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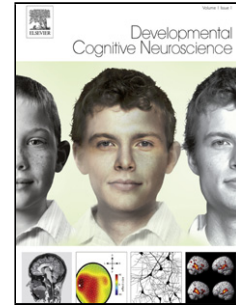
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Beyond Simple Models of Adolescence to an Integrated Circuit-Based Account: A Commentary

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A hallmark of behavioral development is the increasing ability to suppress inappropriate, competing thoughts, desires, emotions and actions in favor of appropriate ones (i.e., self-control). One developmental phase that has received much attention in recent years is that of adolescence, due in part to the significant brain changes of this period (Lee et al., 2014) and also to the heightened risk for psychopathology and criminally relevant behaviors (Casey Glatt & Lee, 2015; Cohen & Casey, 2014). Two interesting articles in this issue, by Shulman and colleagues and Nelson and colleagues, review the developmental science literature and describe potential models for understanding adolescent behavioral and brain development focusing largely on the importance of incentives and social influences, respectively, during adolescence.

A number of theoretical models have emerged to explain challenges to self-control during the period of adolescence. Historically they have been described in the form of dichotomies with G. Stanley Hall claiming the inevitable storm and stress of adolescence while cultural anthropologist (Hall, 1906), Margaret Mead, argued for the importance of the environment (Mead, 2004). Another dichotomy reviewed by Shulman and colleagues in this issue is that proposed by the dual systems model of adolescence that emphasizes divergent trajectories of motivational versus cognitive control systems, based largely on psychological findings. This model has provided perhaps the greatest traction for conveying developmental scientific findings in an accessible way to inform age-related social and legal policies (Steinberg, 2009). However, heuristic accounts can lead to oversimplifications of the science and failure to capture subtle complexities of behavior. A move away from simple dichotomies may enhance our understanding for how self-control varies by content (i.e., actions, emotions or desires to be suppressed) and by context (e.g., alone, with parent, with peer or strangers) during adolescence. Similar advances have been made with the move away from the nature vs nurture dichotomy toward the more nuanced recognition that genetic and environmental factors are inherently intertwined. The environment can impact expression of genes, genes can influence receptiveness to environmental inputs, and so forth.

The imbalance model, unlike dual systems accounts of adolescence (Steinberg, 2008; Luna and Wright, in press) does not propose orthogonal systems, but rather attempts to account for adolescent behavior from an integrated circuit-based

perspective (Casey, Getz & Galvan, 2008; Somerville, Jones & Casey, 2010; Casey, 2015). Accordingly, changes in self-control during adolescence coincide with a series of developmental cascades in the regional fine-tuning of connections within complex subcortical and cortical prefrontal and limbic circuits (Casey et al., 2015). This model focuses on the dynamic neurochemical, connectivity and functional interactions across development in circuits that are essential for self-control and it emerged largely out of developmental findings from a circuit-based study of reward (Galvan et al., 2006). Using a reward paradigm with children, adolescents and adults, previously shown by Shultz and colleagues to differentially impact dopaminergic firing in animal models (Cromwell & Schultz, 2003) this study was the first to show an adolescent-specific sensitivity to reward outcome in subcortical regions relative to orbital frontal regions within a defined basal ganglia thalamo- cortical circuit (Galvan et al 2005, 2006). This model has served the basis for testing how circuits underlying self-control change across development, by content and context, in preparing the adolescent for adulthood.

A key point inherent to the imbalance model is that the development and functioning of components of these neural systems are inextricably linked in their influence over behavior. Much like genes and the environment are co-influenced and highly interactive, so too are the developmental profiles of components of the circuits that are key to evaluating incentives and selecting actions. As such, the imbalance framework diverges from the dual systems account in its assertion that “the two systems contribute to risk taking in an additive manner” (Shulman et al. this issue). Dynamic and interactive models of adolescent brain and behavioral development move away from orthogonal brain systems to distributed interactive networks. Continuing to focus on orthogonal systems may not move the field forward in offering mechanistic accounts of behavior nor offer explanations for subtle temporal shifts in cognitive capacity in different socioemotional situations from childhood through early and late adolescence and into young adulthood. This developmental temporal shift in the capacity of interactive systems to function across different socioemotional contexts is consistent with the developmental cascades perspective of behavior (Masten & Cicchetti, 2010).

A plausible temporal mechanism for the shifts in cognitive capacity from childhood to adulthood is a fine-tuning of circuits from subcortico-subcortical to cortico-subcortical to cortico-cortical consistent with postmortem animal studies of regional synaptic changes (Rakic et al., 1994) and functional connectivity studies (Fair et al., 2009) of refinement of local circuits preceding refinement of distal ones. Thus circuits associated with motivated action (Stuber et al 2011) may be strengthened before top-down projections to these regions have matured with experience and age (Casey, 2015). Although to date, work has focused largely on maturation of cortical- subcortical circuitry implicated in self control, the processing of emotional information and exertion of cognitive control relies on inputs from subcortical circuitry involving the amygdala and ventral striatum as well. These subcortical regions often have been characterized within a dual systems framework too, with valence-specific roles of the amygdala to negatively valenced processes and of the ventral striatum to positively valenced processes (Ernst, Pine, & Hardin, 2006.). However, animal models suggest that binarizing valence onto these two regions in humans may fail to capture the interactive dexterity evinced with sophisticated visualization techniques. For instance, activation of robust unidirectional glutamatergic projections from the amygdala to the ventral striatum (Haber and Knutson, 2010) with optogenetics has been shown to promote cue-triggered motivated behaviors in rodents (Stuber et al., 2011)

independent of valence. Thus development of local subcortical circuitry before corticosubcortical circuitry during adolescence could trigger impulsivity to cues, regardless of valence (positive or negative) or value (rewarding), a finding supported by our recent human developmental studies (Somerville et al 2011; Dreyfus et al 2014). These data provide a second distinction between traditional dual systems and imbalance models with a shift in focus from valence or value to one anchored more on cue-triggered action regardless of reward value or valence (Casey, 2015).

