dopamine release such. Whilst not directly tested in this study, this could thus be a potential mechanism which drives increased rates of delinquent behaviour in children with co-occurring conduct problems and head injuries.

No significant findings were found during reward anticipation after applying FDR-corrections. Whilst some findings were significant prior to this correction, it is important to consider the trade-off between Type I and Type II errors. By applying FDR-corrections, it minimised the risk of incorrectly rejecting a true null hypothesis (Type I error or a false positive). Whilst this correction may increase the risk failing to detect a true effect (Type II error or a false negative), this trade-off was acceptable in the context of this study. Unlike fields such as medical diagnostics, where a Type II error could mean missing a critical diagnosis, the implications here were less severe. In this study, failing to identify all active regions did not pose significant harm to the research outcome, whereas a Type I error could have led to the development of interventions targeting brain regions that are not genuinely implicated. Therefore, prioritising the reduction of Type I error was more appropriate.

The ABCD dataset addressed key limitations of the MCS dataset by providing a detailed differentiation between mild and severe TBI and including clinical measures of conduct disorder. This differentiation allowed the study to focus specifically on children with mTBI and clinical diagnoses of

conduct disorder, rather than relying on broader measures of conduct problems that might only indicate subclinical behaviours and head injuries which could include those with a prolonged loss of consciousness. Consequently, the findings are more precise and aligned with the research objectives of this thesis, namely examining the interaction between non-severe TBIs and clinically diagnosed conduct disorder.

Despite its advantages, the use of the ABCD dataset introduced certain limitations, particularly regarding the generalizability of findings across the UK-based MCS dataset and the US-based ABCD dataset. Cultural and legislative differences between the UK and US may influence findings. For instance, head injury rates are higher in the US, partly due to greater participation in contact sports such as American football and ice hockey, as well as differences in sports-related legislation. In the US, contact sports like tackle football often lack clear age restrictions, whereas in the UK, tackling in rugby is prohibited until age 9. These variations could affect head injury rates and the applicability of findings between the two datasets. Future research should aim to validate the findings of this thesis by conducting primary studies on reward processing in a UK sample and delinquency outcomes in a US sample to evaluate cross-country applicability.

A further limitation relates to the age of the sample within the ABCD dataset. Data was used on children aged 9–10 and may not apply to those with adolescent-onset conduct problems or head injuries. Future research using later waves of the ABCD dataset could explore whether similar neural mechanisms are implicated in older populations. Additionally, the study's cross-sectional design restricts causal interpretation. Whilst the timeline of measures suggests that head injuries and conduct disorder precede the observed neural activation, longitudinal data would help clarify this causal relationship.

Whilst Paper 3 provides evidence of a potential mechanism that could lead to delinquency, analysis directly investigating this is needed. Future work should integrate later ABCD waves to confirm and extend these findings. For example, a mediation analysis could identify whether this reward-based neural processing mediates the relationship from co-occurring conduct disorder and head injury to subsequent delinquency. Nonetheless, these findings create a more detailed picture of the neural mechanisms associated with the co-occurring conduct disorder and mTBI.

5.5 Implications

This thesis comprises of three research papers which collectively provide novel evidence on the associations between childhood head injuries and conduct problems. These findings hold significant implications for research, policy, and clinical practice.

5.5.1 Research Implications

The findings highlight distinct longitudinal associations between childhood head injuries and conduct problems. As such, future research should account for this association as a potential confounder when investigating either condition independently. Failing to do so risks yielding incomplete or misleading conclusions. For example, studies investigating delinquency following head injury without considering the influence of conduct problems may inadvertently attribute outcomes to head injuries alone. This oversight could partially explain why previous studies have reported an association between head injuries and delinquency (Mongilio, 2022). Therefore, it is important that future research studies are mindful of this association and consider this within their analysis.

5.5.2 Policy implications

The findings from this thesis could have important implications for policy. In Paper 2, it was identified that their co-occurrence was associated with a greater rate of early adolescent delinquency and therefore it is important that we reduce their co-occurrence before adolescence. In Paper 1, it was shown that co-occurring conduct problems and head injuries were predicted by cumulative risk at various ecological levels including the household-level. This CRI included SES factors such as occupational status and household income. By reducing the number of SES risks within the household-level CRI, it could help prevent children entering a clinically relevant pathway of linked conduct problems and childhood head injuries and thus potentially reduce the rate of early adolescent delinquency. Such policy implications could include:

- **Expanding Flexible Working Options**: Providing parents from low-income households with more employment opportunities with flexible work arrangements could enhance their access to employment after having a child, improving household employment rates and increasing income. Although employees currently have the right to request flexible working arrangements including adjusted workdays, hours, or remote working, these options are more commonly available to higher-income, degree-educated, and professional employees (Office for National Statistics (ONS), 2023). To promote employment and financial stability across a wider range of households, policymakers should encourage broader access to flexible work arrangements. Whilst certain sectors, such as hospitality, retail, and care, may face greater challenges in implementing flexibility, efforts should be made to introduce adaptable working conditions wherever possible.
- **Promoting Access to Skills Training:** Government initiatives such as ‘Free Courses for Jobs’, which offer Level 3 (A-Level equivalent) qualifications in various sectors, could be actively promoted among parents in low-income households to support career development. Expanding access to flexible work, as suggested above, could also create greater

opportunities for parents to engage in such training programs, ultimately improving long-term employment prospects and household financial stability.

A further key insight from this thesis is that sustaining a mild head injury alone does not appear to significantly influence later delinquency. Consequently, policies aimed at preventing adolescent delinquency should not focus on preventing mild head injuries alone. Instead, policies should prioritise protecting children with conduct problems from sustaining a head injury, given their heightened vulnerability and vice versa. However, implementing such targeted policies poses challenges. For example, it would not be feasible or ethical to exclude children with conduct problems from participating in contact sports. Instead, policies could aim to improve monitoring, training, and care for these children to reduce their injury risk at home and in educational settings. This could include:

- **Enhancing Safety Regulations in Sports:** Contact sports are introduced in late childhood in the UK, with the Rugby Football Union allowing contact from age 7. Whilst under-9s experience controlled and minimal contact, policymakers should consider delaying full-contact play or continuing tag rugby until late childhood. This should allow those at a greater risk of sustaining a head injury (e.g., those with conduct disorder) the equal opportunity to engage in sports whilst preventing the negative outcomes associated with sustaining a head injury.
- **Promoting Awareness Campaigns:** Greater awareness of the risks associated with co-occurring conduct problems and head injuries is needed. Campaigns should target environments where affected children are likely to be present, such as schools, GP surgeries, Child and Adolescent Mental Health Services (CAMHS), and hospitals.
- **Reducing Staff-to-Child Ratios in Early Care Settings:** A lack of supervision can increase the risk of head injuries in young children, especially given their natural curiosity, mobility, and limited awareness of danger (Department for Education, 2024a, 2024b; Schnitzer et al., 2015). In the UK, childminders can care for up to six children under 8, with a maximum of three under 5 (Department for Education, 2024a), whilst group-based settings such as preschools are able to care for 13 children aged 3 and above for every staff member (Department for Education, 2024b). Lowering these ratios could improve the level of supervision to young children and reduce the opportunity for sustaining a head injury.

