

BRAIN

Adolescent Brain Maturation

Jay N. Giedd, MD

Child Psychiatry Branch, National Institute of Mental Health, USA

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Introduction

The teen years have long been noted as a time of dramatic changes in body and behaviour. Insight into the neurobiology underlying these cognitive and behaviour changes has been greatly enhanced by the advent of *magnetic resonance imaging (MRI)*, which allows safe and unprecedented access to the anatomy and physiology of the living brain. Longitudinal MRI studies are beginning to map out the developmental trajectories of brain maturation and to explore the genetic and environmental influences on these trajectories in health and illness.

Subject

Most teenagers successfully navigate the transition from the dependency of childhood to the self-sufficiency of adulthood. However, adolescence may also be a time of substantial turmoil and, for some, the emergence of psychopathology. Understanding the course, mechanisms and influences of adolescent brain maturation may illuminate the path to more effective interventions for illnesses and to the optimization of healthy development.

Problems

Although adolescence is a time when many major life decisions are made and societies grant broader freedoms and responsibilities, surprisingly little research has been done to explore how

changes in cognition, emotion and behaviour affect the decision-making processes. Adolescence is also the most common time for the onset of several classes of psychiatric illnesses including anxiety and mood disorders, psychosis, eating disorders, personality disorders and substance abuse. Even though the risk for somatic illnesses such as cancer or heart disease is relatively low, mortality increases from childhood rates with motor vehicle accidents the leading cause of death.

Research Context

In recent years adolescent neuroscience research has been bolstered by ever-increasing advances in the fields of *neuroimaging* and genetics. Because MRI does not use ionizing radiation it allows not only the scanning of healthy children and adolescents but of repeated scanning throughout the course of development. This longitudinal data regarding the anatomy and physiology of the brain can be integrated with genetic, environmental, cognitive, emotional and behavioural assessments to explore the mechanisms and influences of healthy and unhealthy development.

Key Research Questions

As the goal of characterizing the general trajectories of brain maturation has progressed, research has begun to focus on elucidating: (1) the mechanisms giving rise to anatomical and physiological changes; (2) the relationship between neuroimaging measures and the cognitive, behavioural and emotional changes seen in adolescence; (3) the role of genetic and environmental influences; (4) how and when the developmental trajectories differ between healthy and clinical populations; and (5) what interventions may best optimize healthy development, enhance education, prevent psychopathology and treat disorders in age-appropriate ways if they do happen.

Recent Research Results

Longitudinal studies of subjects from ages 3 to 30 have shown that white matter volumes continue to increase until well into the third decade of life, while gray matter volumes rise and then fall, peaking at a characteristic time during childhood and adolescence which is specific for each brain region. These changes underlie a general pattern of functional and structural increases in connectivity and integrative processing, and a changing balance between *limbic subcortical* and *frontal lobe* functions that extend well into young adulthood.

One of the tenets emerging from a cumulative body of research is that in neuroimaging, as in life, the journey is often as important as the destination. Assessing the trajectories (i.e., size by age) of neuroimaging measures has shown to be more discriminative than static measures in studies

examining male/female differences, linking neuroimaging measures to cognitive abilities, discriminating healthy from clinical populations, and characterizing heritability of brain anatomy.¹ For instance, males and females have differently shaped trajectories, with females tending to reach peak volumes of gray and white matter earlier than males.² Regarding brain/cognitive ability correlates, individuals with a very high IQ have differently-shaped trajectories of cortical thickness than individuals with a normal range IQ, with key brain regions actually starting with thinner cortex, but then growing more rapidly to end up at a similar final value.³ Diagnostically, in Attention-Deficit/Hyperactivity Disorder versus healthy controls, the delay in cortical maturation predicts clinical status better than the final size.⁴ Also, twin studies examining the relative contributions of interacting genetic and environmental factors indicate a robust effect of age on heritability of neuroimaging measures.⁵ For example, brain regions associated with primary and motor sensory functions appear to be most strongly affected by genetic factors early and by environmental factors later in development, while areas associated with more complex functions such as language become more heritable with time. These findings may imply that different brain regions may be more susceptible to environmental interventions at some times than others.

Research Gaps

Although there is a trend toward an increasing number of people, training programs, journals and funding directed toward research of adolescent neurobiology, historically it has been relatively understudied.

