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Review

The neurobiology of adolescence: Changes in brain architecture, functional dynamics, and behavioral tendencies

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ABSTRACT

Adolescence is a period of increased behavioral and psychiatric vulnerabilities. It is also a time of dramatic structural and functional neurodevelopment. In recent years studies have examined the precise nature of these brain and behavioral changes, and several hypotheses link them together. In this review we discuss this research and recent electrophysiological data from behaving rats that demonstrate reduced neuronal coordination and processing efficiency in adolescents. A more comprehensive understanding of these processes will further our knowledge of adolescent behavioral vulnerabilities and the pathophysiology of mental illnesses that manifest during this period.

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1. Introduction

Adolescence is a period in which individuals observe physical changes to their bodies, experience new interests and desires, and find themselves with greater freedom, independence, and responsibility. Although variably defined, adolescence is generally considered to begin with the onset of puberty and ends as one takes on adult social roles (Dahl, 2004; Spear, 2000). The span of puberty—which involves increased growth, changes in body composition, the development of gonads and secondary sexual organs and characteristics, and cardiovascular and respiratory changes—typically occurs from age 10–17 in girls and 12–18 in boys (Falkner and Tanner, 1986). As this occurs the adolescent undergoes a variety of cognitive, behavioral, and psychosocial transitions. The various changes of adolescence do not all start and end together, and thus the puzzle of relating adolescent brain changes with behavior is challenging. Studying adolescence is like shooting at a moving target, with researchers designating "adolescent" groups of different ages and levels of development. Furthermore, from the mid-19th through the 20th century, an earlier average age of menarche has been observed in the western world (Falkner and Tanner, 1986; Tanner, 1990). The educational process is more prolonged and individuals are tending to wait longer before starting their careers, getting married, and having children (Dahl, 2004). Thus, the length of adolescence is not fixed (and has been lengthening) and while the period correlates with many biological developmental processes, it is partially defined according to psychosocial and behavioral criteria. With these caveats in mind,

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the literature reviewed here has primarily defined adolescence in humans as the second decade of life, in monkeys as age two to four years, and in rodents as week four to week six or seven.

Despite the definitional ambiguities, it is well recognized that during this period major transitions do occur, including a variety of characteristic behavioral changes seen across species. There is increased social behavior (Csikszentmihalyi et al., 1977), novelty and sensation seeking (Adriani et al., 1998; Stansfield and Kirstein, 2006; Stansfield et al., 2004), tendencies toward risk taking (Spear, 2000; Steinberg, 2008), emotional instability (Steinberg, 2005), and impulsivity (Adriani and Laviola, 2003; Chambers et al., 2003; Fairbanks et al., 2001; Vaidya et al., 2004). Peer relationships become dominant, and there are greater inclinations to seek out fun and exciting experiences (Nelson et al., 2005). Increased novelty and sensation seeking may be evolutionarily adaptive, as these behaviors could improve the increasingly independent adolescent's chances of finding food and a mate (Spear, 2010). In modern society, however, these features can be associated with taking unnecessary risks. Therefore, adolescence is considered a period of behavioral vulnerability: teens are more likely to experiment with tobacco and illicit drugs and alcohol; drive recklessly; engage in unprotected sex; and have interpersonal conflicts (Arnett, 1992, 1999; Chambers et al., 2003; Spear, 2000). Adolescent risk taking is more likely to occur in groups (e.g., vehicular accidents), when certain behaviors are perceived to be acceptable by one's peers (e.g., unprotected sex, drug use) (Steinberg, 2008), and in emotionally charged situations (Figner et al., 2009). Thus, while adolescents have survived the potential health problems of early childhood their morbidity and mortality rates are twice that of pre-pubescent children (Dahl, 2004).

In addition to the added risks of *normal* adolescent development, it is also the time when symptoms of a variety of mental illnesses often manifest, including mood disorders, eating disorders, and schizophrenia (Paus et al., 2008; Pine, 2002; Sisk and Zehr, 2005; Volkmar, 1996). During this period there is a vast array of neurobiological changes that drive everything from a cascade of hormonal signals that initiate puberty (Sisk and Zehr, 2005), to increased cognitive ability and motivational changes (Doremus-Fitzwater et al., 2009; Luna et al., 2004). Understanding precisely how the brain develops through adolescence, and relating such changes to both normal behavioral tendencies and pathological conditions, is critically important to public health. Here we review some of the behavioral, and neurodevelopmental changes of adolescence and discuss several models that connect them, including our own hypothesis of reduced processing efficiency.