5.5.3 Clinical Implications

From a clinical perspective, this thesis highlights the importance of monitoring children who have sustained a head injury for an increased risk of conduct problems and vice versa. Importantly, this includes not only children who require hospital treatment for their head injuries but also those with

mild injuries that may not require extensive medical attention. Outpatient monitoring could focus on identifying emerging or worsening symptoms of conduct problems, as these may place children at greater risk for maladaptive outcomes, including delinquency. Clinicians could:

- Implement routine follow-ups for children with head injuries to assess behavioural changes over time.
- Collaborate with schools and families to identify early warning signs of conduct problems.
- Develop early intervention strategies to address conduct problems before they escalate.

In terms of those with conduct problems who are at a greater risk of head injury, clinicians responsible for diagnosing conduct disorder could also be educated on the increased risk of sustaining a head injury and routine assessment of head injury should be included as part of any conduct disorder assessment. Further, clinicians should liaise with schools and families to ensure a collective effort is made to reduce the risk of sustaining a head injury.

Failure to monitor and intervene could lead to significant costs for healthcare systems and social services, as well as poorer long-term outcomes for affected children. Early identification and intervention are therefore critical in mitigating these risks and ensuring better outcomes for children with co-occurring childhood head injuries and conduct problems.

5.6 Future Directions

This thesis provides novel evidence for the interplay between conduct problems and head injuries across development, laying the foundations for further research. However, this field of research is still in its infancy, and achieving a more comprehensive understanding will require additional investigation. Consistent with Popper's Falsification Theory, and in line with the postpositivist approach taken in this thesis, an explanation is simply the best explanation we currently have (Popper, 1963). As such, I urge for the research community to not simply accept the findings of this thesis but rather use them as a building block to deepen our knowledge of the association between conduct problems and childhood head injury. Below, I outline areas for future research, focusing on both clarifying and confirming the findings of this thesis and expanding upon them to deepen our understanding.

5.6.1 Clarifying Findings

Whilst this thesis investigates conduct problems broadly, it does not account for all variations of conduct disorder, such as the presence or absence of callous unemotional (CU) traits. CU traits involve deficits in recognising emotional expressions, reduced arousal to emotional stimuli, and a lack of empathy and guilt. Incorporating CU traits in conduct disorder research can often provide

valuable insight by teasing apart underlying mechanisms (Hawes et al., 2021; Zhang et al., 2023). However, CU traits were excluded in this thesis as they do not appear to mediate the direct relationship between head injury and conduct disorder (Khalaf et al., 2023) and are associated more so with genetically predisposed conduct disorder, whereas the focus of this thesis has been on environmental risk factors (Fairchild et al., 2019; Moore et al., 2019). Additionally, by subdividing conduct disorder groups further by CU traits, in combination with head injury status, further small groups would have been created which would result in reduced statistical power. Consequently, this thesis provides a broader overview of the association between conduct problems and head injury. However, I encourage future researchers to investigate the role of CU traits, particularly as a further factor which may contribute to the increased risk for subsequent delinquency (Simmons et al., 2020) and distinct reward-related neural mechanisms (Hawes et al., 2021) in those with co-occurring conduct problems and childhood head injuries. However, researchers must account for potential sample size limitations when examining these subgroups.

Another area that requires further clarification involves the broader role of injury when co-occurring alongside conduct problems. Whilst existing research suggests head injuries, not orthopaedic injuries, are associated with conduct problems and (Khalaf et al., 2023) predict delinquency outcomes (Mongilio, 2022), it remains possible that outcomes following co-occurring conduct problems and head injury such as increased rates of delinquency may result from the general effects of injury amplifying existing conduct problem symptoms rather than a head injury specifically. Future studies should explicitly test whether the findings of this thesis are specific to head injuries or extend to other types of injuries.

Finally, this thesis accounted only for maternal parenting. Whilst maternal influences are important, future research should also consider the role of paternal parenting. Paternal involvement, parenting styles, and potential psychopathology may uniquely contribute to both conduct problems and the risk of head injury. Examining both maternal and paternal influences would provide a more comprehensive understanding of the familial and environmental factors that contribute to these developmental outcomes.

5.6.2 Expanding Findings

This thesis produces novel findings that highlight the association between conduct problems and head injuries. There are thus key opportunities to expand upon its results. Three primary areas which warrant further investigation include:

1. **Identifying Underlying Bidirectional Mechanisms**

Future research should explore the underlying mechanisms that mediate the bidirectional association between conduct problems and head injuries. Research has begun to explore such mechanisms from childhood head injury to conduct problems. For example, Khalaf and colleagues (2023) have highlighted that impulsivity but not CU traits is a potential mediator through which head injuries increase the risk of conduct problems (Khalaf et al., 2023). However, there remains a gap in understanding how conduct problems increase the risk of sustaining head injuries and an investigation of the two in a single model.

2. **Further Exploration of Reward Processing**

   Whilst Paper 3 highlights reward processing as a potential mechanism linking co-occurring head injuries and conduct problems to delinquency, the direct connection to delinquency needs further investigation. Future studies should determine whether reward-related neural activation indeed contributes to increased delinquency or whether other mechanisms, such as impulsivity or emotional regulation, play a more significant role.

   Additionally, as the findings from Paper 3 are based on a cross-sectional design, longitudinal studies that track changes in reward-related neural activation over time are needed to establish causality and examine how these changes influence delinquent behaviour.

   Moreover, future research should also consider how reward processing interacts with other neural, cognitive, and emotional mechanisms, potentially contributing to a more holistic understanding of the pathways from co-occurring conduct problems and head injuries to maladaptive outcomes.

