Scottish Sentencing Council

The development of cognitive and emotional maturity in adolescents and its relevance in judicial contexts

Literature Review

Submitted to the Scottish Sentencing Council in January 2020

Published February 2020

Authors: Suzanne O'Rourke; Heather Whalley; Sarah Janes; Niamh MacSweeney; Asaly Skrenes; Suzy Crowson; Laura MacLean; Matthias Schwannauer[1]

[1] corresponding author: Matthias Schwannauer PhD, Professor of Clinical Psychology, School of Health in Social Sciences, The University of Edinburgh, Teviot Place, Edinburgh, EH8 9AG; Email: M.Schwannauer@ed.ac.uk

www.scottishsentencingcouncil.org.uk
sentencingcouncil@scotcourts.gov.uk

The Scottish Sentencing Council

The development of cognitive and emotional maturity in adolescents and its relevance in judicial contexts

January 2020

THE UNIVERSITY *of* EDINBURGH

Table of Contents

1. Executive Summary

This report provides a synthesis and evaluation of the current neurobiological, neuropsychological and psychological literature on adolescent cognitive maturation. Using an 'umbrella review' methodology, systematic reviews, meta-analyses, and narrative reviews were collated, critically assessed, and then synthesized to provide robust findings and interpretations of the data as it applies to cognitive maturation and juvenile sentencing.

During adolescence and within normal individual development, an imbalanced growth pattern is observed between the brain regions governing emotion and mood, like the amygdala, and those involved in executive functions (those that provide the cognitive abilities which are necessary for prosocial behaviour, successful goal planning and achievement), like the prefrontal cortex. Converging findings suggest that this latter brain region is the last to reach maturity, leaving adolescents with immature and compromised core cognitive abilities for much of this developmental period. This immaturity, when coupled with the increased motivation to achieve rewards observed to coincide with puberty, is thought to be the most likely underlying mechanism contributing to the poor problem solving, poor information processing, poor decision making and risk-taking behaviours often considered to typify adolescence. Evidence suggests that the influence, or presence, of peers further exacerbates these tendencies.

In addition to these normative trajectories of adolescent neurocognitive development, cognitive maturation may be hindered or compromised by several factors including traumatic brain injury, alcohol and substance use, psychiatric and neurodevelopmental disorders and adverse childhood experiences, all of which have the potential to inhibit and disrupt typical development. Notably, adolescent cognitive maturation varies between individuals, and will not be the same for every individual, particularly when impacted upon by the environmental factors listed. Thus, the nature of adolescent cognitive development is not a process that allows us to specify an exact age at which cognitive maturity is definitively reached at an individual level. While we do not therefore recommend the use of stringent age ranges in sentencing guidelines, it is however recommended that the brain's continued growth, until as late as 25-30 years of age, and the resulting cognitive immaturity, is considered during judicial processes involving adolescents and young people.

2. Introduction

The continued maturation of the brain during adolescence has been the subject of research across several modalities in both humans and animals. With increasingly sophisticated brain imaging methods, neurological researchers can now visualise the brain's functioning in real time, enabling them to test hypotheses directly, and draw conclusions that are both novel and robust. Findings from neurological research, typically focused on neural anatomy, pathways and activation, are now informing psychological questions and providing additional means by which they can be tested. Neurological research has helped to reveal the structural and functional[1] changes that the brain undergoes during its development, and psychological and neuropsychological research has evidenced how these changes occur in parallel with the behaviours that might be considered typical during adolescence. Taken together, neurological, psychological, and neuropsychological research creates a complex and multi-level understanding of cognitive development, highlighting how even small changes that occur deep inside the brain can vastly impact human behaviour.

2.1 Adolescent Development

Adolescence is a time of increasing independence and exploration, but one often characterised by poor decisions and impaired problem solving. Definitions of adolescence vary with researchers having historically relied on factors such as age, puberty, and sexual maturation, with acknowledgment that there are individual differences within the developmental trajectory. For the purpose of this review, adolescence will be defined as the 'gradual transition from childhood to adulthood' (1,2). Adolescence can be considered to begin with the onset of puberty which occurs slightly earlier in females, at approximately 10-17 years, than males, at approximately 12-18 years (3). Puberty heralds hormonal changes, a period of increased growth and alterations in the body that continue throughout adolescence (4). Importantly, it brings with it dramatic structural and functional changes in the adolescent brain.

Neurological literature has referred to the adolescent brain as being 'under construction' until early adulthood (5). Between childhood and adulthood, albeit with regional variation, white matter

[1] Across the academic fields consulted in this review the term 'functional' is used in three ways, namely: (a) In the neuroanatomical / neuroimaging literature functional denotes regional brain activation measured as an increase in blood flow; (b) In the neurocognitive literature functional can refer to those cognitive abilities required for age appropriate daily and social functioning; and (c) functional is also used to denote behaviours and interactions that are appropriate for a given context or purpose

volume is observed to gradually increase while cortical grey matter reduces in volume while increasing in density as a result of the 'pruning' of those brain connections that are no longer required (6). Strengthening and building of regional neurocircuitry and pathways also occurs during adolescence, aiding in the development of brain regions which underlie essential cognitive abilities (5). Neuronal changes also emerge during this time through a process called 'plasticity'. Plasticity is essential to brain development and is the occurrence of significant neuronal changes during which new skills are acquired (7). While this process allows adolescents to become more adaptive and permits learning, it also increases vulnerability given the limited or disparate cognitive resources available in this period.

During adolescence, the brain undergoes structural and functional changes that translate into a number of 'stereotypical behaviours' for which adolescents are known. Advances in research have evidenced that, for example, adolescent risk-taking behaviours and poor decision making may not be intrinsically motivated, but instead may be due to the increased activation or underdevelopment of specific brain regions. Specifically, that those regions associated with emotions and rewards become increasingly active at a time when the brain's control centre, the prefrontal cortex, remains unable to deploy the skills required for weighing complex decisions and regulating behavioural and emotional responses (e.g. (5,8,9)). Models therefore suggest that risk-taking behaviour during adolescence is the result of the incongruent growth of two essential brain systems, one that matures earlier and acts as a driver for these behaviours, and one that matures later and acts to inhibit them (10,11). Thus, during adolescence emotions and the motivation to achieve rewards increase but the skills that allow young people to exercise impulse control and evaluate risks and rewards are not yet fully developed, potentially resulting in illegal or dangerous behaviours.

As a result of poor decision-making, problem solving and the increased need for freedom and autonomy as well as reward driven behaviours, adolescents may inadvertently put themselves into situations that have the potential to damage their developing brains. Traumatic brain injuries (TBI), as a result of risky behaviour or experimentation with drugs and alcohol, can have detrimental effects on neurocognitive development with significant implications for behaviour. Particularly relevant in the current context is the increasingly well-established research literature evidencing the role that TBI plays in anti-social behaviour and violent offending. TBI has been examined in incarcerated populations, where those prisoners who have a history of TBI are more likely to have

been incarcerated at an earlier age, to have an increased risk of violence, prison infractions, poorer treatment gains and more convictions (13).

2.2 Relevance to the Judicial System

Taken together, empirical evidence offers a glimpse into the normative developmental trajectory of adolescents and young people, and how this may translate into risk taking, prosocial or anti-social behaviour. Whilst there are several factors which may inhibit normal behaviour and cognitive development, based on neurological models even typically developing adolescents may be prone to making poor decisions and taking increased risks for reasons out with their control. Moreover, adolescents who have sustained brain damage through, for example, TBI, or who have neurodevelopmental disorders, may be even more vulnerable to such behaviours.

Such evidence raises questions regarding the extent to which adolescent offenders, particularly those who have known risk factors for brain injury, should be regarded as fully culpable for their offences and how their age should be considered during sentencing. In Scotland, as elsewhere, a core principle of sentencing is that it must be proportionate and take into consideration relevant factors including individual culpability (14). In its simplest terms, culpability is a measure of the offender's responsibility for the crime, or how much they are to blame (15), often with reference to their intent or their ability to determine, or act on, the best course of action. Arguably, if evidence from neuroscience indicates that, for example, certain essential cognitive abilities do not fully develop until early adulthood, adolescents may be less culpable for their crimes. The principle of proportionality would suggest that offenders who are deemed less culpable for their actions (in this case adolescents), should receive a lesser punishment than an offender functioning at a higher level of cognitive maturity (15,16).

It follows therefore that consideration of adolescent cognitive development is highly relevant to the judicial system given the necessity to:

i. Ensure an adolescent's ability to engage with the court process and their fitness to plead (15)
ii. Consider an adolescent's individual culpability, relative to their cognitive maturity, during sentencing

iii. Consider sentencing decisions with reference to their potential to expose an individual to additional contextual and behavioural factors which may inhibit or disrupt their typical cognitive development.

Commissioned by the Scottish Sentencing Council, the following report describes our current understanding of the developmental trajectory of the adolescent brain, and its functions with reference to behaviours relevant to offending.

Through means of an 'umbrella' review (a systematic review of reviews), recent quantitative and narrative reviews have been systematically collated and critically assessed to provide a current and robust understanding of the field. Informed by the neurological, neuropsychological, and psychological literature, the age at which cognitive maturity is reached will be considered with reference to the following four areas, which also serve as the structure of this review:

a.) Neuro-anatomical development
b.) Factors that affect or inhibit cognitive maturation
c.) Functional development
d.) The state of the evidence

3. Defining Emotional Maturity: Neuro-anatomical Development

Over the past two decades advances in brain imaging and analysis techniques have contributed greatly to our understanding of the development of the adolescent brain. Generally, studies have indicated that the brain undergoes maturational change right up to the age of 25 years and beyond. This development can vary greatly from person to person, since trajectories of development can be influenced by many complex environmental and biological factors (like stress, substance use, pubertal hormones, genetics, etc.), and has gender specific features. The pace of development also varies between brain regions, for example brain regions involved in complex decision making reach biological maturity after brain regions involved in mood and emotion. This mismatch is thought to underlie some of the characteristic (impulsivity/ risk taking, reward driven behaviours) behaviours seen in adolescence, in addition to contributing to significantly increased risk for mental disorders. The variability in these measures, and the influence of pubertal timing differences, points towards the importance of repeated measures within individuals to fully understand these trajectories of brain development and their implications for behaviour.

This section includes reference to several brain regions and neurobiological processes. For clarity, relevant technical terms are introduced here. Gray matter consists of the neuronal cell bodies as well as other support cells called glia. The white matter is made up of the neuron's extensions or axons that allow neurones to communicate i.e. 'wiring'). Brain regions considered to be involved in affective or emotional processing (i.e. in moods and feelings) are regions of the 'limbic network' of the brain. Such regions include the amygdala and anterior cingulate cortex, amongst others (see fig 1) and are situated deep within the brain, underneath the cover of the outer 'cerebral cortex'. Regions which are typically involved in more complex thoughts, planning and decision making include the prefrontal and frontal cortices. These are situated at the very front of the brain, forming the outer layer. Although there is an extensive amount of historical research implicating these specific regions in these functions, it is important to consider that the more modern view is that this may be too simplistic an explanation, and that the brain functions as more as an interacting network of regions for any given function.

In terms of neurobiological processes mentioned, 'myelination' is the process by which the white matter tracts of the brain or 'wiring' is covered with a fatty coating (called myelin), which helps it conduct signals more efficiently. This myelination of brain tracts is one of the key maturational

processes that occurs over adolescence, along with synaptic pruning. This latter process (synaptic pruning) refers to refers to the process by which extra neurons and synaptic connections are eliminated in order to increase the efficiency of neuronal transmissions. In other words the brain's way of removing connections in the brain that are no longer needed. The process is often referred to as following a 'use it or lose it' type principle, emphasising the importance of not only genetic influences over these processed, but also environmental experiences, in shaping an individual's brain maturation.

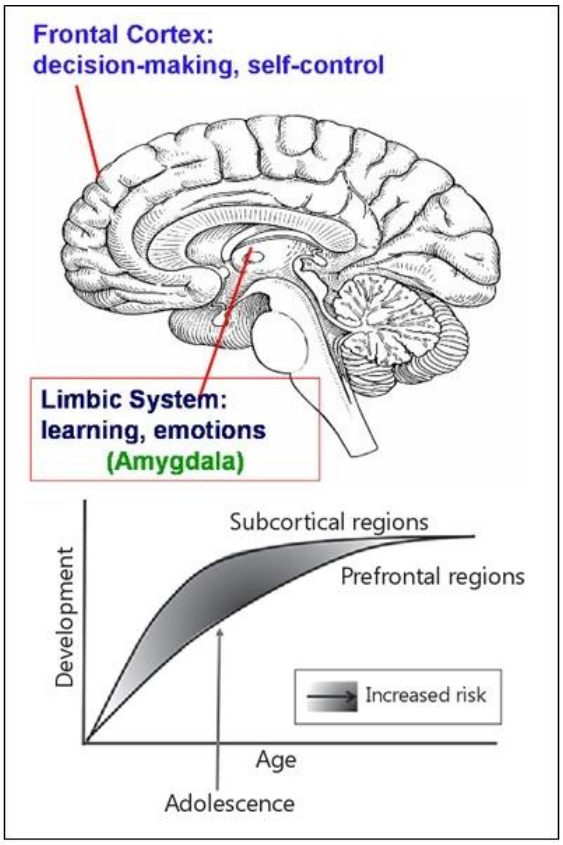

Fig 1: Figure illustrating how the mismatch in regional brain developmental trajectories may contribute to risk-taking in adolescence (From Casey, Jones, & Hare, 2008)

During the last two decades neuroimaging techniques have contributed to significant progress in our understanding of the development of the adolescent brain and emotional maturity. In particular, magnetic resonance imaging (MRI) studies have indicated that the brain remains in an active state of development, particularly in the context of changes in circuitry, neurotransmitter levels, and myelination through to as late as 25 years and beyond (17,18). These neurobiological processes are also understood to be particularly sensitive to the action of sex hormones which, along with other external influences such as substance use, interact with ongoing neural development to manifest in the characteristic behaviours of this period. It is generally considered that significant changes occur in the subcortical limbic regions, governing emotion and mood, and that there is also a significant period of change in myelination in the frontal cortices, implicated in cognitive control. This latter area in particular is considered to be the latest to fully mature. Thus, one of the major theories underlying excessive risk-taking behaviour, emotionally driven decision making, and psychopathology during this developmental period relates to the potential mismatch in the developmental trajectories of these cognitive regions in relation to those that typically concern mood, impulse, reward and emotion (fig 1). It is also important to note, however, that there is considerable inter-individual

variation in these trajectories, and the brain throughout life is in an ever-changing 'plastic' state, making the determination and classification of full maturity challenging. Similarly, the definition of adolescence is problematic. From a purely biological perspective, puberty refers to the period of specific hormonal changes in early youth; however, adolescence spans the entire divide between childhood and adulthood.

In terms of structural brain development, magnetic resonance imaging (MRI) studies consistently report an increase in white matter and a decrease in grey matter volumes in frontal and parietal regions during adolescence (19–21). White matter changes are also accompanied by progressive changes in white matter integrity (as measured by Diffusion Tensor Imaging). Non-linear changes in white matter have also been reported in such studies (22), and it is the case that many trajectories of brain development over this period, for both grey and white matter, do not follow linear longitudinal trajectories. Regarding cortical grey matter density, evolutionary older regions such the sensory and motor cortex are typically the first to mature (in terms of grey matter loss), followed by the rest of the cortex which matures in a posterior-anterior direction (19,21,23). This loss of grey matter, through processes such as synaptic pruning (considered to coincide with increased efficiency), is reported to increase from age 11 years in girls and age 12 years in boys and found to continue up until the age of 25-30 years. Specifically, the prefrontal cortex (PFC) only reaches full biological maturity at ~25 years or older, after significant periods of 'rewiring' (5,9,23), and with a degree of individual variation (24).

A recent review reported that neurodevelopmental processes, including myelinogenesis (the insulation of axons important for neural communication) and the development of complex efficient neurocircuitry, are particularly influenced by sex hormones over this period, (5,23).

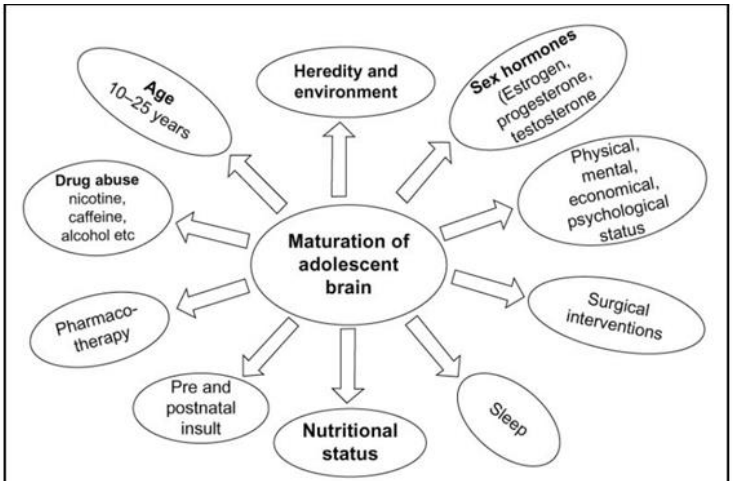

Fig 2: Figure illustrating factors affecting adolescent brain maturation

It is important to also note that pubertal effects do not act in isolation. A review of the factors influencing brain maturation in adolescence reported the importance of a complex interaction of factors including heritability, environment, physical, mental, socio-economical, and (5) (see fig 2). This review notes that drug abuse (caffeine, nicotine and alcohol) and other environmental neurotoxins also have an important influence on brain maturation, specifically impacting synaptic plasticity and neuro-transmitter release. For example, research has demonstrated that socio-economic status (SES) significantly affects brain development, where SES-age interaction effects have been found for amygdala and hippocampal grey matter volume, indicating the complexity and interaction of influencing factors.

Cross-culturally, remarkable similarities have been observed in adolescents - for example risk-taking and sensation-seeking is present across cultures. There have been some cross-cultural neuroimaging studies in adults that have found differences in neural activity across cultures, but few studies have examined whether these differences are present earlier in development (24).

3.1 Other Biological Markers of Maturity

Although puberty falls within the longer period of adolescence, the associated hormonal changes and their influences on neurobiology are important to consider, particularly in relation to behaviour and sex differences (25). It is clear that puberty plays an important role in cortical reorganisation during adolescence. Gonadal hormones are involved in reorganizing neural circuitry for both males and females during puberty (26–28). Increased levels of these result in greater motivation to seek out rewards, to engage in social relationships (romantic and sexual), and greater sensation-seeking behaviour (29).

Pubertal increases in testosterone have been associated with changes in neural activation to threat cues in the amygdala (threat avoidance), changes in the nucleus accumbens (reward processing),

and increased risk-taking behaviour (30–32). Oestradiol and progesterone also contribute significantly to sexual, social, and risk-taking behaviours (33–35). Animal research also illustrates the importance of learning experiences that occur alongside these hormonal transitions, for example in successful coupling (36). In humans, however it is less clear whether increases in testosterone affect individual differences in sexual motivations and behaviour, and in general, in humans, relatively little is known of the association between gender, puberty and neural development (19). There is reported to be some evidence, irrespective of gender, of positive associations between pubertal measures and grey matter in the amygdala, and negative associations with hippocampal volume and frontal cortical thinning (19,37). Some reports of gender-specific effects are, however, emerging. For example, in females positive relationships have been observed between oestrogen levels and limbic grey matter; and in males a negative association has been demonstrated between testosterone and grey matter in the parietal cortex. There are also some studies reporting sex differences in the rate of frontal lobe maturation, but currently this literature is not sufficiently comprehensive to allow for firm conclusions to be drawn.

This research importantly highlights the difficulties and complexities of distinguishing between the biologically mediated effects of gonadal hormones and their influences on neurobiology, and socially mediated effects of bodily change.

3.2 Social Relationships

The unique plasticity in the development of the adolescent brain creates an opportunity for learning and experience in shaping the development of neural networks (25,38–40). This is important for learning and motivation relevant to romantic and sexual behaviour. Pubertal hormones contribute to the neural transitions that prime the brain to learn about romantic love (as opposed to parental love). Whilst sex differences influence these trajectories, this also occurs at a time when adolescent brains are generally overly sensitized to reward learning (41). Romantic love involves increased activation in the dopamine-rich subcortical regions associated with reward processing, emotional processing and motivational systems (42,43), ventral tegmental activation (generally associated with pleasure, focused attention, and motivation to pursue rewards), and sexual arousal which involves ventral striatal activation (associated with motivation and predictive reward value) (43,44). Thus, adolescence can be understood as a period during which there are changes in hormonal levels and increased sensitivity to reward, along with a natural shift from parental and home environments to more independent social relationships.

3.3 Functional Neuroimaging

There have been several neuroimaging studies from a more functional perspective, either investigating brain function directly using cognitive tasks that are completed during scanning or relating measures of social cognition taken independently of the scan and relating them to brain structure. An overview of these studies is described below. It is cautioned however that it remains difficult to frame these studies in relation to adult maturity, since typically there is no direct comparison with adult samples.

In a review of **facial emotion processing** (45), that is the ability to interpret or recognise facial expressions of emotion, all seven studies reported that activation of the amygdala was associated with pubertal development. Notably, this convergence of findings was reported across all measures of pubertal development (e.g., hormone, physical examination, self-report). For **social information processing** tasks, six of the seven studies reported positive associations between measures of neural activation during social information processing tasks and pubertal development. This relationship was observed across multiple task types and measures of pubertal development. In contrast, however, there was no convergence of findings in the neural regions implicated, with multiple areas reported across studies (dorsomedial PFC (dmPFC), ventromedial prefrontal cortex (vmPFC), temporo-parietal junction (TPJ), amygdala, caudate nucleus, ventral striatum, and insula) (45).

Studies on **mentalising**, that is the ability to recognise one's own, and others, thought processes, emotions, intentions and motivational mental states, typically report activity in the dmPFC, TPJ, posterior superior temporal sulcus, and the anterior cingulate cortex. Mentalising is a core individual competency that makes social interactions and the behaviour and reactions of others easier to understand and predictable. Mentalising is a key ability in understanding and detecting our own emotions and intentions as well as those of other people, and it majorly influences social skills and abilities as well as the ability to regulate, tolerate and deal with negative and unwanted emotions as well as complex social situations, such as conflicts or potentially exploitative situations. There is reported to be a differential recruitment of the dmPFC over adolescence and into early adulthood (46,47). In adolescents there is reported to be greater activity in the dmPFC than in adults during a mentalising task compared to a control task (47). Adults showed greater activity in the anterior temporal cortex (ATC), suggesting a shift from medial PFC to ATC over development. It remains unclear why this happens, but it has been suggested that this shift may relate to changes in maturing neurocognitive strategies (19,46).

With regards to **cognitive control and affective (mood and feelings) processing** during adolescence, connectivity between ventromedial PFC and both the amygdala and ventral striatal increases in response to affective processing (30,48–53). Reduced activation reported in the vmPFC, critical in emotional regulation in connectivity with the amygdala, is reported in response to emotional stimuli (54–56).

For studies of online **social rejection**, studies indicate that the subgenual anterior cingulate cortex (ACC) and medial frontal cortex play key roles in adolescent processing of online exclusion (57–59). Several studies reported activity in the ventral striatal with **social acceptance/ social reward** e.g. 'likes' on social media, (60–64). During a **social exclusion** task (Cyberball)[2], adolescents with a history of peer rejection displayed higher activation in the dorsal ACC compared to more stably accepted adolescents (24). Notably, these differences in neural activity during Cyberball tasks were also associated with depressive symptoms in female adolescents (65). In one narrative review, girls were particularly reported to be influenced by body ideals in the media and sensitive to peer feedback embracing this ideal; in females aged 18-19 years, feedback deviated from the norm associated with increased activity in ACC-insula, an important region for modifying behaviour to fit peer feedback norms in adolescents (66). Also noted was increased sensitivity in early adolescence to social media influences in risk perception (66,67), as well as prosocial direction (68). There are only preliminary studies of neural responses to **retaliation and emotional regulation** (46), linking individual difference in responses to media content with brain development. These early studies suggest that the dorsolateral prefrontal cortex may play an important role in regulating emotional responses, consistent with conceptualisations above.

As indicated, there is an important need for further research emanating from these studies, to fully establish whether sensitivity is more pronounced in early or mid-adolescence to these socio-emotional tasks, and at what age this sensitivity reaches maturity, i.e. differences in such functional tasks in relation to adult cognitive activation patterns.

[2] Cyberball is a standardised game-like environment where simple social interactions are modelled. Participants are put in a situation where they experience perceived connection with others in a simple exchange in the game, and subsequently feel rejected when they are excluded from the game by the others.

3.4 Longitudinal Studies

Most studies described above are cross-sectional in nature, providing a snapshot of information at specific time-points between individuals. Arguably more informative are longitudinal studies, those which follow individuals over time, allowing more direct understanding of trajectories and relationships between traits of interest.

Longitudinal studies have reported direct relationships between pubertal changes and the observation of grey matter decreases and white matter increases within individuals across adolescence (69)[3]. Additionally, sex-specific changes in trajectories of brain maturation during puberty were reported in 4 out of the 8 longitudinal studies included in one review (69), suggesting differential effects of physical and hormonal changes on neurodevelopment in males and females. For example, smaller subcortical structural volumes in girls towards later maturation, compared with larger structural volumes of subcortical regions observed in boys in the later stages of puberty (70). Overall, the developmental trajectories of grey matter showed more change during early pubertal maturation, plateauing or even shrinking by late puberty (69). This was observed in subcortical volumes (70), grey, white, and amygdala volumes (69) and in cortical thickness (71,72). Other studies (73,74) have investigated the pattern of maturation in the PFC, amygdala, hippocampus and the nucleus accumbens (NAcc). Here it was found that grey matter in the amygdala increased until mid-adolescence, then change ceased; a small decline in NAcc volume was found across adolescence and there were distinct developmental trajectories between hippocampal sub-regions, but the PFC demonstrated a protracted substantial decline in grey matter during this period. Notably, this pattern was not uniform across all participants, which highlights the presence of heterogeneity in brain maturation.

The authors note the relative absence of longitudinal studies examining other brain regions and white matter microstructure, and the absence of studies examining important inter-individual differences, highlighting the need for further research in order to establish multimodal within-subject changes and variation (24,69).

[3] Note: a decline in grey matter over this period is considered part of normal maturation processes, whereby there is a 'pruning' of brain connections that are not required (those not being actively used), and a focussed strengthening of connections that are important (those circuits that are being actively engaged), in order to maximise efficiency. This process is also considered to be influenced by genetic and environmental factors and is thought to underlie the reason why psychiatric disorders have their peak onset over this developmental period.

3.5 Biological Brain Age and Individual Differences

More generally, Herting and Sowell (23) also indicate the need for future longitudinal research to clarify individual differences in the onset and progression of pubertal maturation in relation to structural brain development. While age infers general developmental changes, the authors highlight the additional benefits of examining pubertal maturation in relation to structural neurodevelopmental trajectories (23).

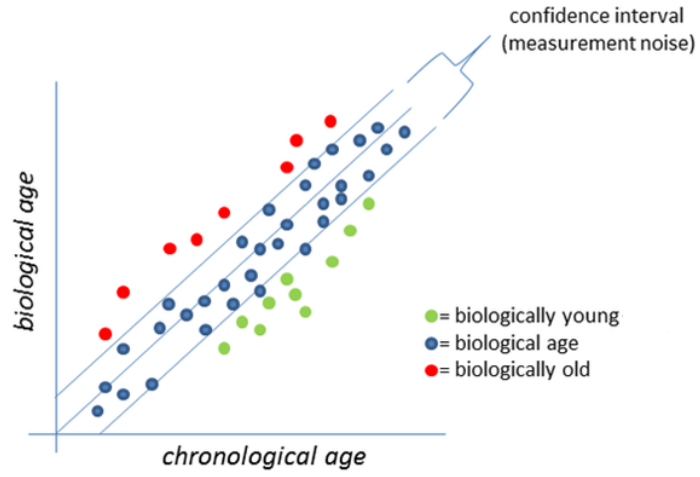

Fig 3: Figure illustrating relation between biological and chronological age, where green represents biologically younger individuals versus their chronological age and red represents biologically older versus chronological age. There is limited study however how these divergences may relate to risk/resilience over the adolescent period.

This concept also ties in with advances in the adult literature in relation to psychiatric and neurological pathology - where there is an increased focus on differences between 'chronological' versus 'biological' age for an individual. This concept was initially derived in relation to studies of 'accelerated ageing' as defined by telomere length and epigenetic age (75), but has recently been applied to biological brain age from imaging measures in adults (76), as well as in adolescents (77). (Fig.3).