2. Adolescent behavior

Studies in rodents and humans have shown that adolescents exhibit greater "impulsive choice," defined as the preference for smaller rewards that occur sooner over larger delayed rewards, as measured with delay-discounting tasks (Adriani and Laviola, 2003; Steinberg et al., 2009). It is notable that in human studies only younger adolescents exhibit this difference; with delay discounting reaching adult levels by age 16–17 (Steinberg et al., 2009). Adolescent humans also score higher on the Sensation-Seeking Scale than adults, with males exhibiting higher levels than females (Zuckerman et al., 1978). Sensation seeking is "the need for varied, novel, and complex sensations and experiences. . ." (Zuckerman, 1979, p. 10), which may occur independently, or together with impulsivity. Sensation seeking is greatest during early- to mid-adolescence and lower thereafter, while impulse control appears to steadily improve through the teenage years, suggesting that they are subserved by different biological processes (Steinberg et al., 2008). Consistent with human evidence of heightened adolescent sensation seeking, adolescent rodents prefer novelty (Adriani et al., 1998; Douglas et al., 2003; Stansfield et al., 2004), exhibit greater novelty-induced locomotion (Stansfield and Kirstein, 2006; Sturman et al., 2010), and spend more time exploring open arms in an elevated plus maze than adults (Adriani et al., 2004; Macrì et al., 2002).

Adolescents' tendencies to seek novel experiences, even at the risk of physical or social harm, might be expected if their capacity to assess risk or compute outcome probability is underdeveloped. Cognitive abilities do continue to develop at this time (Luna et al., 2004; Spear, 2000). According to Piaget, the formal operation period, which is associated with more abstract reasoning, reaches full maturity during adolescence (Schuster and Ashburn, 1992), and may be less well developed in some individuals. Also, the persistence of egocentrism, in which teenagers experience an 'imaginary audience' along with the 'personal fable' of unique feelings, may cause them to believe they are exceptional and give them a sense of invulnerability (Arnett, 1992; Elkind, 1967). However, only modest cognitive improvements appear from mid-adolescence onward (Luna et al., 2004; Spear, 2000), and even young children exhibit an accurate implicit understanding of probability (Acredolo et al., 1989). Furthermore, there is little evidence that adolescents actually perceive themselves as invulnerable or underestimate risk; in fact, they often overestimate risk, such as the chance they will become pregnant within a year, go to jail, or die young (de Bruin et al., 2007). Finally, any cognitive explanation for adolescent risk-taking must account for the fact that children take fewer risks and yet are less cognitively developed than adolescents.

Alternatively, adolescent behavioral disparities could relate to differences in cognitive strategies. One hypothesis, called "fuzzy trace theory," states that far from lacking in cognitive ability, adolescents process the risk/benefit details of choices more explicitly than adults. Paradoxically, adolescents may behave more rationally than adults by more explicitly computing the expected values of different options, but this could lead to greater risk taking (Rivers et al., 2008). According to Rivers et al. (2008), through development we progress from doing more literal "verbatim" to a "fuzzy" gist-level heuristic that captures the essence or bottom line without details. This presumably improves the efficiency of decision making and tends to bias us away from risky choices as we tend to avoid potential adverse outcomes without assessing the actual probabilities involved. For example, unlike adolescents, adults favor choices that attach certainty to increased gains or reduced losses over probabilistic alternatives with identical expected values (Rivers et al., 2008). Overall, the idea that adolescent choices could reflect differences in cognitive strategy—but not deficiencies in outcome prediction—is intriguing. Future neuroimaging and physiology studies of adolescent decision making might benefit from considering the possibility that differences in the precise pattern of neural activity, even within the same brain regions, along with the level of integration between different regions, could facilitate alternative styles of cognitive deliberation.

Adolescents' greater recklessness could be due to differences in how they experience risk and reward. One explanation is that human adolescents experience more negative affect and depressed mood, and may feel less pleasure from stimuli of low or moderate incentive value. Adolescents would therefore seek stimuli of greater hedonic intensity to satisfy a deficiency in their experience of reward (see Spear, 2000). This is supported by studies showing differences in the hedonic value of sucrose solutions to adults versus adolescents. Once sucrose concentrations exceed a critical point, the hedonic value sharply decreases; however such decreases are less pronounced or non-existent in children and adolescents (De Graaf and Zandstra, 1999; Vaidya et al., 2004). An alternative explanation is that adolescents have greater sensitivity to the reinforcing properties of pleasurable stimuli. Either possibil-

