The Transitional Age Brain

"The Best of Times and the Worst of Times"

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KEYWORDS

• Transitional age youth • Brain development • Transitional age brain • Behavior • Neuroscience

KEY POINTS

- Over the past 2 decades, there have been substantial developments in the understanding of brain development.
- Progress in neuroimaging has allowed us to better understand the nuances of the development of cortical, subcortical, and white matter structures.
- Modern neuroscience, genomics, and epigenomic studies allow us a lens through which to develop an understanding of transitional age youth (TAY) behavior from a neurodevelopmental perspective.
- Developing brain building health promotion and illness prevention approaches for TAY will likely yield reductions in morbidity and mortality, enhance individual life trajectories, and have a life-long impact.

INTRODUCTION

A great deal of attention has been paid to the so-called zero to 3 period of brain development. Although clearly an important focus of neuroscience and public health, there is emerging evidence that a second critical period of neurodevelopment exists, bracketed by the onset of the peripubertal process to the completion of cortical organization (roughly ages 13–25). This 'transitional age brain' (TAB) epoch is marked by an increase in risk for morbidity, mortality, drug and alcohol use/misuse, and the onset of persistent psychiatric and nonpsychiatric medical conditions.

The central hypothesis is that the TAB has fully matured risk-taking hardware because of early maturation of subcortical brain regions (amygdala, nucleus

Disclosure Statement: The authors have nothing to disclose.
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Child Adolesc Psychiatric Clin N Am 26 (2017) 157–175
http://dx.doi.org/10.1016/j.chc.2016.12.017
childpsych.theclinics.com

accumbens, etc) but does not yet have matured regulatory hardware (fully pruned prefrontal and related cortical regions). We maintain that adolescents (13–17 of age) and their TABs benefit from imposed external regulatory systems in the form of parents, family members, teachers, and coaches. Even with external control and expectations, transitional age youth (TAY) remain at very high risk for morbidity and mortality associated with suicide, substance use and misuse, psychiatric illness, and accidents. At the same time that TAY and their maturing brains need more external regulatory support and lower risk environments, they instead have easier access to alcohol and drugs, high-risk social activities, and loss of close parenting and supervision. In other words, these negative environmental factors are in play at a very vulnerable time of brain development, in which the regulatory regions of the brain are undergoing the critical process of maturation.

Herein, we discuss the neurodevelopmental processes (with a special emphasis on pruning) that place TAY at high risk to make impulsive, poorly regulated decisions. We present a description of the symphony of brain development (neurogenesis, synaptogenesis, myelination, and pruning) from fertilization to the end of the TAB period to set the stage for just why the TAB epoch is a critical period. Although we emphasize the potential negative consequences of the TAB epoch, we also want to acknowledge that the same features of adolescent and young adult brain development may be a strength that allows TAY and TAB to respond to psychosocial interventions or to changes in environmental context with improved trajectories into adulthood.

EARLY BRAIN DEVELOPMENT

With advances in both structural (MRI) and functional (fMRI) imaging techniques, along with creative experimental designs using fMRI, information about the development of the human brain has been rapidly expanding. Still, research in the field continues to rely on studies the using other mammalian species with the extrapolation of data to humans.[1]

Human brain development begins during the third week of gestation and continues to about the middle of the second decade, when the components involved in executive function become fully formed. It is a process that is intricate and tightly controlled, yet allows for some flexibility to adapt to the idiosyncrasies of the environment. One theme that emerges is that the brain matures by becoming more interconnected and each region becoming more specialized. Another theme that emerges is the process of overproduction before the elimination of excessive cells and connections based on experience, ultimately resulting in an efficient and unique processor.

The process begins with gastrulation, with differentiation of neural progenitor cells, followed by formation of the neural tube, then the neocortex and synaptic pathways. Around gestational week 28, the number of neurons in the human brain is at its peak, a level 40% greater than in adults. Dendritic growth, arborization, and synaptogenesis begin to accelerate rapidly.[2–9] The rate of synaptogenesis reaches its peak around gestational week 34, but the net decrease of synapses does not begin to decrease until the onset of puberty.[2,7–10] At the same time, up to 50% of the neurons undergo cell death to begin the process of establishing definitive connections.[11]

After birth, neurogenesis is largely complete, and a dynamic process of synaptogenesis, myelination, programmed cell death, and pruning ensues as intrinsic and extrinsic signals interact. In the initial critical period up to age 3, development is dominated by synaptogenesis and by age 2 to 3, a toddler has more synapses than an adult and peaks at a level nearly twice that of adults.[12,13] Some networks connections are