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Frontiers of Research on Adolescent Decision Making—  
Contributions from the Biological, Behavioral, and Social Sciences

Background Paper by  
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## INTRODUCTION/OVERVIEW

The charge given for this paper (one component within a broader review of adolescent decision making) was to identify and discuss emerging findings in biological and behavioral research relevant to understanding the development of decision making and competence in adolescence. The general aims include: to identify promising areas of new and emerging research, to describe high-priority questions for future studies, and to consider conceptual frameworks that may help to integrate understanding across biological, behavioral, social, and clinical disciplines relevant to these issues. The central goal, across these efforts, is to advance knowledge that informs *interventions and policies* to improve the health and well being of adolescents.

Although this paper touches upon a wide range of topics, it is organized into two parts, each with a central theme:

**Part One** of this paper focuses on *affective influences on decision making*. A central premise is that motivational and emotional changes during adolescent development represent a crucial (and understudied) dimension to understanding some types of “deficiencies” in responsible decision making. Accordingly, a broad range of questions are raised about affective influences on thinking and behavior. Arguments are presented in favor of approaches based on work emerging from affective neuroscience that consider affective neural signals that influence behavioral control. This perspective appears promising not only in relation to research into the neurobehavioral underpinnings of some aspects of adolescent decision making, but also has important implications for behavioral, clinical and social science research into adolescent risk taking and health behavior.

**Part Two** of this paper focuses on recent advances in understanding *adolescent brain maturation*. An emerging heuristic model is described that emphasizes *gene/brain/behavior/social context interactions* during this important time of neurodevelopment. A key element of this model is based on an emerging body of research that demonstrates that some neurodevelopmental processes continue to show maturational changes through late adolescence and into early adulthood. In contrast, consideration is given to a set of *affective* changes (in association with pubertal maturation) that occurs relatively early in adolescence. The juxtaposition between these early affective changes and the late maturation of systems that underpin mature self-control of behavior are also considered in relation to recent historical changes in the timing of puberty—a trend toward earlier activation of the strong affective influences that emerge during sexual maturation—as well as both genetic and environmental influences.

This model—with its emphasis on affective influences on decision making and slow neurobehavioral maturation of cognitive control—is also used to focus attention on several key research questions. These include questions about the specific genetic and neural underpinnings of affective changes at puberty, questions about the development of cognitive control systems necessary for self-regulation, questions about behavioral, familial, and social factors that promote healthy maturation of these systems and skills, and questions about how to translate these emerging findings into specific policies that protect and support high-risk youth during these important maturational periods.

### *Some Introductory Comments and Caveats:*

Given the charge for this paper—to review research frontiers relevant to adolescent decision making—the range and scope of topics that could be included in this discussion is enormous. Rather than attempting such a comprehensive review of the multitude of emerging areas of research that may have relevance to understanding adolescent decision making, this paper focuses on a subset of approaches that appear promising from the perspective (and personal biases) of the author. The focus of this paper grows from concerns about the *clinical* consequences of risky and reckless decisions in adolescence. This has resulted in an emphasis on pragmatic, clinically-relevant approaches to understanding adolescent behavior—not only questions about how adolescents think through decisions rationally, but more generally *how they develop skills and capacities in reliable self-control over behavior*.

This raises questions about using the term “decision making”, which tends to imply (at least to some) an emphasis on thinking, planning, and *conscious* mental processes. Perhaps a more useful framework (at least from a clinical and social policy perspective) is to consider a broader range of skills in the control of behavior, of which semantically-based rational decision making is one component.

Consider, for example, a clinical perspective on “decision-making” in an obese adolescent trying to lose weight. On one hand, there are important issues in the realm of conscious decisions such as the individual’s choosing the goal of losing weight and numerous choices related to eating and exercising in healthier ways. On the other hand changing behavior is not simply a matter of performing mental evaluations of the advantages/disadvantages of becoming thinner—or logically weighing the benefits/consequences of eating a piece of chocolate cake or sitting in front of the TV after school. Gaining control over behavior involves a broader and complex set of mental processes that include emotional, motivational, and behavioral aspects of “decision making”.