ity is consistent with animal models in which adolescents consume more sucrose solution (Vaidya et al., 2004), prefer chambers previously associated with social interaction (Douglas et al., 2004), and exhibit evidence of higher incentive value for drugs such as nicotine, alcohol, amphetamine, and cocaine than adults (Badanich et al., 2006; Brenhouse and Andersen, 2008; Shram et al., 2006; Spear and Varlinskaya, 2010; Vastola et al., 2002). This is not always seen, however (Frantz et al., 2007; Mathews and McCormick, 2007; Shram et al., 2008), and increased adolescent drug preference could also be related to reduced sensitivity to aversive side-effects and withdrawal (Little et al., 1996; Moy et al., 1998; Schramm-Sapyta et al., 2007, 2009). Similarly, adolescents might perform more risky behaviors if their assessment of possible aversive consequences is less motivating or salient (or if the excitement of risk-taking itself makes such behavior more likely).

Another factor that could account for some adolescent behavioral differences is the impact of emotions (valence, feelings, arousal, and specific emotional states) on behavior. Behavioral disparities may arise if adolescents experience emotions differently, or if emotions differently influence decision making during this period of heightened emotional intensity and volatility (Arnett, 1999; Buchanan et al., 1992). Emotion is often thought to cloud rational decision making. While this may be true in some cases (especially when emotional content is unrelated or irrelevant to a decision context), recent work has examined how emotions may improve certain decisions. For example, the somatic marker hypothesis states that in ambiguous situations, emotional processes can advantageously guide behavior (Damasio, 1994). The Iowa Gambling Task was designed to test decision making under conditions of uncertainty (Bechara et al., 1994). Individuals with lesions of the ventromedial PFC or amygdala have difficulty favoring the advantageous risk-avoiding strategy, suggesting that deficiencies in integrating emotional information can lead to poor decisions (Bechara et al., 1996, 1999). Adolescents and adults may differ in the way they integrate emotional information in decisions: adolescents may be less adept at interpreting or integrating relevant emotional content, or less effective at forming such associations. Cauffman et al. (2010) recently tested children, adolescents, and adults on a modified version of the Iowa Gambling Task; they observed that while both adolescents and adults improved their decision-making over time, adults did this more rapidly. Another study demonstrated that only by mid- to late- adolescence did subjects improve their gambling task performance, and that this improvement coincided with the appearance of physiological correlates of arousal (Crone and van der Molen, 2007). These results suggest that adolescents may be less effective at forming or interpreting the sort of relevant affective information necessary to avoid risky decisions.

According to Rivers et al. (2008) differences in effective gist processing make adolescents more susceptible to potentially deleterious effects of arousal on decision making. In conditions of heightened arousal, a reduction in behavioral inhibition may cause one to switch from a "reasoned" to a "reactive" or impulsive mode. They further argue that the adolescent tendency to perform more verbatim-analytical processing makes this more likely, while the values and biases of the simpler adult "gist" processing is more impervious to arousal state (Rivers et al., 2008). Others have also argued that adolescent behavior may be particularly sensitive to conditions of high emotional arousal (Dahl, 2001; Spear, 2010). A recent study by Figner et al. (2009) directly tested this hypothesis using a task that measured risk taking under different affective conditions. Adolescents and adults performed the Columbia Card Task, in which the level of tolerated risk was examined under conditions of greater/lesser arousal and while varying factors that could be used to make more informed decisions (such as the magnitude of gains/losses and their probability). Adolescents took more risks than adults only in the high-arousal condition, and in this context, adolescents were less affected by gain/loss magnitude and probability, suggesting simplified information usage by adolescents under conditions of heightened arousal (Figner et al., 2009).

Table 1
Adolescent behavioral differences and structural neurodevelopment. Several age-related behavioral differences relevant to adolescent vulnerabilities are listed along with some important neurodevelopmental changes. See text for details and references.

Behavior (compared with adults)	Neurodevelopmental changes
More risk taking	Reductions in gray matter
More impulsive choice	Augmentation of white matter
More sensation seeking	Neurogenesis
More novelty preference	Lifetime peak receptor expression
More reward preference	Increasing forebrain GABA synthesis
Less inhibitory control	Lifetime peak midbrain dopamine activity
More catelepsy from neuroleptics	D2 activation now increases PFC interneuron spiking
Less activation from psychostimulants	NMDA-mediated currents now seen on PFC interneurons

Collectively these studies indicate that although adolescents often reason and behave like adults, in certain contexts there are differences in their cognitive strategy and/or in their response to risk and reward, especially under conditions of heightened emotional arousal. These behavioral changes likely reflect the substantial development of brain networks—including structures in the PFC, basal ganglia, and neuromodulatory systems (e.g., dopamine)—that are critical to motivated behavior (Table 1).

