

THE BIOLOGY OF ADOLESCENCE

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Summary. Adolescence is a time of transformation that is characterized by discrete changes in behavior, cognition and the brain – some of which are likely pubertal-dependent, and others which are not. Although set within cultural contexts, these transformations appear to have biological roots that are deeply embedded in our evolutionary past. Starting from an evolutionary perspective, this paper provides an overview of the neurobiological and hormonal changes of adolescence and the implications of this biology for adolescent risk-taking and other behaviors.

Introduction

Developing organisms across a variety of species must master the transition from the dependence of youth to relative independence from parental support. During this transition, human adolescents, like their counterparts in other mammalian species, are challenged with acquiring the skills necessary to survive away from parents. Notable across-species similarities are seen in the biology of this transition, including not only many hormonal and physiological changes associated with puberty and sexual maturation, but also adolescent-typical transformations in the brain as well. The basics of brain structure and function arose millions of years ago, with similarities in the relative timing of development of these brain structures across species. Adolescents from a variety of mammalian species also show certain age-typical ways of responding to their environment, including an increased focus on peer-directed social interactions, increases in novelty seeking/risk taking, and elevations in a variety of consummatory behaviors, typically including increases in food intake (along with an associated growth spurt), as well as an increased propensity for alcohol/drug use (see Spear, 2000, 2009; Steinberg, 2008, for reviews). These across-species behavioral commonalities presumably have been evolutionarily conserved ultimately because of their adaptive significance. For instance, social interactions with peers may help develop social skills away from the home environment, guide choice behavior, ease the transition to independence away from the family, and provide opportunities to practice and model adult-typical behavior patterns (see Spear, 2010, for references and discussion).

Risk-taking as well has been postulated to serve a number of adaptive functions despite its potentially high cost, with risky behaviors largely driving the elevated adolescent mortality rates across diverse species (e.g., Irwin & Millstein, 1992; Crockett & Pope, 1993). These adaptive functions have been posited to include increasing the probability of reproductive success among males of a variety of species, including humans under some life circumstances (Wilson & Daly, 1985; Steinberg & Belsky, in press), as well as providing opportunities to secure additional resources, explore adult liberties and face and surmount challenges (Csikszentmihalyi & Larson, 1978; Silbereisen & Reitzle, 1992; Steinberg & Belsky, 1996). Risk-taking may also have served to encourage emigration away from the home territory around the time of sexual maturation, thereby avoiding genetic inbreeding and the lower viability of inbred offspring due to greater expression of recessive genes (Bixler, 1992; Moore, 1992).

Indeed, commonly among mammalian species (including our human ancestors, e.g., Schlegel & Barry, 1991), males (or less frequently, females, or both sexes) emigrate away from the home territory around the time of sexual maturation (e.g., Pereira & Altmann, 1985).

Such fundamental biological and behavioral parallels seen among adolescents across a variety of species suggest that these adolescent-typical characteristics have biological roots that are deeply embedded in our evolutionary past. These similarities provide reasonable face, predictive, and construct validity for the judicious use of simple animal models for studying certain features of adolescence not amenable to analysis in human adolescents (see Spear, 2010, for discussion). For instance, consider that the smallest unit of analysis in human brain imaging studies, a voxel, has been estimated to contain up to 5.5 million brain cells (neurons), and between 0.5-5.5 billion neuronal connections (synapses) (Pakkenberg & Gundersen, 1997; Scheff et al, 2001; Logothetis, 2008). This level of complexity provides challenges for the use of imaging studies to extract detailed molecular, neuroanatomical and electrophysiological information about the development of specific neural and synaptic systems – levels of analysis more amenable to the invasive techniques available with animal models of adolescence.

When considering adolescence from an evolutionary perspective, and when using animal models to explore basic aspects of this developmental transition, two important caveats need to be acknowledged. First, although exhibiting certain basic neural and behavioral characteristics of adolescence, organisms undergoing this transition in other species of course lack the rich complexity of human brain and behavioral function seen during adolescence (or at any age). Hence, animal models can be used to model only limited aspects of human adolescence (see Spear, 2000, for discussion). Secondly, viewing adolescence from an evolutionary perspective does not imply biodeterminism; indeed, the biology of adolescence is inexorably interwoven with psychosocial, economic and cultural influences.

As but one example of how biological contributors are shaped and moderated by cultural, economic and psychosocial influences, consider pubertal timing, which has been shown to be influenced by a number of cultural and psychosocial factors. Girls enter puberty earlier in polygamous than monogamous societies (Bean, 1983; cited by Weisfeld, 1999), in cultures with stressful pubertal rite practices than those without initiation ordeals (Surbey, 1998), and when reared in situations involving notable family conflict (e.g., Kim & Smith, 1998) or in homes without the father present (Surbey, 1990). Sociocultural and economic contexts may likewise influence the perception of adolescence as a distinct developmental stage (e.g., see Schlegel, 2009). For instance, it has been argued that the adolescent population provides a means for adjusting the size of the workforce to meet labor needs, with adolescence viewed as a brief developmental transition to maturity when labor needs are high, but as a period of prolonged immaturity needing substantial scaffolding and extended education when unemployment rates are high (Enright et al, 1987). Intriguingly, associations between economic/labor needs and the timing of the transition to maturity are not unique to human populations. Even in honey bees, immature bees (that normally care for brood in the hive) mature earlier than usual when there are too few mature bees to meet the foraging needs of the hive, whereas their maturation is delayed when mature foragers are plentiful (Whitefield et al, 2003).

Thus, although psychosocial, cultural, and economic approaches to the study of adolescence often have been dichotomized from biological analyses, these approaches are bi-directionally linked. That is, recognizing the important role that neural and hormonal changes of adolescence play in influencing the ways adolescents think, feel, and behave does not negate the critical influences exerted by the cultural, social and economic environment. It is to these biological contributors that we now turn.

The impact of puberty on adolescent behavior

Puberty and the attainment of sexual maturation occur during adolescence, although adolescence and puberty are not synonymous terms. Puberty refers to the developmental processes leading to reproductive maturation (Graber et al, 1996), whereas adolescence is the gradual transition from childhood to adulthood that consists of multiple and partially overlapping transformations, some pubertally-related and others not (Pickles et al, 1998). Thus, although “one may define puberty in specific neuroendocrinological terms, ... adolescence is, of its essence, a period of transitions rather than a moment of attainment” (Rosenblum, 1990, p.64) and, as such, is difficult to characterize in terms of its exact onset and offset. The relative timing of puberty within adolescence varies notably across individuals (e.g., Dubas, 1991), which itself has considerable significance for the adolescent, a point to which we return later.

The biology of puberty.