Future research would therefore greatly benefit from large-scale studies of brain development in normative adolescent populations. These would provide data to define both what might be considered normal development in individual brain regions; and, in relation to the pubertal stage, to begin to define and enhance our understanding of the importance of divergences from normative trajectories at an individual level. The overall picture is likely to be considerably more complex than those seen in mid-late life populations, where increased biological age (accelerated ageing) is generally associated with increased mortality and poorer outcome. In contrast, during adolescence, increased ageing may represent increased 'positive' aspects associated with the development of brain regions, e.g. increased maturity, which may be beneficial, particularly in respect to the cortical regions involved in cognitive control and decision making.

3.6 Conclusions

Maturational changes can be observed to continue in some brain regions until as late as 25-30 years, but these trajectories of development are typically not linear, and vary from brain region to region, and from person to person. We have yet to fully understand the considerable inter-individual variation in brain maturation as a field, but this will have critical implications in terms of judicial and clinical decision making and guidelines.

4. Emotional Maturity: Factors that Affect or Inhibit Maturation

Thus far, we have established that brain maturation continues long after the period normally considered to define adolescence and that it is possible to identify common trajectories, including marked periods of vulnerability for poor decision making, problem solving, the understanding of complex social situations and increased risk-taking. Critically however, attempts to define normal development are hampered by the discrepant speeds at which brain regions develop and a marked variability between individuals. Compounding these difficulties is the brain's vulnerability to factors which may interfere with normal development, most commonly by causing damage but also through the removal of factors necessary for optimal development, such as a stable social context or significant adversity. Aggravating this risk further is that the poor decision making and raised risk-taking associated with normal adolescent development may in itself predispose adolescents to greater risk of those factors that may interfere with normal cognitive development; factors such as traumatic brain injury and alcohol and substance abuse. In turn, these risk factors themselves are elevated in individuals who have experienced adverse childhood experiences or trauma, or who are developing neurodevelopmental disorders or significant mental health difficulties, both of which are also associated with delays in adolescent maturation.

Although traumatic brain injury, alcohol and substance abuse, adverse childhood experiences or trauma, and neurodevelopmental disorders may all exert a significant damage on the maturing brain their mechanisms of effect and their breadth of impact across multiple brain regions preclude the ability to draw generalisations and each will be discussed separately in the section that follows.

In this section we will again be referring to many regions of the brain, some of which were described earlier.

Our primary focus in the remainder of this review will be on functions associated with the frontal lobes. The frontal lobe can be considered the brain's management system and, as such, impairments here can have wide reaching effects on an individual's behaviour and functioning. These managerial processes are referred to as the 'executive functions', a term that encompasses the multiple skills that contribute to our ability to 'self-regulate', that is to control our emotions, mood and impulses, and to control our mental processes, particularly with regard to planning our behaviours to reach a desired goal.

> "Executive functions (EFs) make possible mentally playing with ideas; taking the time to think before acting; meeting novel, unanticipated challenges; resisting temptations; and staying focused. Core EFs are inhibition [response inhibition (self-control—resisting temptations and resisting acting impulsively) and interference control (selective attention and cognitive inhibition)], working memory, and cognitive flexibility (including creatively thinking "outside the box," seeing anything from different perspectives, and quickly and flexibly adapting to changed circumstances) (78)."

Reference will also be made to specific parts of the frontal lobe; the prefrontal cortex, which is associated with the higher cognitive functions including concentration and emotion; the orbitofrontal cortex, a part of the prefrontal cortex, associated with decision making, reward seeking and, through its connection with the amygdala, the experience of emotion, and the medial orbitofrontal cortex, which influences our goal directed behaviours. Whereas the lateral prefrontal cortex is responsible for cognitive emotional regulation of your thoughts and rational processing after an event, the amygdala is responsible for the experienced emotional intensity of an event or memory.

We will also refer to gyri, (singular 'gyrus'). Gyri are ridges on the brain's surface that allow the brain to increase its size, and therefore function, within the tight constraints of the skull. In this section we will refer to a number of these, each with its own function and location. The middle temporal gyrus is located in the temporal lobe and responsible for integrating sensory information, visual perception, language and processing semantic memories, those relating to common knowledge. The post central gyrus, located in the parietal lobe, is considered the primary somatosensory cortex, interpreting such sensations as touch and balance while the middle occipital gyrus, in the occipital cortex, contributes to object recognition.

The temporal lobe is responsible for long term memory and learning, hearing and speech comprehension, object perception and face recognition and houses the hippocampus, which, as part of the limbic system, helps to regulate emotional responses and which is also key to our ability to learn and create new memories. Thus, while the amygdala provides the emotional associations that accompany memories, the hippocampus is responsible for remembering the situation that provoked these.

Also mentioned in this section are the cerebellum, responsible for coordination, balance, posture, speech, motor reflexes and learning; and the thalamus, responsible for movement and sensory information.

4.1 The Impact of Head Injury on Adolescent Development

The World Health Organisation has predicted that, by 2020, traumatic brain injury (TBI) will be one of the leading causes of death and disability (79). Defined as an injury to the brain that is acquired as the result of sudden trauma (80) and which disrupts the normal functioning of the brain (81), symptoms can range from mild to severe and be short-term or lead to lasting disability. Commonly, impairments are observed in cognitive abilities, sensory processing, communication, and behavioural and mental health problems (80). Although the symptoms of TBI are largely dependent on severity, mild TBI, also referred to as concussion, can also lead to short and long-term cognitive and behavioural problems in people of all ages, particularly if repeated (81–86).

Historically, it was understood that, due to the potential for healing provided by the increased plasticity of the brain during development, children and adolescents who acquired a TBI were advantaged in comparison to adults (87). However, advances in developmental neuroscience and brain imaging techniques have contradicted this claim. Evidence has instead highlighted the fragility of the adolescent brain, suggesting that even a small impact can cause disruption in the brain's cognitive maturation (87,88).

Findings from a recent review of cross-sectional and longitudinal studies of children and youths under the age of 19 have provided evidence for long-term neurodegenerative changes following a TBI of all severities (87). Longitudinal studies highlighted a significant decrease in cortical thickness at 18 months post-TBI injury in the bilateral frontal, fusiform, and lingual areas of the brain compared to orthopaedic controls (a comparison group with orthopaedic injuries). One study observed a reduction in bilateral regions of the medial parts of the frontal lobes and the anterior cingulate, in addition to an increase in cortical thickness in parts of the medial orbital frontal lobes and bilateral cingulate, as well as the right lateral orbital frontal lobe (89). Additional findings demonstrated that in severely injured children, the area of the corpus collosum decreased between the age of 3 to 36 months, but increased, in line with normal development, in a group with only mild to moderate head injury, indicating the variability of brain impact post-injury (87,90). Similarly, all

the 11 cross-sectional studies reviewed reported findings in support of long-term degeneration (or volume loss) in specific brain regions. Degeneration was identified in the hippocampus, amygdala, globus pallidus, the grey matter area of the thalamus, white matter (periventricular), cerebellum, and the midbrain of the brainstem (87). Of the 5 studies that examined white matter, all findings demonstrated compromised white matter integrity at least 1 year following a TBI compared to controls, indicating a deterioration in white matter microstructure (87).

Similarly, a synthesis of studies examining sports-related concussion indicated brain changes based on multiple brain imaging methods (91). Studies using magnetic resonance spectroscopy (MRS) were suggestive of microstructural alterations during all phases of concussion in young athletes and were in accordance with the limited literature on mild TBI outside of sports (91,92). Research using functional MRI evidenced alterations in functional connectivity in resting states, and changes in activation patterns during tasks, findings which they note have been observed for up to 1 year following an injury, and in those who were asymptomatic, suggesting lasting dysfunction even after symptoms have resolved (91,93).

In summary, brain damage resulting from TBI may result in neural degeneration and volume loss that disrupts normal childhood development and can be both widespread and permanent leading to impairment across the lifespan (87). Importantly, a head injury does not have to be severe to result in life-long impairment; even mild impacts have the potential to cause damage (91).

The impact of head injury on specific functions

The research literature clearly indicates that TBI and concussion in children and adolescents are associated with brain alterations that may disrupt typical developmental trajectories; consequently, it follows that associated cognitive functions may also be impaired. As with the anatomical effects of TBI, the degree to which cognitive impairment occurs also depends on factors such as severity and the age at which the injury takes place. For example, greater severity of TBI is associated with poorer neurocognitive outcomes, and children injured at a young age achieve less recovery than those children injured when older (94–96). Findings from reviews that fit our inclusion criteria have emphasized changes in cognitive functioning, each of which is described in turn below.

Working memory

Individual differences in working memory have been associated with learning and academic performance in typically developing children (97). Working memory is a cognitive function that maintains and stores information temporarily, and which underlies thought processes (98). It is considered responsible for the temporary storage and processing of verbal, visual and spatial information, coordinating memory storage components and retrieving information from long-term memory as well as selective and divided attention and the ability to switch attention (96,99–101). Working memory is largely dependent on the prefrontal cortex; and, due to the slow maturation process of the frontal lobes, is vulnerable to disruption (96).

In a meta-analytic review by Phillips et al. (96) of 27 studies, the impact of TBI on the working memory of children and adolescents under 20 years old was examined in comparison to typically developing children (96). Results showed that there was a statistically significant small-to-medium difference in the ability of children with TBI in measures of two components of working memory. Firstly, central executive functioning: that is, the ability to store and process verbal and visual information, to coordinate memory and to retrieve long term memories, and to select, divide and switch their attention; and, secondly, the phonological loop, responsible for temporary storage of verbal information. Notably, greater severity of TBI was associated only with increased impairment in central executive functioning. No difference was observed in the ability to store visual and spatial information. Additionally, functional neuroimaging studies included in the review examined the correlation between TBI and working memory in children, with four of the five studies reporting significant differences between children with TBI, compared to those without, in brain activation.

The review indicates that children with TBI are at increased risk of working memory impairments, though these impairments appear to be 'component-specific' and are more likely to impact the central executive impairment which increases with the severity of the injury incurred. Consideration of these results should appreciate the significant heterogeneity found between studies, which often indicates methodological differences, querying the appropriateness of synthesising the data using meta-analysis.

Inhibitory control

Impairments in inhibition following childhood TBI have been the subject of narrative review by Sinopoli and Dennis (102) who identified that inhibitory control can be either an *effortful*, voluntary form of control, or an *effortless*, automatic form of inhibition, which involves automatic-type responses, with each component comprising various sub-components (102). The former has been the primary focus of the research literature. As inhibitory control is a multi-faceted construct, it also follows different, but overlapping, developmental trajectories, and this is evident in children with a TBI who exhibit more impairments in some processes, than others. The findings of their review indicate that children with TBI exhibit impairments in processes of effortful inhibition including interference control (the ability to complete a task, while ignoring competing or conflicting information), response flexibility (the ability to shift attention between tasks), and cancellation inhibition (the ability to stop an already initiated action) (102).

The loss or impairment of inhibitory control may impact on the ability to appropriately weigh decisions or achieve the steps necessary to attain goals, and consequently result in inappropriate behaviour. Without intact *effortful* inhibitory control, children and adolescents may find themselves in risky or dangerous situations, in verbal or physical disputes with others, or even under arrest.

Social functioning

Social competence, or appropriate social functioning, plays a key role in successful social, academic, and vocational performances in later life (103,104). Further, social skills are necessary for interactions between children, for solving social problems, and for the evaluation of themselves and others in a social context (104,105). Brain damage, as a result of TBI and other illnesses, has been shown to impair social skills and social performance, resulting in impaired social competence, without which social situations may be wrongfully evaluated, often contributing to adverse outcomes, including aggression (104,105). Arguably, the foundation of social cognition is the ability to recognise emotions from facial expressions, eyes, voices, and body movements (104). Emotion recognition performs an essential role in social interaction by allowing individuals to predict the behaviours of others, which in turn allows them to select an appropriate behavioural response or reaction (104,106). In their meta-analytic review, Kok et al. (104) examined social competence in children aged eighteen years or younger who had experienced a TBI, in comparison to those who had not. Children with moderate to severe TBI had significantly more difficulty recognising emotions

when all types of emotion were measured, and fear, sadness and happiness specifically. It is worthy of note that whether social competence is impaired in children and adolescents with TBI may depend on the severity of their injury, with those with mild TBI evidencing small, statistically non-significant impairments, only when asked to recognise 'all emotions' or fear (104).

The association between childhood TBI and impaired social cognition suggests that children and adolescents with at least moderate to severe TBI may lack the ability to interpret and respond to others appropriately (104). Consequently, their chosen behavioural response may be incongruent with their social situation, particularly in circumstances that require the interpretation of subtle emotional cues such as humour and sarcasm, with the potential to lead to social isolation (104,107).

Intellectual functioning, executive functions & memory

In addition to the effect on inhibition, working memory, and social functioning, studies have reported profound impairments in several neurocognitive abilities following severe paediatric TBI that differ as recovery progresses. Immediately after the injury significant impairments in general intellectual functioning, processing speed, attention, and verbal memory are observed, but by the time recovery has plateaued, where little spontaneous improvement is evident, several other cognitive impairments become apparent (94). In their meta-analytic review, Babikian & Asarnow (2009), found impairments were most apparent in general intellectual functioning, executive functions, and verbal delayed memory, where large effect sizes[4] were observed, but also marked in verbal immediate memory where there was a moderate effect. Small differences were also found in visual perceptual functioning, visual immediate memory, and inhibition (94). Although acknowledging the possibility that the larger effects observed may be due in part to the age at which

[4] Meta-analytic reviews report their findings as effect sizes, a means of standardising statistical findings or associations that provides more information than statistical significance, (the p value), alone which conveys only the likelihood of finding being due to chance. Essentially, where a p value might indicate that an effect or association exists, an effect size will convey the size of any such relationship. Effect sizes might for example refer to the size of an association between two variables, the difference between two groups, or the difference observed in participants over time. Although the interpretation varies slightly according to the type of effect size, conventionally effect sizes are interpreted as follows: d=0.2 is small; d=0.5 is medium, d=0.8 is large where d represents the proportion of a standard deviation such that for a large effect size two groups must differ by 0.8 standard deviations or more. Similarly, for correlations, effect sizes are interpreted as follows: r =0.1-0.3 is small; r=0.3-0.5 is medium and r=0.5-1.0 is large. For clarity, in this report we will refer only the size of the observed effects (302,303).

children were injured, the review robustly emphasises that severe TBI not only has immediate deleterious effects, but also has long-term, profound effects on adolescent and child development. Further, it was observed that children in the severe TBI group were both unable to catch up to the same level of functioning as peers, and that they fell further behind over time, further highlighting that children with severe TBI may be unable to 'keep up' developmentally (94). These findings further demonstrate the long and short-term effects of severe TBI, as well as the profound consequences it has on cognitive development.

4.2 The Impact of Alcohol and Substance Use on Adolescent Development

The increased risk of drug and alcohol use during adolescence is well established, with research confirming that adolescence is a developmental period in which behaviour driven by the reward system, such as risk-taking, novelty seeking, and susceptibility to peer pressure, is at its peak. In response, neurological and psychological research has attempted to understand adolescents' vulnerability to substance use and its consequences. Founded on a cognitive neuroscience framework, there are considered to be two main processes that contribute to addiction: rewards and inhibitory control (108).

The response to positive outcomes and stimuli, as well as the motivation to achieve those outcomes, are known as reward-related processes. Due to the way these processes develop, a hypersensitivity to rewards peaks during adolescence, facilitating reward and sensation-seeking behaviour, in turn creating a vulnerability to experimentation and substance misuse (2,108,109). During this time, adolescents become more sensitive to rewards, which is attributed to the inability of the slow developing cognitive control system to regulate the hypersensitive reward system. In addition to this, inhibitory control, due to its protracted developmental trajectory, is unable to aid in the control of reward-related processes during this time (108).

All typically developing adolescents will endure this period of incongruence between neural systems, as well as the lack of inhibitory control; however, some adolescents may be more at risk for substance use than others. Adolescents deemed to be more 'at risk' for substance use often have a positive family history for addiction. And, interestingly, behavioural studies have indicated that individuals who are high-risk for addiction have greater impairments in inhibitory control compared to adolescents who are not considered high-risk (108,110). Additional studies in this area have reported similar findings and have also suggested that poor behavioural inhibitory control is a risk

factor for increased substance use in both high-risk and typically developing adolescents (108,111–113). Results of these studies postulate that the development of poor or deficient inhibitory control may increase the likelihood for experimentation and use of drugs in non-high-risk adolescents; and in adolescents who are considered high-risk, having deficient inhibitory control may contribute to the progression of disordered use (108).

Whether considered high-risk or low-risk, it is clear that all adolescents go through a period of risk-taking and experimentation, during which time it is not uncommon to experiment with drugs and alcohol. In acknowledgement of this and the adolescent brain's particular vulnerability, research has examined their neurotoxic effects on cognitive development. For example, in their review of brain imaging studies, Silveri and colleagues (2016) reported that the brain region most commonly altered by substance use, inclusive of all types, was the frontal lobe (114). Although the authors acknowledge this could have been anticipated, given that the frontal lobe is the last to develop, they did caution that the observed brain alterations could either be due to the neurotoxic effects of substance use, or to pre-existing differences in the substance abusing groups, including those that potentially predisposed them to such use.

Neurological changes related to alcohol use in adolescence

Several studies have evidenced the effects that alcohol use can have on the developing brain. In comparison to non-using, matched controls, poorer cognitive performance, changes in grey and white matter, and different functional brain patterns are seen in adolescents who meet criteria for alcohol use disorder (AUD), and those who engage in binge-drinking (115). This means that the difficulties linked to a relatively overdeveloped reward system in relation to a regulatory system are amplified and neurodevelopmental adolescent characteristics linked to behaviours such as poor decision making and problem solving, impulsivity and risk taking become far more prominent. Moreover, cortical and subcortical changes are also observed in adolescent alcohol users, including changes in the volume of the prefrontal cortex, hippocampus, and amygdala. Notably, studies that have examined alcohol use with co-occurring substance abuse have found poorer white matter integrity; however, alcohol on its own has been identified as having unique impacts on white matter, particularly in large doses (115). The implications of compromised white matter on neurocognitive functioning can be significant (115,116). For example, certain illnesses such as multiple sclerosis, an autoimmune disease that affects myelin, and schizophrenia, a mental illness that has been associated with abnormalities in white matter, are both characterized by neurocognitive

impairments, further highlighting the link between compromised white matter and deficient neurocognitive functioning (117,118).

Changes in the frontal, temporal, and parietal lobes are also seen in current adolescent alcohol users, and MRI studies suggest that abnormalities in the frontal lobes are not only a consequence of alcohol use, but may also be a pre-existing risk-factor for it (114). Along with the frontal lobes, hippocampal changes have also been reported, though findings are more inconsistent. Studies have found that adolescents with AUD have smaller hippocampal volumes (119), as well as changes in hippocampal asymmetry (120), though similar studies have found no significant changes in hippocampal volume (121,122). The differences in findings may be due to the many confounding factors that might contribute to these changes, such as quantity of alcohol intake, duration of use, and the use of other substances at the same time as alcohol, all of which have the potential to influence results.

Additionally, one of the largest and longest prospective studies to examine alcohol-related changes in brain volume demonstrated similar results. The four-year prospective study following the developmental trajectory of 75 youths who began drinking during adolescence, and 59 controls who did not use alcohol, reported abnormalities and structural changes in heavy drinkers. Findings indicated abnormal neurodevelopmental trajectories in heavy drinkers, compared to controls, and evidenced quickened grey matter volume decreases in the frontal and temporal regions, as well as mitigated increases in white matter volume (123). Replicating earlier findings, this study robustly adds to the evidence that heavy alcohol use negatively impacts the maturation of grey and white matter during adolescence (124).

In conclusion, findings highlight that both the quantity and cumulative use of alcohol may contribute to change or disruption in the adolescent developmental trajectory (115). Dependent on quantity, alcohol use may have distinctive effects on neurocognitive development as well as functioning. Weak inhibitory control has been evidenced as both a risk factor and a consequence of adolescent alcohol use and a large prospective study has confirmed that the brains of heavy drinkers followed abnormal neurodevelopment trajectories. There are clear indications from the research evidence that alcohol, even in the absence of other substance use, has unique and profound effects on the development of adolescents.

Neuropsychological impairments in relation to alcohol use in adolescents

Congruent with the observed effects of alcohol on adolescents' brain maturation, research findings have identified several neuropsychological impairments seen in alcohol-using adolescents. Early findings from cross-sectional studies that compared adolescents that used, and did not use, alcohol identified several domains where the alcohol using group exhibited poorer cognitive performance, including attention, information processing, memory, visuospatial functioning, language abilities and executive functioning (see Jacobus & Tapert, 2013 (115) for review). More recent studies have corroborated these findings, demonstrating that in 12 to 18-year olds, the greater the number of drinks consumed daily, the greater the impairment on measures of attention and executive functioning (115,125). Similarly, a study of 18 to 20-year olds demonstrated that those who engaged in binge drinking had poorer performance on executive functioning and working memory measures, in comparison to controls (115,126).

Longitudinal studies have reported similar results. A 10-year longitudinal study in 13 to 18-year olds found that heavy alcohol use was associated with poor short-term memory, though the participants in this study also reported some use of other substances in addition to alcohol, making it difficult to differentiate the effects (115,127). A three-year follow-up study of adolescents who transitioned into heavy and moderate drinkers found intriguing differences between girls and boys. Findings demonstrated that the amount of 'drinking days' that the girls engaged in over the follow-up period was associated with poor visuospatial performance at follow-up, whereas poor performance on sustained attention at follow-up in boys was associated with more severe hangover symptoms (115,128). In line with this study, adverse post-drinking symptoms, such as withdrawal and hangovers, have also formed the focus of studies based on the belief that the symptoms themselves may have a greater impact on cognitive functioning than the quantity of alcohol consumed (115). A study of 15 to 19-year olds identified significantly impaired verbal learning and memory in those with worse hangover symptoms and was notable for the observation that this did not appear to be the case in those that also used marijuana (115,129).

The link between quantity of alcohol intake and neurocognitive impairment has also been examined in binge-drinking adolescents. A meta-analysis in 2019 analysed 58 primary studies on 10 to 24-year-old adolescents and young adults (130). Their analyses revealed that binge-drinking was associated with significant impairments in overall neurocognition (small effect size), decision-making

(large effect size), inhibition (small effect size), and recognising emotions (large effect size), and, surprisingly, an increase was seen in processing speed (small effect size), which the authors note may indicate increased impulsivity (130). Neurocognitive domains such as mental flexibility, planning, behavioural disinhibition, delayed discounting[5], expressive language, long-term and recent memory, sustained attention, and working memory were all inversely related to binge-drinking, though not significantly. Moreover, receptive language, immediate memory, visual perception, and visuo-construction, were positively related to binge-drinking, but not significantly. Significant statistical heterogeneity, a measure of consistency, was reported for inhibition, decision-making, recent memory, processing speed, and overall neurocognition; the authors noted that this was likely due to the variety of cognitive measures utilised in the primary studies, making the synthesis of findings more variable. Although these findings should be interpreted cautiously, they further highlight the deleterious impacts that alcohol has on adolescent cognitive abilities.

Neurological changes related to drug use in adolescence

Cannabis is one of the most widely used illegal drugs in adolescents and young adults (131). It is considered a psychoactive substance and is often ingested through inhalation or by consumption. When ingested, it interacts with cannabinoid receptor type 1 (CB 1R), which is followed by the activation and release of endocannabinoids (eCB). The main psychoactive ingredient in cannabis is called Delta-9-tetrahydrocannabinol or THC, which also acts as a partial agonist of CB 1R (131).

Brain imaging studies have largely demonstrated that chronic cannabis use contributes to brain changes in adolescents. In a review of 13 brain imaging studies, task-related fMRI findings revealed consistent hyperactivity in the frontotemporal network of the brains of adolescent cannabis users, while findings for other regions, such as the anterior cingulate cortex (ACC), were inconsistent with both hyper and hypoactivity observed. This review also identified changes in the prefrontal region of the brain in adolescent cannabis users and increased prefrontal volumes in female cannabis users. Similarly, in regions of the brain where high levels of CB 1R were found, reductions in grey matter were also observed (132). Commenting on these findings, Lorenzetti and colleagues cautioned that this literature may fail to account for the numerous confounds that may compromise study findings, such as polydrug use and the symptoms of psychopathologies, both of which might contribute to the

[5] Delayed discounting refers to the perceived reduction in the value of a reward associated with the length of time before its receipt.

overestimation of the effects that cannabis has on development (132). Additional functional MRI studies comparing users to non-using controls have reported patterns of activation which are less efficient in users on tasks of working memory, verbal learning (132,133), and cognitive control (132,134,135). Together, these findings suggest that adolescents who use cannabis exhibit abnormal neural profiles.

Changes in grey and white matter have also been observed in adolescent cannabis users. A 3-year longitudinal study examining hippocampal volumes in young adults who used cannabis daily found only changes in grey matter volume and reported no changes in hippocampal volume. The authors concluded that heavy cannabis use in young adults may not disrupt developmental processes affecting hippocampal volume (136). These results contrast findings from other, albeit potentially less robust, cross-sectional studies which have identified an association between cannabis use and hippocampal volume illustrating the need for further high quality studies (136). Similar to that observed in alcohol use, compromised white matter has also been found in the prefrontal, limbic, parietal, and cerebellar tracts of adolescent cannabis users (137).

In common with the literature on TBI, there is evidence that the age at which adolescents begin using cannabis is significant. For example, in comparison to individuals who started using cannabis later in life, males and females who initiated cannabis use before the age of 17 exhibited smaller whole brain and percent grey matter with larger white matter volumes; increased cerebral blood flow was observed in males. Both males and females who began using cannabis before the age of 17 years were smaller in height and weight with this being more marked in males (136,138).

Although the literature presents some inconsistencies, it appears clear that early cannabis use can result in both neural and structural alterations in the developing brain.

Neuropsychological impairments related to drug use in adolescence

In addition to the effect of cannabis use on the structure and functioning of the developing brain, cannabis has also been shown to impact neuropsychological functioning. Adolescent users have demonstrated impairments in attention, memory, processing speed, and some executive functions, including planning (139). Compared to adolescents with minimal cannabis use, heavy users made more perseverative errors on problem-solving tasks (139,140), and regular users had poorer performances on measures of attention, nonverbal memory and learning (139,141). More frequent

use of cannabis in the past month was also associated with poor executive functioning and working memory (141), while cumulative use over an 8-year period predicted poor performance over time on attention measures (139,142). Studies suggest that cannabis users continue to demonstrate some impairment following fourteen days or more abstinence. More generally, there is evidence for impaired attention and concentration in cannabis users more generally, and for sustained impairments in memory function for those with a history of chronic cannabis use (143). Evidence for impairment in executive functioning, primarily in inhibition, impulsivity and decision-making, remains more mixed although demonstrating a trend toward worse performance in cannabis users compared to non-users (143).

Research which has focused on those initiating cannabis use before the age of 17 suggests that this is associated with poor performance on measures of verbal memory, IQ, and fluency, as well as impaired reaction times on visual scanning and attention measures. Notably, impaired verbal memory, IQ and fluency was only seen in those current users who began use before the age of 17 and not in those who initiated use after (139,144,145). Impairment also appears to remain after one month of abstinence with adolescent users continuing to perform poorly on measures of attention, verbal learning and memory, sequencing, and psychomotor speed (120,139). Moreover, those who reported using marijuana more frequently in their lifetime performed very poorly, perhaps indicating a cumulative effect that remained evident even after a period of abstinence (120,139). It is possible, however, that after a longer period of abstinence, certain cognitive functions could recover with one study finding that after a three-month period of abstinence, there were no differences between users and non-users (139,146).

In common with the literature on alcohol use, the neuropsychological literature investigating the effect of marijuana use on neurocognition remains inconsistent due to differential factors such as gender, genetics, psychiatric functioning, amount of THC exposure and poly substance use (139). To obtain a true measure of the cognitive impairments that result from cannabis use, individuals who have entered a period of abstinence may serve as the most reliable measure.

Conclusion

When investigating the differential effects of alcohol versus drug use, there are mixed effects: some studies suggest alcohol use is linked to greater cognitive impairments, while others have demonstrated greater impairments as a result of marijuana use. In any respect, the effects of alcohol, marijuana, and other drugs have been observed in moderate users with no diagnosis of substance use disorder. Although there are apparent inconsistencies within the literature, several studies have highlighted both the neurological and neuropsychological effects of drugs and alcohol. The literature does however suffer from a lack of clarity given the difficulty in obtaining accurate, often self-report measures, of the strength or quantities used of what are illegal or age restricted substances.