3. **The Role of Genetics**

   It was out of the scope of this thesis to consider the role of genetics, despite the moderate heritability of conduct disorder. This genetic predisposition suggests that parents may also exhibit traits of conduct disorder, which could influence the child's risk for developing conduct problems both through genetic transmission and the environment the diagnosed parent creates (Jaffee et al., 2006). Such an environment may be characterised by inconsistent discipline, reduced emotional warmth, or increased exposure to conflict, all of which are known risk factors for the development of conduct problems (Fairchild et al., 2019) and could also increase the risk for sustain a head injury. Future research may thus dive deeper into investigating the role of the parent and their influence on the co-occurrence of conduct problems and childhood head injuries via not only their environment but genetics.

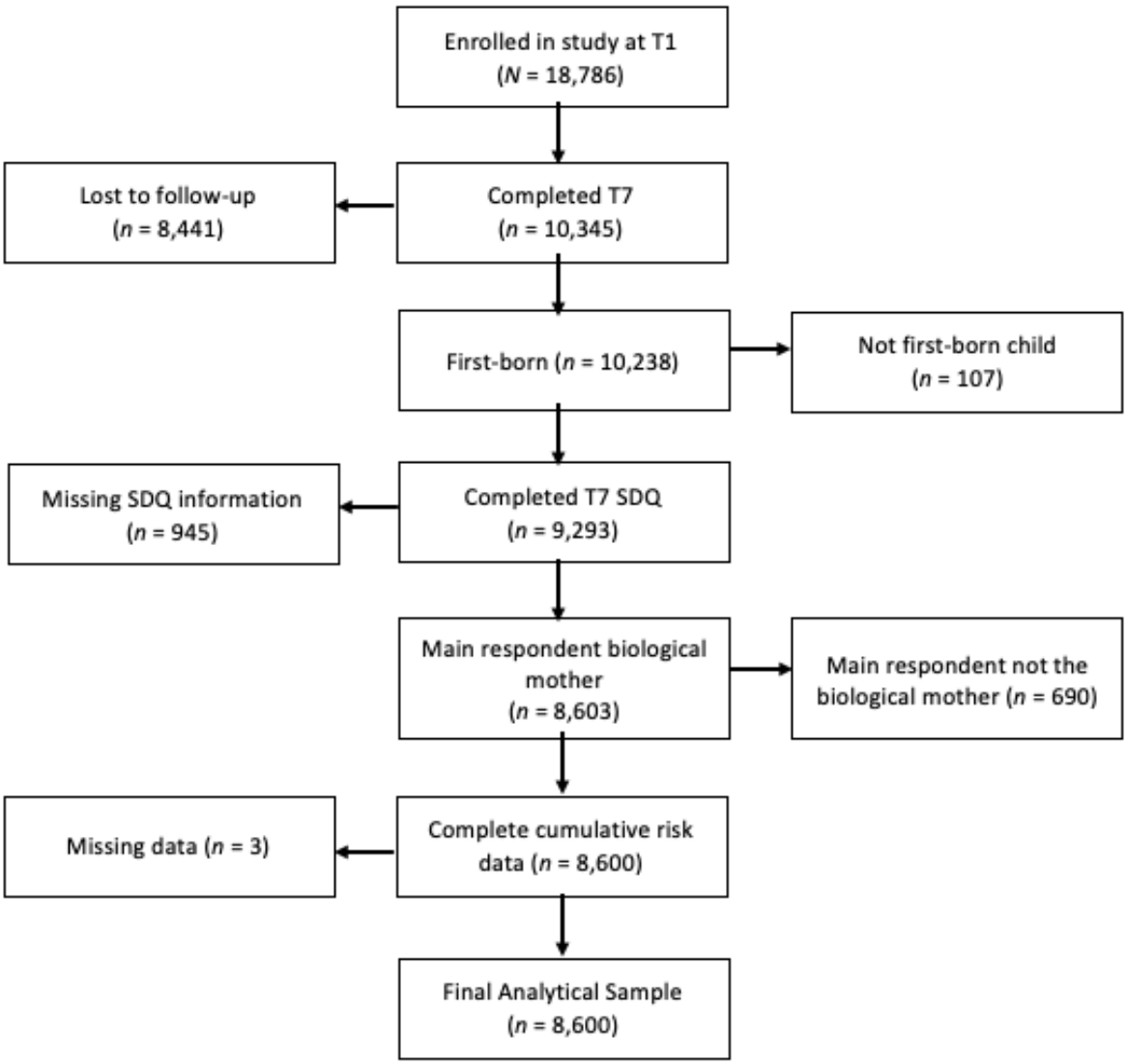
5.7 Concluding Statement

In sum, this thesis represents a significant step forward in understanding the complex relationship between conduct problems and head injuries. Importantly, it shows how conduct problems and head injuries link across development, their increased risk for maladaptive outcomes, and their distinct reward-related neural profile. These findings underscore the importance of considering the co-occurrence of these conditions in both research and practice. Nevertheless, substantial gaps remain to be explored. By addressing the future directions outlined above, researchers can build on this foundation to clarify, expand, and refine our understanding of these complex relationships, ultimately paving the way for more effective prevention and intervention strategies.

Appendix A A Note on the Exclusion Criteria

Exclusions were made to those who were not first-born children to allow for independence of observation (Grawitch & Munz, 2004) and to remove the potential of child-order effects. That is, there appears to be different levels of aggression related schemas in first, second, and third children (Ardebili & Golshani, 2016), as well as higher risks of injuries in first-born children (Honda et al., 2020), which could influence the levels of conduct problem and head injuries highlighted in this study. Further exclusions were made to those whose main respondent in the study was not their biological mother. This exclusion was made because risk factors such as mother to child attachment were measured only for the biological mother. If we did not include this exclusion a proportion of the sample would not have available data for all risk factors at the mother-level. Finally, exclusions were made to those who did not have complete CRI data. As the CRIs were created prior to analysis in Mplus, the missing data method (FIML) could not account for specific missingness a-priori.

Appendix B A Flow Chart of the Total Analytical Sample



Note. This figure shows the exclusions made for the current study. It shows the number of participants excluded from the original total sample of *N* = 18,786 at timepoint 1 (T1) resulting in the final analytical sample of *n* = 8,600.