One aspect of adolescent decision making that has been targeted for future research is to characterize the distinctions between traditional laboratory assessment done with subjects acting alone in low-stress testing environments with hypothetical scenarios (i.e. “cold” cognition) versus real-world decision making which often occurs in group settings with peer pressure, high-conflict/high-stress situations and actual consequences (i.e. “hot” cognition).

Another research challenge is to deepen our understanding of the relationship between neuroimaging findings and specific cognitive abilities or psychological characteristics. As mental functions arise from the activity of distributed neural networks, the practice of attempting to correlate the size of any single structure with a particular ability is giving way to the recognition of the need to understand the complex relationships amongst different nodes of the networks. Mathematical approaches such as graph theory are beginning to be used to explore the network properties of the brain.

Conclusions

A fundamental aspect of adolescent brain maturation is that it is a time of dramatic change. This changeability or “plasticity” has served our species well, allowing us to adapt to the unique challenges of our environment at a time when we leave the protection of our natal families to become self sufficient members of the community. The plasticity of the human adolescent brain makes adolescence a time of great risk and great opportunity.

White matter increases, *functional magnetic resonance imaging (fMRI)* studies showing greater correlation across disparate regions on certain tasks, and *electroencephalogram (EEG)* changes in coherence support a notion of increased “connectedness” among brain subcomponents during adolescence and into adulthood. *Inverted U gray matter* changes may reflect the brain’s increasing refinement for specialization, driven by the demands of the environment – although much work remains to assess this speculation. Studies of twins, male/female differences, specific genes, environmental effects, and psychopathology are underway to examine influences on trajectories of brain development.

Implications for Parents, Services and Policy

Of the neuroimaging findings, the finding that the prefrontal cortex (a critical component of networks involved in judgment, decision making and impulse control) continues to mature into a person’s mid 20s, has most prominently entered discourse, affecting social, legislative, judicial, parenting and educational realms. Despite the temptation to trade the complexity and ambiguity of human behaviour for the clarity and aesthetic beauty of colorful brain images, we must be careful not to over-interpret neuroimaging findings as they relate to public policy. Age-of-consent questions are particularly enmeshed in political and social contexts. For example, currently in the United States a person must be at least 15 to 17 years old (depending on the state) to drive, at least 18 to vote, buy cigarettes or be in the military, and at least 21 to drink alcohol. The minimum age for holding political office varies as well: some municipalities allow mayors as young as 16, and the minimum age for governors ranges from 18 to 30. On the national level, 25 is the minimum age to be a member of the U.S. House of Representatives, and 35 to be a senator or the President. The age of consent to sexual relations varies worldwide from puberty (with no specific age attached) to age 18. Clearly, these demarcations reflect strong societal influences and do not pinpoint a biological “age of maturation.” The optimal use of advances in understanding of adolescent brain maturation will require an integrated effort involving parents, legislators, educators, neuroscientists, clinicians and the teens themselves.

References:

1. Giedd JN, Lenroot RK, Shaw P, Lalonde F, Celano M, White S, Tossell J, Addington A, Gogtay N. Trajectories of anatomic brain development as a phenotype. *Novartis Foundation Symposium* 2008;289:101-112; discussion 112-108,193-105.
2. Lenroot RK, Gogtay N, Greenstein DK, Wells EM, Wallace GL, Clasen LS, Blumenthal JD, Lerch J, Zijdenbos AP, Evans AC, Thompson PM, Giedd JN. Sexual dimorphism of brain developmental trajectories during childhood and adolescence. *Neuroimage* 2007;36(4):1065-1073.
3. Shaw P, Greenstein D, Lerch J, Clasen L, Lenroot R, Gogtay N, Evans A, Rapoport J, Giedd J. Intellectual ability and cortical development in children and adolescents. *Nature* 2006;440(7084):676-679.
4. Shaw P, Eckstrand K, Sharp W, Blumenthal J, Lerch JP, Greenstein D, Clasen L, Evans A, Giedd J, Rapoport JL. Attention-deficit/hyperactivity disorder is characterized by a delay in cortical maturation. *Proceedings of the National Academy of Science of the United States of America* 2007;104(49):19649-19654.
5. Giedd JN, White SL, Celano M. Structural magnetic resonance imaging of typical pediatric brain development. In: Charney DS, Nestler EJ, eds. *Neurobiology of mental illness*. 3rd ed. New York, NY: Oxford University Press; 2008: 1209-1217.