4.3 The Impact of Adverse Childhood Experiences and Interpersonal Trauma on Adolescent Development

Childhood maltreatment, which can include physical and sexual abuse, as well as emotional and physical abuse and neglect, is regarded as one of the most potent predictors for a wide range of psychiatric disorders across the age span (147). However, despite the compelling evidence that maltreatment results in long-term alterations in neurobiological and neurocognitive functioning, the precise mechanisms by which stress and adversity alter an individual's brain are not fully understood. In part, this may be due to the underpinning assumption that individuals meeting clinical criteria for certain psychiatric disorders are comparable, a notion that is now widely regarded as incorrect. Indeed, it is now understood that individuals presenting with the same behavioural symptomatology may vary in terms of their neurobiology and neurocognition (148,149). For example, individuals who present with a history of childhood maltreatment in addition to psychiatric disorder will differ in a number of domains from those with no such history. Psychiatric disorders in individuals who have experienced maltreatment are more likely to have an earlier onset and a more severe symptomatology, as well as an having an increased risk for comorbidity (150,151). Further, the illness course is likely to be persistent, recurrent and less responsive to standard treatments (152–154). This indicates an interaction of mechanisms strongly linking significant childhood adversity to vulnerability to mental health difficulties as well as associated neurobiological and neurocognitive impairments.

The experience of childhood maltreatment is far from homogeneous, being variable in its nature, length of exposure, number of incidents of abuse, abuse severity and frequency, for example, and with exposure to multiple types of abuse and neglect common, providing a further challenge to those seeking to reach generalisable conclusions (155). Disentangling the web of interactions between an individual's biology and environmental risk has, however, become easier with the advent of neuroimaging methods such as structural and functional magnetic resonance imaging (fMRI), which have provided a means to investigate changes in neurobiological and neurocognitive systems following maltreatment (147). From this work, a theory that conceptualises the link between neurobiology, neurocognition and maltreatment has emerged: The Latent Vulnerability Theory (156). According to this prominent theory, maltreatment brings about quantifiable changes in several neurobiological systems that reflect a functional response to the adverse early environment. A central principle of this theory is that these alterations are adaptive, i.e. they benefit the individual in some way within the context of the early maladaptive environment. However, these adaptations are thought to incur costs in the long term as the individual is unable to appropriately adapt to and navigate more normal situations, which therefore increases their vulnerability to future stressors (156). An understanding of the neurobiological and neurocognitive changes that accompany childhood maltreatment are central to an appreciation of adolescent maturation.

Neurobiological effects of childhood abuse, neglect, and trauma

Childhood maltreatment mostly occurs within an interpersonal context. Young people are dependent on their caregivers for safety and love, creating attachment security and a safe haven to explore and develop. Attachment security is one of the key factors that promote positive psychological development, especially in regards to social and interpersonal competencies, but also the capacity of mentalisation, emotion regulation and associated neurocognitive function. When caregivers deviate from this expected caregiving and facilitating social relationship, the development of the brain regions underlying social information processing may be significantly impacted (157). The social information processing network (SINP) comprises specific brain regions that may be affected by maltreatment (158). This network consists of three nodes: a detection node, an affective node, and a cognitive-regulatory node. The detection node is accountable for determining whether a stimulus is social in nature and includes brain regions such as the inferior occipital cortex, inferior temporal cortex, intraparietal sulcus, fusiform face area, superior temporal sulcus, and anterior temporal cortex. The affective node is responsible for processing the social and emotional

components of a stimulus and consists of the amygdala, ventral striatum, septum, bed-nucleus of the stria-terminalis, hypothalamus, and orbitofrontal cortex. Lastly, the cognitive-regulatory node engages in higher order processes such as goal-directed behaviour and inhibitory control, and includes the dorsomedial prefrontal cortex, as well as the dorsal and ventral prefrontal cortices. Research has demonstrated that many of these brain regions undergo a significant development postnatally, which makes them particularly susceptible to the effects of maltreatment. Moreover, given that the brain undergoes extensive development during childhood and adolescence, it is reasonable to anticipate that the effects of maltreatment on neural structure and function will be widespread (159). Although neuroimaging studies in children and adolescents are relatively scarce, there is some evidence to support this hypothesis, primarily from research on adults with a history of maltreatment, albeit this limits our ability to make comparisons with typical development.

Meta-analyses indicate that, in comparison with controls, individuals exposed to childhood maltreatment have demonstrated significantly smaller grey matter volumes in the right orbitofrontal/superior temporal gyrus, as well as in the amygdala, insula, and para-hippocampal and middle temporal gyri, and in the left inferior frontal and post-central gyri (160). Moreover, larger grey matter volume was observed in the right superior frontal and left middle occipital gyri (160). Notably, deficits in the right orbitofrontal-temporal-limbic and left inferior frontal regions remained in a subgroup analysis of participants who were not taking medication, for mental health difficulties for example, suggesting the results are not attributable to prescription drug use (160). Additional analyses indicated that alterations in the left post-central and middle occipital gyri were only present in older individuals with a history of maltreatment (160). No gender differences were found (160). However, when looking at brain volume, rather than grey matter specifically, gender differences in brain structure following maltreatment have been reported in other studies. For example, research has found that childhood emotional abuse is associated with reduced hippocampus volume in males but not females. Nonetheless, it is important to note that many of the existing studies include small samples sizes reducing the confidence with which we can make inferences (161). A small number of studies have looked specifically at structural brain changes in children and adolescents following maltreatment. A review of this literature was notable in concluding that the reduction in hippocampal volume consistently reported in adults with a history of maltreatment could not be confirmed in youths (162). The most consistent finding in children and adolescents with a history of abuse was structural abnormalities in the corpus callosum, the connective pathway between the brain's hemispheres responsible for our ability to integrate sensory, motor and cognitive functions

across the two sides of the brain (162). It is clear that neuroimaging research in this age group lags significantly behind that of adult samples.

Brain function has also been examined in youths and adults following childhood maltreatment. In their meta-analysis Hein and Monk (157) examined the neural response to threat, identifying a significantly increased activation in the bilateral amygdala, which is associated with emotional regulation (163), in those who experienced childhood maltreatment, relative to controls (157). In the SINP regions, as outlined above, the right superior temporal gyrus, associated with social perception and cognition (164), was found to have greater levels of activation in maltreated individuals compared to controls. Moreover, outside of the SINP regions, whole-brain corrected analysis revealed increased activation in the para-hippocampal gyrus, thought potentially implicated in the development of post-traumatic stress disorder (PTSD) (165), and the right insula associated with, among other processes, emotional experience and empathy (166–168), in individuals with a history of maltreatment. Notably, maltreated youths, but not adults, showed hyperactivation in the left lentiform nucleus and globus pallidus, as well as in the left para-hippocampal gyrus (157), which suggests that there may be age-related effects associated with maltreatment.

In the absence of sufficient longitudinal research, it remains to be established whether these neurobiological effects have distinct timetables that unfold at different stages across development. Nonetheless, evidence confirms that the effects of childhood maltreatment extend across the entire brain, which helps explain the profound neurocognitive and psychosocial deficits observed in maltreated individuals. Childhood maltreatment further significantly affects core aspects of psychological maturation, individual resilience and core capacities of mentalisation, emotion regulation and social and interpersonal skills, as well as increased vulnerability to mental health difficulties which can compound the outlined impairments significantly.

Altered neurocognitive functioning following maltreatment and trauma

There is a substantial body of evidence to suggest that childhood maltreatment alters the brain's executive functioning including the partially overlapping processing of threat and rewards and the ability to regulate emotions (147). For example, altered threat reactivity, as indexed by hyper-

reactivity in the amygdala (and other related limbic structures) to threatening stimuli, may represent a neurocognitive system that confers latent vulnerability in young people exposed to adversity, potentially making them over sensitive to potential dangers (157). Functional neuroimaging studies of adolescents have also reported blunted anticipatory responses to reward in reward-processing related subcortical areas, such as the striatum, which, alongside heightened threat reactivity, may reflect an adaptive calibration towards an avoidant behaviour in order to cope with the stressful environment (169). Further, it has been suggested that this altered responsiveness may confer increased risk for affective disorders such as depression (170). In relation to emotion regulation, neuroimaging studies with children exposed to maltreatment report alterations in brain regions and networks associated with emotion regulation. Atypical functional connectivity and focal activity has been found in frontal-limbic neural networks, including the ventral anterior cingulate cortex, the amygdala and lateral-frontal regions, although the direction and pattern of functional alternations were found to vary across studies (147). Much like alterations in the threat response and reward processing systems, it is thought that these neurobiological changes affect the development of effective emotion regulation processes (171).

Neuroimaging research that looked specifically at the neural correlates of executive control in maltreated children and adolescents is limited compared to the research on threat reactivity and reward. However, the existing research demonstrates increased activity during error monitoring and inhibition tasks in medial and lateral frontal regions, such as the dorsal anterior cingulate cortex and frontal motor regions (147). Interestingly, two recent longitudinal cohort studies found that although individuals with a history of childhood maltreatment were characterised by impaired general intelligence and executive control, such deficits were largely accounted for by cognitive deficits prior to the experience of victimisation and by the general effects of childhood socioeconomic deprivation (172). Therefore, caution should be exercised when interpreting the existing neuroimaging findings of executive control, as they may reflect a priori cognitive vulnerability rather than being an after-effect of maltreatment (147).

Neurocognitive impairments following maltreatment and trauma

Given the significant neurobiological changes associated with childhood maltreatment, it is unsurprising that altered neurocognitive functioning is also observed, often resulting in debilitating

and long-term consequences (147). A review by Kavanaugh and colleagues (173) examined neurocognitive impairments in children and young people following maltreatment. The majority of studies included in the review found lower intellectual functioning in young people with a history of maltreatment compared to controls, with group IQ falling in the low-average range, however IQ frequently remained within the range of typical development. Nonetheless, the severity, type, timing, and duration of maltreatment were found to have a significant impact on IQ, which suggests that the association between cognitive functioning and maltreatment should be conceptualised as a continuum rather a categorical model (173).

The effect of childhood maltreatment on executive functions, including attention, has also been the subject of a significant number of studies. Almost all those studies included in Kavanaugh et al.'s (173) review (22 out of 23) found an association between childhood maltreatment and impairment in executive functions. Specific weaknesses were observed in inhibitory control, cognitive flexibility, sustained attention, visual/auditory attention, working memory, planning, and problem solving (173). Notably, certain executive functioning deficits have been associated with specific types of maltreatment. For example, physical abuse has been linked to problem solving deficits, sexual abuse with cognitive flexibility and problem solving, while emotional abuse has been associated with attention and working memory (174–176). Moreover, the overall severity and presence of chronic maltreatment has been associated with the degree of executive function deficits (177).

Further impairments have been found in certain visual-spatial domains such as visual-perception, visual-motor, and visual-construction skills in young people with a history of maltreatment (173). More equivocal is the potential effect of maltreatment on language ability, with mixed results for its effect on the rate of language acquisition and peak in language development, as well as general language skills (e.g., comprehension, vocabulary) (178,179). Although there has been extensive research on memory impairments following maltreatment in adults, there is relatively little research involving child and adolescent samples. Of the research that does exist, the findings are mixed: some studies report no difference in memory functioning following abuse (177,179), while others have identified memory weaknesses in aspects of verbal/visual immediate and delayed recall (178). Additionally, memory ability more generally has been associated with the presence of sexual abuse

and the length of child protection involvement (180). Studies on neurocognitive functioning following maltreatment have also examined motor and psychomotor[6] ability, and although there is a dearth of research in this area, the research that does exist did not find a relationship between maltreatment and psycho-motor functioning (173).

[6] Psychomotor refers to motor activity linked to mental processes e.g. those involved in imitation, manipulation of objects in the completion of a task or precision movements.

4.4 The Impact of Psychiatric and Neurodevelopmental Disorders on Adolescent Development

Although the many biological and psychosocial changes that occur during adolescence can positively influence the life of a young person as they begin to craft their own identity, it is also a period of significant vulnerability for psychiatric and neurodevelopmental disorders and potential developmental and social impairments. In this section we shall focus on mental health and neurodevelopmental difficulties that typically emerge during the adolescent period. Pre-existing mental health and neurodevelopmental disorders which appeared in childhood significantly increase the risks outlined but also interact with adolescent development and neurophysiological and neurocognitive maturation. Fifty percent of mental disorders are established by age 14, and seventy-five percent emerge by age 24 (181). Given that adolescence is a time of critical brain and functional development, the onset of psychiatric disorders can have far reaching consequences that compound this burden. For example, adolescent depression, the chief cause of illness and disability in youth (182) is associated with lower educational attainment, lower perceived social support, relationship difficulties, and greater contact with the criminal justice system (183,184). The psychological and social risk and resilience factors underlying this marked vulnerability to mental health disorders during adolescence have been the subject of extensive enquiry from the very early days of adolescent psychiatric research. However, investigating the neurobiological substrates of psychiatric and neurodevelopmental disorders during adolescence is a more recent field of research, made possible by the advent of neuroimaging techniques, such as structural and functional magnetic resonance imaging (185). Neuroimaging research has thus given us an unparalleled insight into the neuropathology of adolescent psychiatric disorders. However, a key challenge faced by the field is differentiating the typical neurobiological changes that accompany adolescence (e.g. a decrease in grey matter and increase in white matter volume (19)) from atypical alterations in structural and functional brain development that may characterise the emergence of psychopathology (185). Identifying divergent neurodevelopmental trajectories at the earliest stage possible will assist the development of tailored interventions that can help move young people away from ill-health towards recovery. However, as will be discussed, it is evident that while our understanding of the neural circuitry underpinning adolescent psychopathology and neurodevelopmental disorder has advanced significantly, much progress has yet to be made. Undoubtedly, the continued development of neuroimaging techniques, longitudinal and interdisciplinary research will greatly aid this effort.

Cognitive changes leading to the onset of psychiatric disorders

Changes in cognitive functioning are a hallmark of most psychiatric disorders (186). However, the presence of premorbid changes in cognition also merits consideration and existing research in this area has focused on severe mental health difficulties, such as psychotic disorders (bipolar disorder, schizophrenia, and psychosis). A recent narrative review by Mollon and Reichenberg (187), discusses the evidence for subtle premorbid cognitive impairments in individuals who later develop schizophrenia, and examines the possible genetic and environmental mechanisms underlying these deficits (187). They draw upon early and more recent meta-analytic findings which together report that IQ deficits in those who later develop schizophrenia are present early in childhood, (as young as the age of 5), and can be of a magnitude of around 8 IQ points (188,189). Moreover, individuals who go on to develop schizophrenia may demonstrate early, static verbal deficits in addition to increasing non-verbal deficits, which combined, may prevent typical development in other cognitive domains as they grow older (190).

Research on whether these deficits are specific to schizophrenia compared to other psychotic disorders, such as bipolar disorder, is mixed. A systematic review by Parellada and colleagues (191) reports that while both schizophrenia and bipolar disorder are characterized by neurodevelopmental deviations, (both neuromotor and cognitive impairment), and general adjustment problems in childhood, these impairments are more marked, have an earlier onset, and have a greater predictive risk, in individuals who later develop schizophrenia (191). A meta-analysis focusing specifically on cognitive ability reported no premorbid cognitive deficits in future bipolar patients (192) suggesting that premorbid cognitive development differs between schizophrenia and bipolar disorder, indicating there may be distinct neurodevelopmental pathways (193) despite shared genetic determinants (194). Non-psychotic disorders, such as major depression (MDD), have generally been associated with smaller cognitive deficits when compared with schizophrenia (195). Although, evidence on the premorbid aetiology of the deficits associated with psychoses is scarce, the studies reviewed by Mollon and Reichenberg (187) suggest that both common and rare genetic variants, in addition to environmental factors, such as obstetric complications and cannabis use, may play a key role. Moving forward, leveraging prospective population-based cohort longitudinal studies will help unravel the intricacies of the association between premorbid cognitive deficits and psychiatric disorders (187).

Neurobiological and functional changes in adolescents with psychiatric and neurodevelopmental disorders

In their 2016 systematic review, Iorfino and colleagues highlight that most studies that have investigated the neurobiological and functional changes that accompany mood-related psychiatric disorders during adolescence have focused on the clinical syndrome (196). In contrast they highlight a lack of emphasis on related functional domains, such as alcohol and substance abuse, social and economic participation, suicidal and self-harm behaviour and physical health, and their role in the onset, persistence, and impact of the disorder, which the authors argue has significantly impaired the clinical translation of psychiatric research (196). This approach has developed our understanding of the underlying neurobiology suggesting that the heightened amygdala re-activity associated with stress may be linked to the emergence of affective disorders (197). Further, reductions in the volume of the anterior cingulate cortex (ACC) have been linked to MDD with greater reductions associated with illness severity (198). Also reported was an association between an increased cortisol response and the development and persistence of MDD but further research in this area is required to parse out the relationship between cortisol response and symptom severity (196).

A significant body of evidence now demonstrates that neurobiological changes characterise both unipolar (UD) and bipolar disorders (BD) in children and adolescents. A systematic review by Serafini et al., (199) examined the integrity of white matter (WM) and grey matter (GM) within this sample and found that UD and BD have both shared and distinctive impairments in WM and GM domains. For example, more WM abnormalities were found in children and adolescents with BD compared to UD, while volume reductions of basal ganglia and the hippocampus are more greatly associated with paediatric UD compared to BD (199).

Neurobiological and functional changes are also observed in other psychiatric disorders, such as anorexia nervosa (AN). In their review of the literature, Olivo et al. (200) reported altered maturation of the executive network in young people with AN, which may result in impaired cognitive flexibility and working memory and lead to enhanced sensitivity to punishment and negative-feedback association learning. Low BMI and altered pubertal development were key factors associated with these impairments in executive function (200).

Young people with attention-deficit-hyperactivity disorder (ADHD), a condition characterised by behaviours such as inattention, hyperactivity, and impulsiveness (186), show deficits in late developing fronto-cortical and fronto-subcortical neural circuits (201). A systematic review by Arnsten and Rubia (201) found that neuroimaging studies consistently demonstrate structural deficits, most prominently in the basal ganglia, as well as functional impairments in the inferior frontal cortex (IFC) and dorso-lateral prefrontal cortex (DLPFC) circuitries, networks and regions thought to mediate attention and inhibitory control (201).

Furthermore, fMRI studies have revealed disorder specific under-activation of the IFC-DLPFC network in ADHD patients relative to matched paediatric conduct disorder patients and typically developing controls during four different tasks assessing inhibitory and attentional control. Further evidence for disruption to this network in ADHD comes from psychopharmacological studies and is reviewed by Arnsten and Rubia (201): fMRI studies have demonstrated that the commonly used treatment methylphenidate, both when used as an acute and chronic treatment, enhance and even normalise fronto-striatal network activity and connectivity that are impaired in ADHD during disorder-related tasks. There is also some evidence to suggest that ADHD may be associated with a delay to typical brain development, which manifests relatively early in life (202). However, there has been an over-reliance on cross-sectional studies and a lack of medication-naïve, those who are not taking medicines that may affect what a study seeks to examine, in the current literature. A recent systematic review by Marley and colleagues (203) examined advances in ADHD neuroimaging research since the major confound of prior medication use was highlighted by Leo and Cohen (204). In this they suggested that conclusions regarding the neurobiological substrates of ADHD may be premature prior to a thorough examination of the methodological rigour of existing studies, especially the confound of medication (203,204). Further longitudinal research that addresses these methodological concerns will help shed light on the emergence and development of neurodevelopmental disorders such as ADHD, and thus inform novel treatments and interventions.

Neurocognitive changes in psychiatric and neurodevelopmental disorders

In adults depression is associated with a range of neurocognitive impairments such as deficits in information processing, memory, and verbal fluency, which independently predict poorer educational outcomes, occupational and daily functioning (205,206,207). Moreover, these neurocognitive impairments have been shown to reduce the effectiveness of treatment, and thus perpetuate symptoms of depression and increase the risk of experiencing subsequent episodes

(208). Less is known, however, about the effects of depression on the neurocognitive function or maturation of adolescents with depression when compared with healthy controls (209).

Goodall and colleagues (209) addressed this knowledge gap by synthesising the existing research in the field (23 studies). Their systematic review and meta-analysis examined neurocognitive functioning in young people (aged 12-25) with depression (either a diagnosis of MDD or using a self-report or clinician-rated depression symptom scale) compared to controls. Young people with depression were found to demonstrate poorer performance across a range of neurocognitive domains including attention (medium effect size), verbal memory (large effect size), visual memory (medium effect size), verbal reasoning/knowledge (medium effect size), and IQ (small effect size) (209). These findings are largely consistent with those described in an earlier, smaller (7 studies), review by Baune and colleagues (210). However, Baune et al. (210) found that young people with depression exhibited poorer working memory, verbal fluency and executive functioning, results that were not replicated by Goodall and colleagues' (209) considerably larger study. Goodall et al. (209) also observed that those taking medication had impaired attention in comparison to those who did not, although the cross-sectional study design does not allow us to infer a causal relationship (209). Importantly, in the absence of a longitudinal design, as is the case with the studies included in both reviews, it is not known whether the observed neurocognitive impairments are state-related phenomena that accompany depression and will resolve with remission, or whether they reflect a trait-based aspect of the condition, and thus could be an early marker for risk of depression. Finally, neurocognition may worsen as a result of the experience of depression and, therefore, could be considered a scarring effect (211).

Neurocognitive impairment is not restricted to the domain of affective disorders. Indeed, a range of neurocognitive deficits, particularly impaired attention, have been robustly demonstrated in schizophrenia (212). As previously discussed, premorbid neurocognitive impairments are observed in individuals who later develop schizophrenia (187). Furthermore, there is a general consensus that a large majority (75-100%) of patients with schizophrenia are cognitively impaired at any one time e.g., (213–217). However, significant heterogeneity can be observed in the neurocognitive profiles of those with a diagnosis of schizophrenia, ranging from mild to dementia-like impairments (218), likely reflecting variation in premorbid abilities. Notably, there is a relative dearth of longitudinal research on the trajectory of neurocognition over time in this condition, and the findings that do exist are mixed; some report a steady cognitive decline while others suggest a stable composite score

between first episode and later follow-up (212). Nonetheless, it is clear is that individuals diagnosed with schizophrenia experience a significant decline in neurocognitive functioning from the premorbid to post-onset period and that the extent and developmental progression of decline differs across cognitive domains. Importantly, these findings suggest that distinct pathophysiological mechanisms may underlie impairments in different cognitive functions (219).

Although ADHD is characterised by a deficit in attention, other changes to cognition such as an increase in aggressive behaviour have also been associated with this disorder (220). Aggressive behaviour can be categorised into two broad subtypes: 1) reactive/ impulsive and 2) proactive or instrumental, and it is the former that has mostly been associated with ADHD (221,222). In a recent review by Saylor and colleagues, impulsive aggressive was found to be a relatively common comorbidity of ADHD in children and adolescents but it did not imply or require a diagnosis of oppositional defiant disorder. Impulsive aggression was also reported to be a strong predictor of unfavourable developmental outcomes characterised by persistent ADHD; greater psychosocial burden, especially on parents; and serious functional deficits across a range of domains including criminality and anti-social behaviour. Moreover, impulsive aggressive can often trigger peer rejection which can begin a cascade of effects of increasing dysfunction compounding the burden further (222). However, much like the existing research on the other psychiatric and neurodevelopmental disorders previously discussed, whether this aggressive behaviour is a trait, state or scar-related effect remains unknown.

Future research should examine the nature (aetiology), course and severity of neurocognitive deficits associated with adolescent depression, schizophrenia, and ADHD. This would help create a more nuanced understanding of how these challenges may relate to treatment response and prognosis in young people. This can be best achieved through prospective, multi-wave, longitudinal studies so that neurocognition is characterised at important junctures associated with illness and remission. This would have significant implications for future treatment and interventions (209,212,219).

5. Emotional Maturity: Functional Development

Thus far, we have established that adolescence is a critical, and vulnerable, period of development, where the brain undergoes changes that affect the functional ability and behaviours of young people. Over the last two decades, brain imaging studies of animals and humans have highlighted the multiple changes that take place during adolescence, both functional and morphological (5,223). We have reviewed evidence supporting the notion that, during adolescence, the brain remains 'under construction', undergoing continuing maturation of neurocircuitry and myelination both regulated by, and vulnerable to, the increase in sex hormones associated with puberty (5). Changes occur in the adolescent limbic system which may significantly impact on those functions which allow adolescents to behave in a prosocial manner, namely in the areas of self-control, decision making, problem solving, emotion regulation, and risk-taking behaviours (5,223). While many neurotransmitters, the brain's chemical messengers, develop either prenatally or immediately postnatally, some continue to develop during adolescence: for instance, Gamma-aminobutyric acid (GABA), which, as the main inhibitory neurotransmitter, is responsible for inhibiting or reducing aspects of brain activity, particularly in the prefrontal cortex of the brain, and influences factors such as euphoria and risk-taking behaviour (5,7,224). Changes in the neurotransmitter dopamine (central in creating our drive for reward) in the nucleus accumbens during puberty are also reported to increase the vulnerability of adolescents to risk taking behaviours, in that the same levels of reward can only be achieved with higher stimulation. In addition to those changes associated with maturation, the adolescent brain also undergoes neuronal change as new skills are acquired, a process known as "plasticity" (5,7,223,224). While this process contributes to an adolescent's ability to learn, the inherent lack of stability in the context of ongoing development can also contribute to poor decision making (5).

Executive functions have been closely examined in the developmental literature, as they play a key role in the ability to behave appropriately and respond to stimuli. The purpose of the executive functioning system is to organize and deploy cognitive and emotional resources in an efficient and effective way to achieve goals and rewards (225). The system comprises three main dimensions: representational knowledge (e.g. knowledge about rules, actions, and conventions), operational processes (e.g. planning, organization, attention, working memory and connecting intentions to goals), and self-regulation (e.g. being self-aware, initiation, sustained action, inhibitory control, and flexibility in thoughts and actions) (225,226). Evident in early childhood, executive functions

continue to mature through adolescence into adulthood, with many providing a foundation for sociomoral behaviours (225,227).

The prefrontal cortex is the brain region primarily responsible for executive functions and is noteworthy for being the last to fully mature, providing a potential anatomical explanation for the immature behaviours observed during this period (5). Arain et al. (5) highlights functions and abilities, listed below (originally identified by Giedd & Steinberg (109,223,228,229)) which are sub-served by the prefrontal cortex and remain 'under construction' during adolescence, resulting in what might be considered 'stereotypical' adolescent behaviour.

Abilities sub served by the frontal lobes that remain under construction in adolescence and may contribute to behaviours considered typical of this period (adapted from Arain et al. (5).

The ability to:

- consider and predict the future
- direct, sustain and switch attention
- solve problems
- organise one's thoughts
- plan and strategize
- inhibit inappropriate behaviour
- consider multiple streams of information simultaneously
- consider the consequences of behaviour
- adjust behaviour or shift strategies in changing scenarios or situations
- regulate intense emotions
- control impulses
- negotiate the balance between short-term rewards and long-term goals

This list is notable for the key role each function plays in the ability to behave prosocially, an ability that, due to the later development of the prefrontal cortex, adolescents may not yet be able to call upon reliably. Moreover, due to this lasting immaturity in essential cognitive functions, adolescents may participate in risk seeking behaviours, such as unprotected sexual relations, impaired or reckless driving, and drug and alcohol addiction (5).

5.1 The Development of Adolescent Decision-making and Risk-taking

Sensation-seeking, risk-taking and risky-decision making are considered prominent features in adolescence with evidence suggesting consistency across cultures, and that they may serve an evolutionary function (24,230). Given their potential to lead to reckless, dangerous or even lethal consequences (231) they have been the subject of several explanatory models.

The dual systems model suggests that adolescents' vulnerability to risky behaviour is due to the divergent developmental course of two brain systems: one which increases motivation to pursue rewards, and one which restrains impulses (10,11,231–235). In the same vein, such behaviour has been attributed to the changes occurring in the corticostriatal circuitry during this period, specifically the earlier maturation of the amygdala and nucleus accumbens, which are sensitive to emotional cues and the anticipation and attainment of rewards, relative to the prefrontal cortex with its role in controlling behaviour (236,237). The dual systems model submits that risky behaviours peak during adolescence due to activation of the incentive-processing system, also known as the "socioemotional system", which, in processing social and emotional information, allows adolescents to experience increased arousal, emotional intensity and sensitivity to social influence (238). This heightens the attraction of adolescents to exciting, high risk activities, while the "cognitive control" system, which is slower to mature, is not yet developed sufficiently to successfully, or consistently, restrain these urges. A slight variation of this model, proposed by Steinberg (11) agrees that the cognitive control system is slow to mature, and continues to develop through late adolescence, but it suggests that the socioemotional system plays a different role. In the dual systems model, it is indicated that the socioemotional system follows an inverted U-shaped trajectory, where an increase in reward sensitivity occurs in early adolescence and begins to decline in early adulthood, whereas Casey et al. (10)suggested that the socioemotional system is responsible for increases in arousal until mid-adolescence after which it plateaus, remaining consistent until adulthood.

Similar to the dual systems model is the "driven" dual model proposed by Luna and Wright (234), which also suggests that the socioemotional system follows an inverted-U shaped trajectory, but proposes that the cognitive control system plateaus in mid-adolescence, rather than continuing to increase into young adulthood (234) .