Appendix C Model Fit Indices Guiding Optimum Number of Classes

The BIC (Schwarz, 1978) and AIC (Akaike, 1987) were used to examine model fit. The BIC and AIC assess a model's ability to minimize variation within each class whilst maximizing variation between classes (Vermunt & Magidson, 2002). Lower BIC and AIC indices indicate a better fitting model (Collins & Lanza, 2009; Connell et al., 2009). Though there is not a defined guide on how to compare model fit, the BIC has been argued to be the most important factor to consider when comparing model fit and is widely used in LCA research (de Vries et al., 2022; Hamilton et al., 2021; Ma et al., 2022). However, it is not uncommon for the BIC to continue to decrease in size as more classes are introduced, therefore, it is critical to compare model fit indices alongside interpretability of classes produced (Weller et al., 2020).

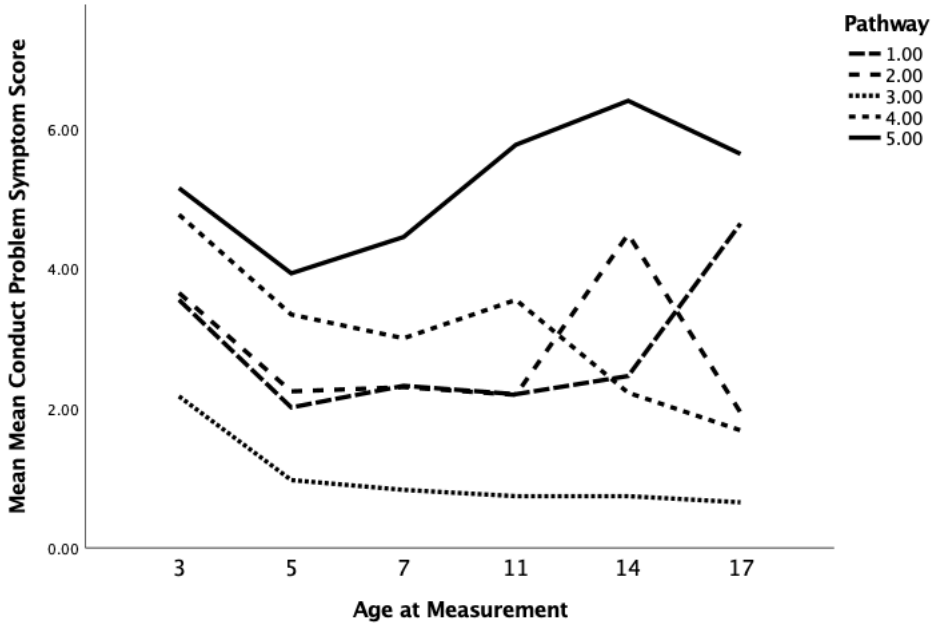
The entropy is a summary statistic. It identifies how accurately the model can define its classes. It can range from 0–1, with a score closer to 1 suggesting better classification; a value of .80 and above is considered acceptable (Clark & Muthén, 2009).

Appendix D Post-Hoc Analysis: Negative Parenting Styles

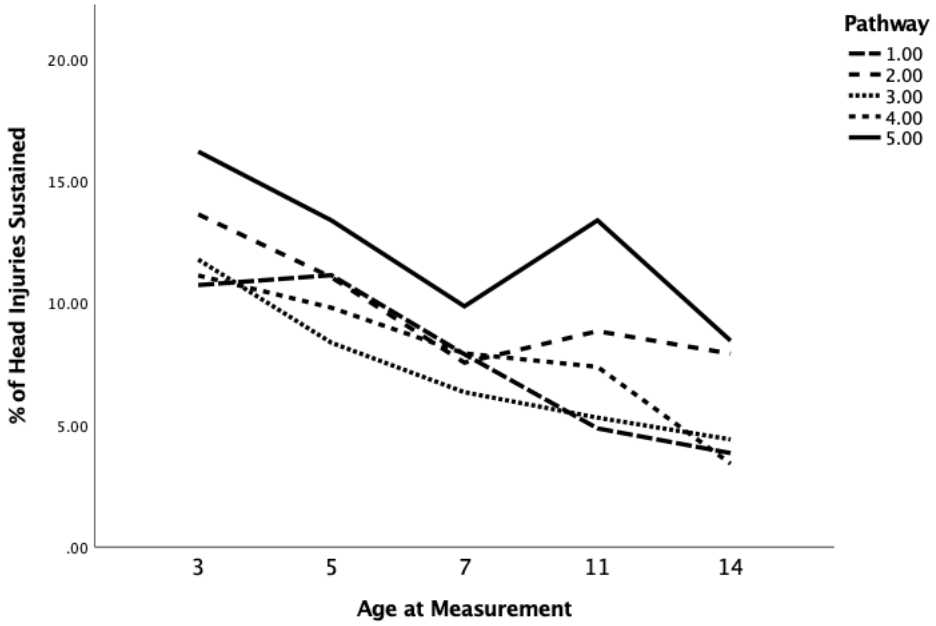
This study aimed to investigate if harsh parenting and withdrawal tactics were associated with group membership. Both have been previously associated with conduct problems (Hukkelberg & Ogden, 2021; Kingsbury et al., 2020; Speyer et al., 2022) and a greater risk of sustaining a head injury (Schnitzer et al., 2015). These were investigated at age 5 for two reasons: 1) there is limited research on the association between withdrawal tactics and conduct problems but of the available research, it suggests that a direct effect is evident from withdrawal tactics at age 5 to conduct problems at age 7 but not from age 3 (Speyer et al., 2022), and 2) as can be seen in Figure 2, the first timepoint where we can start to differentiate between the direction of conduct problems in each pathway is at age 5. Therefore, to tease this apart we decided to investigate how negative parenting at age 5 may be associated with these pathways.