In a similar way, understanding why an adolescent chooses to smoke a cigarette, have unprotected sex, or to stomp on the accelerator on the car while pulling out of the school parking lot in front of a group of friends is unlikely to be completely understood at the level of rational choices. These require moving beyond a focus mental processes at the level of sequences of word and conscious thinking and instead, to a broader consideration of *affective influences on behavior*<sup>1</sup>.

It is also important to emphasize methodological and conceptual advances relevant to understanding these affective processes. There is growing understanding of fast neural processes that underpin emotions, motivations, and the establishment of new cognitive-behavioral patterns that contribute to *sequences of behavior*, which often operate outside the realm of semantic processing (sequences of thoughts and words). These affective processes can impact on the development of behavioral control in ways that may *not* fit into traditional conceptual frameworks of understanding “decision making”.

One traditional argument for focusing on conscious aspects of adolescent decision making is the pragmatic aspects—it is this semantic level of mental processing that is most easily accessible to intervention, by educating adolescents and helping them learn to (consciously) make better choices.

However, additional opportunities for intervention may emerge through a deeper understanding of these affective and implicit aspects of behavioral control—including the importance of emotional and motivational influences on behavior—and to encourage the development of self-control skills through *procedural learning*. Developing competence in behavioral control in adolescence may share features with the process of acquiring skills in a sport or in playing a musical instrument. Accordingly the metaphors of “coaching” and “skill-building” (in relation to behavioral control) may be just as relevant as teaching adolescents how to think (consciously) through the process of making better decisions.

These personal biases—the emphases on a conceptual framework that focus on implicit affective processes, and the acquisition of *skills* as well as knowledge—are reflected in the focus of this review. This is not meant to imply that conscious aspects of adolescent decision making are of less importance, but instead, only to highlight the unique opportunities from these emerging approaches.

Finally, it may be helpful to comment on the inclusion (in Part One of this review) of several anecdotes about decision making. These were selected as examples to illustrate aspects of emotional influences on behavior. *These anecdotes are set off with a row of asterisks in italics so these can be easily skipped over* by readers who might regard these as digressions. In general, Part One serves as an essay that raises provocative questions and arguments for an alternative way of thinking about affective influences; hopefully these can help to provide a framework relevant to research described in Part Two, which will focus on affective changes during adolescent brain development.

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<sup>1</sup> Paul Slovic (see ref 6), among others, has made this argument previously about the limitations of addressing only the rational components of decision-making, and the need to consider the affect heuristic—particularly in adolescence. The emphasis in this paper will be to consider, in greater depth, the set of affective neural processes that underpin this dimension of influences, and the need for further research to advance understanding in these areas of adolescent decision making.

**PART ONE:**  
**AFFECTIVE INFLUENCES ON DECISION MAKING**

*A young guy scanning the crowd at a party notices a girl who he finds strikingly attractive. Immediately smitten, he approaches her and launches a shower of compliments. She tries to rebuff his flattery but finds something about the young man quite appealing. Romantic feelings kindle quickly. As he departs, with a kiss followed by a second kiss, emotions are flaring.*

*On the basis of this one brief meeting, a conversation of less than a hundred words, and two kisses, the emotional lives of two adolescents have been turned upside-down. Each cannot stop thinking about the other and is obsessed with a desire to meet again. They manage a clandestine late-night rendezvous. Passionate feelings now accelerate at a feverish pitch. Their intense motivations to be together quickly rise above all competing priorities. They are willing to spurn friends and family, disregard dangers, ignore pain, and begin to act as if being together is more important than life itself—though they just met four days previously and barely know each other.*

If evaluated by a psychiatrist who did not understand youthful passions, these two adolescents could easily be judged as meeting diagnostic criteria for serious mental disorders or cognitive impairments. Previously learned abilities to think logically and make rational decisions seem to have dissolved in a matter of hours. If viewed without some sympathy and understanding of the emotional power of young love, this scenario of adolescent behavior could appear completely ludicrous.