The triadic model again builds on the dual systems approach but proposes that a third brain system comes into play (231,239). The third system, which lies in the amygdala, is responsible for emotional

intensity and avoidance, and it is speculated that this may increase impulsive decisions, by increasing the 'perceived cost of delay'. Although initially criticised due to the lack of evidence suggesting that the emotion/avoidance system helps to explain risk in adolescents (231), evidence in support of the model is now emerging (240).

It has also been proposed that a hyperactive socioemotional system contributes to increased risk taking by creating excessive demand on the cognitive control system's ability to regulate behaviour (241). Luciana and Collins (241) suggest that adolescents have executive abilities similar to those of an adult, and that rather than considering risk taking as a failure of the system it should instead be attributed to excessive burden on this system moving the debate to one of cognitive capacity (241).

The evidence from neuroimaging

Evidence from neuroimaging agrees that adolescents' overactive reward responsiveness increases their inclination for risky behaviour (242–245). Two studies (246,247) reported decreased, rather than increased, ventral striatum activation but these discrepant findings have been considered a function of complex and different stages of the reward processing (i.e. since there are differential responses to reward anticipation and reward delivery). Interestingly, studies also demonstrate that adolescents make more thought-through decisions for cold (executive) rather than hot (emotive) cognition tasks, consistent with this overall conceptualisation. Additional emotional experiences (e.g. fear of rejection or the excitement of risk) are also reported to make it harder for adolescents to think clearly in relation to emotionally salient decisions (248). Largely, researchers (e.g., Steinberg, Dahl, Johnson) are in agreement that the temporal gap between the development of the socio-emotional areas, linked to surges around pubertal onset, and cognitive control system of the brain, which occurs later in adolescence, may explain some aspects of risk-taking behaviour typical of adolescence.

A more recent review by Dai and Scherf (45) on reward processing specifically, reported little consensus in the studies they reviewed, observing that they failed to meet criterion for convergence in the directionality and locus of effects. In total, 4 studies reported a positive association between reward-related activation and pubertal development where sex hormones were the index of puberty. Another 4 studies reported null effects, while 2 studies found negative associations such that increased hormone levels were related to lower neural activation. The conclusion of this body

of work was that despite the nucleus accumbens being hypothesised by most studies as the locus of effects, the lack of convergence did not support this association (45).

With regard to peer relationships, the literature is even less consistent. In the presence of peers, some studies report that adolescents also experience increased activation of the neural reward circuitry, specifically the ventral striatum (associated with increased risk taking) (25,249,250). Other studies however did not replicate this result, e.g. (251). Instead these studies suggested that activation in the temporal-parietal junction mediated the relationship between adolescents' increased risk taking and their ability to resist peer influence (251). Other studies observed that peer presence can both enhance and impair performance dependent on context, where Van Hoorn and colleagues (68) linked prosocial feedback from peers with increased prosocial behaviour, and antisocial feedback with decreased prosocial behaviour (47,68).

Notably, the theoretical explanations that seek to explain adolescent risk-taking and decision-making all share at their core a struggle in the developing adolescent brain between 'motivational drivers' to action, rooted in the intensity of emotional arousal and increased sensitivity to both rewards and social influence, and their 'cognitive control', their ability to inhibit impulsive behaviours, pause to consider their decisions and plan their actions. Each of these aspects will now be considered in turn.

Motivational drivers

Reward and sensation-seeking

The theoretical models that seek to describe the process of adolescent decision making and risk-taking share a consensus that sensation and reward seeking peaks in adolescence before reducing in adulthood. Sensitivity to incentives or rewards may be highest between the ages of 14 and 16, impairing decision-making capacity such that higher risk strategies are employed in the pursuit of goals (252). While a causal association has yet to be established, this rise appears to parallel the onset of puberty which is associated with a rise in dopamine levels and a change in its transmission, particularly in the striatal and prefrontal cortex where levels rise (11,253). In turn, adolescents may experience increased sensitivity to rewards with a differential bias to those goals based on short term, rather than long term, rewards (253). As the cognitive control system continues to mature, self-regulation of behaviour increases, which in turn decreases reward seeking. Steinberg (11) acknowledged that in order to make mature decisions, both the cognitive control and

socioemotional systems need to be coordinated, and before this occurs, middle adolescents are left "exposed" to increased risk taking behaviours (11,254).

Sensation-seeking is a psychological expression of socioemotional reactivity, and measures of sensation-seeking are often predictive of risk-taking behaviour (231). Longitudinal studies evidence that sensation-seeking increases across adolescence (231,255–257), a finding supported by a review of self-reported sensation-seeking which observed a peak in mid-adolescence followed by a decrease in adulthood (11,15,231,258–263). It is noteworthy however that when data is reported separately by gender, at least one study has identified a differing pattern with sensation-seeking peaking in females before males at ages 16 and 19 respectively (261,264) and reducing more rapidly thereafter (261).

Peer influence in risk taking and risky decision-making

Although many studies have examined incentive processing using measures of risky decision-making in laboratory settings, research has demonstrated that risky behaviours in "real life" more often occur in the presence of friends and peers, which is a limitation of these studies (253). Blakemore (265) highlights the claim that peers are a determinant of adolescent-typical behaviour citing evidence that adolescents are more likely to take risks when with peers than when they are alone (266,267) including, for those aged 13 to 24 years, when engaged in a driving task, something not observed in adults aged 25 and over (267,268). The influence of peers also extends to substance use. In a longitudinal study, perceived peer use of cannabis predicted the onset and extent of an adolescent's own use for the next 3 years (267,269). Indeed, in some studies evidence of increased reward sensitivity has only been observed in the presence of peers. For example, Chein et al. (249) found that adolescents demonstrated more engagement of reward circuitry and more risky behaviours on a simulated driving task, but only in the presence of their peers (249). Equally, evidence suggests that peers can also influence prosocial behaviours, perhaps by diverting adolescents from poor choices (267,270).

The mechanism by which peers exert their influence remains unclear. Spear (271) suggested that adolescents may be subject to greater emotional arousal in the presence of peers which in turn "may be particularly effective in exacerbating adolescent sensitivity to positively valenced (perceived) rewards, while also perhaps further attenuating their sensitivity to aversive stimuli" (271). Blakemore (272) posited that adolescents' increased susceptibility to the influence of peers

may be attributable to a 'hypersensitivity' to possible social exclusion or rejection (272), with the fear of social exclusion and the risk of rejection potentially outweighing more important risks, such as health, safety, and legal censure (273).

Cognitive control

Maturation of cognitive control

Cognitive control is defined as the ability to suppress distracting stimuli in order to achieve a planned response or goal (252,274). Available in childhood, by adolescence it is guided by the executive prefrontal system but continues to mature, particularly in its ability to self-monitor performance and to consistently sustain cognitive control at a level associated with adulthood (274). Adolescents may employ the same neural circuitry as adults in order to perform a cognitive task, however, when doing so in the context of, perhaps excessive, rewarding or stressful stimuli their ability may become compromised resulting in different behavioural outcomes (11,241). Similar impairments in performance may occur in the presence of emotionally salient stimuli with evidence indicating that adolescents may be predisposed to attend and react to emotional stimuli, and perhaps even to approach, rather than avoid, potential threats (10,237,275,276). Their increased sensitivity to reward incentives, particularly between the ages of 14 and 16 years, can impair their ability to inhibit unhelpful responses and distract them, steering them towards emotional stimuli and impairing their decision-making ability.

Ability to plan

Cognitive control has been defined as "the mental abilities or processes that enable the formation and flexible use of internally generated plans to guide behaviour" (253,277–279). In addition to the acquired knowledge needed to identify the actions available to us, a subtle interplay is required between the ability to hold and manipulate this information while we consider the optimal course of action (working memory), our ability to shift our focus between different options as we consider each in turn, and the ability to look to the future and anticipate the consequences of each potential course of action. Working memory, which allows us to hold in mind and manipulate information, follows a linear developmental trajectory, developing at a consistent pace throughout childhood and adolescence (227). Similarly, shifting, or set shifting, which enables individuals to shift between tasks and mental states, essentially to be unimpeded by what has preceded, follows a lengthy developmental course from pre-school through adolescence. Review findings indicate that children

who are of pre-school age can handle shifts between simple tasks, and more complex task-switching reaches adult levels by mid-adolescence (227).

Inhibitory control

In line with the dual-systems model, risk-taking is considered to comprise one or more decisions made in the context of a reward (280). The making of such decisions encompasses both reward processing and cognitive control processes, particularly impulse, or inhibitory, control (274,281–283). As described previously, inhibitory control is the ability to halt a response and is crucial to the organised and voluntary control of behaviour (253). Research has demonstrated that inhibitory control is accessible by early childhood (227,284), and that it continues to improve with age, as evidenced by fewer 'inhibitory failures' in tasks measuring this ability (253,285–288). Several tasks have been developed to measure inhibitory control in laboratory settings, such as the go/no-go task, stop-signal, anti-saccade task, flanker and Stroop tasks (289), and through their use it has become apparent that inhibitory control is not a 'unitary construct', but one for which aspects may be captured by different tasks. For example, the Stroop task measures the ability to suppress goal-inappropriate objects (e.g., selective attention) and the anti-saccade and go/no-go tasks capture the ability to stop planned actions at various time points (253,290). A key component of inhibitory control, commonly measured using the anti-saccade task, is response preparation, which involves the 'internal planning and readying of a motor response' (253,291,292). Studies utilising this task have shown that, generally, inhibitory control improves with age, and that adolescents begin to perform at an adult-level by approximately 14 or 15 years old, though continued more gradual improvement of inhibitory control on this task continues into adulthood (253,284).

Necessary for inhibitory control is the ability to monitor one's responses, an ability that becomes apparent in adolescence (227), but in which adults are observed to be better able to evaluate and change their behaviour when mistakes are made (253). This development of inhibition relies on brain maturation, which brings with it an increased ability to handle complex tasks and use rules, and metacognition (227). While the timing and growth of impulse control is mostly similar for both males and females, the growth in females is slightly faster. As the reasons for this slight discrepancy are currently unclear, they are speculated to be related to evolutionary and societal pressures for females to withhold impulses more than males (262)

Impulsivity and risky decision making

Although many definitions of impulsivity have been proposed there does exist agreement that it is a multidimensional concept which most commonly is considered to comprise an element of both risky decision making (impulsive choice) and disinhibition (impulsive action) (257,293,294). Some authors also consider sensation-seeking a form of impulsivity (264); and, more recently, a three-dimensional model which incorporates sensation-seeking has been suggested for conceptualising impulsivity in offending populations (295). Research suggests that impatience, a form of impulsivity where short term rewards are prioritised over a more valued distal goal similar to acting without thinking (264), is associated with weak executive functions and that impatient adolescents are more likely to engage in drug use (264,294,296).

A series of meta-analyses examining age differences in risky decision-making found that, as expected, adolescents take more risks than adults (small effect size) and, compared to mid-adolescents, early adolescents take more risks (very small effect size). Conversely when adolescents were compared to children, results indicated that they both take risks at equal levels, and similarly, early adolescents and children take equal levels of risk (297).

The evidence suggests that, due to the combination of heightened reward sensitivity and the influence of rewards on inhibitory control regions, decision-making in the presence of rewards may be immature during adolescence. Based on this finding it is posited that adolescents may not have the ability to 'override' the urge to approach rewards, and rewards may heighten the cognitive processes that are involved in approaching the reward, while inhibiting actions toward the alternative (253).

6. Emotional Maturity: The State of the Evidence

6.1 Limitations of the Imaging Literature

There is a critical need for longitudinal research to establish both how within-subject developmental changes occur during adolescence in relation to risk-taking behaviours and psychopathology, and to identify the important causative risk factors. The studies to empirically test such assumptions do not however currently exist and factors of a range of related outcomes and indicators should be addressed in future longitudinal cohort studies. Indeed, one of the overriding conclusions from many of the reviews is the pressing need for detailed large-scale longitudinal research into adolescent neurodevelopment, to understand distinctions between normal and abnormal trajectories and their impact on behaviour and pathophysiology.

Other factors that should be considered in the context of this review are potential confounders. Brain imaging is an exciting and valuable technique; however, it generates considerable amounts of complex data and is expensive to conduct. Many other factors also need to be considered, such as genetics and the environment. For example, there are few studies addressing the mechanisms through which socioeconomic status may impact brain development, a factor which may be critically important in terms of overall outcomes.

Although the field of neuroimaging is now moving to a more robust statistical format of discovery and replication and open science, in the past it has been blighted by small sample sizes, heterogeneity (methodologically, analytically and recruitment-wise), and failure to replicate. The lack of convergence in findings reflects critical theoretical, methodological, and analytic issues within the field that need to be addressed if our understanding of the association between pubertal and functional neural development is to be improved.

However, with the advent of large-scale multi-modal imaging resources, network analytic approaches, data repositories, and the necessity to make data publicly available, there are significant opportunities to leverage such assets to gain a more thorough understanding and evidence base of trajectories of normal and abnormal adolescent brain development of significant translatable relevance and potential to inform legal and educational policies. The field will benefit greatly from multidisciplinary, prospective, longitudinal research with large sample sizes that incorporate individual variability. There are numerous clinical and policy applications that may arise from this burgeoning field of research and we would urge future policymakers to consider both the

characteristics of typical adolescent development and due consideration of the factors that impact on neurocognitive maturation and which may place typical development at risk.

6.2 Limitations of the Non-imaging Literature

Those studies that did not utilise imaging techniques were primarily observational in design given that the nature of the subject matter rarely lends itself to experimental designs. As such the field remains reliant on primarily clinical samples, those in whom a difficulty has already been identified, resulting in its continued limitation by small sample sizes and significant heterogeneity, contributing to difficulty in replications.

In particular, the literature examining factors that may disrupt cognitive maturation suffer from high levels of heterogeneity, the inconsistent make up of samples, such that only studies on significantly larger scales are likely to provide robust conclusions. For example, the TBI literature lacks consistency in its definition and measurement of the severity of injuries and in defining common time points during recovery. Indeed, it is perhaps in an effort to overcome this that the literature on mild TBI was notable for its focus only on sports related concussion, which may not always be generalizable to other mechanisms of TBI. In those reviews included, there was little information on repeated TBI as well as mild TBI and concussion. The literature on substance abuse struggles with similar issues given the variation in substance type, quality, quantity and frequency that may be relevant in a context where polydrug use is common. While it may be easy to call for research to characterise the distinct effects of different substances on maturation, it is more difficult to suggest how this might be achieved. Notably, existing studies appear to lack racial diversity and often exclude those with co-occurring mental illnesses, challenges which may be easier to overcome. Lastly, substance use is often reported via self-report, using qualitative markers, possibly further contributing to heterogeneity (124) and potentially impacting the accuracy of data. Heterogeneity was also evident in the literature exploring psychiatric and neurodevelopmental disorders, arising from differences in methodologies and measures, duration of illness, comorbidities, family history, and socioeconomic status, all of which have the potential to influence results.

More robust evidence on the maturation of cognitive abilities and the factors which affect this will require longitudinal cohort studies from representative populations where typically developing young people are observed in addition to those who subsequently experience potentially harmful

environmental factors. Such studies would also have the opportunity to examine factors which have yet to be examined in depth, such as the effect of diet, gender, and sleep on cognitive maturation (5). Arguably, even more important for the consideration of cognitive maturation is the need for studies that identify the differential effect of neurological insults during each stage of both childhood and adolescence given that their effect is likely to be mediated by the individual's current level of developmental maturity or to impact their ability to achieve subsequent developmental milestones. Indeed, the effects of an insult that occurs early in childhood may not become apparent until the brain lacks the resources to achieve a subsequent maturational milestone. This is particularly the case for TBI where participants should be recruited based on a smaller age range corresponding to the age at which their injury occurred (94).

Lastly, there is evidence that children who have developmental or behavioural problems are at a higher risk of being in a situation where they are abused or neglected (173,298). Thus, findings of neurocognitive impairments following mistreatment should be interpreted with caution until there are more longitudinal studies which employ a pre-abuse and post-abuse measure (173).

6.3 The Quality of Published Reviews

Despite a rigorous search strategy, very few systematic and meta-analytic reviews were available for inclusion, precluding the umbrella meta-analyses originally planned. The preponderance of narrative reviews in the field presents a significant limitation given their potential for increased risk of bias in both the papers chosen for inclusion and results reported. Systematic reviews and meta-analyses are considered to offer more robust findings given their use of rigorous, replicable search strategies and inclusion criteria. To quantify and address this limitation, all narrative reviews were critically appraised using the Scale for the Quality Assessment of Narrative Reviews (SANRA) (299), and the majority were found to be of either 'good' or 'fair' quality. Reviews that received lower scores failed to describe search strategy or any methodology, state concrete aims, or formulate/report research questions. In addition, all included systematic reviews and meta-analyses were assessed for risk of bias using the Risk of Bias in Systematic Reviews (ROBIS) tool (300). While the majority of these were rated as at low risk of bias, there were four to which the rating of 'unclear' was assigned as insufficient information was reported. All those reviews rated as unclear failed to state whether a second reviewer had been engaged to check for bias and to measure inter-rater reliability, and some

did not use a quality appraisal tool to assess quality and risk of bias in the primary studies included in their reviews. Additional limitations noted were non-adherence to review guidelines and failure to report primary studies in data tables, heterogeneity, evidence of sensitivity analyses or funnel plots. Notwithstanding these limitations, based on the ratings of the quality review rating tools that the majority of the included papers were either of fair/good quality or had a low risk of bias, we consider there is likely to be a low risk of bias in this review.

The current review took an 'umbrella' approach to synthesising the literature. Umbrella reviews provide a clear understanding of a broad topic area, as well as a means for decision makers to gather evidence in various settings (301). Further, umbrella reviews allow for the inclusion of all review types and allow researchers to compare and contrast findings from reviews rather than primary studies, allowing them to answer questions with a far wider scope. In conjunction with a robust methodology, all of the reviews were critically assessed, and care was taken when extracting and interpreting the data.

Taken together, the findings from this review are both robust and current; and, while bearing the limitations in mind, it is recommended that the evidence from this review be considered in relation to sentencing guidelines.

7. Conclusion

This report has synthesised recent neurological and neuropsychological evidence pertaining to the age at which adolescents achieve cognitive maturity. In doing so it has outlined the development of neurocognitive functions and the stages at which they occur, discussed factors that have the potential to temporarily or permanently disrupt the typical developmental trajectory, and examined the links between cognitive and emotional maturity. In doing so we have endeavoured to answer the following aims:

To identify evidence that emotional maturity is linked to maturation of the brain, and of the age at which the brain is fully developed.

The advancement of neuroimaging methods has played a key role in our understanding of adolescent cognitive development. MRI studies in particular have demonstrated that the brain remains in an active state of development until between approximately 25 and 30 years of age. During this developmental period, an immature prefrontal cortex, and consequent dysfunctional cognitive control over phylogenically older emotion and reward-related regions, are suggested to be responsible for the normative risk-taking behaviour characteristic of the adolescent period; and to contribute to difficulties in self-regulation (5,8). In short, immaturity of cognitive regions along with overactivation of emotion and reward-related regions contributes to adolescents finding it difficult to think rationally and critically before making complex decisions (9). Pubertal onset is reported to trigger this increased behavioural responsiveness to emotionally salient stimuli, again reflected in aberrant fronto-limbic functional connectivity (5,8).

To identify evidence that continuing development of the brain during adolescence and young adulthood means that young people have less impulse control, ability to plan and make rational decisions, and greater susceptibility to negative influences and peer pressure.

The brain's continued maturation during adolescence and into early adulthood limits the functional abilities of young people, impacting their capacity to control their behaviour. Most affected are those skills that form the executive functions (including the ability to plan, control impulses and pay attention), which are located in the last region of the brain to achieve maturity, the prefrontal

cortex, meaning that adolescents are unable to call upon them reliably. Concurrently, a rise in dopamine is associated with an increased sensitivity to incentives and rewards, particularly those associated with short term gain, peaking between the ages of 14 and 16 years of age. Brain regions associated with emotional responses become more active and sensation-seeking is observed to increase. Occurring together as they do, it is the immaturity of the executive functions, coupled with their emotional context, that impairs decision-making in the presence of rewards, making it difficult for adolescents to 'override' their drive towards short term gratification. This is particularly the case in males, where, in comparison to females, higher levels of sensation-seeking and lower levels of impulse control are observed (262). The presence of peers has also been observed to exert an influence on decision making, although the mechanism for this remains unclear.

To identify evidence around any factors which inhibit, either temporarily or permanently, cognitive maturation including, but not limited to, adverse childhood experiences (ACEs) and traumatic head injuries.

The ongoing development of the brain during adolescence increases its vulnerability to factors that may slow, or permanently disrupt cognitive maturation. Findings have evidenced that factors including traumatic brain injury, alcohol and substance use, psychological and neurodevelopmental disorders, and adverse childhood experiences, contribute to abnormal cognitive maturation and functioning. Adverse experiences are a particularly potent and significant risk factor as these also compound and increase the risk and vulnerability to develop significant mental health problems, accumulate further stressors and adverse experiences, and affect key factors of resilience and cooping, such as the abilities to mentalise, emotion regulate and utilise support.

To Identify areas of risk or controversy around this area, with a particular focus on implications for using this evidence in relation to setting sentencing policy

7.1 Areas of Risk or Controversy

The literature, in both neuroimaging and cognitive research, remains limited by its reliance on small, clinical samples and the difficulty in implementing experimental designs which retain ecological

validity in this area. Although reporting limitations were observed in those studies reviewed the use of structured quality appraisal tools suggested that the risk of bias remained low.

7.2 Application in Judicial Contexts

The neurobiological and cognitive developmental trajectories associated with cognitive maturation are non-linear, and differ between individuals, limiting our ability to definitively pinpoint the beginning and end of cognitive maturation. There is however converging evidence that this process continues into the mid to late twenties, an age range typically considered adult rather than adolescent and that we should consider *biological,* rather than chronological age. Most striking is that the last region to develop is that which provides the foundation for those functions most likely to be relevant in a judicial context, the executive functions. Significantly, evidence supports theoretical models that position poor decision-making and increased risk-taking in adolescence as the result of typical maturational processes rather than solely reflective of preference or personality. It would appear therefore that the consideration of culpability, and by extension sentencing, in both adolescents *and* young adults should include due regard to their cognitive maturity. More difficult will be attempts to support such deliberations with assessments of cognitive maturity on an individual level. Currently, the widespread use of imaging is both impractical and unlikely to be helpful given the variability between individuals but, as the number of epidemiological studies mapping normal brain development increase, it may in the future be possible to develop growth curves similar to those used routinely for height and weight. The comparison of offenders' performance on psychometric measures where normative data exists to illustrate typical functioning in both adolescents and adults is perhaps feasible in a minority of more serious cases but the measurement of many aspects of cognitive maturity may prove elusive.

It follows therefore that consideration of adolescent cognitive development is highly relevant to the judicial system given the necessity to:

i. Ensure an adolescent's ability to engage with the court process and their fitness to plead (15)
ii. Consider an adolescent's culpability, relative to their cognitive maturity and linked ability, during sentencing

iii. Consider sentencing decisions with reference to their potential to expose an individual to additional contextual and behavioural factors which may inhibit or disrupt typical cognitive development.

8. Bibliography

1. Spear LP. The adolescent brain and age-related behavioral manifestations. Neurosci Biobehav Rev. 2000;24(4):417–63.
2. Dahl RE. Adolescent brain development. Ann N Y Acad Sci. 2004;1021(1):1–22.
3. Falkner FT, Tanner JM. Human growth : a comprehensive treatise. 2nd ed. Falkner FT, Tanner JM (James M, editors. New York: Plenum Press; 1986.
4. Sturman DA, Moghaddam B. The neurobiology of adolescence: Changes in brain architecture, functional dynamics, and behavioral tendencies. Neurosci Biobehav Rev. 2011 Aug;35(8):1704–12.
5. Arain M, Haque M, Johal L, Mathur P, Nel W, Rais A, et al. Maturation of the adolescent brain. Neuropsychiatr Dis Treat. 2013;13(9):449–61.
6. Tamnes CK, Østby Y, Fjell AM, Westlye LT, Due-Tønnessen P, Walhovd KB. Brain maturation in adolescence and young adulthood: Regional age-related changes in cortical thickness and white matter volume and microstructure. Cereb Cortex. 2010 Mar;20(3):534–48.
7. Wahlstrom D, Collins P, White T, Luciana M. Developmental changes in dopamine neurotransmission in adolescence: behavioral implications and issues in assessment. Brain Cogn [Internet]. 2010 [cited 2019 Nov 28];72(1):146–59. Available from: https://www.sciencedirect.com/science/article/pii/S027826260900205X
8. Oron Semper J V., Murillo JI, Bernacer J. Adolescent emotional maturation through divergent models of brain organization. Front Psychol. 2016 Aug 23;7(AUG).
9. Bjork JM, Pardini DA. Who are those “risk-taking adolescents”? Individual differences in developmental neuroimaging research. Dev Cogn Neurosci [Internet]. 2015;11:56–64. Available from: http://dx.doi.org/10.1016/j.dcn.2014.07.008
10. Casey BJ, Getz S, Galvan A. The adolescent brain. Dev Rev. 2008 Mar;28(1):62–77.

11. Steinberg L. A social neuroscience perspective on adolescent risk-taking. Dev Rev. 2008;28(1):78–106.

12. Dahl RE. Affect regulation, brain development, and behavioral/emotional health in adolescence. CNS Spectr [Internet]. 2001 [cited 2019 Dec 1];6(1):60–72. Available from: https://www.cambridge.org/core/journals/cns-spectrums/article/affect-regulation-brain-development-and-behavioralemotional-health-in-adolescence/AAE9F543E2165C0EA497C406C1FAAEA1

13. Williams WH, Chitsabesan P, Fazel S, McMillan T, Hughes N, Parsonage M, et al. Traumatic brain injury: a potential cause of violent crime? The Lancet Psychiatry [Internet]. 2018 [cited 2019 Nov 28];5(10):836–44. Available from: https://www.sciencedirect.com/science/article/pii/S2215036618300622

14. Scottish Sentencing Council. Principles and Purposes of Sentencing: Consultation analysis. 2018;(November):1–5. Available from: https://www.scottishsentencingcouncil.org.uk/media/1639/principles-and-purposes-of-sentencing-consultation-analysis.pdf

15. Steinberg L. Adolescent Development and Juvenile Justice. Annu Rev Clin Psychol. 2009 Apr;5(1):459–85.

16. Scott, Elizabeth; Steinberg L. Rethinking Juvenile Justice. 2008 [cited 2019 Nov 28]; Available from: https://books.google.co.uk/books?hl=en&lr=&id=QEkbMyBLJXIC&oi=fnd&pg=PP6&dq=Rethinking+Juvenile+Justice.&ots=a7-eTdWukJ&sig=LDpBhI-xNqqlmssSok8HVYY5mho#v=onepage&q=Rethinking Juvenile Justice.&f=false

17. Kaplan PS. Adolescence. Boston:MA: Houghton Mifflin Company; 2004. 84–88 p.

18. Gavin L, MacKay A, Brown K, Harrier S, Ventura S, Kann L, et al. Centres for Disease Control and Prevention (CDC). Sexual and reproductive health of persons aged 10-24 years - United States, 2002-2007. MMWR Surveill Summ. 2009;58:1–58.

19. Blakemore SJ. Imaging brain development: The adolescent brain. Neuroimage [Internet]. 2012;61(2):397–406. Available from: http://dx.doi.org/10.1016/j.neuroimage.2011.11.080

20. Blakemore SJ, Burnett S, Dahl RE. The role of puberty in the developing adolescent brain. Hum Brain Mapp. 2010 Jun;31(6):926–33.

21. Johnson SB, Blum RW, Giedd JN. Adolescent Maturity and the Brain: The Promise and Pitfalls of Neuroscience Research in Adolescent Health Policy. J Adolesc Heal. 2009 Sep;45(3):216–21.

22. Lebel C, Beaulieu C. Longitudinal development of human brain wiring continues from childhood into adulthood. J Neurosci [Internet]. 2011 Jul 27 [cited 2019 Nov 27];31(30):10937–47. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21795544

23. Herting MM, Sowell ER. Puberty and structural brain development in humans. Front Neuroendocrinol. 2017 Jan 1;44:122–37.

24. Foulkes L, Blakemore SJ. Studying individual differences in human adolescent brain development. Nat Neurosci [Internet]. 2018 [cited 2019 Nov 21];21(3):315–23. Available from: https://doi.org/10.1038/s41593-018-0078-4

25. Suleiman AB, Galván A, Harden KP, Dahl RE. Becoming a sexual being: The 'elephant in the room' of adolescent brain development. Dev Cogn Neurosci [Internet]. 2017;25:209–20. Available from: http://dx.doi.org/10.1016/j.dcn.2016.09.004

26. Schulz KM, Sisk CL. The organizing actions of adolescent gonadal steroid hormones on brain and behavioral development. Neurosci Biobehav Rev. 2016 Nov 1;70:148–58.