A hallmark event of puberty is an increase in the release of gonadal hormones – e.g., testosterone released from the testes in males and estrogen and progesterone released at various stages of the egg maturation process by the ovaries and uterus of females. These hormones represent the endpoint of a hormonal cascade that begins in the brain with the release of gonadotropin releasing hormone (GnRH) from the hypothalamus that in turn stimulates the release of other hormones (follicle-stimulating hormone [FSH] and luteinizing hormone [LH]) from the pituitary gland into the blood, which pass through the circulation to reach the gonads and stimulate hormone release there. The pubertal rise in gonadal hormones contributes to the development of secondary sexual characteristics, and influences neural function and behavior via binding to testosterone and estrogen receptors in brain.

“Organizational” vs. “activational” effects of gonadal hormones at puberty. In males, the rise in activity of the hypothalamic-pituitary-gonadal (HPG) axis at puberty actually represents a reinstatement of high levels of gonadal hormones seen prior to, and for some time after birth, where they serve to promote differentiation of the brain (and reproductive organs) into a male-typical pattern. The absence of significant gonadal hormone stimulation at this time, in contrast, channels differentiation of the brain and reproductive organs into female-typical patterns. Traditionally, sex differences in brain structure/function were thought to be established early in life by “organizational” effects of the presence or absence of gonadal hormones, with the later increases in gonadal hormones merely serving to “activate” these latent sex differences (e.g., see Gorski, 2002, for review). Relatively recently, however, convincing evidence has emerged from basic science studies that the developing brain remains sensitive to organizational effects of gonadal hormones from very early in life through adolescence, with normal developmental increases in gonadal hormones during puberty not only exerting adult-typical “activational” effects, but also triggering a second organizational period, further

differentiating the brain to produce the final sex-specific neural maturation needed to support sexually dimorphic behaviors (e.g., Sisk et al, 2003; Schulz et al, 2009a,b). Thus, the pubertal rises in gonadal hormones may contribute to sex differences seen in some regions of the mature brain, but not others. For instance, keeping in mind that causality is not implied in correlational analyses, such analyses have reported stage of pubertal development to account for 13-15% of the variance in volume of the amygdala (boys>girls in proportional size) and hippocampus (girls>boys), but to be unrelated to volume of another sexually dimorphic brain region, the striatum (where size in girls>boys)(Neufang et al, 2009). Pubertal rises in gonadal hormones were also recently reported to be associated with declines in gray matter in several cortical regions among girls, although not in boys among the 10-15 year olds examined (Peper et al, 2009).

Puberty and behavior. Stage of pubertal development has been correlated with a variety of behavioral changes, including, of course, rises in sexual activity and interests. Among the behaviors hypothesized to be influenced by pubertal maturation are adolescent-typical changes in arousal and the salience of socioemotional stimuli, with chronological age postulated to be more associated with cognitive maturational processes (e.g., see Steinberg, 2005). Indeed, a number of studies comparing adolescents at different stages of puberty have found stage of pubertal maturation to be associated with a variety of adolescent-typical behaviors, including increased conflicts with parents (Steinberg, 1988), later onset of sleep (Carskadon et al, 1993), and increased risk-taking behaviors, including alcohol and drug use (Harrell et al, 1998; Wilson et al, 1994). And in animal models, the presence or absence of testosterone during adolescence has been shown to program not only adult male sexual behavior, but also perhaps other social behaviors, certain indices of anxiety, and spatial cognition (see Schulz et al, 2009a, for discussion and references). Yet, other studies have not found reliable relationships between pubertal status and behavior (e.g., Laursen et al, 1998; Feinberg et al, 2006), in part perhaps because of the different strategies used across studies when attempting to disentangle maturational age from pubertal status, given the strong correlations between these variables (see Spear, 2010, for discussion). An additional complication is that it is not just puberty per se, but also the relative timing of puberty that is important.

Pubertal timing. The timing of puberty is ultimately driven by changes in the hypothalamus that stimulate GnRH secretion, precipitating the HPG hormonal cascade. The “trigger” for this rise in GnRH appears to be a recently discovered group of peptides called “kisspeptins” and their hypothalamic receptors (termed “GPR54 receptors”) that increase at the time of puberty and are essential for reproductive maturity (e.g., Kaiser & Kuohung, 2005; Tena-Sempere, 2006). Kisspeptin-containing neurons have receptors for leptin, a hormone released by fat cells that signals body fat availability (e.g., Shalitin & Phillip, 2003), and that rises in females approaching puberty, presumably signaling that the body contains sufficient energy stores to support a pregnancy and lactation (Grumbach, 2002; Mann & Plant, 2002). Indeed, body weight and amount of body fat is strongly linked to puberty in a variety of species, especially in females, with pubertal timing delayed among individuals who are anorexic or engaged in sports encouraging low levels of body fat (e.g., ballet, wrestling)(see Roemmich et al, 2001), while accelerated among individuals with elevated body weights (e.g., Karlberg, 2002).

Early puberty has been found to be associated with an increase in a variety of adverse outcomes in both boys and girls, including earlier use of alcohol and other drugs,

greater levels of risky drinking in high school, earlier and risky sexual behavior, as well as increased delinquency (see Spear, 2010, for review and references). These pubertal timing effects undoubtedly have multiple determinants, including prominent psychosocial influences. There is also emerging evidence to support the suggestion that “the developing adolescent brain can be intercepted by pubertal hormone secretions at various time points” (Schulz et al, 2009a, p.600), thus variations in pubertal timing may influence which specific aspects of brain morphology and behavior are altered (see Schulz et al, 2009b). In the case of testosterone, earlier rises in testosterone were found to exert a greater facilitatory effect on later sexual behavior, presumably via induction of somewhat different organizational influences on the brain, than seen when the rise in testosterone occurred later in adolescence (Schulz et al, 2009a,b). The generality of these effects to non-reproductive behaviors and to pubertal increases in gonadal hormones in females remains to be determined, as well as the degree to which similar timing-dependent development occurs in the adolescent human brain (see Schulz et al, 2009a).

The biology of adolescence: adolescent brain transformations

The adolescent brain is a work in progress. Changes are seen during adolescence at molecular, cellular, anatomical and functional levels in ways that are both progressive and regressive, including among the latter, notable decreases in the number of connections (synapses) between neurons as well as reductions in the volume of certain brain regions. Other prominent changes include the myelination of axonal pathways interconnecting different brain regions, speeding conduction along these pathways and increasing the coordination of brain effort across greater distances via the formation of networks of functionally interrelated brain regions. Such adolescent-typical transformations in brain are regionally- and temporally-specific, with changes generally evident earlier in adolescence in areas implicated in modulating affect/emotional reactivity and reward responsivity, whereas regions critical for impulse control and other indices of executive function mature later. Together these transformations notably economize brain energy needs, decreasing the brain’s demands for energy as it reaches maturity.