Appendix E A Figure of the 5-class Solution

a) Conduct Problems



b) Head Injuries

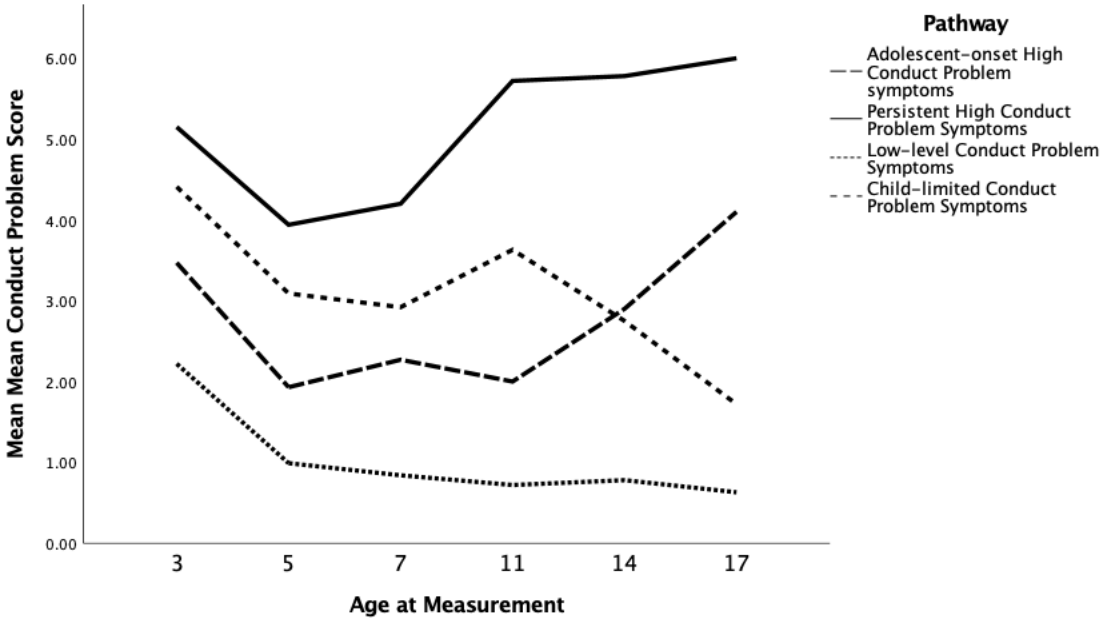


Note. This figure shows the linked pathways of a) conduct problems and b) head injuries within the 5-class solution. As can be seen, similarly to the 4-class solution, there appears to be a low-level pathway (3) and three pathways characteristic of the "clinically-relevant" forms of conduct problems: an adolescent-onset (1), child-limited (4), and persistent pathway (5). However, there is an additional pathway which appears to

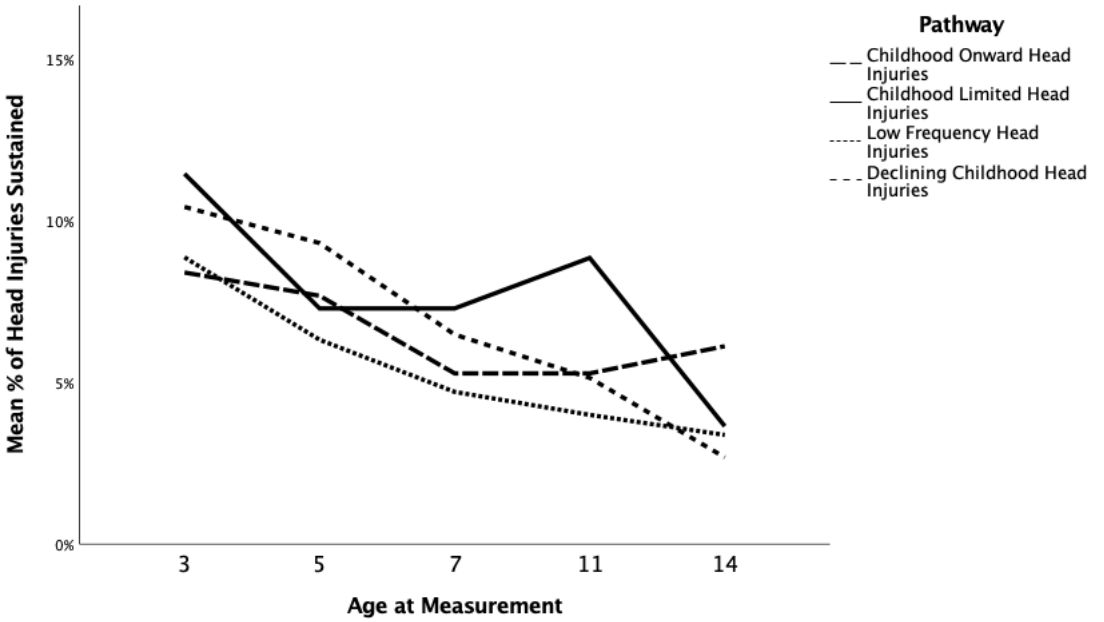
show a single spike in high conduct problem levels at age 14 linked with similarly higher levels of head injuries compared to the other pathways around this time (except for the persistent pathway). Whilst conduct problem symptoms remain somewhat interpretable alongside the previous literature; it seems unusual for two separate adolescent pathways to be present. Further, their linked head injury pathways do not make as much theoretical sense in comparison to the 4-class solution. For example, in the 4-class solution (Figure 1) the child-limited pathway is characterised by high conduct problem symptoms during early childhood as well as the highest rates of early head injuries (except for the other pathway with high conduct problems at that period: the persistent pathway). In the 5-class solution, this is not the case, and the child-limited pathway shows similar levels to the stable and adolescent-onset pathway. In fact, the head injury rates associated with pathway 2 do not as well fit the timings of high conduct problems that is so well documented in the 4-class solution and makes more theoretical sense regarding the association between the two.

Appendix F A Figure of the 4-class Solution Conducted in a Whole Sample Analysis.

a) Conduct Problem Symptoms



b) Head Injury Frequency



Note. This figure shows the 4-class solution of conduct problem symptoms (a), and head injures (b) pathways across development when no exclusion criteria were applied. Figure 2a shows the same four conduct problems symptom pathways as when relevant exclusion criteria were applied. These are: low-level, persistent high, childhood-limited, and adolescent-onset high conduct problem symptoms. Figure 2b

show similar pathways of head injuries as when relevant exclusion criteria were applied. These are: low frequency, childhood onward, childhood limited, and declining head injuries.

Appendix G Supplementary Group Classifications

There are different trajectories or sub-types of conduct problems (Gutman et al., 2019), even when accounting for their association with head injury (Carr, Brandt, et al., 2024). These sub-types include a childhood-limited (symptoms present only in early childhood, i.e., < 11 years old), persistent (present across childhood and into adolescence), and adolescent-onset (present from age 11 onwards). However, a recent meta-analysis suggests that whilst persistent and adolescent-onset conduct problems are significant predictors of later delinquency, earlier levels of conduct problems (i.e., childhood-limited) show weak or non-significant associations (Bevilacqua et al., 2018). Thus, whilst our age 14 analyses consider conduct problem symptoms across development, we have limited our group classifications to conduct problem symptoms measured at ages 11 or 14 only for age 17 delinquency.

