Adolescent brain development

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Abstract

Adolescence starts with puberty and ends when individuals attain an independent role in society. Cognitive neuroscience research in the last two decades has improved our understanding of adolescent brain development. The evidence indicates a prolonged structural maturation of grey matter and white matter tracts supporting higher cognitive functions such as cognitive control and social cognition. These changes are associated with a greater strengthening and separation of brain networks, both in terms of structure and function, as well as improved cognitive skills. Adolescent-specific sub-cortical reactivity to emotions and rewards, contrasted with their developing self-control skills, are thought to account for their greater sensitivity to the socio-affective context. The present review examines these findings and their implications for training interventions and education.

Introduction

Adolescence is the period of transition from childhood to adulthood. The start of adolescence is defined by the onset of puberty, while its end is defined socially, as the time when an individual takes an independent role in society. The timing and length of adolescence has varied historically and varies between cultures. Research in the last two decades has used techniques such as magnetic resonance imaging (MRI) to study the healthy developing brain. Although total brain volume reaches adult levels at the end of childhood, it was found that adolescence is associated with significant, region-specific, changes in brain structure and brain function, leading to unique adolescent patterns of brain responses and behaviour. Here, I will present recent findings and reviews of this research, and consider the implication of the findings for training and education.

Structural brain development

A key finding from longitudinal MRI studies of brain development has been that there are during adolescence significant changes in white matter, which contains myelin-covered axons, and grey matter, which contains neuronal cell-bodies, dendritic trees and synapses [1,2]. Volumetric measures broadly show that white matter volume increases linearly during the first two or three decades of life, while grey matter volume peaks in mid- to late childhood, and decreases during adolescence [3,4].

White matter

The developmental increase in white matter volume is thought to reflect increased axon diameter and increased myelination. Diffusion tensor imaging (DTI) techniques allow the investigation of the organisation of white matter tracts using fractional anisotropy (FA) and mean diffusivity (MD), which measure the direction and mean diffusion of water, respectively. The first large longitudinal DTI study showed tract-specific non-linear developmental changes in FA and MD, with prolonged maturation of association tracts during adolescence, in particular frontal tracts [3]. Interestingly, there was extensive individual variability in developmental change, notably in the 20s, with for example, 40–50% of 19-32 year-olds showing increasing FA in the inferior longitudinal and fronto-occipital fasciculi between scans, demonstrating prolonged development in these regions, while 5–

15% of this age group showed decreased FA between scans [3]. This individual variability may inform our understanding of psychiatric disorders, many of which emerge during adolescence and show frontal white matter anomalies [5].

Grey matter

Synaptic density, i.e. the number of synapses per neuronal volume, increases during the first months and years of life, reflecting dendritic arborisation, and later decreases first in somatosensory regions during childhood and in the prefrontal cortex (PFC) during adolescence [6,7]. Changes in grey matter volumes, thought to reflect synaptic pruning, show a later development of frontal and temporal lobes than occipital and parietal lobes, indicating a prolonged maturation of brain structure in higher association areas. A recent longitudinal study suggests that the developmental decrease in cortical thickness may be accelerated in adolescence compared to childhood and early adulthood in all four lobes [8], although there is significant variability in developmental changes. This variability appears to be meaningful. For instance, delayed or greater changes in cortical thickness in the PFC during adolescence have been associated with higher IQ [9] and verbal working memory [10]. These findings can be related to heritability studies suggesting that more intelligent individuals show a longer period of sensitivity to the environment extending into adolescence [11].

Sex and Puberty

Although sexual maturation, growth, and body fat redistribution, are related to puberty, very little is currently known in humans of the effect of hormones on brain development during adolescence [12,13]. Recent studies collecting puberty assessments or salivary levels of pubertal hormones and have demonstrated that age and puberty status could independently account for aspect of brain maturation during adolescence, e.g. volume of subcortical regions [12], cortical thickness [14], and MD measures of white matter tracts in boys [15]. In animal studies, androgens and oestrogens have differential effects on different brain areas [12,13]. Although brain differences between sexes in humans mostly reflect differences in total volume, some region-specific differences in brain maturation can be observed, both cortically and subcortically [2,12,16] and may be driven by differential hormone effects. This spatially sexually specific dimorphic cortical maturation may provide a

framework to better understand sex differences in cognition and behaviour, such as differences in risk-taking and antisocial behaviour, or differences in the emergence of psychiatric disorders [5].