Synaptic pruning.

Many more synaptic connections are formed between neurons than ultimately will be maintained. Early in life, synaptic overproduction is followed by pruning to eliminate non-functional synapses while retaining effective ones, a process long thought to help match brain connectivity to need (e.g., Rakic et al, 1994), and to environmental characteristics (e.g., Blakemore, 1974). Synaptic pruning undergoes a resurgence during adolescence as well, with almost half of the synaptic connections eliminated in some brain regions during this developmental transition (e.g., Rakic et al, 1994). Given that some of the synapses lost include connectivity established much earlier in life (e.g., Lewis, 1997), it seems improbable that such pruning simply reflects exceptionally delayed elimination of nonfunctional synapses. Indeed, this pruning is highly selective – e.g., more pronounced in cortical than subcortical regions (e.g., see Giedd et al, 1999a) and more evident among excitatory (glutamate) inputs to cortex than among inhibitory (GABA) synapses there (e.g., Woo et al, 1997). Such pruning during adolescence may contribute to the fine-tuning of brain connectivity necessary for emergence of adult-typical networks of brain activity (Zehr et al, 2006), and may even provide a final

enhanced opportunity for the brain to be sculpted by the environment, a possibility discussed in more detail later.

Myelination.

Neuronal information is transmitted over long distances via electrical impulses passed along special appendages of neurons called axons; this transmission occurs faster in larger diameter axons as well as when the axons are wrapped by a fatty cover called myelin. Although the process of myelination begins early in life and continues into adulthood, its production escalates notably during adolescence (e.g., see Lu & Sowell, 2009). Relatively long axons interconnecting distant regions are particularly targeted for myelination, and as a result their input is received more quickly and with a likely greater impact relative to input provided by more local, unmyelinated connections (e.g., see Markham & Greenough, 2004, for discussion). This could provide one means by which patterns of connectivity across and within brain regions could change in strength during adolescence, contributing to the emergence of adult-typical networks interrelating relatively distant brain regions.

Increases in brain efficiency.

The brain requires the most blood flow, energy and nutrients to function from roughly 3-4 years of age through the remainder of childhood, with glucose utilization rates at this time more than twice than seen in adulthood (or in infancy) (e.g., Chugani, 1994, 1996). These glucose utilization rates begin to decline in late childhood/early adolescence to reach more efficient, adult-typical rates by early adulthood (Chugani, 1998). Substantial energy is needed by the brain to restore normal ion balance across neuronal membranes following message-conveying ion changes induced by synaptic activity and axon potentials, with the latter process particularly costly when axons are unmyelinated. Adolescent-associated reductions in synaptic connectivity and increases in the proportion of cost-effective myelinated axons likely contribute considerably to the decline in brain energy needs at this time. And, to the extent that the emergence and refinement of neural networks requires fewer neurons to be recruited for a given task, these changes as well would be expected to reduce further the energy needed to power the brain (e.g., Laughlin & Sejnowski, 2003; Devous et al, 2006).

Regional specificity of adolescent brain transformations.

Regional differences in brain development have been illustrated in structural imaging studies through assessing brain volumes and white/gray matter ratios between cortical areas enriched in axon tracts (many of which are myelinated and appear white in unstained tissue because of myelin's high fat content) and those largely containing cell bodies and processes of neurons and glia support cells (that appear grayish in unstained tissue). Gray matter volume generally shows an inverted U-shaped pattern over time in the cortex, increasing to reach a gentle plateau, and modestly declining thereafter. This timing is regionally- (and in some cases, sex-) specific (e.g., Lenroot & Giedd, 2006; Lenroot et al, 2007), with these plateaus generally occurring earlier in sensory and motor areas than in prefrontal cortex (PFC) and other cortical association areas thought to subservise relatively advanced cognitive functions (Gogtay et al, 2004; Lenroot & Giedd, 2006; Østby et al, 2009). In part, these gray matter declines may reflect synaptic pruning as well as associated declines in overall volume of neurons and in the number of the non-neuronal support cells necessary to sustain synaptic functions. In animal studies, these regionally specific declines in cortical gray matter are also accompanied by some

genetically-programmed death (apoptosis) of neurons (Markam et al, 2007). Given that mature skull size is reached in well before adolescence, developmental declines in gray matter within the skull cavity may also reflect in part increases in the amount of brain partitioned into white matter, as axons continue to grow in diameter and/or become myelinated during adolescence (e.g., Sowell et al, 1999; Paus, 2005). The net result is considerable increases in the ratio of white-to-gray matter during adolescence, with a timing that varies across cortical regions.

Changes in gray matter volume are also seen during adolescence in subcortical regions as well, although they are generally of lesser magnitude than those seen cortically. Regions showing gray matter declines include dorsal striatum (caudate) and other regions of the basal ganglia, as well as ventral striatum (nucleus accumbens) (Østby et al, 2009; also see Lu & Sowell, 2009). In contrast, gray matter volumes of the amygdala and, to some extent, the hippocampus, have been reported to increase through adolescence and into young adulthood, whereas volume of the thalamus showed no developmental changes across the age span from 8-30 years (Østby et al, 2009).

Structural imaging data have been found to be associated with a variety of cognitive and behavioral changes during adolescence, with for instance associations between impulse control and volume of the PFC and the basal ganglia (Casey et al, 1997). Relationships between brain structure and function during development can be more directly examined in human imaging studies through the use of functional magnetic resonance imaging (fMRI). Based on the principle that regions with elevated neural activity require a transient increase in blood flow to provide the energy to power that synaptic and axonal activity, fMRI uses blood-oxygen-level-dependent (BOLD) signals to assess changes in regional blood flow when performing a target task relative to a baseline condition (Attwell & Iadecola, 2002). Developmental fMRI studies have escalated rapidly over the last decade or so, and have revealed sometimes notable differences in regional patterns of cortical and subcortical brain activation from childhood through adolescence and into adulthood during performance of a variety of tasks involving risky decision making and impulsive choices, data that will be reviewed later.

In studies of brain maturation, the emphasis is beginning to turn from viewing development as a sequential series of brain regions maturing and coming “online” at differing ages to considering brain maturation as a dynamic process of emerging regional activities that become more strongly interrelated and linked over time into functional networks that serve to interconnect functionally related but often spatially separated brain regions (e.g., Johnson, 2001; Fair et al, 2008; Stevens et al, 2009). Given that network interconnections linking distant regions are thought to be driven in part by myelinated excitatory pathways (e.g., Fingelkurts et al, 2005), it could be speculated that increases in within-network functional connectivity could be in part a consequence of pathway myelination, with decreases in connectivity with other regions or networks perhaps reflecting selective synaptic pruning of network-irrelevant associations. Although clearly much remains to be understood about how networks emerge and strengthen during adolescence, viewing brain development as a dynamic and iterative process of emerging regional activities and associated across-region competition, influence and cooperation adds an additional dimension to considerations of developmental differences in brain activation patterns during risk-related cognitions and behavior.