We created further supplementary groups, which aimed to replicate previously identified associations between delinquency and conduct problem symptoms or head injuries separately (i.e., without taking the presence of the other into consideration; Hammerton et al., 2019; Hopfer et al., 2013; Mongilio, 2022; Picoito et al., 2021).

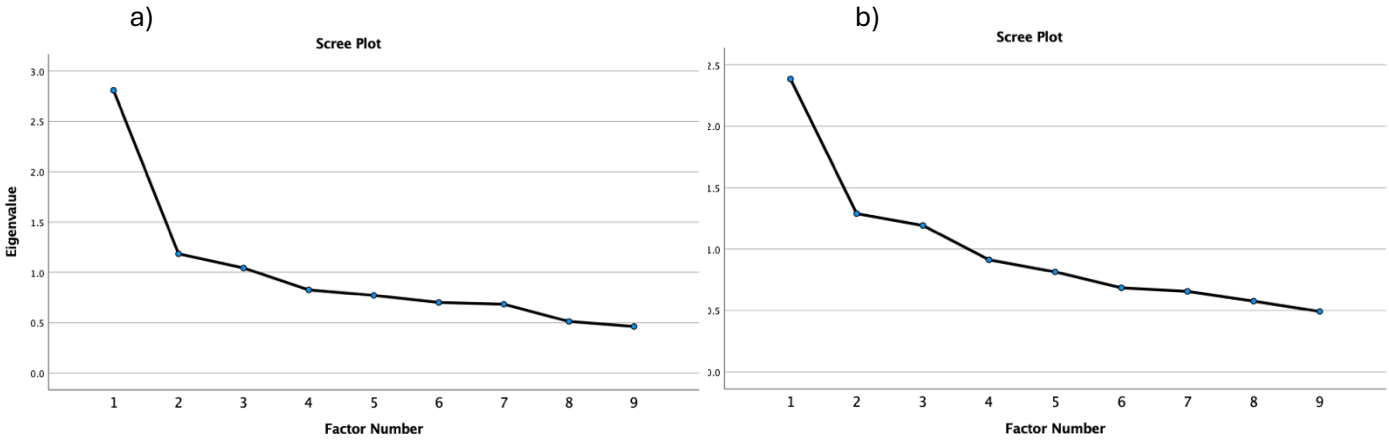
We further specified a head injury group consisting of those who sustained a head injury with a loss of consciousness only. As this is a much smaller subsample, we had to compare this group to a random subsample as opposed to the entire MCS population without a history of head injury.

Appendix H Exploratory Factor Analysis of Delinquency Items

Whilst the three chosen sub-categories of delinquency were guided by previous literature (Jackson, Testa, et al., 2022; Picoito et al., 2021), an exploratory factor analysis with a direct oblimin rotation was computed to ensure that these categories were appropriate. The scree plots below show that a 3–factor solution was the most appropriate at ages 14 and 17 (Figure S1). Results of this solution are further shown in the pattern matrices below (Table S1).

Figure S1

Scree Plots Highlighting the Appropriate Number of Factors from an Exploratory Factor Analysis for Delinquency at a) 14 and b) 17 Years



Note. This figure highlights the scree plots produced from a factor analysis of the delinquency items at ages (a) 14 and (b) 17. They show that at both ages, a 3-factor solution appears to be appropriate.

Table S1

Pattern Matrix of the Factor Loadings for an Exploratory Factor Analysis with a Three-factor Solution at Ages 14 and 17

	Factor loading (age 14)			Factor loading (age 17)		
Delinquency item	1	2	3	1	2	3
Factor 1: Substance use						
Ever smoked cigarettes?	**.69**	-.02	.004	.61	.04	.06
Ever tried cannabis?	**.79**	-.004	-.03	.77	.01	.02
Had more than five alcoholic drinks at one time [a]	**.41**	.07	.09	.53	-.02	-.01
Factor 2: Antisocial Behaviour						
Stolen something from someone…[a]	-.04	**.32**	-.01	.02	**.30**	-.01
Taken something from a shop without paying…[a]	.15	**.41**	-.02	-.10	**.51**	-.03
Written things or spray painted…[a]	.01	**.57**	-.01	.002	**.53**	.01
Damaged something in a public place…[a]	.04	**.50**	.12	.03	**.67**	.04
Factor 3: Crime						
Ever been stopped or questioned by police?	-.01	.03	**.73**	-.04	.001	**.67**
Ever been given a formal warning or caution from police?	.02	-.02	**.65**	.02	-.001	**.67**

[a] In the last 12 months.

Appendix I Details of Study Covariates

Prenatal covariates included low birth weight (< 2.5kg; Reijneveld et al., 2006; Whiteside-Mansell et al., 2009), premature birth (<= 252 days; Reijneveld et al., 2006; Whiteside-Mansell et al., 2009), and mother smoking and drinking during pregnancy (Van Adrichem et al., 2020).

SES covariates included parental education level (not achieved a high school diploma/GCSE's; Trentacosta et al., 2008; Van Adrichem et al., 2020), parental occupation status (semi-skilled or less; Greitemeyer & Sagioglou, 2016), single parent household (Northerner et al., 2016; Trentacosta et al., 2008), low household income (below 60% median poverty indicator; Northerner et al., 2016; Trentacosta et al., 2008), and teenage pregnancy (< 18 years-old; Trentacosta et al., 2008).

Negative parenting styles were measured using Straus's Conflict Tactic Scale at T2 (Straus et al., 1998) and encompasses harsh parenting (smacking, shouting at, or telling off the child) and parental withdrawal tactics (ignoring child, sending them to their room, and taking away their toys). All items were measured on a 5-point Likert scale to ascertain the frequency of the behaviours from 1 (*never*) to 5 (*daily*) and were summed to create an overall harsh parenting (range 3–15) and an overall withdrawal tactics score (range 3–15). A higher scored indicated harsher parenting or greater use of withdrawal tactics.

ADHD was measured by parent-reports of an ADHD diagnosis for their child. This was asked from T3–T6 (age 5–14) and was summarized via a binary variable (0 [*no diagnosis*], 1 [*ADHD diagnosis*]).