3. Adolescent structural neurodevelopment

The adolescent brain undergoes dramatic changes in gross morphology. Human structural imaging studies have demonstrated that throughout the cerebral cortex there is a loss of gray matter during adolescence, with gray-matter reductions in portions of the temporal lobe and dorsolateral PFC occurring in late adolescence (Gogtay et al., 2004; Sowell et al., 2001, 2002, 2003). Gray matter reductions are also apparent in the striatum and other subcortical structures (Sowell et al., 1999, 2002). These changes may be related to a massive pruning of synapses observed during this period from animal studies (Rakic et al., 1986, 1994), although some question this connection as synaptic boutons make up only a small proportion of cortical volume (Paus et al., 2008). Human imaging has also revealed that white matter increase through adolescence in cortical and subcortical fiber tracts (Asato et al., 2010; Benes et al., 1994; Paus et al., 1999, 2001), resulting from increased myelination, axon caliber, or both (Paus, 2010). Changes in the patterns of connectivity also occur during adolescence. For example, axonal sprouting and growth have been observed in circuits connecting the amygdala to cortical targets (Cunningham et al., 2002), and increasing measures of white matter are observed between the PFC and striatum and other areas (Asato et al., 2010; Giedd, 2004; Gogtay et al., 2004; Liston et al., 2006; Paus et al., 2001; Sowell et al., 1999).

At a finer scale, rat and primate studies have demonstrated numerous differences in adolescent neurotransmitter systems. Adolescents tend to over-express dopaminergic, adrenergic, serotonergic and endocannabinoid receptors across many regions followed by pruning to adult levels (Lidow and Rakic, 1992; Rodriguez de Fonseca et al., 1993). They express D1 and D2 dopamine receptors at higher levels in subcortical targets such as the dorsal striatum and nucleus accumbens, although some have not found reduced adult expression in this latter region (Gelbard et al., 1989; Tarazi and Baldessarini, 2000; Tarazi et al., 1999;

Teicher et al., 1995). During adolescence, there are also changes in dopamine production and turnover, as well as evidence for changes in downstream effects of receptor–ligand binding (Badanich et al., 2006; Cao et al., 2007; Coulter et al., 1996; Laviola et al., 2001; Tarazi et al., 1998). Functionally, there is evidence from anesthetized rats that the spontaneous activity of midbrain dopamine neurons peaks during adolescence and then decreases (McCutcheon and Marinelli, 2009). Developmental changes in mesocorticolimbic dopamine circuitry and activity may underlie some differences in motivated behavior generally, as well as risk taking and addiction vulnerability in particular. Several studies have observed reduced psychomotor effects of stimulant drugs in adolescent animals but enhanced or similar reinforcing effects (Adriani et al., 1998; Adriani and Laviola, 2000; Badanich et al., 2006; Bolanos et al., 1998; Frantz et al., 2007; Laviola et al., 1999; Mathews and McCormick, 2007; Spear and Brake, 1983). In contrast, adolescents are more sensitive to the cataleptic effects of neuroleptics (e.g., haloperidol), which are antagonists for dopamine receptors (Spear and Brake, 1983; Spear et al., 1980; Teicher et al., 1993). Some have proposed that this pattern, along with the increased exploration and novelty-seeking, indicates that the adolescent dopamine system is near a "functional ceiling" at baseline (Chambers et al., 2003).

Several lines of evidence suggest that the balance of large-scale excitatory and inhibitory neurotransmission is vastly different in adolescents compared to adults. Levels of GABA, the main inhibitory neurotransmitter in the brain, increases linearly through adolescence in rat forebrain (Hedner et al., 1984). The expression of the activating glutamate NMDA receptors on fast-spiking neurons (thought to be inhibitory interneurons) changes dramatically in the PFC of adolescents. At this time the vast majority of fast-spiking interneurons exhibit no synaptic NMDA receptor-mediated currents (Wang and Gao, 2009). Additionally the modulatory impact of dopamine-receptor binding shifts during adolescence (O'Donnell and Tseng, 2010). It is only by this time that the activation of dopamine D2 receptors increases interneuron activity (Tseng and O'Donnell, 2007). Furthermore, the synergistic interaction between dopamine D1 receptor activation and the NMDA receptor changes during adolescence, allowing for plateau depolarizations which may facilitate context-dependent synaptic plasticity (O'Donnell and Tseng, 2010; Wang and O'Donnell, 2001). These adolescent dopamine, glutamate, and GABA signaling changes suggest fundamental neural activity differences in the adolescent brain. All of these systems are essential to cognitive and emotional processes. Their dysfunction is implicated in numerous psychiatric illnesses ranging from mood disorders and addiction to schizophrenia.