Plasticity in the adolescent brain.

Although the brain is most malleable to experience-induced modification early in life, there is growing evidence that significant neuroplasticity is retained in some regions well into adolescence. Such plasticity could represent relatively delayed “developmental programming” of the brain, potentially providing continued opportunities for the adolescent brain to be sculpted and “customized” to match the interests, activities, and experiences of the adolescent. One example of residual brain plasticity in adolescence was discussed earlier: the retention of sensitivity to “organizational” influences of gonadal hormones in some brain regions through adolescence (e.g., see Schulz et al, 2009a,b). There are a number of possible neural mechanisms by which plasticity could persist into adolescence. Both synaptic pruning and the formation of new synapses have been linked to environmentally-induced plasticity during development, depending on the brain region involved, the nature of the environmental manipulation and its timing (e.g., see Carpenter-Hyland & Chandler, 2007; Zuo et al, 2005a). Adolescence is characterized not only by synaptic pruning, but by notable fluxes in synaptic organization, with axonal (presynaptic) endings often extending and retracting within a matter of minutes during adolescence – a process that is much more prevalent and notably faster than in mature neurons (Gan et al, 2003). Moreover, although the vast majority of neurons are formed during early brain development, modest populations of new neurons are formed from small populations of stem cells throughout life – a rate of neurogenesis 4-5 fold higher among adolescents than adults (He & Crews, 2007).

Evidence is mounting that myelination as well may be a dynamic process, instigated in part by activity in the to-be-myelinated axons, with this electrical activity inducing release of chemical substances from the axons that stimulate nearby glia cells to initiate myelination processes (e.g., Stevens et al, 2002; Fields, 2008). There are hints from both basic science and human imaging studies that life experiences may influence such activity-dependent myelination. For instance, although causal associations cannot be inferred, it is nevertheless intriguing that the amount of practice during childhood and early-mid adolescence among a group of professional musicians was found to be correlated with white matter integrity in a number of performance-relevant axonal tracts (Bengtsson et al, 2005). In basic science studies, laboratory animals raised through adolescence in an enriched environment were found to have a larger corpus callosum (the huge bundle of axons that crosses the midline to connect the left and right sides of the brain) and more heavily myelinated brains than animals raised in restricted environments (Markham & Greenough, 2004).

Despite these tantalizing hints, more research is necessary to substantiate the degree to which adolescence represents a delayed sensitive period for experience-dependent brain sculpting. Work is also needed to characterize the circumstances under which these adaptations occur, the extent to which such plasticity represents an opportunity for long-lasting beneficial adaptations or a time of vulnerability for lasting perturbation (see Spear, 2010, for further discussion), and the potential role of risk-taking in these processes.

The biology of adolescent risk behavior

Adolescents may be prone to display risky behaviors for a number of reasons. They may differ from adults in the ways they make decisions regarding risks, in their

sensitivity to the rewards and costs potentially associated with risk-taking, in their capacity for inhibitory control or propensity to react impulsively, and in their sensitivity to, or impact of stressful or emotional circumstances on risk-taking. Each of these potential contributors to adolescent risk-taking reflects to a certain extent separable although overlapping biological processes and developmental time-lines, some of which have been posited to be related to pubertal changes, and others not. Major threads within this developmental interweaving of biological contributors to adolescent risk-taking are considered in the following sections.

(1) Adolescent risk-taking in part reflects relatively delayed maturation of PFC and related regions critical for cognitive control and for modulating activity in regions processing emotional and rewarding stimuli.

Although present to some extent even in early childhood, inhibitory control is one of a series of executive control functions that continue to mature through adolescence (e.g., Leon-Carrion et al, 2004; Luna et al, 2004). Like other executive function tasks, the capacity to inhibit responding is thought to be associated in part with activity in frontal regions. For instance, a longitudinal study of young adolescents found age-associated increases in focal activation within ventral PFC during a response inhibition task; performance-related correlations were also evident, with individuals showing greater ventral PFC activation on trials when they successfully withheld responding than on unsuccessful trials (Durston et al, 2006). Other studies as well have reported developmental increases through adolescence in focal activation within ventral areas of the PFC during tasks involving response inhibition (Rubia et al, 2007; Tamm et al, 2002; Stevens et al, 2007) and risky decision-making (Bjork et al, 2008; Eshel et al, 2007; Galvan et al, 2006; see also, however, van Leigenhorst et al, 2006). Indirect support for the importance of ventral PFC in developmental improvements in risk-taking is provided by evidence that adults with damage sustained to ventromedial regions of PFC performed similarly to children on a modified gambling task, with both groups showing less advantageous choice behavior relative to adults who were neurologically intact (Crone & van der Molen, 2004).

Along with reduced activation of ventral PFC regions during risk taking and response inhibition tasks, adolescents also often show more diffuse activation across a variety of PFC regions (Casey et al, 1997; Tamm et al, 2002; Durston et al, 2006). Indeed, maturation of neural systems involved in cognitive control has often been characterized as a shift from a broader and more diffuse pattern of activation to greater regionally-specific activation, a shift particularly pronounced in PFC (e.g., Booth et al, 2003; Durston et al, 2006). Such developmental shifts from diffuse to focal activation could reflect, in part, age differences in task performance, with perhaps broader activation patterns associated with the increased effort required to perform the task at younger ages (see Rubia et al, 2007, for discussion). Yet, in at least some instances, regions showing declining activation with age were found to be largely unrelated to task performance (Durston et al, 2006), data more consistent with the suggestion that the immature brain may be characterized by inefficiencies in neural recruitment. Others have proposed that maturational changes in regional patterns of brain activation may reflect alternative cognitive strategies across age, resulting in age differences in the brain regions engaged when performing the task (Rubia et al, 2007).

Consistent with the increasing emphasis on changes in network connectivity during adolescence, several recent developmental studies of cognitive control mechanisms found associations between the maturation of inhibitory control and the emergence of networks interconnecting frontal/PFC regions with subcortical regions – e.g., fronto-striato-thalamic, frontal-parietal and fronto-cerebellar networks (e.g., Rubia et al, 2007; Stevens et al, 2007). Evidence for increasing integration of networks interconnecting frontal brain areas with other regions during adolescence is reminiscent of the hypothesis of the relatively late maturation of a “top-down”, “dorsal”, or “cognitive control” system that includes the PFC as one of its major components. As this “top-down” control system continues to mature into late adolescence/early adulthood, it has been posited to increasingly modulate earlier reactive, largely subcortical, “affective”, “bottom-up” systems that respond to rewarding and emotional stimuli (e.g., Ernst et al, 2005b; Casey et al, 2008). This theme will be revisited later, following discussion of these earlier emerging, “bottom-up” emotional affect and reward systems.