Yet, the story of *Romeo and Juliet* has moved audiences to tears for centuries. It has evoked sympathetic responses across many translations and cultures because of a nearly universal appreciation for the emotional intensity—and potential for tragedy—from the influences of rapidly-igniting adolescent passions. It is interesting to reflect for a moment, on Juliet's age. In an early Italian version of the story penned in 1535 by Luigi da Porto (who first placed the scene in Verona and named the feuding families Montecchi and Capellati), Juliet (Giuletta) was 18 years old. However, in 1595, when Shakespeare adapted the play, he made Juliet 13 years old.

*Why did Shakespeare create a heroine so young in this romantic tragedy? He seems to have intentionally juxtaposed adult-like passions with the cognitive naïveté of a young teenager. It is likely that he had noted what many have observed about these years of early adolescence—it is a time of life that seems to create a natural tinderbox for igniting passions—a period of development when surging emotions have a particularly dramatic capacity to influence decisions and behavior.*

Clearly, some aspects of these emotional influences on adolescent behavior have been well recognized for many centuries. Over the past decade, however, the tools of modern neuroscience are creating a deeper understanding of affective influences on behavior, and more specifically about this developmental period—neurobehavioral changes during pubertal maturation. These lines of work are generating new insights into the roots of emotional and motivational changes in adolescence.

However, before focusing on these neurobehavioral changes during adolescent brain development (these will be discussed in Part Two of this paper) it is valuable to consider a broader range of questions—and an emerging conceptual framework—that leads toward new ways of understanding some of these affective influences.

The perspective that will be described—based on work in affective neuroscience—does not focus simply on emotions, but considers a range of affective influences that share some similar features. These are based in neural systems that operate through affective signals experienced as *feelings*. These include appetitive feelings (like hunger and thirst), emotional feelings (like sadness, fear, disgust, anger) motivational feelings (like drive, ambition, and desire), and “gut” feelings (the hunches, intuitions and impulses that are experienced as affective signals).

On one hand there are important differences between these different categories of feelings—an appetitive feeling like thirst *is* very different from an emotional feeling like fear. On the other hand there are also some advantages in considering (together) the broad set of affective systems that create similar types of action-tendencies in the brain—and to consider the *adaptive* function of many of these affective neural signals in the way they influence thinking and behavior.

### ***Affective Signals: Action-Tendencies in the Brain***

Consider this scenario: A young woman walking through a park on a summer day is faced with a “decision” as to whether to take a drink of water from a public fountain. At one level, this decision could be parsed into a set of semantic processes about the advantages/disadvantages (or the benefits/risks) related to taking a drink. These could include thoughts about how good the water will taste, thoughts about the value of replenishing body fluids on a hot summer day, considerations about whether there are other fountains or sources of water that will be encountered on this walk, and considerations about the cleanliness of drinking from a public fountain.

However this “decision” is also likely to be strongly influenced by inputs from affective neural systems—specifically, the degree of thirst this individual is experiencing at this particular moment. This level of thirst is *not* simply a subjective feeling; it is *not* simply a thought about how good the water will taste. Thirst is an affective biologic signal. It is the output of neural computations based in physiological systems that integrate several variables related to water and salt balances in the body.

If thirst levels are high—if this person has just completed a strenuous run through the park on a hot day and has lost a considerable amount of free water through sweating—there will be a strong physiological need for water, and this affective thirst system will activate a strong *action-tendency* to motivate water drinking behavior. This affective signal is experienced subjectively as a *feeling* of thirst. A strong signal of thirst can exert a powerful influence on her “decision” to stop at this water fountain and take a drink.