4. Adolescent functional neurodevelopment

Neuroimaging studies have shown differences in human adolescent functional activity in several forebrain regions. These differences are primarily observed in brain regions that encode emotional significance (e.g., the amygdala) integrate sensory and emotional information for the computation of value expectations (e.g., the orbitofrontal cortex), and play various roles in motivation, action selection, and association learning (e.g., the striatum). Compared to adults, adolescents have a reduced hemodynamic response in lateral orbitofrontal cortex and increased activity in ventral striatum to rewards (Ernst et al., 2005; Galvan et al., 2006). Others have found reduced activity in right ventral striatum and right extended amygdala during reward anticipation, with no observed age-related activity differences after gain outcome (Bjork et al., 2004). In a decision-making task, adolescents had reduced right anterior cingulate and left orbitofrontal/ventrolateral PFC activation compared to adults during risky choices (Eshel et al., 2007). Adolescents also activated their ventral striatum and orbitofrontal cortex more strongly than did adults as they took greater risks during a Stoplight driving game—an effect driven by implicit peer pressure (Chein et al., 2011).

Several studies have observed immaturity of adolescent cognitive control systems, along with poorer behavioral performance (Luna et al., 2010). For example, during tasks that require the inhibition of a prepotent response (the performance of which improves with age), adolescents have increased PFC activity in some subregions and decreased activity in others (Bunge et al., 2002; Rubia et al., 2000; Tamm et al., 2002). During an antisaccade cognitive control task, adolescent (but not adult) ventral striatum activity was reduced while viewing a cue that indicated if reward was available during a given trial, but it was more activated than its adult counterpart during reward anticipation (Geier et al., 2009). Thus adolescents generally activate similar cognitive and affective structures as adults, although often with different magnitudes or spatial and temporal patterns, or levels functional interconnectivity (Hwang et al., 2010).

Maturation of intra- and inter-regional connectivity and neuronal coordination may play a central role in adolescent behavioral development. There is a direct relationship between measures of frontostriatal white matter, which increases through adolescence, and inhibitory control performance (Liston et al., 2006). White-matter development is also directly related to improved functional integration of gray matter regions, suggesting more-distributed network activity through development (Stevens et al., 2009). This is corroborated by a study that, using resting state functional connectivity MRI along with graph analyses, observed a shift from greater connectivity with anatomically proximal nodes to networks that were more extensively integrated across all nodes in adulthood regardless of distance (Fair et al., 2009). Similarly, age-related increases in the functional integration of frontal and parietal regions support improved top-down inhibitory control performance in an antisaccade task (Hwang et al., 2010). White matter development, the rapid pruning of synapses (which are largely local excitatory connections), and developmental shifts in local interneuron activity may together facilitate more extensive functional coordination between brain regions through development. Less widely distributed activity in adolescents has also been demonstrated in another cognitive control task (Velanova et al., 2008). At the same time, diffuse functional signal uncorrelated with task-performance decreases through development (Durston et al., 2006). Thus, the adult pattern of utilizing more-distributed networks is coincident with reduced task-irrelevant activity, indicating greater efficiency in the pattern and extent of cortical processing.

Electrophysiological studies have also found evidence of further development of neuronal responses and greater local and long-range coordinated activity through adolescence. For example, the Contingent Negative Variation, which is a negative voltage event-related potential during response preparation, only develops in late childhood and continues to become larger through adolescence (Bender et al., 2005; Segalowitz and Davies, 2004). This is thought to reflect age-related differences in the distribution of PFC processing of attention and executive motor control (Segalowitz et al., 2010). Another age-related electrophysiological change is the development of strong positive peak (P300) approximately 300 ms after attending to a stimulus. A mature P300 pattern does not appear until approximately age 13 (Segalowitz and Davies, 2004). Finally, the Error-Related Negativity is a negative voltage centered over the anterior cingulate cortex during error trials of different tasks. Although there is some variability in the age of its appearance, it seems to arrive around mid-adolescence (Segalowitz and Davies, 2004). These findings provide additional evidence for the continued maturation of prefrontal cortical processing during adolescence. Segalowitz and colleagues also found that the signal-