Mismatch model

In 2008, two research teams proposed that the increased risk-taking and sensation-seeking observed during adolescence compared to childhood and adulthood may emerge from differential developmental of two brain systems [17,18]. The suggestion was that adolescent-specific behaviour emerged from a mismatch between earlier, puberty-driven, maturation of sub-cortical regions supporting emotional and reward processing, and later maturation of parietal, frontal and temporal cortex regions supporting self-regulation and social cognition [17–19]. Although this theoretical framework is likely too simple, considering for example the different time courses of structural changes observed in individual sub-cortical regions [12], a recent study contrasting PFC cortical thickness and volumes of the nucleus accumbens (NAcc) and amygdala, provides support for the mismatch model [20]. This study reports greater and later developmental changes in the PFC than in the amygdala and NAcc, and evidence of mismatch in most participants at the individual level [20].

Functional brain development

Neuroimaging techniques have allowed the investigation of not only the structural changes occurring during adolescence, but also of functional changes. Findings from resting state connectivity and electroencephalogram (EEG) oscillation studies will first be presented. As there is little event-related potential (ERPs) research on adolescence [21], the subsequent sections will focus on functional MRI (fMRI) studies of cognitive, social and emotional development (see [21,22] for more detailed reviews).

Resting state

The analysis of correlations of fluctuations in blood-oxygen level dependent (BOLD) signal at rest has shown a pattern of (i) decreased short-range connectivity and increased long-range connectivity, and (ii) increased within-functional network (e.g. default, sensorimotor, fronto-parietal) and decreased between-functional network connectivity during

development. Reanalysis of these data suggests however that developmental differences are smaller than first thought because of confounding effects of motion [23], an issue the field is currently trying to address [24]. Importantly, individual differences in functional connectivity at rest and during task performance associate with cognitive performance during adolescence (e.g. for cognitive control [25]). EEG coherence patterns, thought to reflect increased communication between sites, continue to mature until at least mid-adolescence [21], and have been found to predict motor skill acquisition in young adults [26]. A good correlation between networks showing high EEG temporal correlation and networks identified using tractography from structural MRI data demonstrates the possibility of linking structural and functional measures [27].

Cognitive control

Cognitive control can be broadly defined as the ability to flexibly adapt one's behaviour in the pursuit of an internal goal by the coordination of thoughts and actions. Cognitive control abilities improve steeply during childhood, and more slowly through adolescence. During adolescence basic executive functions tasks assessing working memory (WM), inhibition, or task switching are associated with increased activation in the parietal cortex and both increases and decreases in activation in the lateral PFC [22,28] (**Figure 1**). Functional changes are also observed for more complex cognitive control tasks of performance monitoring, feedback learning and relational reasoning [22]. An unspecific broad PFC recruitment at young ages may be replaced by the activation of increasingly specialised PFC regions for particular aspect of cognitive control, such as the inferior frontal gyrus for response inhibition [29], or the rostrolateral PFC for relational reasoning [30]. Little is known regarding synaptic and neurotransmitter changes underlying cognitive control development [31]; however studies using common genetic variants affecting neurotransmitter systems allow for indirect investigations of these changes, and can demonstrate associations with individual differences in cognitive development (e.g. for working memory [32]).

Adolescence is a period when students become increasingly responsive and able to learn from negative feedback [33], which may have implications for education. Other links between cognitive control abilities and school performance have been made. For example, working memory performance and its neural correlates are associated with arithmetic skills

[34], while improved reasoning about increasingly complex relations may support maths learning [35]. Improved cognitive control also allows adolescents to improve their ability to organise and monitor memory representations and memory retrieval [36].

Social cognition and emotion

Adolescence is also a period of major social cognitive changes [37]. Within the social brain, adolescents consistently show greater activation than adults in the medial PFC (MPFC) and reduced activation in the temporal cortex (**Figure 1**) [4,22]. Adolescents become increasingly socially oriented towards their peers, and show greater sensitivity to the presence of peers and evaluation by peers both at the behavioural and the neural level [37]. Although adolescents can be more self-centred than adults, for instance they are less likely to take another individual's perspective into account [38], they are also more sensitive to peer exclusion [39], and more risk-taking in the presence of peers [17,19]. A better understanding of the brain basis of social functioning and social development during adolescence could help foster social competence [37].