Appendix J Adolescent Cumulative Delinquency at Age 14 Predicted by Childhood Conduct Problems, a Bang to the Head, or a Loss of Consciousness during ages 3 to 11

	Overall delinquency	Substance use	Crime	Antisocial behaviour
	IRR [95% CI]	*IRR* [95% CI]	*IRR* [95% CI]	*IRR* [95% CI]
HI vs no HI	**1.19* [1.06–1.34]**	**1.28* [1.08–1.50]**	1.07 [0.94–1.21]	1.19 [0.97–1.46]
LoC vs no HI [a]	**2.04* [1.25–3.31]**	**4.27** [1.80–10.15]**	1.70 [0.85–3.42]	1.10 [0.51–2.37]
CP vs no CP	**1.35** [1.18–1.55]**	**1.37* [1.14–1.65]**	**1.44** [1.25–1.67]**	1.21 [0.96–1.52]

Note. X vs Y, Y is the reference group. IRR = incidence rate ratio; HI = head injury (a bang to the head with or without a loss of consciousness); LoC = loss of consciousness; CP = conduct problem symptoms.

[a] When using a random subsample of those without a history of head injury

*p<.05

**p<.001

Appendix K Adolescent Cumulative Delinquency at Age 17 Predicted by Childhood Conduct Problems from ages 11 and 14, or a Bang to the Head or a Loss of Consciousness during ages 3 to 14

	Overall delinquency	Substance use	Crime	Antisocial behaviour
	IRR [95% CI]	*IRR* [95% CI]	*IRR* [95% CI]	*IRR* [95% CI]
HI vs no HI	1.06 [0.97–1.16]	1.06 [0.97–1.16]	1.20 [0.94–1.52]	0.98 [0.79–1.22]
LoC vs no HI	1.12 [0.88–1.42]	1.10 [0.87–1.38]	1.88 [0.90–3.89]	1.48 [0.60–3.64]
CP vs no CP	**1.24* [1.07–1.45]**	**1.20* [1.03–1.39]**	1.09 [0.71–1.67]	**1.65* [1.12–2.44]**

Note. X vs Y, Y is the reference group. IRR = incidence rate ratio; HI = head injury (a bang to the head with or without a loss of consciousness); LoC = loss of consciousness; CP = conduct problem symptoms.

*p<.05

**p<.001

Appendix L Addition of IQ as a Covariate

Whilst the study included relevant covariates appropriate when investigating children with conduct disorder and/or mTBI and reward processing, IQ is a further factor generally considered when conducting neuroimaging analyses in children with conduct disorder (Fairchild et al., 2019). Although direct measures of IQ were not available in the ABCD study, the NIH Toolbox Cognition Battery (NIHTB-CB) was included and provides validated fluid and crystalised composite scores that can serve as proxies for IQ (Heaton et al., 2014), which have been used in the literature as IQ substitutes (e.g., Bernanke et al., 2022; Zhao et al., 2022). The NIHTB-CB includes seven tasks aimed at assessing attention, memory, processing speed, vocabulary, and cognitive flexibility. A detailed overview of the battery can be found elsewhere (Luciana et al., 2018). The crystalised composite score is derived from scores obtained on the Picture Vocabulary Test and Oral Reading Recognition Test whilst the fluid composite score is derived from scores obtained on the Flanker, List Sorting Working Memory Test, Dimensional Change Card Sort, Pattern Comparison Processing Speed, and Picture Sequence Memory Test.

As can be seen below in Tables S2 and S3, adding these proxies for IQ as covariates within the model (as well as the already controlled for covariates, see Section 4.3.2.4), does not seem to drastically change the results. After applying an FDR-correction, the same ROIs remain significant with the odd ratios generally becoming slightly larger.

Table S2. Multinomial Regression Model Results Comparing Activation During Reward Anticipation across Groups, Including IQ as a Covariate

	Group comparisons					
	CD vs TD	**mTBI vs TD**	**mTBI+CD vs TD**	**mTBI+CD vs CD**	**mTBI+CD vs mTBI**	**CD vs mTBI**
ROI	***OR* [95% CI]**	***OR* [95% CI]**	***OR* [95% CI]**	***OR* [95% CI]**	***OR* [95% CI]**	***OR* [95% CI]**
Left hemisphere						
Amygdala	1.13 [0.72–1.80]	1.37 [0.91–2.06]	1.02 [.60–1.73]	0.90 [0.60–1.41]	0.74 [0.46–1.20]	0.83 [0.55–1.25]
NAc	1.10 [0.70–1.70]	1.26 [0.90–1.78]	1.94 [1.11–3.41]	1.78 [1.06–2.96]	1.54 [0.91–2.59]	0.87 [0.59–1.27]
Caudal ACC	1.33 [0.76–2.35]	1.51 [0.97–2.37]	2.45 [1.26–4.79]	1.84 [1.04–3.25]	1.62 [0.87–3.03]	0.88 [0.53–1.47]
Rostral ACC	1.39[0.77–2.51]	1.36 [0.96–1.93]	2.31 [1.27–4.21]	1.66 [0.93–2.98]	1.69 [0.98–2.93]	1.02 [0.61–1.70]
Medial OFC	1.01 [0.78–1.32]	0.98 [0.82–1.16]	1.39 [1.00–1.94]	1.37 [1.01–1.86]	1.43 [1.04–1.95]	1.04 [0.82–1.32]
Hippocampus	1.13 [0.58–2.18]	1.47 [0.86–2.52]	1.18 [0.52–2.69]	1.05 [0.50–2.23]	0.80 [0.37–1.73]	0.77 [0.42–1.39]
Thalamus	1.49 [0.76–2.93]	1.72 [0.99–2.97]	2.04 [0.90–4.65]	1.37 [0.64–2.91]	1.19 [0.56–2.55]	0.87 [0.48–1.58]
Insula	1.24 [0.58–2.66]	1.41 [0.81–2.46]	1.98 [0.80–4.92]	1.60 [0.70–3.65]	1.40 [0.59–3.30]	0.88 [0.44–1.75]
Right hemisphere						
Amygdala	1.08 [0.66–1.78]	1.33 [0.88–2.02]	1.03 [0.57–1.84]	0.95 [0.57–1.60]	0.77 [0.46–1.31]	0.81 [0.53–1.25]