(2) Adolescents sometimes show greater physiological and neural responses to emotional and stressful stimuli than adults.

Although by mid-adolescence, rational decision making of adolescents reaches levels typical of adults (e.g., see Steinberg, et al, 2009), adolescents seem particularly prone to have their decision-making influenced by stressful, exciting and emotionally charged situations (“hot cognitions”; Arnsten, 1998; Dahl, 2001). Research has shown that stressful and emotionally arousing situations often increase activity in the amygdala and other regions critical for rapid and instinctive behavioral responses (“hot cognitions”), while attenuating activity in PFC regions critical for logical thinking and cognitive control (“cold cognitions”) (Arnsten, 1998, Liston et al, 2009). Responses to stressful and emotional stimuli also include physiological signs mediated through activation of the stress hormone system (the hypothalamo-pituitary adrenal axis [HPA]), as well as the two components of the autonomic nervous system (ANS): (a) the sympathetic nervous system (SNS) that facilitates “fight-or-flight” reactions, increasing HR and blood pressure (BP), and shunting blood flow away from digestion to skeletal muscles; and (b) the parasympathetic nervous system (PNS), which slows HR, lowers BP and facilitates rest/recovery. Such ANS-mediated somatic (bodily) reactions have been argued not only to reflect emotional reactions, but also to serve as cues for making emotional self-attributions (e.g., “my heart is racing, so I must be unusually anxious about giving this talk”) (see Verdejo-Garcia et al, 2006). Adolescent-typical alterations in these neural and somatic responses to emotional/stressful stimuli likely contribute to the increased propensity of adolescents to engage in risky behaviors under stressful, exciting or other emotion-arousing circumstances.

Although little studied to date, the pubertal/adolescent transition has generally been reported to be associated with increased ANS and stress hormone reactivity to stressors (e.g., Walker et al, 2004; Gunnar et al, 2009; Stroud et al, 2009), along with slower post-stress hormonal recovery relative to adults (Romeo & McEwen, 2006). The available data also hint to the provocative possibility that these somatic signs may not be as strongly linked to emotional expression (e.g., Quas et al, 2000; Stroud et al, 2009) or to optimizing risky decision-making (e.g., Crone & van der Molen, 2007) during development as in adulthood. For instance, a study examining cardiovascular reactivity

to emotional stimuli found no clear association between children's cardiovascular reactivity and emotional expression, with children that showed greater cardiac reactivity to a needle puncture for blood draw even tending to exhibit *less* behavioral evidence of negative affect and emotional distress to the procedure (Quas et al, 2000). Likewise, the changes in physiological responses to stressors observed by Stroud et al (2009) during the pubertal transition "were not mirrored by differences in *affective* responses to the stressors" (p.62). These data raise the speculative but intriguing possibility that, despite increases in ANS emotional reactivity during adolescence, the ability to link these physiological reactions to perceived emotions may develop only slowly.

The amygdala is an evolutionarily ancient group of spatially adjacent, but sometimes functionally opposing, subregions that play critical roles in responding to, learning about, and remembering stressful and other emotional circumstances (Zald, 2003; Dalgleish, 2004), as well as in the processing of social signs of emotions (Amaral et al, 2003), including signs of emotions conveyed in facial expressions (e.g., see Zald, 2003). These subregions are well positioned to facilitate physiological and behavioral responding to emotional stimuli, with portions of the amygdala projecting to hypothalamic and brainstem areas critical for emotion-related behaviors, release of stress hormones, ANS activity, and so on (Armony & LeDoux, 1997). In a number of studies, adolescents have been found to exhibit greater amygdalar activation to fearful faces (relative to neutral faces) than adults (Killgore et al, 2001; Monk et al, 2003; Guyer et al, 2008) or than both children and adults (Hare et al, 2008). These findings, however, are by no means ubiquitous (see Pine et al, 2001; Thomas et al, 2001b; McClure et al, 2004; Deeley et al, 2008), perhaps in part due to differences across studies in test parameters, including the subregions included within amygdala-defined areas (e.g., see Zald, 2003).

Signs of greater amygdala activation to emotional stimuli during adolescence under some test circumstances have been proposed to reflect an increased reactivity of adolescents to the emotional properties of social stimuli (Monk et al, 2003; Nelson et al, 2005; Hare et al, 2008), a bias which may lower the likelihood of adolescents responding effectively to other situational or task demands. For instance, Hare and colleagues (2008) found that increased amygdalar activation to emotional stimuli was correlated with slower response times to these stimuli in a go/no-go task, with adolescents overall responding more slowly than adults in this task. Likewise, in an fMRI study using a fearful face perception task, greater amygdala activation was correlated with poorer emotional and social capacities in a group of 8-15 year olds (Killgore & Yurgelun-Todd, 2007). Although such correlations do not necessarily reflect causality, it is nevertheless interesting that elevated activity in amygdala induced by emotional stimuli was associated with poorer affect-relevant performance during development – findings consistent with the notion of "hot cognitions".

(3) Adolescents differ notably from adults in their brain reward neurocircuitry and in the way they process and respond to rewarding and aversive stimuli.

Novel and exciting stimuli, as well as alcohol and other drugs used for their rewarding effects, tap into phylogenetically old brain reward circuitry that is critical for seeking out, finding and "consuming" survival-essential natural rewards such as food, water, sexual reproduction and other social rewards. In both basic science studies as well as human imaging work, marked transformations are seen in this reward circuitry during

adolescence. Major components of the reward system that undergo particularly dramatic change during adolescence include projections from dopamine (DA) neurons deep in the back of the brain to subcortical limbic regions such as the ventral striatum (nucleus accumbens) – a particularly critical node in reward-related circuitry – as well as the hippocampus, amygdala and dorsal striatum, along with portions of the PFC. Even in the mature brain, controversy continues as to how these DA projections, their forebrain targets, interconnecting circuitry, and associated brain regions are related to specific psychological components of rewards (e.g., see Baxter & Murray, 2002; Cardinal et al, 2002; Berridge & Kringelbach, 2008) – even such fundamental questions as to whether reward sensitivity is modulated by DA or non-DA systems (e.g., Gardner, 1999; Robinson & Berridge, 2003) or whether reward seeking is a result of less active or hypersensitive DA systems (e.g., Volkow et al, 2003; Robinson & Berridge, 2003). Some researchers have drawn distinctions between anticipatory/ “wanting” vs. consummatory/ “liking” of rewards, with the former DA-dependent and the latter reflecting non-DA (opiate and cannabinoid) systems (Robinson & Berridge, 2003). These ongoing controversies provide special challenges for understanding the significance of the marked alterations in the DA system and other components of brain reward circuitry during adolescence.