The importance of the social context is paralleled by the importance of the emotional, affective and reward context during adolescence, both impacting on decision making [40]. In an extension of the mismatch model [17,18], developing cognitive control skills are proposed to compete with increased reactivity to emotional stimuli, for example observed via greater amygdala response to emotional faces during adolescence [41], and increased reactivity to rewards, apparent through increased striatal activation observed when adolescents receive rewards [22,42] (**Figure 1**). This adolescent-specific reactivity to emotion and rewards, and the salience of the social context for adolescents, associated with diminished self-control (e.g. inhibition inappropriate emotions, desires, and actions) are thought to be behind the small increase in mortality compared to childhood [43]. However, as this increase continues into early adulthood, risk-taking is not unique to adolescents, but they are likely to differ from adults in what they find tempting or rewarding [44].

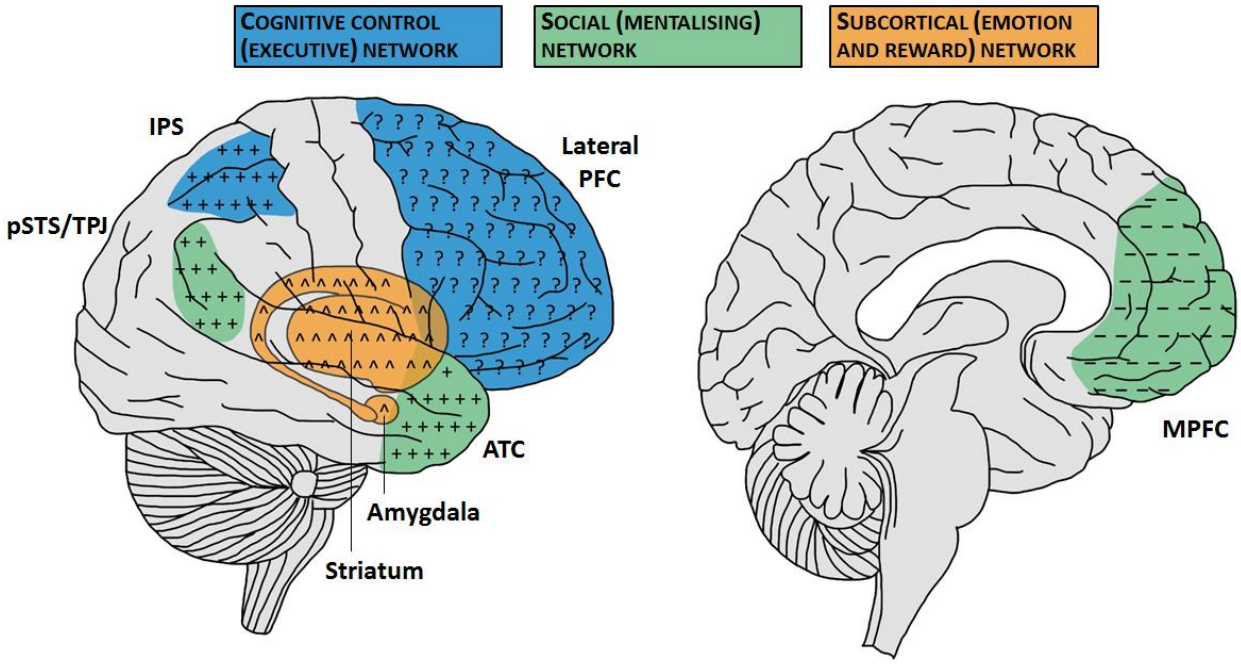

Figure 1: Summary of key aspects of brain development during adolescence. Lateral PFC and IPS are the main regions of the cognitive control network. While there is a consistent increase in IPS activation during cognitive control tasks into adulthood **(+)**, the findings in the dorsal aspect of the lateral PFC are more mixed **(?)**. The ventral aspect of the lateral PFC also shows both increases and decreases in activation with age in tasks requiring self-control in an affective or reward context. The MPFC, ATC and pSTS/TPJ are key region of the mentalising network of the social brain. MPFC activation consistently decreases with age **(-)** in social cognition tasks, while temporal cortex activation tends to increase with age **(+)**. Finally, the striatum and amygdala show peaks in activation during adolescence **(^)** when participants receive a reward or are presented with emotional stimuli, respectively. All cortical regions highlighted here show decreased grey matter volume and cortical thickness during adolescence, while amygdala volume increases during adolescence, and striatum volume decreases during adolescence. Age and puberty stage both play a role in structural and functional changes taking place during adolescence. ATC: anterior temporal cortex; IPS: Intraparietal sulcus; MPFC: medial prefrontal cortex; PFC: prefrontal cortex; pSTS: posterior superior temporal sulcus; TPJ: temporo-parietal junction.