to-noise ratio of the electrical signals of children and adolescents were often lower than that of adults. This could be due to functional immaturity or intra-individual instability of brain regions producing these signals (Segalowitz et al., 2010). It might also reflect reduced adolescent neural coordination within and between brain regions. This interpretation is consistent with work performed by Uhlhaas et al. (2009b), in which electroencephalograms (EEGs) were recorded in children, adolescents, and adults during a facial recognition task. They observed reduced theta (4–7 Hz) and gamma band (30–50 Hz) oscillatory power in adolescents compared to adults. Additionally there was greater long-range phase-synchrony in theta, beta (13–30 Hz), and gamma bands, along with improved task performance in adults. EEG oscillations are due to fluctuations in neuronal excitability and are thought to fine-tune the timing of spike output (Fries, 2005). Measures of synchrony in specific frequency bands facilitate communication between neuronal groups, and may be critical to numerous perceptual and cognitive processes (Uhlhaas et al., 2009a). Thus, these findings are evidence of enhanced coordinated local processing and improved inter-regional communication from adolescence to adulthood (Uhlhaas et al., 2009b).

Another useful approach for examining neural activity changes through adolescence is with *in vivo* electrophysiological recording from implanted electrode arrays in awake behaving animals. This technique enables one to record the activity of individual neurons as well as larger-scale field potentials. We recently carried out such a study, in which adolescent and adult rats performed a simple goal-directed behavior (Fig. 1a) as recordings were taken from orbitofrontal cortex. While adolescents and adults performed the same behavior, striking age-related neural encoding differences were observed, especially to reward (Sturman and Moghaddam, 2011). This indicates that even when behavior may appear similar, the adolescent prefrontal cortex is in a different state than that of adults. Specifically, adolescent orbitofrontal cortex neurons became far more excited to the reward, while the proportion of adolescent inhibited neurons was substantially smaller at that time and at other points in the task (Fig. 1b). As neural inhibition is critical for controlling the precise timing of spikes and entraining synchronized oscillatory activity (Cardin et al., 2009; Fries et al., 2007; Sohal et al., 2009), reduced task-related adolescent orbitofrontal cortex neuronal inhibition may be directly related to larger-scale neural encoding differences observed in this study and described by others. Finally, throughout much of the task adolescents exhibited greater cross-trial spike-timing variability, which could indicate lower signal-to-noise in adolescent prefrontal cortex. Therefore, as the prefrontal cortex develops, increased phasic inhibition at the single-unit level could support greater intra- and inter-regional neural coordination and processing efficiency.

5. Neurobehavioral hypotheses

With all of the neurodevelopmental changes of adolescence, what accounts for the particular behavioral differences and vulnerabilities of this period? The previous sections outline evidence for a variety of adolescent neurodevelopmental changes and age-related behavioral differences and vulnerabilities. Here we present several hypotheses or models that explicitly connect adolescent differences in motivated behavior, social development, and behavioral inhibition with the maturity of specific neural circuits (Table 2).

Adolescent refinement of a social information processing network is one model connecting adolescent social development with brain changes (Nelson et al., 2005). This framework describes three interconnected functional nodes with distinct neural structural underpinnings: the detection node (inferior occipital cortex, inferior and anterior temporal cortex, intraparietal sulcus, fusiform gyrus, and superior temporal sulcus), the affective node (amygdala, ventral striatum, septum, bed nucleus of the stria terminalis, hypothalamus, and orbitofrontal cortex in some conditions), and the cognitive-regulatory node (portions of the prefrontal cortex). The detection node determines whether stimuli contain social information, which is further processed by the affective node which imbues such stimuli with emotional significance. The cognitive-regulatory node further processes this information, performing more complex operations related to perceiving the mental states of others, inhibiting prepotent responses, and generating goal-directed behavior (Nelson et al., 2005). Adolescent changes in the sensitivity and interaction of these nodes is hypothesized to intensify social and emotional experiences, strongly influence adolescent decision making, and contribute to the emergence of psychopathologies during this period (Nelson et al., 2005).

The triadic node model (Ernst et al., 2006) posits that the specific developmental trajectory of brain regions subserving affective processing and cognitive control, and the balance between them, may underlie the risk-taking propensity of adolescents. This model is also based on the activity of three nodes corresponding to specific brain regions. In this case a node responsible for reward approach (ventral striatum) is in balance with a punishment-avoidance node (amygdala). A modulation node (prefrontal cortex) affects the relative influence of these countervailing forces, and risky behavior will result from a final calculus favoring approach. According to this model, in situations involving some probabilistic trade-off between appetitive and aversive stimuli, the approach node is more dominant in adolescents. Hyperactivity or hypersensitivity of a reward-approach system might otherwise be adjusted by activity in portions of the prefrontal cortex, however its underdevelopment in adolescents does not permit adequate self monitoring and inhibitory control (Ernst and Fudge, 2009).