Connections among reward-related regions undergo considerable elaboration during adolescence, including PFC projections to ventral striatum (Brenhouse et al, 2008), DA and amygdala projections to the PFC (Benes et al, 2000; Cunningham et al, 2008), and the inhibitory control exerted on the PFC by these DA projections (Tseng & O’Donnell, 2006). Developmental transformations are particularly dramatic in the DA system. The density of receptor sites binding DA peaks in dorsal striatum early in adolescence in humans and laboratory animals, followed by a loss of 1/3-1/2 of these receptors by young adulthood (Seeman et al, 1987; Tarazi & Baldessarini, 2000; Teicher et al, 2003). Similarly timed but more modest (20-35%) declines have been reported in ventral striatum (Andersen, 2002; Tarazi & Baldessarini, 2000; but see also Andersen et al, 2000). In contrast, DA receptor density in PFC does not peak until late adolescence, with pruning of these receptor populations not occurring until young adulthood (Andersen et al, 2000; Weickert et al, 2007). Similar adolescent peaks and later declines may be seen in other reward-critical receptor systems, with cannabinoid receptors peaking during adolescence in dorsal striatum and limbic forebrain and declining thereafter (Rodriguez de Fonseca et al, 1993).

It is not straightforward to relate developmental changes in DA receptors to alterations in reward processing during adolescence, given that the DA system is highly regulated, with alterations in one part of the DA system typically inducing compensations in other parts in an attempt to restore balance (e.g., Zigmond, 1998), and baseline (tonic) levels of DA activity (“DA tone”) often influencing how easily the DA system can be acutely activated (phasic activity) (see Goto et al, 2007). Yet, it is abundantly clear that DA and other reward-relevant neurocircuitry are substantively altered during adolescence, with not only the losses of up to 50% of the DA receptors in some reward-relevant regions as discussed above, but also marked (2-7 fold) changes in regional DA tone (e.g., Andersen, 2002). In the face of such dramatic molecular and cellular transformations, it would be remarkable if adolescents did not differ from adults in their responsiveness to rewarding stimuli, including novel, exciting and risky stimuli.

Indeed, evidence is mounting from fMRI studies that the adolescent brain processes rewarding (and aversive) stimuli differently than do adults. The strongest evidence is for greater ventral striatum activation among adolescents than adults in response to the *receipt* of a reward, although several studies have found adolescents to exhibit attenuated ventral striatum activation when *anticipating* rewards, suggesting the possibility that adolescents may be characterized by both underactive and overactive reward systems at different points in the processing of reward-relevant stimuli (see Geier et al, 2009). These distinctions are reminiscent of the anticipatory/“wanting” vs. consummatory/“liking” distinctions drawn by Robinson & Berridge (2003), and with animal data showing adolescents to exhibit less “wanting” behavior (indexed via attenuated “sign-tracking” toward reward-predictive cues) than adults, while finding a variety of natural rewards and drugs more rewarding than their adult counterparts (see Doremus-Fitzwater et al, 2010, for discussion).

Specifically, during *cue assessment* and when *anticipating* a reward, adolescents have been reported to show less fMRI activation in the ventral striatum than adults (Bjork et al, 2004; Geier et al, 2009). This ventral striatal underactivation, however, was not seen when adolescents were responding to a cue signaling an uncertain reward possibility (van Leijenhorst et al, in press), perhaps reflecting once again the complexities of reward attribution and incentive motivation processes and their neural substrates. At first blush, any evidence for attenuated ventral striatal responses during cue-induced anticipation/“wanting” among adolescents seems counterintuitive, given the avidity with which many adolescents pursue new sensations and alcohol/drugs. Yet, individuals with attentional-deficit/hyperactivity disorder likewise exhibit less activation in ventral striatum than control subjects during anticipation of gains in a monetary incentive task, with the magnitude of this hypoactivation correlated with impulsivity ratings (Scheres et al, 2007; Ströhle et al, 2008). Work remains to confirm these initial findings, determine their generality, and “connect the dots” between ventral striatal hypoactivation and impulsivity and risk-taking behavior among adolescents.

During *receipt* of positive rewards, however, adolescents have been reported by a number of groups to show heightened activation of the ventral striatum (Ernst et al, 2005a; Galvan et al, 2006; Geier et al, 2009; van Leijenhorst et al, in press). Interpretation of adolescent-associated elevations in ventral striatum activation to receipt of rewards seems relatively straightforward, with evidence (albeit correlational in nature) that the magnitude of ventral striatum recruitment predicts level of excitement (Bjork et al, 2004, 2008) and positive affect (Ernst et al, 2005a) when receiving rewards, as well as the propensity for sensation-seeking and risk-taking (Galvan et al, 2007; Bjork et al, 2008). The relationship between ventral striatal activation and reward magnitude may be exaggerated during adolescence, with adolescents tending to show weaker responses in the ventral striatum to small rewards (Galvan et al, 2006), but showing more dramatic signal increases (Galvan et al, 2006) or more sustained activation (Delgado et al, 2000) in the ventral striatum to rewards of larger magnitude than do adults.

In contrast to findings of sometimes greater ventral striatal activation to rewards, adolescents have been reported to exhibit less pronounced activation of the amygdala during punishment (response omission) than do adults (Ernst et al, 2005a). Ernst and colleagues (2005a) reported that level of ventral striatum recruitment correlated with positive affect to reward receipt only among adolescents, with adults (but not

adolescents) showing a correlation between negative emotion and decreased amygdala activation on punishment (reward omission) trials, leading them to propose that adolescence is associated with relatively delayed development of a “harm-avoidant” system (Ernst et al, 2005b). These findings are reminiscent of other evidence for earlier maturation of neural responses to positive than negative feedback (Crone et al, 2008; van Duijvenvoorde et al, 2008; but see also van Leijenhorst et al, 2006). Collectively, the findings suggest potential biological contributors to the propensity of adolescents to attach greater benefit and less cost to risky behavior such as alcohol and cigarette use than attributed by individuals at other ages (see Millstein & Halpern-Felsher, 2002).