27. Sisk CL, Zehr JL. Pubertal hormones organize the adolescent brain and behavior. Front Neuroendocrinol. 2005 Oct;26(3–4):163–74.

28. Sisk CL. Hormone-dependent adolescent organization of socio-sexual behaviors in mammals. Curr Opin Neurobiol. 2016 Jun 1;38:63–8.

29. Crone EA, Dahl RE. Understanding adolescence as a period of social-affective engagement and goal flexibility. Nat Rev Neurosci. 2012 Sep;13(9):636–50.

30. Spielberg JM, Olino TM, Forbes EE, Dahl RE. Exciting fear in adolescence: Does pubertal development alter threat processing? Dev Cogn Neurosci. 2014;8:86–95.

31. Op De MacKs ZA, Moor BG, Overgaauw S, Gürolu B, Dahl RE, Crone EA. Testosterone levels correspond with increased ventral striatum activation in response to monetary rewards in adolescents. Dev Cogn Neurosci. 2011 Oct;1(4):506–16.

32. Peper JS, Dahl RE. The Teenage Brain. Curr Dir Psychol Sci [Internet]. 2013 Apr 16 [cited 2019 Nov 27];22(2):134–9. Available from:

http://journals.sagepub.com/doi/10.1177/0963721412473755

33. Romeo RD. Puberty: A period of both organizational and activational effects of steroid hormones on neurobehavioural development. J Neuroendocrinol. 2003 Dec;15(12):1185–92.

34. Tackett JL, Reardon KW, Herzhoff K, Page-Gould E, Harden KP, Josephs RA. Estradiol and cortisol interactions in youth externalizing psychopathology. Psychoneuroendocrinology. 2015 May 1;55:146–53.

35. Vermeersch H, T'Sjoen G, Kaufman JM, Vincke J. The relationship between sex steroid hormones and behavioural inhibition (BIS) and behavioural activation (BAS) in adolescent boys and girls. Pers Individ Dif. 2009 Jul;47(1):3–7.

36. Wallen K. Sex and context: Hormones and primate sexual motivation. Horm Behav. 2001;40(2):339–57.

37. Juraska JM, Willing J. Pubertal onset as a critical transition for neural development and cognition. Brain Res [Internet]. 2017 Jan 1;1654:87–94. Available from: http://dx.doi.org/10.1016/j.brainres.2016.04.012

38. Hensch TK. Bistable parvalbumin circuits pivotal for brain plasticity. Cell. 2014;156(1–2):17–9.

39. Takesian AE, Hensch TK. Balancing plasticity/stability across brain development. In: Progress in Brain Research. Elsevier B.V.; 2013. p. 3–34.

40. Werker JF, Hensch TK. Critical Periods in Speech Perception: New Directions. Annu Rev Psychol [Internet]. 2015 Jan 3 [cited 2019 Nov 27];66(1):173–96. Available from: http://www.annualreviews.org/doi/10.1146/annurev-psych-010814-015104

41. Galván A. The Teenage Brain. Curr Dir Psychol Sci [Internet]. 2013 Apr 16 [cited 2019 Nov 27];22(2):88–93. Available from: http://journals.sagepub.com/doi/10.1177/0963721413480859

42. Aron A, Fisher H, Mashek DJ, Strong G, Li H, Brown LL. Reward, motivation, and emotion systems associated with early-stage intense romantic love. J Neurophysiol. 2005 Jul;94(1):327–37.

43. Fisher HE, Brown LL, Aron A, Strong G, Mashek D. Reward, addiction, and emotion regulation systems associated with rejection in love. J Neurophysiol. 2010 Jul;104(1):51–60.

44. Diamond LM, Dickenson JA. THE NEUROIMAGING OF LOVE AND DESIRE: REVIEW AND

FUTURE DIRECTIONS. Clin Neuropsychiatry [Internet]. 2012 [cited 2019 Nov 28];9. Available from: https://pdfs.semanticscholar.org/71d5/58512b5589ce62a04d951be337f51283b674.pdf

45. Dai J, Scherf KS. Puberty and functional brain development in humans: Convergence in findings? Dev Cogn Neurosci [Internet]. 2019 Oct [cited 2019 Nov 21];39:100690. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1878929318303621

46. Kilford EJ, Garrett E, Blakemore SJ. The development of social cognition in adolescence: An integrated perspective. Neurosci Biobehav Rev. 2016 Nov 1;70:106–20.

47. Blakemore S-J. The social brain in adolescence. Nat Rev Neurosci [Internet]. 2008 Apr [cited 2019 Nov 28];9(4):267–77. Available from: http://www.nature.com/articles/nrn2353

48. Gee DG, Humphreys KL, Flannery J, Goff B, Telzer EH, Shapiro M, et al. A developmental shift from positive to negative connectivity in human amygdala-prefrontal circuitry. J Neurosci. 2013 Mar 6;33(10):4584–93.

49. Guyer AE, Lau JYF, McClure-Tone EB, Parrish J, Shiffrin ND, Reynolds RC, et al. Amygdala and ventrolateral prefrontal cortex function during anticipated peer evaluation in pediatric social anxiety. Arch Gen Psychiatry. 2008 Nov;65(11):1303–12.

50. Pfeifer JH, Masten CL, Moore WE, Oswald TM, Mazziotta JC, Iacoboni M, et al. Entering Adolescence: Resistance to Peer Influence, Risky Behavior, and Neural Changes in Emotion Reactivity. Neuron. 2011 Mar 10;69(5):1029–36.

51. Somerville LH, Jones RM, Ruberry EJ, Dyke JP, Glover G, Casey BJ. The Medial Prefrontal Cortex and the Emergence of Self-Conscious Emotion in Adolescence. Psychol Sci. 2013;24(8):1554–62.

52. Spielberg JM, Forbes EE, Ladouceur CD, Worthman CM, Olino TM, Ryan ND, et al. Pubertal testosterone influences threat-related amygdala-orbitofrontal cortex coupling. Soc Cogn Affect Neurosci. 2013 Sep 3;10(3):408–15.

53. Van Den Bos W, Cohen MX, Kahnt T, Crone EA. Striatum-medial prefrontal cortex connectivity predicts developmental changes in reinforcement learning. Cereb Cortex. 2012 Jun;22(6):1247–55.

54. Barbalat G, Bazargani N, Blakemore SJ. The influence of prior expectations on emotional face

perception in adolescence. Cereb Cortex. 2013 Jul;23(7):1542–51.

55. Etkin A, Egner T, Peraza DM, Kandel ER, Hirsch J. Resolving Emotional Conflict: A Role for the Rostral Anterior Cingulate Cortex in Modulating Activity in the Amygdala. Neuron. 2006 Sep 21;51(6):871–82.

56. Hare TA, Tottenham N, Galvan A, Voss HU, Glover GH, Casey BJ. Biological substrates of emotional reactivity and regulation in adolescence during an emotional go-nogo task. Biol Psychiatry. 2008;63(10):927.

57. Achterberg M, Peper JS, van Duijvenvoorde ACK, Mandl RCW, Crone EA. Frontostriatal white matter integrity predicts development of delay of gratification: A longitudinal study. J Neurosci. 2016 Feb 10;36(6):1954–61.

58. Silk JS, Stroud LR, Siegle GJ, Dahl RE, Lee KH, Nelson EE. Peer acceptance and rejection through the eyes of youth: Pupillary, eyetracking and ecological data from the chatroom interact task. Soc Cogn Affect Neurosci. 2012 Jan;7(1):93–105.

59. Rodman AM, Powers KE, Somerville LH. Development of self-protective biases in response to social evaluative feedback. Proc Natl Acad Sci U S A. 2017 Dec 12;114(50):13158–63.

60. Silverman MH, Jedd K, Luciana M. Neural networks involved in adolescent reward processing: An activation likelihood estimation meta-analysis of functional neuroimaging studies. Neuroimage. 2015 Nov 15;122:427–39.

61. Schreuders E, Braams BR, Blankenstein NE, Peper JS, Güroğlu B, Crone EA. Contributions of Reward Sensitivity to Ventral Striatum Activity Across Adolescence and Early Adulthood. Child Dev [Internet]. 2018 May [cited 2019 Nov 27];89(3):797–810. Available from: http://doi.wiley.com/10.1111/cdev.13056

62. Braams BR, van Duijvenvoorde ACK, Peper JS, Crone EA. Longitudinal changes in adolescent risk-taking: A comprehensive study of neural responses to rewards, pubertal development, and risk-taking behavior. J Neurosci. 2015 May 6;35(18):7226–38.

63. Sherman LE, Payton AA, Hernandez LM, Greenfield PM, Dapretto M. The Power of the Like in Adolescence: Effects of Peer Influence on Neural and Behavioral Responses to Social Media. Psychol Sci. 2016 Jul 1;27(7):1027–35.

64. Sherman LE, Greenfield PM, Hernandez LM, Dapretto M. Peer Influence Via Instagram:

Effects on Brain and Behavior in Adolescence and Young Adulthood. Child Dev [Internet]. 2018 Jan [cited 2019 Nov 27];89(1):37–47. Available from: http://doi.wiley.com/10.1111/cdev.12838

65. Rudolph MD, Miranda-Domínguez O, Cohen AO, Breiner K, Steinberg L, Bonnie RJ, et al. At risk of being risky: The relationship between "brain age" under emotional states and risk preference. Dev Cogn Neurosci [Internet]. 2017 Apr 1 [cited 2019 Nov 28];24:93–106. Available from: https://www.sciencedirect.com/science/article/pii/S1878929316301074?via%3Dihub

66. Crone EA, Konijn EA. Media use and brain development during adolescence. Nat Commun. 2018 Dec 1;9(1).

67. Knoll LJ, Magis-Weinberg L, Speekenbrink M, Blakemore SJ. Social Influence on Risk Perception During Adolescence. Psychol Sci [Internet]. 2015 May 25 [cited 2019 Nov 28];26(5):583–92. Available from: http://journals.sagepub.com/doi/10.1177/0956797615569578

68. van Hoorn J, van Dijk E, Meuwese R, Rieffe C, Crone EA. Peer Influence on Prosocial Behavior in Adolescence. J Res Adolesc [Internet]. 2016 Mar 1 [cited 2019 Nov 28];26(1):90–100. Available from: http://doi.wiley.com/10.1111/jora.12173

69. Herting MM, Sowell ER. Puberty and structural brain development in humans. Front Neuroendocrinol [Internet]. 2017;44(2017):122–37. Available from: http://dx.doi.org/10.1016/j.yfrne.2016.12.003

70. Goddings AL, Mills KL, Clasen LS, Giedd JN, Viner RM, Blakemore SJ. The influence of puberty on subcortical brain development. Neuroimage. 2014 Mar;88:242–51.

71. Nguyen TV, McCracken JT, Ducharme S, Cropp BF, Botteron KN, Evans AC, et al. Interactive effects of dehydroepiandrosterone and testosterone on cortical thickness during early brain development. J Neurosci. 2013;33(26):10840–8.

72. Nguyen T-V, McCracken J, Ducharme S, Botteron KN, Mahabir M, Johnson W, et al. Testosterone-Related Cortical Maturation Across Childhood and Adolescence. Cereb Cortex [Internet]. 2013 Jun 1 [cited 2019 Nov 27];23(6):1424–32. Available from: https://academic.oup.com/cercor/article-lookup/doi/10.1093/cercor/bhs125

73. Tamnes CK, Herting MM, Goddings AL, Meuwese R, Blakemore SJ, Dahl RE, et al.

Development of the cerebral cortex across adolescence: A multisample study of inter-related longitudinal changes in cortical volume, surface area, and thickness. J Neurosci [Internet]. 2017 [cited 2019 Nov 21];37(12):3402–12. Available from: https://www.jneurosci.org/content/jneuro/37/12/3402.full.pdf

74. Mills KL, Lalonde F, Clasen LS, Giedd JN, Blakemore SJ. Developmental changes in the structure of the social brain in late childhood and adolescence. Soc Cogn Affect Neurosci [Internet]. 2014 Jan 1 [cited 2019 Nov 28];9(1):123–31. Available from: https://academic.oup.com/scan/article/9/1/123/1675831

75. Horvath S, Raj K. DNA methylation-based biomarkers and the epigenetic clock theory of ageing. Nat Rev Genet [Internet]. 2018 Jun 11 [cited 2019 Nov 28];19(6):371–84. Available from: http://www.nature.com/articles/s41576-018-0004-3

76. Cole JH, Ritchie SJ, Bastin ME, Valdés Hernández MC, Muñoz Maniega S, Royle N, et al. Brain age predicts mortality. Mol Psychiatry [Internet]. 2018 May 25 [cited 2019 Nov 28];23(5):1385–92. Available from: http://www.nature.com/articles/mp201762

77. de Nooij L, Harris MA, Hawkins EL, Shen X, Clarke T-K, Stella WY, et al. Trajectory of brain maturation in adolescent individuals at familial risk of mood disorder. bioRxiv [Internet]. 2019 Oct 17 [cited 2019 Nov 28];537951. Available from: https://www.biorxiv.org/content/10.1101/537951v3.full

78. Diamond A. Executive functions. Annu Rev Psychol. 2013;(64):135–68.

79. Hyder AA, Wunderlich CA, Puvanachandra P, Gururaj G, Kobusingye OC. The impact of traumatic brain injuries: A global perspective. NeuroRehabilitation. 2007;22:341–53.

80. Traumatic Brain Injury Information Page: National Institute of Neurological Disorders and Stroke (NINDS) [Internet]. [cited 2019 Nov 27]. Available from: https://www.ninds.nih.gov/disorders/All-disorders/traumatic-brain-injury-information-page

81. Care of Children with Concussion (also called mTBI) | CDC [Internet]. [cited 2019 Nov 27]. Available from: https://www.cdc.gov/injury/features/pediatric-mtbi-guideline/index.html

82. Collins MW, Lovell MR, Iverson GL, Cantu R, Maroon J, Field M. Cumulative-Effects-of-Concussion-in-HS-Athletics. Neurosurgery. 2002;51:1175–9.

83. Gaetz M, Goodman D, Weinberg H. Electrophysiological evidence for the cumulative effects

of concussion. Brain Inj. 2000;14(12):1077–88.

84. Guskiewicz KM, Mccrea M, Marshall SW, Cantu RC, Randolph C, Barr W, et al. The NCAA Concussion Study. J Am Med Assoc. 2003;290(19):2549–55.

85. Iverson GL, Gaetz M, Lovell MR, Collins MW. Cumulative effects of concussion in amateur athletes. Brain Inj. 2004;18(5):433–43.

86. Kirkwood MW, Yeates KO, Wilson PE. Pediatric sport-related concussion: a review of the clinical management of an oft-neglected population. Pediatrics. 2006;117(4):1359–71.

87. Keightley ML, Sinopoli KJ, Davis KD, Mikulis DJ, Wennberg R, Tartaglia MC, et al. Is there evidence for neurodegenerative change following traumatic brain injury in children and youth? A scoping review. Front Hum Neurosci. 2014 Mar 19;8(MAR).

88. Anderson V, Catroppa C, Morse S, Haritou F, Rosenfeld J. Outcome from mild head injury in young children: A prospective study. J Clin Exp Neuropsychol. 2001;23(6):705–17.

89. Wilde EA, Merkley TL, Bigler ED, Max JE, Schmidt AT, Ayoub KW, et al. Longitudinal changes in cortical thickness in children after traumatic brain injury and their relation to behavioral regulation and emotional control. Int J Dev Neurosci. 2012 May;30(3):267–76.

90. Levin, H., Benavidez, D., Verger-Maestre,K., Perachio, N., Song, J., Medndelsohn, D.B. et al. Reduction of corpus callosum growth after severe traumatic brain injury in children. Neurology. 2000;54:647–53.

91. Chamard E, Lichtenstein JD. A systematic review of neuroimaging findings in children and adolescents with sports-related concussion. Brain Inj. 2018 Jun 7;32(7):816–31.

92. Bartnik-Olson BL, Holshouser B, Wang H, Grube M, Tong K, Wong V, et al. Impaired neurovascular unit function contributes to persistent symptoms after concussion: a pilot study. J Neurotrauma. 2014 Sep 1;31(17):1497–506.

93. Orr CA, Albaugh MD, Watts R, Garavan H, Andrews T, Nickerson JP, et al. Neuroimaging biomarkers of a history of concussion observed in asymptomatic young athletes. J Neurotrauma [Internet]. 2016 May [cited 2019 Nov 27];33(9):803–10. Available from: http://www.liebertpub.com/doi/10.1089/neu.2014.3721

94. Babikian T, Asarnow R. Neurocognitive Outcomes and Recovery After Pediatric TBI: Meta-Analytic Review of the Literature. Neuropsychology. 2009 May;23(3):283–96.

95. Anderson V, Godfrey C, Rosenfeld J V., Catroppa C. Predictors of cognitive function and recovery 10 years after traumatic brain injury in young children. Pediatrics. 2012;129(2).

96. Phillips NL, Parry L, Mandalis A, Lah S. Working memory outcomes following traumatic brain injury in children: A systematic review with meta-analysis. Child Neuropsychol. 2017 Jan 2;23(1):26–66.

97. Alloway TP. Working Memory, but Not IQ, Predicts Subsequent Learning in Children with Learning Difficulties. Eur J Psychol Assess [Internet]. 2009;25(2). Available from: http://www.psycontent.com/content/1015-5759

98. Baddeley A. Working memory: Looking back and looking forward. Nat Rev Neurosci. 2003;4(10):829–39.

99. Baddeley AD, Hitch G. Working memory. Psychol Learn Motiv - Adv Res Theory. 1974 Jan 1;8(C):47–89.

100. Baddeley A. Memory: Recording Experience in Cells and Circuits. 1996;93:13468–72.

101. Baddeley A. Working memory, thought, and action. Vol. 45. OUP Oxford; 2007.

102. Sinopoli KJ, Dennis M. Inhibitory control after traumatic brain injury in children. Int J Dev Neurosci. 2012 May;30(3):207–15.

103. Gest SD, Sesma A, Masten AS, Tellegen A. Childhood peer reputation as a predictor of competence and symptoms 10 years later. J Abnorm Child Psychol. 2006 Aug;34(4):509–26.

104. Kok TB, Post WJ, Tucha O, De Bont ESJM, Kamps WA, Kingma A. Social competence in children with brain disorders: A meta-analytic review. Neuropsychol Rev. 2014;24(4):219–35.

105. Yeates KO, Bigler ED, Dennis M, Gerhardt CA, Rubin KH, Stancin T, et al. Social Outcomes in Childhood Brain Disorder: A Heuristic Integration of Social Neuroscience and Developmental Psychology. Psychol Bull. 2007 May;133(3):535–56.

106. Thomas LA, De Bellis MD, Graham R, LaBar KS. Development of emotional facial recognition in late childhood and adolescence: REPORT. Dev Sci. 2007 Sep;10(5):547–58.

107. Turkstra LS, Williams WH, Tonks J, Frampton I. Measuring social cognition in adolescents: Implications for students with TBI returning to school. NeuroRehabilitation. 2008;23(6):501–9.

108. Hardin MG, Ernst M. Functional Brain Imaging of Development-Related Risk and Vulnerability for Substance Use in Adolescents. 2009;

109. Steinberg L. Risk taking in adolescence: What changes, and why? Ann N Y Acad Sci. 2004;1021:51–8.

110. Habeych M, Folan M, Luna B, Alcohol RT-D and, 2006 undefined. Impaired oculomotor response inhibition in children of alcoholics: The role of attention deficit hyperactivity disorder. Elsevier [Internet]. [cited 2019 Nov 27]; Available from: https://www.sciencedirect.com/science/article/pii/S0376871605002589

111. Nigg JT, Wong MM, Martel MM, Jester JM, Puttler LI, Glass JM, et al. Poor response inhibition as a predictor of problem drinking and illicit drug use in adolescents at risk for alcoholism and other substance use disorders. J Am Acad Child Adolesc Psychiatry. 2006 Apr;45(4):468–75.

112. Habeych ME, Sclabassi RJ, Charles PJ, Kirisci L, Tarter RE. Association among parental substance use disorder, P300 amplitude, and neurobehavioral disinhibition in preteen boys at high risk for substance use disorder. Psychol Addict Behav. 2005;19(2):123–30.

113. Kamarajan C, Porjesz B, Jones K, Chorlian D, Padmanabhapillai A, Rangaswamy M, et al. Event-related oscillations in offspring of alcoholics: Neurocognitive disinhibition as a risk for alcoholism. Biol Psychiatry. 2006 Apr 1;59(7):625–34.

114. Silveri M, Dager A, Cohen-Gilbert & S. Neurobiological signatures associated with alcohol and drug use in the human adolescent brain. Elsevier [Internet]. 2016 [cited 2019 Nov 27]; Available from: https://www.sciencedirect.com/science/article/pii/S0149763416301518

115. Jacobus J, Tapert SF. Neurotoxic Effects of Alcohol in Adolescence. Annu Rev Clin Psychol. 2013;9(1):703–21.

116. Filley CM. White matter: Organization and functional relevance. Neuropsychol Rev. 2010 Jun;20(2):158–73.

117. Chiaravalloti ND, DeLuca J. Cognitive impairment in multiple sclerosis. Lancet Neurol. 2008 Dec;7(12):1139–51.

118. Elofson J, Gongvatana W, Carey KB. Alcohol use and cerebral white matter compromise in adolescence. Addict Behav. 2013 Jul;38(7):2295–305.

119. De Bellis MD, Clark DB, Beers SR, Soloff PH, Boring AM, Julie Hall B, et al. Hippocampal

Volume in Adolescent-Onset Alcohol Use Disorders. Am J Psychiatry. 2000;157(5).

120. Medina KL, Hanson KL, Schweinsburf AD, Cohen-Zion M, Nafel BJ, Tapert SF. Neuropsychological functioning in adolescent marijuana users: Subtle deficits detectable after a month of abstinence. J Int Neuropsychol Soc. 2007;13(5):807–20.

121. Wilson S, Malone SM, Thomas KM, Iacono WG. Adolescent drinking and brain morphometry: A co-twin control analysis. Dev Cogn Neurosci. 2015 Dec 1;16:130–8.

122. Squeglia LM, Boissoneault J, Van Skike CE, Nixon SJ, Matthews DB. Age-Related Effects of Alcohol from Adolescent, Adult, and Aged Populations Using Human and Animal Models. Alcohol Clin Exp Res. 2014;38(10):2509–16.

123. Squeglia LM, Tapert SF, Sullivan E V, Jacobus J, Meloy MJ, Rohlfing T, et al. Brain Development in Heavy-Drinking Adolescents. Am J Psychiatry [Internet]. 2015;172:531–42. Available from: http://www.nitrc.org/proj-

124. Squeglia LM, Gray KM. Alcohol and Drug Use and the Developing Brain. Curr Psychiatry Rep. 2016 May 1;18(5).

125. Thoma RJ, Monnig MA, Lysne PA, Ruhl DA, Pommy JA, Bogenschutz M, et al. Adolescent Substance Abuse: The Effects of Alcohol and Marijuana on Neuropsychological Performance. Alcohol Clin Exp Res. 2011;35(1):39–46.

126. Parada M, Corral M, Mota N, Crego A, Rodríguez Holguín S, Cadaveira F. Executive functioning and alcohol binge drinking in university students. Addict Behav. 2012 Feb;37(2):167–72.

127. Hanson KL, Medina KL, Padula CB, Tapert SF, Brown SA. Impact of Adolescent Alcohol and Drug Use on Neuropsychological Functioning in Young Adulthood:10-year Outcomes. J Child Adolesc Subst Abus. 2011 Apr;20(2):135–54.

128. Squeglia LM, Spadoni AD, Infante MA, Myers MG, Tapert SF. Initiating Moderate to Heavy Alcohol Use Predicts Changes in Neuropsychological Functioning for Adolescent Girls and Boys. Psychol Addict Behav. 2009 Dec;23(4):715–22.

129. Mahmood OM, Jacobus J, Bava S, Scarlett A, Tapert SF. Learning and Memory Performances in Adolescent Users of Alcohol and Marijuana: Interactive Effects*. 2010;

130. Lees B, Mewton L, Stapinski LA, Squeglia LM, Rae CD, Teesson M. Neurobiological and Cognitive Profile of Young Binge Drinkers: a Systematic Review and Meta-Analysis.

Neuropsychol Rev. 2019 Sep 1;29(3):357–85.

131. Krebs MO, Kebir O, Jay TM. Exposure to cannabinoids can lead to persistent cognitive and psychiatric disorders. Eur J Pain (United Kingdom). 2019 Aug 1;23(7):1225–33.

132. Lorenzetti V, Alonso-Lana S, Youssef GJ, Verdejo-Garcia A, Suo C, Cousijn J, et al. Adolescent Cannabis Use: What is the Evidence for Functional Brain Alteration? Curr Pharm Des [Internet]. 2016 [cited 2019 Nov 20];22:1–14. Available from: https://www.researchgate.net/profile/Janna_Cousijn/publication/306434093_Adolescent_cannabis_use_What_is_the_evidence_for_functional_brain_alteration/links/57dbcf0508ae4e6f1845e068.pdf

133. Schweinsburg AD, Schweinsburg BC, Lisdahl Medina K, McQueeny T, Brown SA, Tapert SF. The Influence of Recency of Use on fMRI Response During Spatial Working Memory in Adolescent Marijuana Users. J Psychoact Drugs. 2010;42(116B):401–12.

134. Tapert SF, Schweinsburg AD, Drummond SPA, Paulus MP, Brown SA, Yang TT, et al. Functional MRI of inhibitory processing in abstinent adolescent marijuana users. Psychopharmacology (Berl). 2007 Oct;194(2):173–83.

135. Bava S, Tapert SF. Adolescent brain development and the risk for alcohol and other drug problems. Neuropsychol Rev. 2010;20(4):398–413.

136. Koenders L, Lorenzetti V, De Haan L, Suo C, Vingerhoets WAM, Van Den Brink W, et al. Longitudinal study of hippocampal volumes in heavy cannabis users. J Psychopharmacol. 2017 Aug 1;31(8):1027–34.

137. Gruber SA, Sagar KA. Marijuana on the Mind? The Impact of Marijuana on Cognition, Brain Structure, and Brain Function, and Related Public Policy Implications. Policy Insights from Behav Brain Sci. 2017 Mar 1;4(1):104–11.

138. Wilson W, Mathew R, Turkington T, Hawk T, Coleman RE, Provenzale J. Brain morphological changes and early marijuana use: A magnetic resonance and positron emission tomography study. J Addict Dis. 2000 Mar 9;19(1):1–22.

139. Jacobus J, Bava S, Cohen-Zion M, Mahmood O, Tapert SF. Functional consequences of marijuana use in adolescents. Pharmacol Biochem Behav [Internet]. 2009 [cited 2019 Nov 27];92(4):559–65. Available from: https://www.sciencedirect.com/science/article/pii/S0091305709001051

140. Lane SD, Cherek DR, Tcheremissine O V., Steinberg JL, Sharon JL. Response perseveration and adaptation in heavy marijuana-smoking adolescents. Addict Behav. 2007 May;32(5):977–90.

141. Harvey MA, Sellman JD, Porter RJ, Frampton CM. The relationship between non-acute adolescent cannabis use and cognition. Drug Alcohol Rev. 2007 May;26(3):309–19.

142. Tapert SF, Granholm E, Leedy NG, Brown SA. Substance use and withdrawal: Neuropsychological functioning over 8 years in youth. J Int Neuropsychol Soc. 2002;8(7):873–83.

143. Ganzer F, Bröning S, Kraft S, Sack PM, Thomasius R. Weighing the Evidence: A Systematic Review on Long-Term Neurocognitive Effects of Cannabis Use in Abstinent Adolescents and Adults. Neuropsychol Rev. 2016 Jun 1;26(2):186–222.

144. Ehrenreich H, Rinn T, Hanns ·, Kunert J, Moeller MR, Poser W, et al. Specific attentional dysfunction in adults following early start of cannabis use. Psychopharmacology (Berl). 1999;142:295–301.

145. Pope HG, Gruber AJ, Hudson JI, Cohane G, Huestis MA, Yurgelun-Todd D. Early-onset cannabis use and cognitive deficits: What is the nature of the association? Drug Alcohol Depend. 2003 Apr 1;69(3):303–10.

146. Fried PA, Watkinson B, Gray R. Neurocognitive consequences of marihuana - A comparison with pre-drug performance. Neurotoxicol Teratol. 2005;27(2):231–9.