Casey et al. hypothesize that differences in the developmental trajectory of adolescent prefrontal cortex versus subcortical structures (e.g., ventral striatum and amygdala), along with the connections between them, might account for adolescent behavioral propensities (Casey et al., 2008; Somerville and Casey, 2010; Somerville et al., 2010). During a task involving the receipt of different reward values, the extent of adolescent activity in the nucleus accumbens was similar to that of adults (although with greater magnitudes) whereas the pattern of orbitofrontal cortical activity looked more like that of children than adults (Galvan et al., 2006). The relative maturity of subcortical systems and the immaturity of the prefrontal cortex, which is critical to cognitive control, may lead to a greater adolescent propensity toward sensation seeking and risk taking. The key here, as in the triadic node model, is the concept of a relative inter-regional imbalance during adolescence, in contrast to childhood when these regions are all relatively immature and adulthood when they are all mature (Somerville et al., 2010). This model is also similar to Steinberg's framework, in which the relative decrease in risk taking from adolescence to adulthood is due to the development of cognitive control systems, connections facilitating the integration of cognition and affect among cortical and subcortical regions, and differences in reward salience or sensitivity (Steinberg, 2008).

The central theme of these models is that in adolescents, there are differences in the sensitivity, level, or effect of activity in cortical and subcortical regions within networks that subserve emotional processing and cognitive control. Based on our data and other evidence, we hypothesize that such differences may be the result of reduced neuronal coordination and processing efficiency in adolescents which manifests as a result of less-effective information transfer between regions and imbalances in neuronal excitation and inhibition within critical brain regions, such as the orbitofrontal cortex and portions of the basal ganglia. As described earlier, *in vitro* work has demonstrated dramatic changes in the expression pat-