Signs of enhanced responsivity to positive rewards and attenuated sensitivity to aversive outcomes (including punishment) are often seen among adolescents, with for instance sensitivity to rewards found to be high in early adolescence and to peak at around 13-16 years of age, whereas punishment sensitivity was observed to be low during early-mid adolescence, and to increase gradually with age thereafter (see Steinberg, 2008). In animal studies, adolescents likewise have been reported to be more sensitive than adults to the positive rewarding effects of social peers (Douglas et al, 2004), novelty (Douglas et al, 2003), and a variety of drugs, including cocaine (e.g., Brenhouse & Andersen, 2008; Brenhouse et al, 2008), nicotine (e.g., Shram et al, 2006; Torres et al, 2008), and alcohol (e.g., Pautassi et al, 2008), while being less sensitive to aversive stimuli (Shramm-Sapyta et al, 2006), including the aversive consequences of these drugs of abuse (e.g., Infurna & Spear, 1979; Shramm-Sapyta et al, 2006; Varlinskaya et al 2006). The presence of social peers may exacerbate these appetitive/aversive biases even further, enhancing the rewarding properties of cocaine and nicotine among adolescents (Thiel et al, 2008, 2009), while further attenuating adolescent sensitivity to aversive effects of alcohol, an effect not seen in adults (Vetter-O’Hagen et al, 2009). In human studies as well, the presence of peers considerably exacerbated risk-taking among adolescents, but not adults (Gardner & Steinberg, 2005), and increased ventral striatum activation of adolescents when making risky decisions (Steinberg, 2010). Indeed, most sensation-seeking and risky behaviors occur in social situations, supporting the view that “the presence of peers activates the same neural circuitry implicated in reward processing, and that this impels adolescents towards greater sensation seeking” (Steinberg, 2008, p.91).

Adolescents vary from adults not only in their sensitivity to rewarding and aversive effects of drugs such as alcohol, but in their sensitivity to other alcohol effects as well, including its intoxicating effects. In a study where 8-15 year old boys were given alcohol, Behar and colleagues (1983) reported that “little behavioral change was noted clinically, subjectively, or on a validated objective test of intoxication...” and that they “were impressed by how little gross behavioral change occurred in the children...after a dose of alcohol which had been intoxicating in an adult population” (p.407). Although ethical concerns now generally prohibit giving alcohol to youth for research purposes, in studies using animal models, adolescents likewise have been found to be less sensitive to many intoxicating effects of alcohol, including ethanol-induced social impairment, sedation, motor impairment, dysphoria, and even some “hangover” effects (reviewed by Spear & Varlinskaya, 2005). In contrast, these studies have also found adolescents to not only be more sensitive than adults to positive rewarding effects of alcohol and other drugs as discussed earlier, but also to the facilitation of social behavior by alcohol (e.g.,

Varlinskaya & Spear, 2002) as well as to the disruption in brain plasticity and memory seen at higher levels of alcohol exposure (White & Swartzwelder, 2005). An attenuated sensitivity to alcohol cues serving to moderate intake could contribute to the 2-3 fold greater per episode alcohol intakes seen among adolescents than adults in both humans (SAMHSA survey data, 2006) and laboratory animals (e.g., Doremus et al, 2005). Indeed, a decreased sensitivity to alcohol is a known risk factor for problematic alcohol involvement (Schuckit, 1994), with such attenuated sensitivities evident genetically in both humans and laboratory animals (Shuckit, 1994; Green & Grahame, 2008), perhaps further exacerbated by a history of repeated alcohol use (Varlinskaya & Spear, 2008) or prior stress (Doremus-Fitzwater et al, 2007), and potentially contributing to a pattern of elevated alcohol exposure during adolescence that may lead vulnerable youth on a trajectory toward problematic use and dependence (Spear & Varlinskaya, 2005).

When examining how adolescents process and respond to rewarding and aversive stimuli it is important to show inflections in adolescent behavior and brain function that are distinct from those of children and adults. Several groups have begun to show inflections in response to rewarding and emotional cues. For instance, Sternberg and colleagues using a gambling task (Cauffman et al, 2010) and a delay discounting task (Steinberg, et al., 2009) have shown that sensitivity to rewards and incentives actually peaks during adolescence, with a steady increase from late childhood to adolescence and subsequent decline from late adolescence to adulthood. These findings illustrate a \cap -shaped function, peaking between 14 and 16, and then declining (Steinberg, 2010). Hare and colleagues (2008) have shown a similar pattern in response to emotional stimuli with teens relative to younger children and adults, showing an exaggerated response and worse performance in detection of emotional cues relative to neutral ones. Parallel \cap -shaped patterns in functional development further support these findings (Van Leijenhorst et al., in press; Geier et al, in press). These data suggest exaggerated reactivity to affective and rewarding stimuli under some circumstances that, as they continue to mature, receive progressively more “top-down” cognitive control from later maturing prefrontal regions

(4) Putting the pieces together: Adolescent risk-taking may be promoted by exaggerated reactivity in early emerging and perhaps pubertally-driven “bottom-up” reward and affective regions that dominate prior to maturation of cognitive, “top-down” control regions.

Thus far, we have talked about two phylogenetically ancient and largely subcortical systems that show greater reactivity under some circumstances in adolescence than adulthood: the reward system (with a focus on DA, the ventral striatum and other forebrain DA target regions) and an affective system critical for emotional attribution and responding to socio-emotional stimuli (whose brain substrates were exemplified in the earlier discussion by the amygdala). While separable to some extent, these two systems overlap considerably. They are anatomically interconnected and closely functionally interrelated, with for instance socio-emotional stimuli influencing salience of rewarding stimuli (e.g., Thiel et al, 2008, 2009), and the presence or omission of potential or expected rewards often contributing to emotional affect (e.g., see Figner et al, 2009). And, as we have seen, responsiveness within each of these systems emerges early, although it may be somewhat of a misnomer to classify them as “early maturing” in that they often demonstrate different and sometimes exaggerated patterns of reactivity relative

to that seen at maturity. Both of these interrelated systems are also highly stress sensitive, with stressors tending to increase activation in the ventral striatum, amygdala and other subcortical regions such as the hippocampus, while attenuating functional efficacy within the PFC (Arnsten, 1998, Liston et al, 2009), regional shifts in activity that are in part DA-mediated (Arnsten, 2009).