NAc	1.07 [0.69–1.66]	1.14 [0.83–1.56]	1.83 [1.05–3.19]	1.71 [1.02–2.87]	1.60 [0.96–2.68]	0.94 [0.64–1.38]
Caudal ACC	1.12 [0.62–2.01]	1.13 [0.71–1.78]	1.79 [0.89–3.58]	1.59 [0.83–3.05]	1.59 [0.83–3.03]	1.00 [0.59–1.68]
Rostral ACC	1.16 [0.69–1.96]	1.04 [0.70–1.53]	2.14 [1.14–4.05]	1.85 [1.01–3.39]	2.07 [1.14–3.77]	1.12 [0.70–1.79]
Medial OFC	0.89 [0.69–1.17]	0.93 [0.77–1.12]	1.27 [0.88–1.82]	1.42 [1.02–1.96]	1.37 [0.97–1.92]	0.97 [0.77–1.21]
Hippocampus	0.94 [0.46–1.92]	1.59 [0.95–2.68]	1.14 [0.48–2.69]	1.21 [0.54–2.71]	0.71 [0.32–1.60]	0.59 [0.31–1.10]
Thalamus	1.41 [0.69–2.85]	1.63 [0.97–2.76]	2.15 [0.88–5.24]	1.53 [0.67–3.48]	1.31 [0.57–3.01]	0.86 [0.46–1.60]
Insula	1.01 [0.50–2.04]	1.24 [0.74–2.07]	1.92 [0.81–4.55]	1.90 [0.87–4.17]	1.55 [0.69–3.50]	0.82 [0.44–1.53]

Note. This model includes all of the original covariates (sex, ethnicity, age, ADHD, internalizing problems, low birth weight, premature birth, smoking or alcohol consumption during pregnancy, low parental education, low household income, and family conflict as a covariate) as well as IQ. CD = conduct disorder only; TD = typically developing controls; mTBI = mild traumatic brain injury only; mTBI+CD = co-occurring mild traumatic brain injury and conduct disorder; OR = odds ratio; NAc = nucleus accumbens; ACC = anterior cingulate cortex; OFC = orbitofrontal cortex.

Table S3. Multinomial Regression Model Results Comparing Activation During Reward Receipt across Groups, Including IQ as a Covariate

	Group comparisons					
	CD vs TD	mTBI vs TD	mTBI+CD vs TD	mTBI+CD vs CD	mTBI+CD vs mTBI	CD vs mTBI
ROI	***OR* [95% CI]**	***OR* [95% CI]**	***OR* [95% CI]**	***OR* [95% CI]**	***OR* [95% CI]**	***OR* [95% CI]**
Left hemisphere						
Amygdala	1.05 [0.70–1.56]	0.87 [0.63–1.22]	2.23 [1.32–3.78]*	2.14 [1.30–3.52]*	2.65 [1.53–4.29]*	1.20 [0.81–1.77]
NAc	1.28 [0.91–1.81]	1.07 [0.81–1.43]	1.57 [0.97–2.52]	1.22 [0.79–1.89]	1.46 [0.92–2.30]	1.20 [0.87–1.63]
Caudal ACC	1.38 [0.85–2.23]	1.27 [0.86–1.89]	2.49 [1.27–4.90]	1.81 [0.97–3.36]	1.96 [1.00–3.84]	1.09 [0.68–1.73]
Rostral ACC	1.38 [0.91–2.09]	1.19 [0.84–1.69]	1.72 [1.03–2.88]	1.25 [0.78–2.00]	1.44 [0.79–1.70]	1.15 [0.88–2.36]
Medial OFC	1.30 [1.02–1.65]	1.20 [1.00–1.45]	1.47 [1.10–1.98]	1.14 [0.88–1.47]	1.22 [0.93–1.61]	1.08 [0.86–1.34]
Hippocampus	1.64 [0.95–2.85]	1.15 [0.73–1.80]	4.24 [2.09–8.60]*	2.58 [1.39–4.80]*	3.69 [1.86–7.33]*	1.43 [0.85–2.41]
Thalamus	1.26 [0.72–2.22]	1.12 [0.72–1.73]	2.16 [0.9– 5.13]	1.71 [0.77–3.77]	1.93 [0.83–4.49]	1.13 [0.67–1.90]
Insula	1.28 [0.71–2.29]	1.08 [0.67–1.73]	2.62 [1.22–5.62]	2.05 [1.01–4.16]	2.43 [1.18–5.02]	1.19 [0.70–2.01]
Right hemisphere						

Amygdala	1.19 [0.81–1.76]	0.88 [0.64–1.22]	1.54 [0.94–2.52]	1.29 [0.82–2.05]	1.75 [1.07–2.88]	1.35 [0.92–2.00]
NAc	1.17 [0.82–1.65]	0.90 [0.66–1.21]	1.39 [0.82–2.36]	1.19 [0.74–1.90]	1.55 [0.92–2.61]	1.30 [0.93–1.83]
Caudal ACC	1.30 [0.79–2.12]	1.10 [0.74–1.64]	2.40 [1.29–4.48]	1.85 [1.04–3.30]	2.18 [1.18–4.01]	1.18 [0.73–1.88]
Rostral ACC	1.63 [1.07–2.47]	1.36 [0.96–1.93]	1.73 [1.05–2.86]	1.07 [0.68–1.66]	1.27 [0.78–2.08]	1.19 [0.79–1.79]
Medial OFC	1.35 [1.05–1.74]	1.19 [0.98–1.46]	1.49 [1.09–2.05]	1.11 [0.86–1.43]	1.25 [0.93–1.69]	1.13 [0.90–1.42]
Hippocampus	1.65 [0.91–3.01]	1.28 [0.79–2.10]	3.17 [1.57–6.38]*	1.92 [1.13–3.27]	2.47 [1.32–4.62]*	1.29 [0.76–2.17]
Thalamus	1.39 [0.83–2.33]	1.35 [0.89–2.07]	3.00 [1.45–6.18]*	2.15 [1.10–4.22]	2.21 [1.07–4.56]	1.03 [0.62–1.69]
Insula	1.10 [0.60–2.02]	1.09 [0.69–1.73]	1.63 [0.72–3.69]	1.48 [0.70–3.11]	1.49 [0.68–3.28]	1.01 [0.58–1.76]

Note. This model includes all of the original covariates (sex, ethnicity, age, ADHD, internalizing problems, low birth weight, premature birth, smoking or alcohol consumption during pregnancy, low parental education, low household income, and family conflict as a covariate) as well as IQ. CD = conduct disorder only; TD = typically developing controls; mTBI = mild traumatic brain injury only; mTBI+CD = co-occurring mild traumatic brain injury and conduct disorder; OR = odds ratio; NAc = nucleus accumbens; ACC = anterior cingulate cortex; OFC = orbitofrontal cortex.

*p <.05 (FDR-corrected)

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