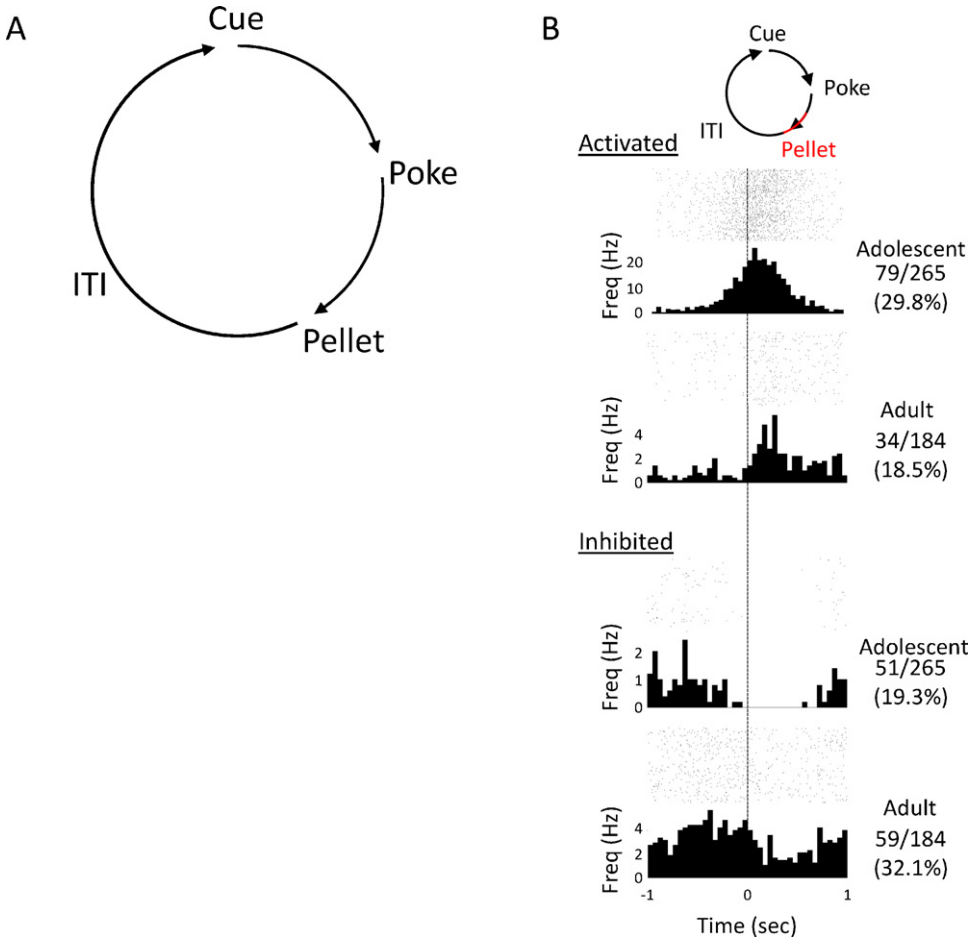

Fig. 1. (A) Schematic of the behavioral task. Rats performed an instrumental behavior inside of a standard operant chamber. Each trial began with the onset of a cue light within a nose-poke hole (Cue). If the rat poked into that hole while the light was on (Poke) the light turned off and a food pellet was delivered to a food trough on the opposite wall. Once the animal poked into the food trough to retrieve the pellet (Pellet) a 5 s inter-trial interval (ITI) was triggered, followed by the next trial. Rats could perform a maximum of 100 trials within a 30 min session. (B) Adolescent and adult unit firing-rate activity during pellet retrieval after learning the task. Each graph is the activity of a representative adolescent or adult unit. Raster plots, which indicate the timing of spikes for each trial (row) are displayed above peri-event time histograms which average across trials in 50 ms bins. Units that were significantly activated (upper plots) or inhibited (lower plots), relative to a baseline period, are shown around the time of reinforcement. To the right of each plot is the proportion and percentage of units classified with the corresponding response pattern in a 500-ms window centered at pellet retrieval. As indicated, adolescents had substantially larger proportions of units that were activated during this period. Conversely, adults had a larger proportion of inhibited units. These age-related proportional differences were statistically significant (Chi-square test, $p < 0.01$).
Adapted from Sturman and Moghaddam (2011).

Table 2
Neurobehavioral hypotheses integrating adolescent behavioral changes with brain development.

Hypothesis	Description	References
Social information processing network	Changes in adolescent social behavior reflect the development of specific brain networks that integrate the detection of social information with cognitive and affective processing regions.	Nelson et al. (2005)
Triadic node	Adolescent risky behavior can be explained in terms of the relative strength of ventral striatum-mediate approach versus amygdala-mediated avoidance and an immature supervisory prefrontal cortex.	Ernst et al. (2006)
Differential development of limbic reward versus top-down control systems	The relatively earlier development of bottom-up limbic regions versus the prefrontal cortex, biases behavior toward risk and reward.	Casey et al. (2008)
Arousal of socio-emotional systems at puberty	Increased sensation-seeking and risk-taking during adolescence are due to changes in reward salience and sensitivity as a result of brain remodeling (e.g., changes in dopamine and oxytocin systems) and immature cognitive control systems.	Steinberg (2008)
Inefficient neuronal processing	Adolescent neural processing is less well-distributed and coordinated due to immature myelination, pruning, interneuron development, and other factors. This leads to imbalances in local activation and inhibition in systems that underlie motivated behavior, and precipitate both altered sensitivities to salient stimuli and less-effective top-down control in certain contexts.	Sturman and Moghaddam (2011)

terns of various receptors, and the effects of receptor activation, including the response of inhibitory fast-spiking interneurons to dopamine and NMDA receptor stimulation. Such changes would be expected to affect both the balance of excitation and inhibition and the coordination of neuronal groups. As fast-spiking interneuron activity is critical to controlling the precise timing of neural activity and the entrainment of oscillations, the developmental shifts in adolescent interneuron activity and their response to neuromodulators like dopamine may be central to some of these age-related processing differences. As a result of this, adolescent neural activity may be less well-coordinated, noisier, and more local, and also perhaps more sensitive to the behaviorally activating effects of rewards, novelty, or other salient stimuli. Reduced inter-regional oscillatory coordination, further hampered by incomplete myelination, could together account for the less-distributed functional activity observed in imaging studies. The previously mentioned tendency for adolescents to favor risky choices in emotionally charged contexts could also be related to a combination of reduced inter-regional communication (e.g., failure of the prefrontal cortex to effectively dampen subcortical "go" signals in the basal ganglia), and exaggerated activation and/or reduced inhibition to salient cues in the context of motivated behavior, as we observed during reward anticipation in the orbitofrontal cortex.

6. Summary

As we have learned more about the specific brain and behavioral changes of adolescence several neurobehavioral models have been proposed. Central to most of these is the notion that immature neuronal processing in the prefrontal cortex and other cortical and subcortical regions, along with their interaction, leads to behavior that is biased toward risk, reward, and emotional reactivity during the adolescent period. Recent work on the development of inhibitory interneuron circuits and their changing interaction with neuromodulatory systems during adolescence may also shed light on why illnesses like schizophrenia typically manifest at this time. Using techniques like fMRI in humans and electrophysiological recordings in laboratory animals, we are beginning to identify more precisely how adolescents process reward and other aspects of motivated behavior differently from adults. Doing so is a critical step toward ascertaining the brain-based vulnerabilities of normal adolescent behavior and in understanding the pathophysiology of the psychiatric illnesses that develop during this period.

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