Collectively, the data reviewed above support a view of adolescent brain development characterized by a developmental dissociation between the emergence early in adolescence of two interrelated (and perhaps cross-reactive) “bottom-up” systems that express exaggerated reactivity to affective and rewarding stimuli under some circumstances and that, as they continue to mature, receive progressively more “top-down” cognitive control from the PFC and related later maturing control regions. This view draws strongly upon and bears considerable similarity to other models of adolescent brain development, although those have largely emphasized early maturation of a single “bottom-up” affective or reward system (with one perhaps subsumed within the other), with this initially unconstrained bottom-up system stimulating risk-taking behavior, but gradually losing its competitive edge with the progressive emergence of “top-down” regulation provided by a later maturing, cognitive control system in the PFC and related cortical regions (e.g., Dahl, 2001; Chambers et al, 2003; Ernst et al, 2005b; Nelson et al, 2005; Casey et al, 2008; Hare et al, 2008; Steinberg, 2008). In view of findings that these early emerging reward- and affect-related regions tend to exhibit exaggerated patterns of reactivity, or at least are differently reactive than in adulthood, it remains to be seen whether this reactivity merely reflects unconstrained activity of “bottom-up” systems in the absence of sufficient expression of “top-down” control, or whether they reflect, as postulated here, ongoing transformations within these reward and affective systems that continue to be elaborated during adolescence. Given the magnitude of alterations seen in reward- and affect-relevant DA projection regions during adolescence, it does not seem beyond the realm of possibility that such dramatic transformations could contribute to the transient appearance of greater reactivity within these systems during early and mid-adolescence.

Another common theme in many theories of adolescent brain development is that the early emergence of “bottom up” affect or/reward systems is posited to be triggered by rises in pubertal hormones, in contrast to later, pubertally-independent maturation of “top-down” cognitive control in regions such as the PFC. This theme of adolescent risk-taking prompted by developmental discontinuities between pubertally-driven and puberty-independent brain maturation is intuitively appealing. Indeed, critical neural components of the affective and reward systems, including portions of the amygdala, hypothalamus and ventral striatum, as well as DA neurons themselves, contain receptors for estrogen and/or testosterone (e.g., Finley & Kritzer, 1999; Stevens, 2002; Kritzer & Creutz, 2008; Sakuma, 2008), and hence activity in these regions could be modified, perhaps dramatically, by pubertally-related rises in these gonadal hormones. Yet, direct evidence for the role of pubertal hormones in development of affective and reward systems is as yet sparse. As discussed earlier, a number of studies in young human adolescents have found significant correlations between pubertal status and various adolescent-typical behaviors, including risky behaviors and alcohol/drug use. In research using surgical or other manipulations in laboratory animals to examine the importance of gonadal hormones at puberty, there are early reports that pubertal

hormones may exert effects on some behaviors beyond sexual behaviors per se (e.g., see Schulz et al, 2009a). Similar studies examining the impact of pubertal hormones on neural development of reward and affective systems, however, have yielded surprisingly few differences, although work in this area is limited (e.g., see Kuhn et al, in press). For instance, in one of the few studies examining consequences of pre-pubertal gonadectomy on the DA system, DA receptor pruning in striatum was found to be disappointingly unaffected by pubertal rises in gonadal hormones (Andersen et al, 2002). With the increasing emphasis on puberty as a critical variable in adolescent research, however, data to assess the contribution of puberty to development within affective and reward-relevant systems will likely accumulate rapidly.

The biology of adolescence: Conclusions and implications for adolescent risk-taking

So, what impact does consideration of the biology of adolescence have for understanding adolescent risk-taking?

(1) Basic neurobehavioral characteristics of adolescents have biological roots that are deeply imbedded in our evolutionary past. Given the magnitude of the neural changes seen during adolescence in brain regions critical for mediating or modulating sensitivity to rewards and aversive stimuli, perception and expression of emotions, and inhibitory control and impulsivity, some degree of adolescent risk-taking would seem to be inevitable. Thus, rather than trying to eliminate adolescent risk-taking behaviors, a strategy that has not proved successful to date (see Steinberg, 2008, for discussion), a better tactic might be to reduce the costs of adolescent risk-taking by limiting access to particularly harmful risk-taking opportunities, while perhaps providing access to risky and exciting activities under circumstances designed to minimize chance of harm.

(2) Adolescents view rewarding and aversive stimuli differently than do adults. Their neural and behavioral sensitivity to rewards, especially strong rewards, often appears to be heightened, whereas adolescents may sometimes appear less reactive during anticipation of rewards, and perhaps when receiving relatively weak rewards. Along with these seeming exaggerations in reward reactivity, adolescents often appear less sensitive to aversive outcomes and stimuli. There are hints that this adolescent propensity to exhibit accentuated responses to intense, appetitive stimuli but attenuated responsiveness to aversive stimuli may be further intensified when in social (and perhaps stressful situations). Such hedonic shifts could encourage risk-taking, especially when in the presence of peers, for its thrilling and exciting aspects, and may help promote continued engagement in risky activities when prior activities have proved exciting but without catastrophic consequences. Such adolescent-typical hedonic shifts toward greater rewarding and attenuated aversive properties seems to extend to drugs and alcohol as well, and at least in the case of alcohol, may combine with genetic and other environmental risk factors to encourage sufficiently high intakes to lead to patterns of problematic alcohol use and dependence among vulnerable individuals.

There are a number of potential implications of viewing adolescence as a time of shifts in hedonic sensitivity toward exaggerated reward and attenuated aversive responding. As one example, evidence that adolescent-typical hedonic shifts may be exacerbated by social and arousing situations supports manipulations involving control of social context when providing increased responsibilities to adolescents (e.g., graduated

driving licenses). To take another very different example, findings that vulnerable adolescents appear to be even more resistant to aversive alcohol effects that normally serve to limit intake than normal adolescents may be an important message to include in alcohol education efforts, given that youth (and probably many adults as well) seemingly associate greater capacities to “hold one’s liquor” with a resistance to adverse alcohol outcomes rather than to an enhanced probability of developing alcohol problems and dependence.

(3) The adolescent brain does not seem to merely reflect a series of regions attaining maturity at different times, but in some sense can be characterized as a brain that reacts differently to stimuli than does the mature brain. Current models of adolescent brain development, with their general emphasis on developmental discontinuities in maturation across a few regions (e.g., “bottom-up” affective or reward systems vs. a “top-down” cognitive control system), are clearly simplistic but provide useful heuristics to guide research beginning to parse the complexities of adolescent brain maturation with its multiple and often partially overlapping neural, regional, and network transitions, differential timing and perhaps even developmental plasticities. One important implication of this approach is that neural underpinnings of adolescent behavioral proclivities are likely to vary dynamically during the adolescent period. Consequently, effective strategies for scaffolding risk-taking proclivities of adolescents may vary with age, with the provision of “safer” risk-taking options perhaps most promising for early- to mid-adolescents, whereas approaches focusing on strengthening emerging cognitive control capacities may be more efficacious among older adolescents (Steinberg, 2009). And with increasing evidence for plasticity in the brain transformations of adolescence, important questions can be asked as to the degree to which adolescent experiences – including perhaps experiences provided by adolescent risk-taking – customize the maturing brain in ways commensurate with those experiences, and the degree to which these various adaptations may be beneficial or detrimental.

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