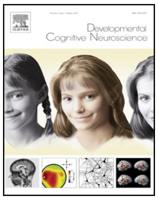
Developmental Cognitive Neuroscience 16 (2015) 192–193

Contents lists available at ScienceDirect

Developmental Cognitive Neuroscience

journal homepage: http://www.elsevier.com/locate/dcn



Commentary

Adolescent neuroscience of addiction: A new era

Jay N. Giedd

Director, Division of Child and Adolescent Psychiatry, University of California, San Diego, 9500 Gilman Drive, MC 0949, La Jolla, CA 92093, United States

Adolescence has long been recognized as a time of dramatic changes in body and behavior. More recently it is being recognized as a time of dramatic changes in brain as well. Advances in neuroimaging technologies have made knowledge of the anatomy and physiology of the developing brain increasingly accessible.

Several large scale initiatives using magnetic resonance imaging (MRI) to characterize adolescent brain maturation in health and illness, often integrated with genetics and progressively sophisticated behavioral and environmental measures, are beginning to yield insights into why adolescence is a time of both opportunity and of vulnerability.

During adolescence the brain does not mature by becoming larger and larger. It matures by becoming more interconnected and more specialized.

The increasing interconnectedness, or communication amongst disparate brain regions comprising an elaborately embedded hierarchy of neural circuits, is demonstrated across multiple modalities and levels of investigation. Studies of long term potentiation indicate the formation of stronger synaptic connections during adolescence. Greater coherence of electrical activity (the degree to which activity in one area can be predicted from activity in another) is shown by studies using EEG. Similarly, fMRI studies assessing blood oxygenation also show a general trend toward greater co-activation amongst spatially distinct regions. And structural MRI studies find increases in white matter volume during adolescence reflecting myelination and concomitant increases in the speed of neural communication.

Characterization of how brain structures are interconnected has benefited enormously from the application of graph theory, a branch of mathematics that is used to quantify the relationship between "nodes" and "edges." Nodes can be any object or measurable entity ranging from quarks to galaxies. Examples of brain nodes may be a neuron, a structure such as the hippocampus, or a region such as the prefrontal cortex. Edges can be any connections between nodes, from a physical connection such as a synapse between neurons or a statistical correlation, such as when two parts of the brain are activated similarly at rest or during a given cognitive task. Graph theory approaches help us to quantify the relationship between maturation of different neural circuits and how differences in maturational timing may relate to variation in behavior and cognition.

For instance, a changing balance between earlier maturing limbic regions, which undergo dramatic changes during puberty and later maturing prefrontal regions, which continue to undergo substantial changes well into the third decade are hypothesized to underlie many of the observed phenomena of adolescence (Somerville et al., 2010).

The increasing specialization of the adolescent brain is indirectly expressed as decreases in gray matter volumes during the second decade, although much work remains to be done to understand the molecular and microscopic processes underlying the observation. Increases in myelination, which may flip the designation of an MRI voxel at the inner border of the cortex from gray to white, account for some of the "reduction" in gray matter volume, but converging evidence from post mortem studies and regionally specific mismatches between developmental trajectories of gray and white matter volumes suggest other processes are contributing as well. The extent to which "pruning" of synapses contributes to the gray matter volume reductions is unknown. This is an important question to resolve in order to shed light on the over simplified notion that specialization is subserved by the phenomenon of fewer but faster/firmer connections. Understanding the mechanisms is fundamental to guiding interventions and refining hypotheses for future investigations.