147. McCrory EJ, Gerin MI, Viding E. Annual Research Review: Childhood maltreatment, latent vulnerability and the shift to preventative psychiatry - the contribution of functional brain imaging. J Child Psychol Psychiatry [Internet]. 2017 Apr [cited 2019 Nov 25];58(4):338–57. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28295339

148. Gottesman II, Gould TD. The Endophenotype Concept in Psychiatry: Etymology and Strategic Intentions. Am J Psychiatry [Internet]. 2003 Apr 1 [cited 2019 Nov 26];160(4):636–45. Available from: http://psychiatryonline.org/doi/abs/10.1176/appi.ajp.160.4.636

149. Cicchetti D, Rogosch FA. Equifinality and multifinality in developmental psychopathology. Dev Psychopathol [Internet]. 1996 Mar 4 [cited 2019 Nov 26];8(4):597–600. Available from: https://www.cambridge.org/core/product/identifier/S0954579400007318/type/journal_article

150. Harkness KL, Wildes JE. Childhood adversity and anxiety versus dysthymia co-morbidity in major depression. Psychol Med [Internet]. 2002 [cited 2019 Nov 26];32(7):1239–49. Available from: https://doi.org/10.1017/S0033291702006177

151. Hovens JGFM, Wiersma JE, Giltay EJ, Van Oppen P, Spinhoven P, Penninx BWJH, et al. Childhood life events and childhood trauma in adult patients with depressive, anxiety and comorbid disorders vs. controls. Acta Psychiatr Scand [Internet]. 2010 Oct 30 [cited 2019 Nov 26];122(1):66–74. Available from: http://doi.wiley.com/10.1111/j.1600-0447.2009.01491.x

152. Hovens JGFM, Giltay EJ, Wiersma JE, Spinhoven P, Penninx BWJH, Zitman FG. Impact of childhood life events and trauma on the course of depressive and anxiety disorders. Acta Psychiatr Scand [Internet]. 2012 Sep 1 [cited 2019 Nov 26];126(3):198–207. Available from: http://doi.wiley.com/10.1111/j.1600-0447.2011.01828.x

153. Nanni V, Uher R, Danese A. Childhood maltreatment predicts unfavorable course of illness and treatment outcome in depression: A meta-analysis. Am J Psychiatry [Internet]. 2012 Feb [cited 2019 Nov 26];169(2):141–51. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22420036

154. Agnew-Blais J, Danese A. Childhood maltreatment and unfavourable clinical outcomes in bipolar disorder: A systematic review and meta-analysis. The Lancet Psychiatry [Internet]. 2016 Apr 1 [cited 2019 Nov 26];3(4):342–9. Available from: https://www.sciencedirect.com/science/article/pii/S2215036615005441

155. Finkelhor D, Ormrod RK, Turner HA. Polyvictimization and trauma in a national longitudinal cohort. Dev Psychopathol [Internet]. 2007 [cited 2019 Nov 26];19(1):149–66. Available from: https://www.cambridge.org/core/services/aop-cambridge-core/content/view/3A067DFF8C45A87C9131F04F1D860C60/S0954579407070083a.pdf/polyvictimization_and_trauma_in_a_national_longitudinal_cohort.pdf

156. McCrory EJ, Viding E. The theory of latent vulnerability: Reconceptualizing the link between childhood maltreatment and psychiatric disorder. Dev Psychopathol [Internet]. 2015 [cited 2019 Nov 26];27(2):493–505. Available from: https://www.cambridge.org/core/services/aop-cambridge-core/content/view/552648FD22ACD298D00125693C2CB743/S0954579415000115a.pdf/theory_of_latent_vulnerability_reconceptualizing_the_link_between_childhood_maltreatment_and_psychiatric_disorder.pdf

157. Hein TC, Monk CS. Research Review: Neural response to threat in children, adolescents, and adults after child maltreatment – a quantitative meta-analysis. J Child Psychol Psychiatry Allied Discip [Internet]. 2017 Mar 1 [cited 2019 Nov 26];58(3):222–30. Available from: http://doi.wiley.com/10.1111/jcpp.12651

158. Nelson EE, Leibenluft E, McClure EB, Pine DS. The social re-orientation of adolescence: A neuroscience perspective on the process and its relation to psychopathology. Psychol Med [Internet]. 2005 [cited 2019 Nov 26];35(2):163–74. Available from: https://doi.org/10.1017/S0033291704003915

159. Teicher MH, Andersen SL, Polcari A, Anderson CM, Navalta CP, Kim DM. The neurobiological consequences of early stress and childhood maltreatment. Neurosci Biobehav Rev [Internet]. 2003 Jan [cited 2019 Nov 26];27(1–2):33–44. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0149763403000071

160. Lim L, Radua J, Rubia K. Gray matter abnormalities in childhood maltreatment: A voxelwise metaanalysis. Am J Psychiatry [Internet]. 2014 Aug 1 [cited 2019 Nov 26];171(8):854–63. Available from: http://psychiatryonline.org/doi/abs/10.1176/appi.ajp.2014.13101427

161. Teicher MH, Samson JA. Annual Research Review: Enduring neurobiological effects of childhood abuse and neglect. J Child Psychol Psychiatry Allied Discip [Internet]. 2016 [cited 2019 Nov 26];57(3):241–66. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4760853/pdf/nihms741660.pdf

162. Rinne-Albers MAW, Van Der Wee NJA, Lamers-Winkelman F, Vermeiren RRJM. Neuroimaging in children, adolescents and young adults with psychological trauma. Eur Child Adolesc Psychiatry [Internet]. 2013 [cited 2019 Nov 26];22(12):745–55. Available from: https://link.springer.com/content/pdf/10.1007%2Fs00787-013-0410-1.pdf

163. Phelps EA, LeDoux JE. Contributions of the amygdala to emotion processing: From animal models to human behavior. Neuron. 2005;48(2):175–87.

164. Pelphrey K, Adolphs R, Morris JP. Neuroanatomical substrates of social cognition dysfunction in autism. Ment Retard Dev Disabil Res Rev. 2004;10(4):259–71.

165. Francati V, Vermetten E, Bremer JD. Stress Disorder : Review of Current Methods and. Depress Anxiety. 2007;24(3):202–18.

166. Singer T, Critchley H, Preuschoff K. A common role of insula in feelings, empathy and

uncertainty. J Clin Epidemiol. 2009;13(8):334–440.

167. Eisenberger NI. Social Pain and the Brain: Controversies, Questions, and Where to Go from Here. Annu Rev Psychol. 2015;66(1):601–29.

168. Smith AR, Steinberg L, Chein J. The role of the anterior insula in adolescent decision making. Dev Neurosci. 2014;36(3–4):196–209.

169. Teicher MH, Samson JA, Anderson CM, Ohashi K. The effects of childhood maltreatment on brain structure, function and connectivity. Nat Rev Neurosci [Internet]. 2016 [cited 2019 Nov 26];17(10):652–66. Available from: www.nature.com/nrn

170. Pizzagalli DA, Holmes AJ, Dillon DG, Goetz EL, Birk JL, Bogdan R, et al. Reduced Caudate and Nucleus Accumbens Response to Rewards in Unmedicated Individuals With Major Depressive Disorder. Am J Psychiatry [Internet]. 2009 Jun [cited 2019 Nov 26];166(6):702–10. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19411368

171. McLaughlin KA, Sheridan MA, Lambert HK. Childhood adversity and neural development: Deprivation and threat as distinct dimensions of early experience. Neurosci Biobehav Rev. 2014;47:578–91.

172. Danese A, Moffitt TE, Arseneault L, Bleiberg BA, Dinardo PB, Gandelman SB, et al. The origins of cognitive deficits in victimized children: Implications for neuroscientists and clinicians. Am J Psychiatry [Internet]. 2017 Apr [cited 2019 Nov 26];174(4):349–61. Available from: http://ajp.psychiatryonline.org/doi/10.1176/appi.ajp.2016.16030333

173. Kavanaugh BC, Dupont-Frechette JA, Jerskey BA, Holler KA. Neurocognitive deficits in children and adolescents following maltreatment: Neurodevelopmental consequences and neuropsychological implications of traumatic stress. Appl Neuropsychol Child [Internet]. 2017 [cited 2019 Nov 26];6(1):64–78. Available from: https://www.tandfonline.com/action/journalInformation?journalCode=hapc20

174. Fishbein D, Warner T, Krebs C, Trevarthen N, Flannery B, Hammond J. Differential Relationships Between Personal and Community Stressors and Children's Neurocognitive Functioning. Child Maltreat [Internet]. 2009 Nov 29 [cited 2019 Nov 26];14(4):299–315. Available from: http://journals.sagepub.com/doi/10.1177/1077559508326355

175. Kavanaugh B, Holler K, Selke G. A Neuropsychological Profile of Childhood Maltreatment Within an Adolescent Inpatient Sample. Appl Neuropsychol Child [Internet]. 2015 Jan 2 [cited

2019 Nov 26];4(1):9–19. Available from: http://www.tandfonline.com/doi/abs/10.1080/21622965.2013.789964

176. Spann MN, Mayes LC, Kalmar JH, Guiney J, Womer FY, Pittman B, et al. Childhood abuse and neglect and cognitive flexibility in adolescents. Child Neuropsychol [Internet]. 2012 Mar [cited 2019 Nov 26];18(2):182–9. Available from: http://www.tandfonline.com/doi/abs/10.1080/09297049.2011.595400

177. Cowell RA, Cicchetti D, Rogosch FA, Toth SL. Childhood maltreatment and its effect on neurocognitive functioning: Timing and chronicity matter. Dev Psychopathol [Internet]. 2015 May [cited 2019 Nov 26];27(2):521–33. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25997769

178. Beers SR, De Bellis MD. Neuropsychological function in children with maltreatment-related posttraumatic stress disorder. Am J Psychiatry [Internet]. 2002 Mar 1 [cited 2019 Nov 26];159(3):483–6. Available from: http://psychiatryonline.org/doi/abs/10.1176/appi.ajp.159.3.483

179. Kavanaugh B, Holler K. Executive, emotional, and language functioning following childhood maltreatment and the influence of pediatric PTSD. J Child Adolesc Trauma [Internet]. 2014 Jun 29 [cited 2019 Nov 26];7(2):121–30. Available from: http://link.springer.com/10.1007/s40653-014-0014-z

180. De Bellis MD, Woolley DP, Hooper SR. Neuropsychological Findings in Pediatric Maltreatment: Relationship of PTSD, Dissociative Symptoms, and Abuse/Neglect Indices to Neurocognitive Outcomes. Child Maltreat [Internet]. 2013 Aug 25 [cited 2019 Nov 26];18(3):171–83. Available from: http://journals.sagepub.com/doi/10.1177/1077559513497420

181. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. Arch Gen Psychiatry. 2005 Jun;62(6):593.

182. Swartz JR, Knodt AR, Radtke SR, Hariri AR. A neural biomarker of psychological vulnerability to future life stress. Neuron. 2015;85(3):505–11.

183. Clayborne ZM, Varin M, Colman I. Systematic Review and Meta-Analysis: Adolescent Depression and Long-Term Psychosocial Outcomes. J Am Acad Child Adolesc Psychiatry. 2019

Jan;58(1):72–9.

184. Hampel P, Petermann F. Age and gender effects on coping in children and adolescents. J Youth Adolesc. 2005;34(2):73–83.

185. Miguel-Hidalgo JJ. Brain structural and functional changes in adolescents with psychiatric disorders. Int J Adolesc Med Health. 2013;25(3):245–56.

186. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington, DC: American Psychiatric Association; 2013.

187. Mollon J, Reichenberg A. Cognitive development prior to onset of psychosis. Psychol Med [Internet]. 2018 [cited 2019 Nov 23];48(3):392–403. Available from: https://doi.org/10.1017/S0033291717001970

188. Aylward E, Walker E, Bettes B. Intelligence in Schizophrenia: Meta-analysis of the Research. Schizophr Bull [Internet]. 1984 Jan 1 [cited 2019 Nov 23];10(3):430–59. Available from: http://www.ncbi.nlm.nih.gov/pubmed/6382590

189. Khandaker GM, Barnett JH, White IR, Jones PB. A quantitative meta-analysis of population-based studies of premorbid intelligence and schizophrenia. Schizophr Res [Internet]. 2011 Nov [cited 2019 Nov 23];132(2–3):220–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21764562

190. Cannon M, Moffitt TE, Caspi A, Murray RM, Harrington H, Poulton R. Neuropsychological performance at the age of 13 years and adult schizophreniform disorder. Br J Psychiatry [Internet]. 2006 Nov 2 [cited 2019 Nov 23];189(5):463–4. Available from: https://www.cambridge.org/core/product/identifier/S0007125000232972/type/journal_article

191. Parellada M, Gomez-Vallejo S, Burdeus M, Arango C. Developmental Differences between Schizophrenia and Bipolar Disorder. Schizophr Bull [Internet]. 2017 [cited 2019 Nov 20];43(6):1176–89. Available from: https://academic.oup.com/schizophreniabulletin/article-abstract/43/6/1176/4554270

192. Trotta A, Murray RM, MacCabe JH. Do premorbid and post-onset cognitive functioning differ between schizophrenia and bipolar disorder? A systematic review and meta-analysis. Psychol Med [Internet]. 2015 Jan 23 [cited 2019 Nov 23];45(2):381–94. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25065268

193. Murray RM, Sham P, Van Os J, Zanelli J, Cannon M, McDonald C. A developmental model for similarities and dissimilarities between schizophrenia and bipolar disorder. Schizophr Res [Internet]. 2004 Dec 1 [cited 2019 Nov 23];71(2–3):405–16. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15474912

194. Purcell SM, Wray NR, Stone JL, Visscher PM, O'Donovan MC, Sullivan PF, et al. Common polygenic variation contributes to risk of schizophrenia and bipolar disorder. Nature [Internet]. 2009 Aug 1 [cited 2019 Nov 23];460(7256):748–52. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19571811

195. Koenen KC, Moffitt TE, Roberts AL, Martin LT, Kubzansky L, Harrington H, et al. Childhood IQ and Adult Mental Disorders: A Test of the Cognitive Reserve Hypothesis. Am J Psychiatry [Internet]. 2009 Jan [cited 2019 Nov 23];166(1):50–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19047325

196. Iorfino F, Hickie IB, Lee RSC, Lagopoulos J, Hermens DF. The underlying neurobiology of key functional domains in young people with mood and anxiety disorders: A systematic review. BMC Psychiatry [Internet]. 2016 [cited 2019 Nov 20];16(1). Available from: https://bmcpsychiatry.biomedcentral.com/track/pdf/10.1186/s12888-016-0852-3

197. Hariri AR, Drabant EM, Munoz KE, Kolachana BS, Mattay VS, Egan MF, et al. A Susceptibility Gene for Affective Disorders and the Response of the Human Amygdala. Arch Gen Psychiatry [Internet]. 2005 Feb 1 [cited 2019 Nov 23];62(2):146. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15699291

198. Pannekoek JN, van der Werff SJA, van den Bulk BG, van Lang NDJ, Rombouts SARB, van Buchem MA, et al. Reduced anterior cingulate gray matter volume in treatment-naïve clinically depressed adolescents. NeuroImage Clin [Internet]. 2014 [cited 2019 Nov 23];4:336–42. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24501702

199. Serafini G, Pompili M, Borgwardt S, Houenou J, Geoffroy PA, Jardri R, et al. Brain changes in early-onset bipolar and unipolar depressive disorders: a systematic review in children and adolescents. Eur Child Adolesc Psychiatry [Internet]. 2014 [cited 2019 Nov 20];23(11):1023–41. Available from: https://link.springer.com/content/pdf/10.1007%2Fs00787-014-0614-z.pdf

200. Olivo G, Gaudio S, Schiöth HB. Brain and Cognitive Development in Adolescents with Anorexia Nervosa: A Systematic Review of fMRI Studies. Nutrients [Internet]. 2019 [cited 2019 Nov

20];11(8):1907. Available from: www.mdpi.com/journal/nutrients

201. Arnsten AFT, Rubia K. Neurobiological circuits regulating attention, cognitive control, motivation, and emotion: Disruptions in neurodevelopmental psychiatric disorders. J Am Acad Child Adolesc Psychiatry [Internet]. 2012 Apr 1 [cited 2019 Nov 23];51(4):356–67. Available from: https://www.sciencedirect.com/science/article/pii/S0890856712000433?via%3Dihub

202. Shaw P, Eckstrand K, Sharp W, Blumenthal J, Lerch JP, Greenstein D, et al. Attention-deficit/hyperactivity disorder is characterized by a delay in cortical maturation. Proc Natl Acad Sci U S A [Internet]. 2007 Dec 4 [cited 2019 Nov 25];104(49):19649–54. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18024590

203. Marley C, O'Leary AM, Nikopoulou VA. Broken brains or flawed studies? An update on Leo and Cohen's critical review of ADHD neuroimaging. J Mind Behav. 2018;39(3):205–28.

204. Leo J, Cohen D. Broken Brains or Flawed Studies? A Critical Review of ADHD Neuroimaging Research. Source J Mind Behav [Internet]. 2003 [cited 2019 Nov 25];24(1):29–55. Available from: https://www.jstor.org/stable/pdf/43853990.pdf?refreqid=excelsior%3A9ad226a3d54373c27e3b542d083c5632

205. Lee RSC, Hermens DF, Porter MA, Redoblado-Hodge MA. A meta-analysis of cognitive deficits in first-episode Major Depressive Disorder. J Affect Disord [Internet]. 2012 Oct [cited 2019 Nov 25];140(2):113–24. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22088608

206. Rock PL, Roiser JP, Riedel WJ, Blackwell AD. Cognitive impairment in depression: a systematic review and meta-analysis. Psychol Med [Internet]. 2014 Jul 29 [cited 2019 Nov 25];44(10):2029–40. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24168753

207. Jaeger J, Berns S, Uzelac S, Davis-Conway S. Neurocognitive deficits and disability in major depressive disorder. Psychiatry Res [Internet]. 2006 Nov 29 [cited 2019 Nov 25];145(1):39–48. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17045658

208. Kaygusuz CC, Arisoy O, Boztas MH, Sercan M. Comparison of first episode and recurrent major depression patients in terms of cognitive function. Dusunen Adam J Psychiatry Neurol Sci [Internet]. 2013 [cited 2019 Nov 25];26(4):320–32. Available from: https://pdfs.semanticscholar.org/02cf/81afa628e50411ba7471e5ac98e2d3ca33ba.pdf

209. Goodall J, Fisher C, Hetrick S, Phillips L, Parrish EM, Allott K. Neurocognitive Functioning in Depressed Young People: A Systematic Review and Meta-Analysis. Neuropsychol Rev [Internet]. 2018 [cited 2019 Nov 25];28(2):216–31. Available from: https://link.springer.com/content/pdf/10.1007%2Fs11065-018-9373-9.pdf

210. Baune BT, Fuhr M, Air T, Hering C. Neuropsychological functioning in adolescents and young adults with major depressive disorder – A review. Psychiatry Res [Internet]. 2014 Aug 30 [cited 2019 Nov 25];218(3):261–71. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24851725

211. Allott K, Fisher CA, Amminger GP, Goodall J, Hetrick S. Characterizing neurocognitive impairment in young people with major depression: state, trait, or scar? Brain Behav [Internet]. 2016 [cited 2019 Nov 25];6(10). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5064339/

212. Seidman LJ, Mirsky AF. Evolving Notions of Schizophrenia as a Developmental Neurocognitive Disorder. J Int Neuropsychol Soc [Internet]. 2017 [cited 2019 Nov 25];23:881–92. Available from: https://doi.org/10.1017/S1355617717001114

213. Schaefer J, Giangrande E, Weinberger DR, Dickinson D. The global cognitive impairment in schizophrenia: Consistent over decades and around the world. Scizophrenia Res. 2013;150(1):42–50.

214. Fioravanti M, Bianchi V, Cinti ME. Cognitive deficits in schizophrenia: An updated metanalysis of the scientific evidence. BMC Psychiatry. 2012;12.

215. Fatouros-Bergman H, Cervenka S, Flyckt L, Edman G, Farde L. Meta-analysis of cognitive performance in drug-naïve patients with schizophrenia. Schizophr Res [Internet]. 2014;158(1–3):156–62. Available from: http://dx.doi.org/10.1016/j.schres.2014.06.034

216. Kremen WS, Seidman LJ, Faraone S V., Toomey R, Tsuang MT. The paradox of normal neuropsychological function in schizophrenia. J Abnorm Psychol [Internet]. 2000 [cited 2019 Nov 25];109(4):743–52. Available from: http://doi.apa.org/getdoi.cfm?doi=10.1037/0021-843X.109.4.743

217. Palmer BW, Heaton RK, Paulsen JS, Kuck J, Braff D, Harris MJ, et al. Is it possible to be schizophrenic yet neuropsychologically normal? Neuropsychology [Internet]. 1997 [cited 2019 Nov 25];11(3):437–46. Available from:

http://doi.apa.org/getdoi.cfm?doi=10.1037/0894-4105.11.3.437

218. Kremen WS, Seidman LJ, Faraone S V., Toomey R, Tsuang MT. Heterogeneity of schizophrenia: a study of individual neuropsychological profiles. Schizophr Res [Internet]. 2004 Dec 1 [cited 2019 Nov 25];71(2–3):307–21. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15474901

219. Meier MH, Caspi A, Reichenberg A, Keefe RSE, Fisher HL, Harrington H, et al. Neuropsychological decline in schizophrenia from the premorbid to the postonset period: evidence from a population-representative longitudinal study. Am J Psychiatry [Internet]. 2014 Jan [cited 2019 Nov 25];171(1):91–101. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24030246

220. Jensen PS, Youngstrom EA, Steiner H, Findling RL, Meyer RE, Malone RP, et al. Consensus report on impulsive aggression as a symptom across diagnostic categories in child psychiatry: Implications for medication studies. J Am Acad Child Adolesc Psychiatry [Internet]. 2007 Mar 1 [cited 2019 Nov 25];46(3):309–22. Available from: https://www.sciencedirect.com/science/article/pii/S0890856709616750?via%3Dihub

221. Vitiello B, Stoff DM. Subtypes of aggression and their relevance to child psychiatry. J Am Acad Child Adolesc Psychiatry [Internet]. 1997 Mar 1 [cited 2019 Nov 25];36(3):307–15. Available from: https://www.sciencedirect.com/science/article/pii/S0890856709664339

222. Saylor KE, Amann BH. Impulsive Aggression as a Comorbidity of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. J Child Adolesc Psychopharmacol [Internet]. 2016 Feb [cited 2019 Nov 25];26(1):19–25. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26744906

223. Giedd JN, Blumenthal J, Xavier Castellanos F, Zijdenbos AP, Jeffries NO, Castellanos FX, et al. Brain development during childhood and adolescence: a longitudinal MRI study. J Comput Assist Tomogr [Internet]. 1999 [cited 2019 Nov 28];51(2):648–60. Available from: http://neurosci.nature.com

224. Li K, Xu E. The role and the mechanism of γ-aminobutyric acid during central nervous system development. Neurosci Bull. 2008 Jun;24(3):195–200.

225. Barrasso-Catanzaro C, Eslinger PJ. Neurobiological Bases of Executive Function and Social-Emotional Development: Typical and Atypical Brain Changes. Fam Relat. 2016;65(1):108–19.

226. Eslinger P. Conceptualizing, describing, and measuring components of executive function: A summary. 1996 [cited 2019 Nov 29]; Available from: https://psycnet.apa.org/record/1995-98902-019

227. Best JR, Miller PH. A Developmental Perspective on Executive Function. Child Dev [Internet]. 2010 Nov [cited 2019 Nov 28];81(6):1641–60. Available from: http://doi.wiley.com/10.1111/j.1467-8624.2010.01499.x

228. Giedd JN. Structural magnetic resonance imaging of the adolescent brain. Ann new york Acad Sci. 2004;1021(1):77–85.

229. Ziva Kunda. The case for Motivated Reasoning. Psychol Bull [Internet]. 1990;108(3):480–98. Available from: http://synapse.princeton.edu/~sam/kunda90_psychol_bulletin_the-case-for-motivated-reasoning.pdf

230. Machluf K, Bjorklund DF. Social cognitive development from an evolutionary perspective. Evol Perspect Soc Psychol. 2015;149–58.

231. Shulman EP, Smith AR, Silva K, Icenogle G, Duell N, Chein J, et al. The dual systems model: Review, reappraisal, and reaffirmation. Dev Cogn Neurosci. 2016 Feb 1;17:103–17.

232. Duckworth AL, Steinberg L. Unpacking Self-Control. Child Dev Perspect [Internet]. 2015 Mar [cited 2019 Nov 28];9(1):32–7. Available from: http://doi.wiley.com/10.1111/cdep.12107

233. Evans JSB, Science KS-P on P, 2013 undefined. Dual-process theories of higher cognition: Advancing the debate. JSTOR [Internet]. [cited 2019 Nov 28]; Available from: https://www.jstor.org/stable/44289870

234. Luna B, Wright C. Adolescent brain development: Implications for the juvenile criminal justice system. In: APA handbook of psychology and juvenile justice. American Psychological Association; 2015. p. 91–116.

235. Metcalfe J. A Hot/Cool-System Analysis of Delay of Gratification: Dynamics of Willpower. 1999 [cited 2019 Nov 28]; Available from: https://www.researchgate.net/publication/13101564

236. Fareri DS, Martin LN, Delgado MR. Reward-related processing in the human brain: Developmental considerations. Dev Psychopathol. 2008;20(4):1191–211.

237. Somerville LH, Casey BJ. Developmental neurobiology of cognitive control and motivational

systems. Curr Opin Neurobiol [Internet]. 2010;20(2):236–41. Available from: http://dx.doi.org/10.1016/j.conb.2010.01.006

238. Temple University. Teenage Risk-taking: Biological And Inevitable? -- ScienceDaily [Internet]. 2007 [cited 2019 Nov 28]. Available from: https://www.sciencedaily.com/releases/2007/04/070412115231.htm

239. Ernst M. The triadic model perspective for the study of adolescent motivated behavior. Brain Cogn [Internet]. 2014 [cited 2019 Nov 28];89:104–11. Available from: https://www.sciencedirect.com/science/article/pii/S0278262614000086

240. Mueller SC, Cromheeke S, Siugzdaite R, Nicolas Boehler C. Evidence for the triadic model of adolescent brain development: Cognitive load and task-relevance of emotion differentially affect adolescents and adults. Dev Cogn Neurosci. 2017 Aug 1;26:91–100.

241. Luciana M, Collins PF. Incentive Motivation, Cognitive Control, and the Adolescent Brain: Is It Time for a Paradigm Shift? Child Dev Perspect [Internet]. 2012 Aug [cited 2019 Nov 28];n/a-n/a. Available from: http://doi.wiley.com/10.1111/j.1750-8606.2012.00252.x

242. Van Leijenhorst L, Zanolie K, Van Meel CS, Westenberg PM, Rombouts SARB, Crone EA. What motivates the adolescent? brain regions mediating reward sensitivity across adolescence. Cereb Cortex. 2010 Jan;20(1):61–9.

243. Ernst M, Nelson EE, Jazbec S, McClure EB, Monk CS, Leibenluft E, et al. Amygdala and nucleus accumbens in responses to receipt and omission of gains in adults and adolescents. Neuroimage. 2005 May 1;25(4):1279–91.

244. Van Leijenhorst L, Moor BG, Op de Macks ZA, Rombouts SARB, Westenberg PM, Crone EA. Adolescent risky decision-making: Neurocognitive development of reward and control regions. Neuroimage. 2010 May;51(1):345–55.

245. Galvan A, Hare TA, Parra CE, Penn J, Voss H, Glover G, et al. Earlier development of the accumbens relative to orbitofrontal cortex might underlie risk-taking behavior in adolescents. J Neurosci. 2006;26(25):6885–92.

246. Bjork JM, Smith AR, Chen G, Hommer DW. Adolescents, Adults and Rewards: Comparing Motivational Neurocircuitry Recruitment Using fMRI. Lauwereyns J, editor. PLoS One [Internet]. 2010 Jul 6 [cited 2019 Nov 27];5(7):e11440. Available from: http://dx.plos.org/10.1371/journal.pone.0011440

247. Bjork JM, Knutson B, Fong GW, Caggiano DM, Bennett SM, Hommer DW. Behavioral/Systems/Cognitive Incentive-Elicited Brain Activation in Adolescents: Similarities and Differences from Young Adults. 2004 [cited 2019 Nov 27]; Available from: https://www.jneurosci.org/content/jneuro/24/8/1793.full.pdf

248. Benes FM. Handbook of Developmental Cognitive Neuroscience. In: Nelson CA, Luciana M, editors. Handbook of Developmental Cognitive Neuroscience [Internet]. Cambridge, MA: MIT Press; 2001 [cited 2019 Nov 27]. p. 79–92. Available from: https://books.google.co.uk/books?hl=en&lr=&id=_xAEKoSYPPUC&oi=fnd&pg=PR5&ots=egu3Wn43wo&sig=HTTsTxMLPeosF-JitP7R6usBaE4&redir_esc=y#v=onepage&q&f=false

249. Chein JM, Albert D, O'Brien L, Uckert K, Steinberg L. Peers increase adolescent risk taking by enhancing activity in the brain's reward circuitry. Dev Sci. 2011 Mar;14(2).