These developmental cascades could serve a critical function in stimulating neurodevelopment in that robust subcortical signaling could provide the key functional inputs to provoke strengthening of cortical projections. Subsequently, the capacity for top down control of cortico-subcortical circuits may be dependent in part on the functional development of these circuits as part of a dynamic cascade. This view is consistent with Thelen's notion of development as hierarchical (Thelen, 2005) with the need for certain aspects of development (e.g., heightened function of subcortical circuits) to precede others (e.g. top-down cortical control) in order for them to develop. In other words, cortical systems need something to respond to in order to develop (i.e. strengthen of connections). Only then can cortico-subcortical development serve as the building block for the next cognitive hurdle (e.g. cortico-cortical driven goal-oriented behavior).

Our perspective is not dissimilar from Nelson's notion of interactive specialization of different organizing social forces at different times in development that shape social development. However, we place as much emphasis on evolutionary-based expectations of the social environment as the environment itself, which we posit may underlie significant changes in the brain to enhance receptivity to environmental inputs and facilitate the capacity for meeting changing social pressures during this developmental window (Casey et al., 2010).

The imbalance framework emphasizes shifts in the flow of information through brain networks that are continually being refined with experience and maturation. Likewise, Shulman and colleagues acknowledge that insights into the neurodevelopmental mechanisms of risky behavior can be gained from examining brain connectivity and circuit-level coordination. We would additionally suggest that the dual systems account may benefit from developmental frameworks that acknowledge dynamic and hierarchical development of brain circuitry to explain changes in behavior throughout adolescence. The foundational brain systems that support these behaviors are not orthogonal- they are interactive and integrative. Decades of research in human and nonhuman models of goal-directed behavior emphasize parallel, integrative basal ganglia thalamocortical loops that integrate signals of value, context, and inhibitory demands to select goal-directed actions (Casey, 2000, 2015; Haber & Knudson, 2010).

Perhaps the most prominent difference between dual systems and imbalance models is how one would *approach* the study of brain mechanisms. Rather than focusing on regions (Mills et al 2014) or nodes (e.g., ventral striatum, prefrontal cortex) this approach would examine developmental shifts in the flow of information and output within and across circuits. Viewing developmental findings through a circuit lens is not only faithful to the organization of the underlying biological systems and to knowledge gained from elegant nonhuman studies, but it readily accommodates key findings demonstrating how the *interactive* effects of motivation signals on cognitive

control change over development (e.g., Geier et al., 2010; Somerville et al., 2011, Teslovich et al., 2013, van den Bos et al., 2012; Cohen et al., 2015).

Collectively, understanding the cascade of changes in behavior throughout adolescence may be most informed by focusing on temporal changes in functional connectivity within and between brain circuits. An over-simplified illustration of these possible changes in circuitry with development is below (Fig. 1). For the sake of example, this figure highlights specific changes within and between medial and lateral prefrontal circuits implicated in different computations and functions important for self-control. The medial prefrontal cortex, implicated in emotion regulation can modulate activity in both the amygdala and ventral striatum to suppress outputs that otherwise lead to emotive responses and actions. The ventral striatum, a region implicated in learning and prediction of rewarding outcomes, also receives inputs from the basolateral amygdala. The amygdala is important in learning the emotional significance of cues in the environment, and can facilitate ventral striatal activity through its direct inputs, leading to motivated action (Stuber et al., 2011). With development and experience, connectivity within prefrontal corticosubcortical circuitry is strengthened and provides a mechanism for top-down modulation of the subcortical output that diminishes emotive processes and habitual actions observed more subcortically. Subsequently, the lateral prefrontal cortex implicated in cognitive control and goal oriented behavior can modulate these frontolimbic circuits via cortico-cortical projections from lateral to medial prefrontal circuits. Thus, it is the interconnections among these regions that change with development to integrate regulation of emotional responses. Examining each of these regions alone and how they function in isolation could fail to identify the key developing features of these systems. Incorporating circuit-based changes with development may improve our understanding of why adolescents engage in the behaviors they do, which situations compromise self-control in adolescents the most (Casey, 2015), and how development of this capacity can be protracted and vary by emotional context (Cohen et al., 2015).

Regional changes in connectivity are indicated with dotted and bolded lines and darkening of circles. Medial prefrontal cortex, mPFC; lateral prefrontal cortex, lPFC; ventral striatum, VS; amygdala, Amy; Ventral tegmentum area, VTA.

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Fig. 1 Simplistic Illustration of hierarchical changes in connectivity from subcortico- subcortical to cortico-subcortical to cortico-cortical circuits with age.