Perhaps the most striking change of adolescent brain development is the degree of change itself. A key feature of adolescent brain development is plasticity, the ability of the brain to change in response to demands of the environment. Some degree of plasticity is maintained throughout life but in general there is a developmental gradient of decreasing plasticity as myelin releases proteins such as Nogo-A, MAG and OMgp that inhibit axon sprouting and the creation of new synapses (Fields, 2008). However, humans have a uniquely long period of high plasticity allowing us to be remarkably adaptable to a wide range of conditions. Prolonged plasticity may be related to prolonged dependency on caregivers as across species. A longer period of dependence is associated with more complex social and food securing behavior. By "keeping options open" in terms of brain specialization, humans can assess the demands of their particular environmental and develop the skills to survive. Humans can thrive everywhere from the frigid North and South poles to the balmy islands on the equator. We have adapted to cultural changes as well. Ten thousand years ago, a brief amount of time in evolutionary terms, we spent much of our time securing

---

E-mail address: jgiedd@ucsd.edu

http://dx.doi.org/10.1016/j.dcn.2015.11.002

food and shelter. Now most humans can secure shelter and calories with far less time and effort, which via epigenetic or other factors may be related to earlier puberty and greater size. Instead of securing food many of us now spend the majority of our time interacting with words or symbols. This is a notable adaptation given that reading is only 5000 years old and did not exist for much of human history.

Further support for the advantage of prolonged plasticity comes from the observation that our last increase in brain size about 500,000 years ago correlates not with the harshness of climate but the degree of climate change. This is in contrast to Neanderthals, our close genetic relatives. Maturational rates can be assessed from fossilized teeth in much the same way that tree rings can be used to discern growth rates for trees. Evidence from fossilized Neanderthal teeth indicate that they had a much more rapid maturation (Ramirez Rozzi and Bermudez De Castro, 2004). Although there brains were about 10% larger and they were able to survive in harsh environments, their tool use did not change over 100,000 years. They lacked the adolescent plasticity and adaptability of humans.

Adolescent brain plasticity has served our species well, however it comes at a price. It creates vulnerabilities as well as opportunities. Over half of all mental illness emerges during adolescence. One in five adolescents has a mental illness that will persist into adulthood. It is the peak time for the emergence of anxiety disorders, bipolar disorder, depression, eating disorders, and psychosis. It is also the most common time for the onset of substance abuse.

In this Special Edition of Developmental Cognitive Neuroscience top experts in the field report on investigations of the neurobiology of adolescent substance misuse. Consistent themes are relationships between the onset, amount and type of use as correlated with changes in the brain's reward, impulse control, and decision making circuitry. Although the studies represent the finest efforts to date, substantial challenges remain in order to discern specificity of effects, cause/effect dynamics, and mechanisms.

As the path, mechanisms, and influences of adolescent brain development are being elucidated more resources and more researchers are being drawn into the field. Adolescence is increasingly being recognized as a distinct developmental stage with distinct biology rather than just as an intermediate stage between childhood and adulthood. This special edition contains seminal findings from many of the prominent researchers exploring the interface between adolescent neurobiology and addiction.

Adolescence is the peak time of onset for the majority of mental illness, the time of several major life choices having lifelong consequences, and a time when the brain's plasticity may make interventions more effective. However, funding for adolescent research was until recently a small fraction of the budget. This has changed with the Adolescent Brain Cognitive Development (ABCD) Study – a national longitudinal initiative that will assess the short- and long-term impact of substance use on brain development. The project will recruit 10,000 youths before they begin using alcohol, marijuana, tobacco and other drugs, and follow them over 10 years into early adulthood. The ABCD project provides a fantastic platform for young or established investigators to pursue interest in adolescent neurobiology and may serve as a catalyst to bring much needed support and talent to the field.

References

Fields, R.D., 2008. White matter in learning, cognition, and psychiatric disorders. Trends Neurosci. 31 (7), 361.

Ramirez Rozzi, F.V., Bermudez De Castro, J.M., 2004. Surprisingly rapid growth in Neanderthals. Nature 428 (April (6986)), 936–939.

Somerville, L.H., Jones, R.M., Casey, B.J., 2010. A time of change: behavioral and neural correlates of adolescent sensitivity to appetitive and aversive environmental cues. Brain Cogn. 72, 124–133, http://dx.doi.org/10.1016/j.bandc.2009.07.003.