250. Telzer EH, Fuligni AJ, Lieberman MD, Miernicki ME, Galván A. The quality of adolescents peer relationships modulates neural sensitivity to risk taking. Soc Cogn Affect Neurosci. 2013 Sep 3;10(3):389–98.

251. Peake SJ, Dishion TJ, Stormshak EA, Moore WE, Pfeifer JH. Risk-taking and social exclusion in adolescence: Neural mechanisms underlying peer influences on decision-making. Neuroimage [Internet]. 2013 Nov 15 [cited 2019 Nov 28];82:23–34. Available from: https://www.sciencedirect.com/science/article/pii/S1053811913005557

252. Somerville LH, Casey BJ. Developmental neurobiology of cognitive control and motivational systems. Vol. 20, Current Opinion in Neurobiology. Elsevier Ltd; 2010. p. 236–41.

253. Geier CF. Adolescent cognitive control and reward processing: Implications for risk taking and substance use. Horm Behav. 2013 Jul;64(2):333–42.

254. Kambam P, Thompson C. The development of decision-making capacities in children and adolescents: Psychological and neurological perspectives and their implications for juvenile defendants. Behav Sci Law. 2009;27(2):173–90.

255. Collado A, Felton JW, MacPherson L, Lejuez CW. Longitudinal trajectories of sensation seeking, risk taking propensity, and impulsivity across early to middle adolescence. Addict Behav. 2014;39(11):1580–8.

256. Lynne-Landsman SD, Graber JA, Nichols TR, Botvin GJ. Is Sensation Seeking a Stable Trait or Does it Change Over Time? J Youth Adolesc. 2011;40(1):48–58.

257. MacPherson L, Magidson JF, Reynolds EK, Kahler CW, Lejuez CW. Changes in sensation seeking and risk-taking propensity predict increases in alcohol use among early adolescents. Alcohol Clin Exp Res. 2010 Aug;34(8):1400–8.

258. Harden KP, Tucker-Drob EM. Individual differences in the development of sensation seeking and impulsivity during adolescence: Further evidence for a dual systems model. Dev Psychol. 2011 May;47(3):739–46.

259. Peach HD, Gaultney JF. Sleep, impulse control, and sensation-seeking predict delinquent behavior in adolescents, emerging adults, and adults. J Adolesc Heal. 2013 Aug;53(2):293–9.

260. Quinn PD, Harden KP. Differential changes in impulsivity and sensation seeking and the escalation of substance use from adolescence to early adulthood. Dev Psychopathol. 2013 Feb;25(1):223–39.

261. Romer D, Hennessy M. A biosocial-affect model of adolescent sensation seeking: The role of affect evaluation and peer-group influence in adolescent drug use. Prev Sci. 2007 Jun;8(2):89–101.

262. Shulman EP, Harden KP, Chein JM, Steinberg L. Sex Differences in the Developmental Trajectories of Impulse Control and Sensation-Seeking from Early Adolescence to Early Adulthood. J Youth Adolesc. 2014;44(1):1–17.

263. Steinberg L, Chein JM. Multiple accounts of adolescent impulsivity. Proc Natl Acad Sci U S A. 2015;112(29):8807–8.

264. Romer D. Adolescent risk taking, impulsivity, and brain development: Implications for prevention. Dev Psychobiol. 2010;52(3):263–76.

265. Blakemore SJ. Avoiding Social Risk in Adolescence. Curr Dir Psychol Sci. 2018 Apr 1;27(2):116–22.

266. Reniers RLEP, Beavan A, Keogan L, Furneaux A, Mayhew S, Wood SJ. Is it all in the reward? Peers influence risk-taking behaviour in young adulthood. Br J Psychol. 2017 May 1;108(2):276–95.

267. Blakemore SJ. Avoiding Social Risk in Adolescence. Curr Dir Psychol Sci. 2018;27(2):116–22.

268. Gardner M, Steinberg L. Peer Influence on Risk Taking, Risk Preference, and Risky Decision Making in Adolescence and Adulthood: An Experimental Study. 2005;

269. D'Amico EJ, McCarthy DM. Escalation and Initiation of Younger Adolescents' Substance Use: The Impact of Perceived Peer Use. J Adolesc Heal. 2006;39(4):481–7.

270. Maxwell KA. Friends: The role of peer influence across adolescent risk behaviors. J Youth Adolesc. 2002;31(4):267–77.

271. Spear LP. Rewards, aversions and affect in adolescence: Emerging convergences across laboratory animal and human data. Dev Cogn Neurosci. 2011;1(4):390–403.

272. Blakemore SJ, Robbins TW. Decision-making in the adolescent brain. Nat Neurosci. 2012 Sep;15(9):1184–91.

273. Blakemore S-J, Mills KL. Is Adolescence a Sensitive Period for Sociocultural Processing? Annu Rev Psychol [Internet]. 2014 [cited 2019 Nov 28];65:187–207. Available from: http://psych.annualreviews.org

274. Luna B, Paulsen DJ, Padmanabhan A, Geier C. The Teenage Brain: Cognitive Control and Motivation. Curr Dir Psychol Sci. 2013;22(2):94–100.

275. Cohen AO, Casey BJ. Rewiring juvenile justice: The intersection of developmental neuroscience and legal policy. Trends Cogn Sci. 2014 Feb;18(2):63–5.

276. Somerville LH, Jones RM, Casey BJ. A time of change: Behavioral and neural correlates of adolescent. Brain Cogn. 2010;72(1):1–21.

277. Fuster JM. The Prefrontal COrtex. New York: Raven Press; 1997.

278. Luna B, Thulborn KR, Munoz DP, Merriam EP, Garver KE, Minshew NJ, et al. Maturation of Widely Distributed Brain Function Subserves Cognitive Development. 2001 [cited 2019 Nov 28]; Available from: http://www.idealibrary.com

279. Miller EK, Cohen JD. An Integrative Theory of Prefrontal Cortex Function. Annu Rev Neurosci. 2001 Mar;24(1):167–202.

280. Geier C, Luna B. The maturation of incentive processing and cognitive control. Pharmacol Biochem Behav. 2009 Sep;93(3):212–21.

281. Balleine BW, Leung BK, Ostlund SB. The orbitofrontal cortex, predicted value, and choice. Ann N Y Acad Sci. 2011;1239(1):43–50.

282. Hooper CJ, Luciana M, Conklin HM, Yarger RS. Adolescents' performance on the iowa

gambling task: Implications for the development of decision making and ventromedial prefrontal cortex. Dev Psychol. 2004 Nov;40(6):1148–58.

283. Pierrot-Deseilligny C, Müri RM, Ploner CJ, Gaymard B, Demeret S, Rivaud-Pechoux S. Decisional role of the dorsolateral prefrontal cortex in ocular motor behaviour. Brain. 2003 Jun 1;126(6):1460–73.

284. Luna B, Garver KE, Urban TA, Lazar NA, Sweeney JA. Maturation of Cognitive Processes from Late Childhood to Adulthood. Source Child Dev. 2004;75(5):1357–72.

285. Bedard AC, Nichols S, Barbosa JA, Schachar R, Logan GD, Tannock R. The development of selective inhibitory control across the life span. Dev Neuropsychol. 2002;21(1):93–111.

286. Luna B, Garver KE, Urban TA, Lazar NA, Sweeney JA. Maturation of cognitive processes from late childhood to adulthood. Child Dev. 2004 Sep;75(5):1357–72.

287. Ridderinkhof KR, Band GPH, Logan GD. A study of adaptive behavior: Effects of age and irrelevant information on the ability to inhibit one's actions. Acta Psychol (Amst). 1999;101(2–3):315–37.

288. Wise LA, Sutton JA, Gibbons PD. Decrement in Stroop Interference Time with Age. Percept Mot Skills. 1975 Aug;41(1):149–50.

289. Luna B. Developmental Changes in Cognitive Control through Adolescence. Adv Child Dev Behav [Internet]. 2009 [cited 2019 Nov 28];37:233–78. Available from: https://www.sciencedirect.com/science/article/pii/S0065240709037069

290. Kok A. Varieties of inhibition: Manifestations in cognition, event-related potentials and aging. Acta Psychol (Amst). 1999 Apr;101(2–3):129–58.

291. Connolly JD, Goodale MA, Menon RS, Munoz DP. Human fMRI evidence for the neural correlates of preparatory set. Nat Neurosci. 2002 Dec 1;5(12):1345–52.

292. Fuster JM. Frontal lobe and cognitive development The neurophysiological mechanisms of the major cognitive functions: attention, perception, memory, intelligence and language View project Metal toxicity View project. Artic J Neurocytol [Internet]. 2002 [cited 2019 Nov 28]; Available from: https://www.researchgate.net/publication/10701247

293. Dalley JW, Everitt BJ, Robbins TW. Impulsivity, Compulsivity, and Top-Down Cognitive Control. Neuron. 2011 Feb 24;69(4):680–94.

294. Reynolds B. A review of delay-discounting research with humans: relations to drug use and gambling. Behav Pharmacol. 2006;17:651–67.

295. Tonnaer F, Cima M, Arntz A. Modeling impulsivity in forensic patients: A three-dimensional model of impulsivity. Am J Psychol. 2016;129(4):429–41.

296. Romer D, Duckworth AL, Sznitman S, Park S. Can adolescents learn self-control? Delay of gratification in the development of control over risk taking. Prev Sci. 2010 Sep;11(3):319–30.

297. Defoe IN, Dubas JS, Figner B, Van Aken MAG. A meta-analysis on age differences in risky decision making: Adolescents versus children and adults. Psychol Bull. 2015;141(1):48–84.

298. Olson K, Jacobson KK. The Importance of Assessing for Abuse and Neglect in Children With Chronic Health Conditions Referred for Neuropsychological Evaluation. Appl Neuropsychol Child. 2014;3(1):66–72.

299. Baethge C, Goldbeck-Wood S, Mertens S. SANRA—a scale for the quality assessment of narrative review articles. Res Integr Peer Rev [Internet]. 2019 Dec 26 [cited 2019 Nov 28];4(1):5. Available from: https://researchintegrityjournal.biomedcentral.com/articles/10.1186/s41073-019-0064-8

300. Whiting P, Svovic J, Higgins J, Caldwell D, Reeves B, Shea B, et al. ROBIS : Tool to assess risk of bias in systematic reviews Guidance on how to use ROBIS. Univ Bristol Sch Soc Community Med [Internet]. 2018;1–39. Available from: https://www.bristol.ac.uk/media-library/sites/social-community-medicine/robis/robisguidancedocument.pdf%0Ahttp://www.bristol.ac.uk/media-library/sites/social-community-medicine/robis/robisguidancedocument.pdf

301. Aromataris E, Fernandez R, Godfrey CM, Holly C, Khalil H, Tungpunkom P. Summarizing systematic reviews: Methodological development, conduct and reporting of an umbrella review approach. Int J Evid Based Healthc. 2015;13(3):132–40.

302. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. Hillsdale, NJ: Erlbaum.e; 1988.

303. Cohen J. A power primer. Psychol Bull. 1992;(122):155–9.

9. Appendix A: Methodology

The review was commissioned by the Scottish Courts and Tribunals Service (contract Reference: SCTS-2019-011) with the following stated aims:

To carry out a literature review of the latest neurological research into the age at which cognitive maturity is reached, and any evidence of gender differences in brain maturation. In particular, this should evaluate:

i. evidence that continuing development of the brain during adolescence and young adulthood means that young people have less impulse control, ability to plan and make rational decisions, and greater susceptibility to negative influences and peer pressure; *(functional development)*
ii. evidence that emotional maturity is linked to maturation of the brain, and of the age at which the brain is fully developed; *(neuro-anatomical development)*
iii. evidence around any factors which inhibit, either temporarily or permanently, cognitive maturation including, but not limited to, Adverse Childhood Experiences (ACEs) and traumatic head injuries; *(factors that affect or inhibit maturation)*
iv. any areas of risk or controversy around this area, with a particular focus on implications for using this evidence in relation to setting sentencing policy. *(the state of the evidence and conclusions)*

Design

An umbrella review, that is a systematic collection and assessment of multiple published meta-analyses and systematic reviews on a topic of interest[1], was conducted using search terms designed to capture the stated aims.

Literature Search

During November 2019 three separate systematic searches were conducted corresponding to the first three of these aims; functional development, neuroanatomical development and factors that affect or inhibit maturation. Each had its own search terms and inclusion and exclusion criteria (listed in appendices b-d). All searches were limited to the years 2009-2019, all were limited to reviews and articles written in the English language and all searched were conducted on the following databases; PsycInfo, Embase, Medline.

Data Extraction and Quality Review

All papers were assessed for quality by members of the review team who used a common data collection tool to extract information from each review prior to assessing its quality. For narrative reviews the data extracted comprised; author, year, title and summary of main findings. For quantitative reviews the data extracted comprised: citation details, objectives, review type, participant details, setting and context, number of databases sourced and searched, date range of database searching, number of studies included, study type, study country of origin, rating instrument, relevant outcomes reported and synthesis method.

The quality of narrative reviews was assessed using the Scale for the quality assessment of narrative reviews (SANRA) (299) and the quality of quantitative reviews using Risk of Bias in Systematic Reviews (ROBIS) tool (300).

The extraction tables and summary outcome of the quality rating for each review are provided in Appendix E (quantitative reviews) and Appendix F (narrative reviews).

10. Appendix B: Search Strategy — Functional Development

Search completed on 1 November 2019

Database	Papers Imported	Duplicates removed	Excluded by title/abstract	Kept for full-text review	Included
PsycInfo	353	0	326	26	8
Embase	382	68	289	25	5
Medline	345	128	213	4	1

Search Terms:

Concepts	Keywords
Adolescence & young adulthood	Adolesc* OR adolescence OR youth OR "young adult"
Brain development	Brain matur* OR cognitive matur* OR puberty* OR matur* OR cog* devel* OR cognitive development
Factors	Impuls* OR "impulse control" OR plan* OR decision* OR "decision making" OR "decision-making" OR negative influenc* OR "peer pressure" OR suggestibility OR executive function* OR cognitive abilit*
Topic area	Neuro* OR neuropsych* OR neurocog* OR "cognitive psych*"

Limitations applied: 2009-2019; English only; limit to reviews only

Inclusion/Exclusion criteria

Inclusion	Exclusion
Article published in English, peer reviewed journals	Chapters from books, posters, conference extracts
Neurological, neuropsychological, and cognitive psychology studies exploring typical development	Papers which focus on specific clinical groups
Research with human participants between the ages of 12-25	
Papers published between 2009-2019	
Relevant to cognitive development as it applies to the aims of the review	

11. Appendix C: Search Strategy — Neuroanatomy

Search completed in August 2019

Database	Papers Imported	Duplicates removed	Excluded by title/abstract	Kept for full-text review	Included
PsycInfo	50	0	38	12	9
Embase	35	3	29	3	1
Medline	14	5	9	0	0

Search Terms:

Concepts	Keywords
Adolescence & young adulthood	adolesc* OR child* OR youth
Brain development	brain matur* OR cognitive matur* OR pubert* OR matur*
Topic area	neuro*

Limitations applied: English only.
Limitations applied subsequently: 2009-2019; limit to reviews only.

Inclusion/Exclusion criteria

Inclusion	Exclusion
Article published in English, peer reviewed journals	Chapters from books, posters, conference extracts
Neurological, neuropsychological, and cognitive psychology studies exploring typical development	Papers which focus on specific clinical groups
Research with human participants between the ages of 12-25	
Relevant to cognitive development as it applies to the aims of the review	

12. Appendix D: Search Strategy — Factors that Affect Development

Search completed on 13 November 2019

Database	Papers Imported	Duplicates removed	Excluded by title/abstract	Kept for full-text review	Included
PsycInfo	376	0	301	79	23
Embase	2,876	464	2,313	70	8
Medline	4	2	0	0	0

Search Terms:

Concepts	Keywords
Adolescence & young adulthood	Adolesc* OR adolescence OR youth OR "young adult"
Brain development	Brain matur* OR cognitive matur* OR puberty* OR matur* OR "cog* devel*" OR cognitive development OR psychological development OR "cognitive impairment" OR impairment OR deficit OR "cognitive deficit" OR "neuropsychological impairment" OR "functional impairment" OR function* OR "functional changes"
Factors	"adverse childhood experiences" OR ACES OR "head injury" OR TBI OR "traumatic brain injury" OR "substance misuse" OR drugs OR substance OR alcohol OR "alcohol misuse" OR "mental illness" OR mental* ill* OR "developmental disability" OR disability OR devel* disabil* OR medic*OR medication OR child abuse OR sexual abuse OR trauma OR neurodevelopment OR neglect OR "interpersonal trauma"
Topic area	Neuro* OR neuropsych* OR neurocog* OR cognitive psych*

Limitations applied: 2009-2019; English only; limit to reviews only

Inclusion/Exclusion criteria

Inclusion	Exclusion
Article published in English, peer reviewed journals	Chapters from books, posters, conference extracts
Neurological, neuropsychological, and cognitive psychology studies	

Research with human participants between the ages of 12-25	
Papers published between 2009-2019	
Relevant to cognitive development as it applies to the aims of the review	

Quality Assessment and Risk of Bias: All included systematic reviews and meta-analyses were rated using the ROBIS tool. All included narrative reviews were rated using the SANRA tool.

13. Appendix E: Summary Table of Quantitative Reviews

Citation details	Objectives	Review Type	Participant Details	Setting and Context	No. databases sourced and searched	Date range of data base searching	No. studies included	Study Type	Study country of origin	Rating instrument	Relevant outcomes reported	Synthesis method	Risk of Bias
Babikian & Asarnow, 2009	Review effects of injury severity, time since injury, outcomes in ped. TBI	Systematic & Meta-analysis	Not reported	Pediatric TBI, English, reporting neurocognitive outcomes after TBI	PubMed	1988-2007	28	Original research	USA	Not reported	general intellectual functioning, executive functions, and verbal delayed memory-impaired after severe TBI, verbal immediate memory-mod es; Small differences found in visual perceptual functioning, visual immediate memory, and inhibition	Meta-analysis	Unclear
Chamard and Lichtenstein, 2018	Review literature on MRS, DTI, fMRI and cortical thickness following a sports related concussion (SRC).	Systematic	Young people aged 0-19 who had sustained a SRC	Included males and females, studies in English. Geographic context not reported.	1 (PubMed)	March 2017	26	Original research study	Not reported	Not reported	Studies demonstrated metabolic, microstructural, and functional changes in the brain of young athletes in acute, subacute and chronic phase of concussion recovery.	Not reported	Unclear
Dai & Scherf, 2019	To review neuroimaging studies (fMRI and EEG/ERP) investigating the association between pubertal and functional brain development in humans.	Systematic	Adolescents (age range across studies: 8-27 years old)	Not reported	2 (PubMed and Google Scholar)	Not reported	28	Original research studies (mix of cross sectional and longitudinal).	Not reported	Not reported	Face processing was the only domain to demonstrate convergence in the locus of effects in the amygdala, while social information processing exhibits convergence of positive effects. (directionality). Clear that much more human research is needed on the association between pubertal and functional brain development.	Not reported	Low
DeFoe,	to elucidate why	Meta-	Children,	Did not include children's age	(5) PsycINFO, Scopus,	Not	32	Primary	Not	Not	Adolescents take more	Meta-	Low

2015	adolescents, engage in more risky behaviour than children and adults in real-life settings but not always within the laboratory context. Focus on 1) whether adolescents engage in more risk-taking than children and adults, and 2) differences in the degree of risk-taking behaviour in early and late adolescents.	analysis	adolescents, adults (5-65 years); only studies in English and Dutch	groups that contained children younger than 5 and adults' age groups that contained adults older than 65.	Medline, ERIC, and Google Scholar	reported		studies, case-control	reported	reported	risks than adults (g =.37), while early adolescents engage in more risk-taking behaviour than mid-late adolescents. Adolescents and children were found to take the same amount of risk; meta-regression analyses demonstrated that, compared to adults, adolescents take more risks on hot tasks that have immediate outcome feedback on rewards and losses. Adolescents do not take as many risks as children on tasks where there is a sure/safe option.	analysis	
Ganzer et al., 2016	Focus on understanding sustained effects of cannabis	Systematic & Meta-analysis	Not reported	Studies only on subjects with regular consumption of cannabis or Marijuana; only studies with a period of at least 14 days of abstinence were included	(5) EMBASE, Ovid MEDLINER, PsycInfo, P SYNDEXplus Literature and Audio-visual Media, PSYNDEXplus Tests	2004 and 2015	38	Original research study	Not reported	SIGN	"Mean ES in cannabis users versus non-using controls Attention: r=.273; EF r= .294; Motor function: r=.478; memory and learning: r= .229; Visuospatial: r=.094"	Meta-analysis	Low
Goodall et al., 2018	To synthesise the literature on neurocognitive functioning in currently depressed adolescents compared to healthy controls.	Meta-analysis	Young people aged 12-25	English language; peer-reviewed; minimum sample size of five participants. Excluded samples of depressed young people with a comorbid diagnosis of bipolar disorder or any form of psychotic disorder or had a documented intellectual disability.	3 (PsychINFO;Embase;Medline)	January 2016	23	Original research studies	UK, USA, Australia, Israel, Canada, Germany, New Zealand.	Newcastle-Ottawa Quality Assessment Scale	Depressed youth (compared to control) had poorer performance in the domains of attention, verbal memory, visual memory, verbal reasoning/knowledge, and IQ; moderator analysis found in depressed youth vs. control an existence of a tendency for poorer set-shifting ability, and moderator analysis of medication status showed taking medication was	Not reported	Low

											associated with poorer attentional functioning.		
Hein et al., 2017	A quantitative meta-analysis to that confirms that heightened bilateral amygdala activation is related to child maltreatment in a large sample across studies; to investigate other altered SIPN structures; to identify additional regions that show altered function in maltreated children, teens, and adults.	Meta-analysis	adolescents and adults	Not reported	(3) Google Scholar, PubMed, PsycInfo	Up to March 2016	20	Original research studies, Meta-analysis	Not reported	ALE	Maltreatment is related to increased bilateral amygdala reactivity; childhood maltreatment affects several additional structures in the brain.	meta-analysis of whole-brain voxel-based morphometry studies	Low
Kok et al., 2014	Review the role of social-affective functions to explain social adjustment problems after TBI	Meta-analysis	Young people with an acquired brain injury or a neurological disorder (0-18)	English	1 (PubMed)	1964 to November 2011	9	Original research study	Not reported	Not reported	Emotion recognition: children with brain disorders score 0.69 SDs lower than controls. Facial affect recognition is impaired in children with brain disorders Recognition of fear and sadness was the largest impairment. Ability to recognize emotions was not directly associated with social adjustment. Moderate to large associations between internalising problems and facial emotion recognition	Random-effects meta-analyses	Unclear

Lees et al., 2019	To provide an update of literature on binge drinking and neurodevelopment	Systematic review & Meta-analysis	Youth aged 10 to 24 years	Adolescents and adults	(5) PubMed, EMBASE, Medline, PsychINFO, ProQuest	2004 to 2018	58	Original research study	Not reported	Grade	Abnormal or delayed development of key frontal executive-control regions can predispose youth to binge drink, which exacerbates these abnormalities as well as alcohol-related neural aberrations in reward-seeking and incentive salience regions; cognitive deficits and maladaptive alcohol associations. A meta-analysis of neuropsychological correlates identified that binge drinking in youth was associated with a small overall neurocognitive deficit and decision-making deficits.	Not reported	Low
Lim et al., 2014	To conduct a meta-analysis of	Meta-analysis	children, adolescents, and	Both men and women, mostly women; Excluded studies that	(4) PubMed, ScienceDirect, Web of	up to January	12	Original research	Not reported	Not reported	Maltreated participants displayed significantly	meta-analysis of	Low

	published whole-brain voxel-based morphometry studies in childhood maltreatment to explain the most robust volumetric gray matter abnormalities		adults	used fewer than 10 patients; all studies excluded participants with substance abuse or medical conditions that could adversely affect growth and development	Knowledge, and Scopus	2014		study			smaller grey matter volumes in the right orbitofrontal/superior temporal gyrus extending to the amygdala, insula, and Para hippocampal and middle temporal gyri and in the left inferior frontal, postcentral, and right middle temporal gyri compared to non-maltreated participants; additionally had larger grey matter volumes in the right superior frontal and left middle occipital gyri. Age was positively correlated with left middle occipital grey matter volumes and negatively correlated with left postcentral.	whole-brain voxel-based morphometry studies	
Lorenzetti et al., 2016	Examine the impact of adolescent cannabis use on brain function by reviewing FmRI studies in adolescent sample	Systematic	Adolescents aged 13-18 who were regular cannabis users, as defined by each study protocol	Mostly or exclusively male participants recruited from primarily through the community, and some through substance support services.	1 (PubMed)	Not reported	13	Original research study	Not reported	Not reported	Studies showed abnormal activity in the fronto-parietal network in adolescent cannabis users, especially heavier users, compared to controls.	Not reported	Unclear
Marley et al., 2018	Examine neuroimaging results on ADHD comparing children and adolescents with ADHD focusing on the major confound of prior medication use first brought to attention by Leo and Cohen (2003) and thereafter acknowledged in the literature.	Systematic	Children and adolescents with ADHD 5-18 years old	Studies with participants with co-morbidities excluded	BIOSIS, WOS Core Collection, EMBASE, psychINFO	2003-2015	14	Case-control studies with matched controls	UK	Not reported	The understanding of neurobiological underpinnings of ADHD has not advanced since the Leo and Cohen review despite technological advances.	Not reported	Low

Parellada et al., 2017	To review studies of premorbid (adjustment and functionality) and early developmental milestones in schizophrenic (SZ) and Bipolar patient (BP).	Systematic	Recruited from cohort studies or national registries. Exact age range not given.	Mostly cohort or national registry studies based in Europe, US, Israel, New Zealand and Australia.	1 (PubMed)	June 2017	30	8 prospective cohorts, 15 retrospective studies, 7 national based registries.	UK, Sweden, Norway, Finland, Germany, Spain, Israel, New Zealand, Australia, USA.	Not reported	Psychomotor developmental deviations and general adjustment problems in childhood precede the development of SZ and BP. These pathologies vary between SZ and BP and tend to be more severe in SZ.	Not reported	Low
Phillips et al., 2017	Systematically examine literature of multicomponent working memory and specific systems in pediatric TBI.	Systematic & Meta-analysis	predominantly included school-aged children and adolescents under 20 yrs who had sustained a TBI	English; Excluded if it involved children and adults but did not report on outcomes of children separately; assessed WM but did not report on the scores of distinct components of WM; mostly cross-sectional	(3) MEDLINE, PsychINFO, EMBASE	28 October 2014	27	Original research study	Not reported	Newcastle-Ottawa Scale	those with TBI scored significantly lower on VSSP; Severity: Worse CE performance was associated with more severe injury. No significant association was found between TBI of any severity and storage components (PL and VSSP); Age at injury was not associated with CE performance. Children who sustain a TBI are at risk of working memory impairments, which are often component-specific; More severe TBI was related to worse working memory on CE; Younger age at injury and shorter time since injury were linked with poor CE functioning. Functional brain activity changes were associated with impairments in working memory after TBI	Meta-analysis	Low
Serafini et al., 2014	To determine whether the integrity of brain white matter	Systematic	Paediatric and adolescent samples with BP and UD.	Excluded studies explicitly conducted on high risk subjects.	3 (PubMed/MedLine; Scopus; Science Direct).	January 2014	17	Original research study (mostly	Not reported	Not reported	More WM abnormalities have been reported in children and adolescents with BD than UD. UD and	Not reported	Low

	(WM) and grey matter (GM) may be considered common trait markers or may be used to distinguish bipolar disorder (BP) from unipolar disorder (UD).							cross-sectional in design)			BD have both shared and distinct WM and GM abnormalities.		