Limitations of functional imaging research

The BOLD signal is an indirect measure of neural activity, and as such may be subject to the influence of a broad range of factors affecting the link between neural activity and BOLD during development [45]. Developmental differences in brain activation may be associated with either quantitative or qualitative differences [28], and may reflect underlying changes in brain structure [46], and changes in task-related functional connectivity [25,47]. EEG offers a somewhat more direct measure of neural activity, associated with a better time

resolution; however, the interpretation of age group differences is also difficult [21]. A common limitation to both techniques is the difficulty in dissociating the impact of age or performance on BOLD or ERPs, and confounding effects of movement [21,22,48].

Interventions

Adolescence as a sensitive period

The research reviewed above demonstrates adolescents' brains and cognition are in a state of flux. Studies in adults have shown that training interventions can lead to changes in behaviour, brain function, and brain structure [49]. Animals studies indicate that mechanisms of neural plasticity, implemented via synaptic reinforcement and pruning, differ between brain regions [50], however little is known of developmental changes in neural plasticity, in particular in humans. It has been suggested that the changes in neural efficiency and integration of networks occurring during adolescence may render this period particularly sensitive to training interventions. Indeed, despite suggestions that earliest interventions are the most effective [51], this may not be true for aspects of cognition and mental health problems which are developing during adolescence [37,52]. There is however currently little evidence of adolescence as a sensitive period [52]. Brain structure and current level of cognitive functioning, as well as genetic differences [54], may constrain the maximum level of performance achievable through training [49]. It is also necessary to consider whether accelerating all aspects of development may be useful, as, for example, the specificities of adolescents' cognition may render them more flexible, explorative and adaptable [22], which may be beneficial in a range of contexts. For example, while improving inhibitory control may improve behaviour in class overall, it may limit adolescents' creativity in arts. Such trade-offs will need to be fully considered [53].

Training interventions

Training interventions targeting adolescents have taken a variety of forms, from cognitive computerised training of working memory or selective attention, to mindfulness meditation training and physical activity. A number of these interventions have been implemented in a school context and aim to improve academic performance by improving cognitive skills (e.g. CogMed working memory training [55]) or indirectly by improving self-regulation, social

interactions, and well-being (e.g. Mindfulness in Schools Programme [56]). This work demonstrates that findings from cognitive neuroscience and psychology can lead to school-based intervention programmes, however much more research needs to be done to develop evidence-based training interventions for education. One key challenge of cognitive training is transfer of improved performance to a wider range of measures, in particular school attainment measures. This may require the implementation of domain-specific (e.g. within the science curriculum), rather than domain-general training [49]. A second challenge is the need to assess which intervention would be most beneficial. Executive functions seem to be particularly important in achieving positive life outcomes despite adversity in low-socio-economic status children and adolescents [57], however interventions focusing on physical exercise, boosting brain functioning and improving body health, or on parental care, may have broader benefits. A third challenge regards the consideration of individual differences [49], i.e. the identification of who may benefit most from what type of training, and of which measures, from genetics [54] to functional connectivity [26] and socio-economic status, may best predict the success of an intervention at the individual level.

Conclusions

This review summarised recent research on the adolescent brain. Adolescence is seen as a period of continued structural changes in association areas, which allow for a prolonged development of cognitive abilities such as social cognition and cognitive control. Functionally, adolescent brains show increased integration and individuation of brain networks, task-specific changes in activation in both posterior brain regions and the PFC, and increased responses in the striatum to emotions and rewards. These adolescent-specific patterns of brain activation are thought to lead to a greater influence of the social, emotional and reward context on decision-making. The prolonged development of the adolescent brain, and its specificities, may render adolescents particularly sensitive to certain types of interventions. Testing this hypothesis and the implications of the findings reviewed here for adolescent education is an important direction for future research.

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