14. Appendix F: Summary Table of Narrative Reviews

Author	Year	Title	Summary of findings	QA (score out of 12)

Arain et al.	2013	Maturation of the adolescent brain	Factors influencing brain maturation in adolescence include heredity, environment, physical, mental, economical, and psychological stress and sex hormones. **PFC** matures during adolescence only reaching full maturity at age 25. An immature PFC may be responsible for risk-seeking behaviour in adolescents. **Limbic system**: risk taking and sensation-seeking behaviours associated with increased activity in the nucleus accumbens and amygdala. Decreases in DA in the nucleus accumbens during puberty may increase the vulnerability of adolescents to risk taking behaviours as the same levels of reward can only be achieved with higher DAergic stimulation. Sex differences reported in the DAergic functions during adolescence, also sex differences in drug and alcohol abuse and dependence outlined. **Risk perception:** Studies demonstrate adolescents make more thought out decisions in cold than hot cognition - thought to results from immature connections between the limbic system and PFC.	8
Arnsten & Rubia	2012	Neurobiological circuits regulating attention, cognitive control, motivation, and emotion: Disruptions in neurodevelopmental psychiatric disorders	Neuroimaging studies of young people with neurodevelopmental disorders demonstrate altered brain structure and function in PFC circuitries. Children with ADHD show abnormalities in inferior PFC, while those with ODD have alterations in the paralimbic system. Young people with MDD demonstrated irregularities in ventral orbital and limbic activity whereas children with OCD appeared to show dysregulation in orbito-fronto-striatal inhibitory control pathways. Evidence for good correspondence between neurobiological and compromised behavioural functioning.	11
Barrasso-Catanzaro et al.	2016	Neurobiological bases of executive function and social-emotional development: Typical and atypical brain changes.	Maturation of executive functions, social cognition, and moral judgement in typical and atypical neurodevelopment, seem necessary for ample development in both adults and adolescents. They require increased connectivity and sculpting of the PFC and related networks that are influenced by social and caregiving experiences in addition to neurobiological factors, and cognitive and social stimulation.	8
Bava et al.	2010	Adolescent Brain Development and the Risk for Alcohol and Other Drug Problems	Heavy drinking during adolescence may be associated with deficient cognitive performance and brain health. Attention, memory and executive functions impairments in adolescent substance users are evident and are associated with changes in prefrontal, hippocampal, and cerebellar structure and function, and poor white matter integrity.	8

Best et al.	2010	A developmental perspective on executive function	Executive functions begin to emerge early in life, they continue to develop throughout childhood and adolescence. By age 4, children demonstrate successful performance on response inhibition tasks, and continues to improve. Development of executive working memory is gradual and continues refinement through adolescence- namely on tasks requiring maintenance and manipulation of items. A prolonged increase in the specialisation of working memory neural circuitry during childhood and adolescence shows only limited task improvements, especially in adolescence. Maturation of specific cognitive functions during late childhood and adolescence is associated with maturation of specific neural circuits, not with global maturation. Performance on complex working memory tasks shows improvements through adolescence, research suggests working memory follows a linear developmental trajectory from preschool through adolescence. A mechanism for developing accurate set-shifting may be improved meta-cognition. Set-shifting follows protracted development through adolescence. Behavioural and physiological measures suggest that self-monitoring is evident during adolescence, tasking switching is evident by middle adolescence and often has reached adult levels.	7
Blakemore	2012	Imaging brain development: The adolescent brain	**Structural development: MRI** studies consistently find an increase in white matter and decrease in grey matter volumes in frontal and parietal regions during adolescence. White matter changes are also accompanied by progressive changes in white matter integrity as measured by MTR in MRI and FA in DTI. Non-linear changes in white matter have also been reported in DTI studies (Lebel & Beaulieu, 2011). Regarding cortical grey matter density, sensory and motor regions were the first to mature (in terms of grey matter loss), followed by the rest of the cortex which matured in a posterior-anterior direction. Posterior temporal regions are the last to mature. Loss of grey matter was found to continue up until the age of 30. Non-linear changes in grey matter have also been reported an interpreted in various ways. **Functional Development: Focus on the social brain and mentalising tasks (MT).** ROIs —posterior superior temporal sulcus (pSTS)/temporo-parietal junction (TPJ), anterior temporal cortex (ATC) the medial prefrontal cortex (MPFC). Studies consistently demonstrate greater activity in the dorso-medial PFC than adults during a MT compared to a control task. In emotional MTS, similar developmental patters have also been observed. Adults showed greater activity in the ATC suggesting a shift from MPFC to ATC over development — still unclear why this happens. **Gender differences:** relatively little is known the association between gender puberty and neural development in humans. Some evidence to suggest that irrespective of gender, positive associations between pubertal measures and GM in the amygdala and negative association with hippocampal volume. But some gender-specific effects are emerging: e.g., positive relationship observed between oestrogen levels and limbic GM in females, and males showed neg. association between testosterone and GM in parietal cortex. Findings need to be replicated. **Functional and effective connectivity:** emerging rsFMRI studies have shown that significant changes between and within network occur during adolescence. Some suggest that the decreased interactions between different networks that occurs with age may be accounted for by more efficient within-network connectivity. Blakemore also recommends that future research examines the relationship between functional and structural development but acknowledges that current methodological limitations may hinder this**. Blakemore concludes by outlining the numerous clinical and policy applications that may arise from this burgeoning field of research.**	10

Blakemore et al.	2018	Avoiding social risk in adolescence.	Evidence from real-life situations and laboratory experiments both demonstrate that adolescents are more likely to take risks when in the company of their peers. For example, they are more likely to engage in reckless behaviours such as trying drugs, smoking and alcohol and fast driving. However, the same effect is not observed in adults (>25 years old) (Gardner & Steinberg, 2005; Reniers et al. 2016). Importantly, peer influence on risk taking an also have a positive effect. For example, a young person discouraging their peer from partaking in a risky activity reduces their tendency to do so (Maxwell, 2002).	7
Blakemore et al.	2012	Decision making in the adolescent brain	Non-linear development of reward system, hyper-responsiveness to rewards in adolescents, decision making may be modulated by emotions and social factors.	7
Blakemore et al.	2014	Is adolescence a time for sociocultural processing?	Changes in social environment during this developmental period may interact with functions and social sensitivity resulting in behaviours.	7

Blakemore et al.	2010	The role of puberty in the developing adolescent brain	**Sex differences:** Grey Matter (GM): positive associations between testosterone levels and global GM in males, while females exhibit a negative association between estradiol levels and global and regional GM density. White Matter (WM): males demonstrate significantly steeper age-related changes in WM density than females. Perrin et al. (2008) report that the sexually dimorphic relationship between WM volume and age may be due expression levels in the gene encoding for the testosterone receptor. Blakemore notes although pubertal onset does seem to have an effect on cognitive development, further longitudinal research that assesses sex hormones as the measure of puberty is needed.	7
Crone & Konijn	2018	Media use and brain development during adolescence	**Neural responses to online social rejection**: Subgenual anterior cingulate cortex (ACC) and medial frontal cortex play key roles in adolescent processing of online exclusion (Rodam et al., 2017; Achterberg et al., 2016; Silk et al., 2012). **Neural responses to online social acceptance**: Several studies reported activity in ventral striatum, region associated with experience of pleasure and reward, in response to monetary rewards (Silverman et al., 2015; Schreuders et al., 2018; Braams et al., 2015). This heightened reward sensitivity associated with monetary rewards also seen in response to social rewards e.g. likes on social media (Sherman et al., 2016; Sherman et al., 2017). **Neural responses to online peer influence:** Girls are particularly influence by body ideals in the media and sensitive to peer feedback embracing this ideal; in females aged 18-19 feedback deviating from the norm associated with increased activity in ACC-insula, an important region for modifying behaviour to fit peer feedback norms in adolescents. **Neural responses to prosocial peer feedback**: Increased sensitivity in early adolescence to social media influences in risk perception (Knoll et al., 2015) as well as prosocial direction (Van Hoorn et al. 2016); further research needed to establish whether sensitivity is more pronounced in early or mid-adolescence, relevant for future target interventions. Neural responses to retaliation and emotion regulation: only preliminary studies linking individual difference in responses to media content with brain development, but these suggest the dorsolateral prefrontal cortex may play an important role in regulating emotional responses. **Sensation-seeking**: New forms of risk-taking observed within social media including excessive self-disclosure or sexting (van Oosten et al., 2017). This	10

			points to social media as a more recent platform for the expression of sensation-seeking behaviours in adolescence.	
Elofson et al.	2013	Alcohol use and cerebral white matter compromise in adolescence	Heavy drinking in adolescence compared to controls, has measurable differences in white matter integrity. Patterns of binge drinking and AUDs during early adolescence is associated with white matter integrity and impaired cognitive functioning.	9

Foulkes & Blakemore	2018	Studying individual differences in human adolescent brain development	Brain development at the individual level: emerging longitudinal research (n=270, aged 8-28, three scans for each participant) has demonstrated distinct developmental trajectories within hippocampal sub regions (Tamnes et al. 2018). Inspection of raw data revealed large variance in structural development in subcortical and cortical regions — this is likely due to individual differences. But crucially, very few studies have examined individual differences. Another study (Mills et al. 2014) investigated pattern of maturation in PFC, amygdala and NAcc. Found that GM in amygdala increased until mid-adolescence, then change ceased; a small decline in NAcc vol. was found across adolescence but the PFC demonstrated a protracted substantial decline during this period. Notably, this pattern was not uniform across all participants, which highlights the presence of heterogeneity in brain maturation. **Socioeconomic Status:** research demonstrates that SES affects brain development (e.g., an SES-age interaction was found on grey matter volume in amygdala and hippocampus). In adolescents, SES has been associated with neural response to social cognition tasks, but the majority of studies were cross-sectional and the trajectory of neural processing during these tasks is not known. Future research needs to characterise the mechanisms through which SES impact brain development. **Culture:** Remarkable similarities have been observed cross-culturally in adolescents - for example risk-taking and sensation-seeking is present across cultures. There have been some cultural neuroimaging studies in adults that have found differences in neural activity across cultures, but few studies have examined whether these differences are present earlier in development, i.e., adolescence. Of the limited studies in this area, cultural differences in susceptibility to peer influence (e.g. smoking behaviour) during adolescence have been reported. **Peer environment:** During a social exclusion task (Cyberball), adolescents with a history of peer-rejection displayed higher activation in the dorsal ACC compared to stably accepted adolescents (Will et al. 2016). These differences in neural activity during cybermall tasks were also associated with depressive symptoms in female adolescents (Rudolph et al. 2016). Individual differences in peer environment need to be considered in future research. Conclusion: The authors highlight that there are many other factors that need to be considered and that the field will benefit greatly from prospective, longitudinal research with large sample sizes that incorporates individual variability.	10
Geier	2013	Adolescent cognitive control and reward processing: Implications for risk taking and substance use.	Protracted gray matter changes, specifically in the lateral PFC, may inhibit the ability to process and integrate multiple sources of information, and decision making in the context of rewards in adolescents Increased sensitivity to rewards during adolescence in addition to the influence of rewards on inhibition, indicates that decision-making in a rewards context are immature in adolescents compared to adults. Compared to adults, in decision making, adolescents might not be able to 'override' strong urges for rewards, and rewards may largely increase reward and inhibiting action toward alternatives.	9
Geier et al.	2009	The maturation of incentive processing and cognitive control	Compared to adults, adolescents have decrease anticipatory processing and assessment of risk, increased consummatory response.	7

Hardin et al.	2009	Functional Brain Imaging of Development-Related Risk and Vulnerability for Substance Use in Adolescents	Studies show that discrepancies in the developmental trajectories of reward and inhibitory processes are larger than normal in adolescents at risk of developing SUD. Discrepancy is between the exaggerated hyper-responsive reward system and abnormally developed inhibitory processes.	9
Herting & Sowell	2016	Puberty and structural brain development in humans	**Cross-sectional studies** suggest physical and hormonal changes influence grey and white matter development. **Longitudinal studies** establish a direct relationship between pubertal changes and grey matter decreases and white matter increases in adolescence. Sex-specific changes in trajectories of brain maturation during puberty reported in 4 out of the 8 longitudinal studies suggesting, in some cases, distinct effects of physical and hormonal changes on neurodevelopment in boys and girls e.g. smaller subcortical structural volumes in girls towards late maturation as compared with larger structural volumes observed in boys at later stages of puberty (Goddings et al., 2013). The developmental trajectories of grey matter showed more change during early pubertal maturation, plateauing or even shrinking by late puberty. This was observed in subcortical volumes (Goddings et al., 2013), grey, white, and amygdala volumes (Herting et al., 2014), and cortical thickness (Nguyen et al., 2013a, 2013b). Absence of longitudinal studies for pituitary and white matter microstructure, authors point to need for further research in order to establish relationships between structures/properties and within subject changes in adolescent boys and girls. More generally, future longitudinal research needed to clarify individual differences in onset and progression of pubertal maturation on structural brain development. While age infers general developmental changes, authors highlight the additional benefits of examining pubertal maturation in relation structural neurodevelopmental trajectories.	10

Jacobus et al.	2013	Review findings from neurocognitive studies looking at alcohol-related toxicity in adolescents.	Compared to controls, teens who meet criteria for alcohol use disorders, and those who engage in binge drinking behaviours, often exhibit poor neurocognitive performance (Learning and memory), changes in grey and white matter, and discrepancies in functional brain activation patterns. Teens who misuse alcohol have changes in overall volume of the PFC, hippocampus, and amygdala, alcohol related changes are also seen in cortical thickness. Poor white matter integrity is seen in teens with alcohol use history, and binge drinkers with co-occurring substance use. Adolescents who report significant use exhibit increases and decreases in BOLD activation when compared to controls with minimum use. Girls may be more vulnerable to vulnerable to effects of alcohol than boys.	8
Johnson et al.	2009	Adolescent Maturity and the Brain: The Promise and Pitfalls of Neuroscience Research in Adolescent Health Policy	Highlight that biological explanations for stereotypical adolescent behaviour (e.g., risk-taking, sensation-seeking) have often been taken out of context by the media and policy makers. There is a lack of empirical support for a causal link between neurobiological processes and real-world behaviour. Summarise current research on brain development during adolescence: see an increase in pruning in grey matter from age 11 in girls and age 12 in boys. Loss of grey matter generally progresses from the posterior to anterior regions (Sowell et al. 2001). An increase in myelination occurs in pre-frontal regions but evidence suggests that this does not occur until at least the early 20s. Some researchers (e.g., Steinberg, Dahl) have suggested that a temporal gap between the development of socioemotional areas (surges at pubertal onset) and cognitive control system of brain (occurs later in adolescence) may explain some aspects of risk-taking behaviour typical of adolescence. Authors consider the recent advancements in neuroimaging technology and the promise that these methods hold for future research. Give examples of use of neuroscience in court and conclude that future policy must consider conditions under which adolescents' and maturity are most at risk and most resilient. Highlights that the overemphasis on the pathologies, deficits and lack of capacity of the adolescent brain - need to illuminate the many strengths of the adolescent brain as well.	6

Juraska & Willing	2017	Pubertal onset as a critical transition for neural development and cognition	**Neural development:** decrease in overall cortical volume during adolescence with the largest decrease seen in the PFC - interesting given that behaviours mediated by this region undergo substantial change during adolescence. Some evidence to suggest increase in synaptic density in PFC and that peak in cortical size could be affected by puberty (as noted by Giedd et al. 1999) but lack of statistical power in included studies for researchers to draw any clear inferences. **Hormonal effects:** Pubertal status as measured by Tanner stage (self-report or physical exam) was associated with a thinning in cortical regions (particularly frontal areas) in males and females. Increasing levels of testosterone and DHEA across adolescence was associated with cortical thinning in both sexes. Some studies report sex-differences in the rate of frontal maturation, but this review of literature is not comprehensive enough to draw conclusions. Clear that puberty plays important role in cortical reorganisation during adolescence, but this review does not thoroughly examine the underlying mechanisms in humans - focus is on rats. **Behaviour:** PFC maturation is associated with decreases in inhibitory control - thought to reflect interactions between frontal and limbic regions. Puberty onset seems to trigger increased behavioural responsiveness to emotionally salient stimuli, again reflected in increased fronto-limbic functional connectivity.	4
Kambam et al.	2009	The development of decision-making capacities in children and adolescents: Psychological and neurological perspectives and their implications for juvenile defendants.	Overview of cognitive control and socioemotional systems	7
Kavanaugh et al.	2017	Neurocognitive deficits in children and adolescents following maltreatment: Neurodevelopmental consequences and neuropsychological implications of traumatic stress.	Neurocognitive impairments were frequently reported in children and adolescents following maltreatment with impairments in executive functioning being the most common and severe. IQ, language, visual-spatial skills and memory also stand significant risk of impairment following maltreatment. Individual factors such as: abuse/neglect duration, type, severity, and timing in development were all associated with neurocognitive functioning. These neurocognitive deficits appear to result from known neurobiological and brain development abnormalities, which suggests that trauma and adversity can be potential causes of neurodevelopmental disorders. Such findings have many implications for clinical practice and future research.	12

Keightley et al.	2014	Is there evidence for neurodegenerative change following traumatic brain injury in children and youth? A scoping review	There is evidence for long-term neurodegenerative change in children following TBI. Volume loss in certain brain regions: hippocampus, amygdale, globus pallidus, thalamus, periventricular white matter, cerebellum, and brain stem. Decreased whole brain volume, increased CSF, and ventricular space. Hippocampus sensitivity and limbic structures have also been highlighted in paediatric populations.	11
Kilford et al.	2016	The Development of Social Cognition in Adolescence: An Integrated Perspective	**Mentalising**: Neuroimaging studies found activity in the dmPFC, TPJ, pSTS, and ATC during the process of mentalising. fMRI studies of mentalising report decreases in dmPFC recruitment between adolescence and adulthood (reviewed in Blakemore, 2008). It has been suggested that the decrease in recruitment of the dmPFC across adolescence may relate to changes in neuroanatomy or maturing neurocognitive strategies (Blakemore, 2008). **Cognitive control and affective processing**: During adolescence connectivity between vmPFC and both the amygdala and VS increases in response to affective processing (Gee et al., 2013; Guyer et al., 2008; Pfeifer et al., 2011; Somerville et al., 2013; Spielberg et al., 2015, 2014; van den Bos et al., 2012a). Reduced activation reported in the vmPFC, critical in emotional regulation in connectivity with the amygdala, in response to emotional stimuli (Barbalat et al., 2013; Etkin et al., 2006; Hare et al., 2008). **Peer influence**: Adolescent sensitivity to the presence of peers in risk or reward-related tasks influences decision-making (O'Brien et al., 2011; Smith et al., 2015, 2014a; Gardner and Steinberg, 2005). Studies observe that peer presence can both enhance and impair performance; further research is needed to see how direction of performance effects is determined. Van Hoorn et al. (2014) linked prosocial feedback from peers with increased prosocial behaviour, and antisocial feedback with decreased prosocial behaviour. Discussion of factors associated with individual differences in brain regions associated with top-down cognitive control: cognitive control processes identified by Cascio et al., (2014); greater behavioural risk-taking among adolescents with low self-reported resistance to peer influence (RPI), lower RPI associated with increased activity in right TPJ and reduced activity in lateral PFC during crashes following social exclusion. **Conclusion**: behavioral and cognitive changes during adolescence situated within context of mental health and problem behaviours	7
Krebs et al.	2018	Exposure to cannabinoids can lead to persistent cognitive and psychiatric disorders	When used in adolescence, alterations from cannabis may lead to cognitive impairments or psychiatric disorders, namely psychosis. When a psychotic disorder pre-exists, some individuals are more at risk of persistent impairments. It is unclear if ongoing regular cannabis use impairs cognition and educational achievement. Risk of cognitive and psychiatric adverse effects depend on: the kind of cannabinoid used, level and duration of exposure, and individual vulnerability, and age of exposure.	7
Luna et al.	2013	The teenage brain: Cognitive control and motivation.	The ability to make an inhibitory response is present in early development, but ability to monitor performance after errors are committed, continues to mature into adulthood. Basic architecture of the brain remains stable throughout development- which supports refinements in neural connectivity during	8

			'biobehavioural' transition into adulthood. Prefrontal executive networks are established by adolescence- this supports that adolescence can behave like adults, but differences in behaviour depend on context- which is a result of the immaturities and connection strengths between brain regions. Cognitive control is available in childhood, becomes guided by executive prefrontal systems by adolescence, and continues to mature in specific areas: performance monitoring, sustaining a cognitive manner of responding to the level of an adult. Sensitivity to rewards in adolescence can enhance performance by increasing activities reward regions of the brain. Adolescents have delayed reward reactivity which becomes enhanced when response preparation and reward anticipation occurs, which then leads to increased activity in regions which support behaviour that leads to the receipt of a reward. Temporal proximity of increased reward reactivity which occurs right before a reward-motivated response- may be a mechanism for impulsivity and sensation-seeking.	
McCrory, Gerin & Viding	2017	Annual research review: Childhood maltreatment, latent vulnerability and the shift to preventative psychiatry-The contribution of functional brain imaging	Research on threat processing reveals altered neural responsiveness in maltreated individuals, particularly in the amygdala. Studies on reward processing show blunted neural response to anticipation and receipt of rewards, especially in striatal regions, regarding emotion regulation, studies report increased activation in the anterior cingulate cortex (ACC) in individuals with a history of maltreatment. Research on executive control reveals increased dorsal ACC activity during error monitoring and inhibition. Together, findings suggest that altered neurocognitive functioning follows maltreatment, even in the absence of psychopathology but can strongly predict future symptoms of psychopathology.	11
Miguel-Hidalgo et al.	2013	Brain structural and functional changes in adolescents with psychiatric disorders.	Adolescent-onset of schizophrenia associated with accelerated loss of GM density and WM intensity. Adolescent mood disorders have been linked to increased reactivity in amygdala and vmPFC areas. Alcohol misuse during adolescence associated with reduced WM integrity and GM density. Neuroimaging findings should be considered alongside genetic and environmental factors when examining the aetiology of adolescent psychiatric disorders	9

Mollon & Reichenberg	2018	Cognitive development prior to onset of psychosis.	IQ deficits can be present early in childhood in future schizophrenia patients but not bipolar patients. Premorbid deficits found across a number of cognitive domains including language, executive functions, and processing speed. Evidence from the few longitudinal studies that exist suggests that an increasing trajectory of cognitive impairment is present prior to onset of psychosis. Research suggests that genetic and environmental factors play a role in this risk and warrant further investigation.	9
Rinne-Albers et al.	2013	Neuroimaging in children, adolescents and young adults with psychological trauma.	Neuroimaging studies in children and adolescents with a history of psychological trauma were found to be scarce and lag significantly behind adult research. Of those that do exist, most are structural and undertaken using small samples in the USA. The reduction in hippocampal volume found in adult PTSD could not be replicated in a youth sample. Structural abnormalities in the corpus collosum was the most consistent finding reported in maltreated youth.	12
Romer et al.	2010	Adolescent risk taking, impulsivity, and brain development: implications for prevention.	The findings of the review suggest that a key source of risk-taking behaviour during adolescence is impaired impulse control present earlier in development, and that this is greatly influenced by experience. Adolescent risk taking is a multi-faceted phenomenon and is shaped by individual differences. It is unclear how PFC activation relates to risky decision making — it is important to note that this review is over 10 years old, so we now have a much clearer understanding of this relationship.	9

Saylor and Amann	2016	Impulsive Aggression as a Comorbidity of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents.	impulsive aggressive was found to be a relatively common comorbidity of ADHD in children and adolescents but it does not imply or require a diagnosis of oppositional defiant disorder. Impulsive aggression was also reported to be a strong predictor of unfavourable developmental outcomes characterised by persistent ADHD; greater psychosocial burden, especially on parents; and serious functional deficits across a range of domains including criminality and anti-social behaviour. Impulsive aggressive can often trigger peer rejection which can begin a cascade of effects of increasing dysfunction compounding the burden further.	8
Seidman & Mirsky	2017	Evolving Notions of Schizophrenia as a Developmental Neurocognitive Disorder	Neurocognitive impairments are present in the vast majority of individuals with schizophrenia, vary from mild to severe, and can be present from the first episode, or can even be premorbid. Limited evidence to suggest that these impairments can be reversed via pharmacological treatment, but promising results have recently emerged from cognitive remediation studies. Great deal of evidence to support the definition of schizophrenia as a developmental neurocognitive disorder.	8
Semper et al.	2016	Adolescent Emotional Maturation through Divergent Models of Brain Organization	The componential computational account (CCA) suggests brain functions are localized in specified modules whereas dynamic systems perspective (DSP) supports the idea that functionality is dependent on the brain system as a whole. In terms of understanding emotional management, the prevailing view in the literature base is in support of CAA wherein regions of the adolescent brain related to emotion lack the regulation of the necessary cognitive regions. Since explicit research embracing DSP is limited, article examines models of emotion in line with this interpretation. These models reject idea of specialised cognitive regulatory bodies for emotional responses. The CCA and its understanding of emotional regulation highlight the vulnerability of adolescents to harming themselves or others due to imbalanced and immature brain development; authors claim legal and educational policies must thus foster a context in which adolescents are protected better from such harm. DSP, in emphasizing personal responsibility rather than adolescent vulnerability, better aligns with an educational system that goes beyond the resolution of harmful situations instead aiding personal growth (e.g. emphasizing the importance of contextualizing decisions in the bigger picture)	10

Shulman et al.	2016	The dual systems model: Review, reappraisal, and reaffirmation	The dual systems model provides a better explanation of adolescent risk taking than prior models that have attributed adolescent recklessness to cognitive impairments.	9
Silveri et al.	2016	Neurobiological signatures associated with alcohol and drug use in the human adolescent brain	Studies included in the review indicate that the most common alteration reported across all substances and magnetic resonance modalities, is in the frontal lobes. A neurobiological consequence of drug and alcohol use is neurotoxic effects. These effects could be from antecedents: age of first use, family history of addiction, childhood maltreatment, and/or co-morbid psychiatric conditions. Mixed results when it comes to the substance that creates greater impairments, some studies suggest that alcohol use is associated with greater impairments, while other studies have shown greater impairments with marijuana. Effects of alcohol, marijuana, nicotine and other drugs are apparent in moderate users with no diagnosis of SUD. The association between substance use and neurocognition and patterns of continued use remain unclear.	9
Sinopoli et al.	2012	Inhibitory control after traumatic brain injury in children	Many factors influence the expression of deficits following TBI: age at injury, time since injury, post injury ADHD symptoms, and presence of rewards. Inhibitory control is not unitary, and each follows different but overlapping trajectories, and different but overlapping neural areas within the basal ganglia and frontal cortex.	8
Somerville et al.	2010	Developmental neurobiology of cognitive control and motivational systems	Adolescents demonstrate unique sensitivity and motivational cues which challenge the immature cognitive control system and result in an imbalance between systems. This leads to patterns of behaviour unique to adolescents. Cognitive control improves in a linear function from childhood to adulthood, but when it is advantageous to suppress a responded to incentive-relate cues, cognitive control suffers. Inverted U-shaped function of rewards and incentive; peaks between 14 and 16 and then declines. Motivational cues of potential rewards are unique and may lead to riskier or poor choices, which in turn diminish goal-oriented behaviour. When represented at the level of the striatum, increased sensitivity to motivational cues in adolescence, modulate cognitive control-related processes in a different way than children and adults.	8

Squeglia et al.	2016	Alcohol and Drug Use and the Developing Brain	Pre-existing features that increase substance use include poorer neuropsychological dysfunction on measures of working memory and inhibition. Smaller grey and white matter volumes, changes in white matter integrity and altered brain activation in inhibition, working memory, reward and resting state. Alcohol and marijuana are linked with poorer cognitive functioning, verbal memory, visuospatial functioning, psychomotor speed, working memory, attention, cognitive control and overall IQ. Heavy alcohol use associated with accelerated decreases in gray matter and attenuated increases in white matter volumes Increased brain activation during inhibition and working memory tasks, compared to controls.	8
Squeglia et al.	2014	The effect of alcohol use on human adolescent brain structures and systems	Impaired inhibition precedes heavy alcohol use Alcohol use is associated with worsening cognitive functioning- spatial and attentional processing- deficits continue into young adulthood. Neural response patters may serve as a risk factor for future substance use Heavy alcohol use during adolescence has been linked with subtle changes in brain functioning. Humans 12-18: pre-existing differences: decreased cognitive inhibition and neural response Initiation of alcohol: decreased attention, visuospatial functioning, and white matter integrity. Increase in neural response in frontal regions.	9
Suleiman et al.	2016	Becoming a sexual being: The 'elephant in the room' of adolescent brain development	Paper highlights that adolescence is also a sensitive period for romantic and sexual development, an area on which there has been surprisingly little focus. Authors conclude that we need to broaden our understanding of puberty and acknowledge that in addition to be a period of somatic changes that are critical for physical reproductive maturation, it also involves an array of neurobiological changes that are key for the social, emotional and cognition maturation, necessary for reproductive success.	10

Teicher et al.	2016	Annual research review: Enduring neurobiological effects of childhood abuse and neglect.	Research suggests that parental verbal abuse, being a witness to domestic violence, and sexual abuse target specific brain regions (auditory, visual and somatosensory cortex) and pathways that process and convey the stressful experience. A strong association is found between morphological alterations in anterior cingulate, dorsal lateral prefrontal and orbitofrontal cortex, corpus callosum and adult hippocampus. Further, increased amygdala reactivity when processing emotional faces and diminished striatal response to rewards has also been demonstrated. These brain regions and functional networks were found to be highly interconnected and also to have sensitive periods when they are most vulnerable to change. Authors argue that structural and functional irregularities are often attributed to psychiatric illness, but they may instead be a more direct consequence of abuse — this should be considered in future research.	10

Scottish Sentencing Council
Parliament House
Parliament Square
Edinburgh
EH1 1RQ

sentencingcouncil@scotcourts.gov.uk
www.scottishsentencingcouncil.org.uk

ISBN: 978-1-912442-16-4