Now, however, imagine that she bends over to get a drink of water and sees a vile looking ball of phlegm that someone has spit into the basin of the fountain. At this moment there is a good chance that she will “decide” to tolerate her thirst a bit longer. Even if she is able to determine, rationally, that the source of water is protected from any chance of direct contamination and could drink without coming into any contact with the offending substances—even if she logically determines that the benefits of replenishing her fluids are much greater than any risk of being harmed by an infection, there is a good chance that this affective signal (her *feelings* of disgust) will influence her decision.

In this scenario it is quite clear that the decision to drink (or not to drink) is heavily influenced by the activation of specific affective signals being generated by biological systems (in this example, feelings of thirst and feelings of disgust). The presence and strength of these affective signals are as important as the lines of thought about benefits/risks. As will be argued in this paper, there are *often* emotional, motivational, and appetitive signals adding to the complex mental vectors that underpin the process of making choices. These affective signals can have powerful but insidious influences on behavior. These affective signals work through fast neural connections that often operate (at least partially) outside the realm of semantic processing—even as they exert direct influences on thoughts and behavior.

On one hand, our species has developed remarkable mental abilities—we can consciously analyze the costs and benefits of our choices, we can picture things that might happen in the future, and can calculate, in probabilistic terms, the chances that a particular decision may lead to a good or bad outcome. On the other hand, we still behave in response to affective signals: we become thirsty, hungry, exhausted, afraid, lonely, develop cravings and addictions, and fall in love.

If we look deeply into patterns of human behavior—through personal reflection, as well as in the results of some elegant scientific experiments—we often find evidence that a great deal of “decision-making” is reflecting the activation and influence of a multitude of affective signals.

More times than not, one’s decision to take a drink of water is not based primarily on logical evaluations of the benefits of adding fluids to the body. The decision to eat a chocolate dessert at the end of a large meal is not usually the product of rational analyses of its benefits. An adolescent’s

decision to smoke his first cigarette is not likely to be the product of consciously weighing the immediate benefits of smoking against the risks of addiction and health consequences of lung cancer. Instead, these choices reflect several types of affective signals that push and pull on behavior.

The adolescent who makes the choice to smoke that first cigarette, for example, might be influenced by the *feeling* of excitement of doing something bold, the *feeling* of desire to please or impress one's peers, the *feeling* that smoking contributes to desirable traits like being older, tougher, or "cool".

In a similar way, the adolescent who decides to refuse that cigarette may be strongly influenced by *feelings* of fear of doing something wrong, fear of getting in trouble, *feelings* of disgust from the associations with bad breath and stained teeth, or a general *feeling* that smoking has become "uncool" in his social setting—rather than a "decision" based on thinking through the health risks of getting cancer thirty years in the future.

### ***Feelings: Fast Automatic Evaluations in the Brain***

Key insights regarding the nature and characteristics of these affective signals—and their capacity to influence behavior and choice—have been emerging from research in affective neuroscience. This work is demonstrating that many of these affective signals (that we experience as feelings) involve rapid, unconscious mental processes that are performing *evaluative* computations. They are based in neural systems that are calculating personal salience—making rapid automatic estimates of the value of a particular set of stimuli with regard to that individual at that point of time, in that context.

These affective signals are capable of generating *action-tendencies* in the brain. An action-tendency is an automatic propensity to think and act in a particular way, often in service to some biological need or physiologic priority.

For example, a feeling of thirst creates an action-tendency to seek fluids. Thirst is an internal signal that helps to shift behavioral priorities in a specific, adaptive way: to ingest needed fluids. Thirst naturally inclines one's thoughts, attention, and behavior toward drinking—it creates an *automatic* tendency to think and act in ways that increase the likelihood of finding and consuming water.

In a similar way, a feeling of fear creates an action-tendency regarding the priority of assessing danger and seeking safety. Fear is typically activated when a potential threat has been detected, consciously or subconsciously, and this feeling naturally promotes patterns of thinking and behavior directed at evaluating possible danger and making preparations for escape. This includes a wide range of automatic processes including changes in heart rate, tensing of muscles, and shifts in attention and arousal that support the action-tendency of vigilance and escape.

Many different types of feelings—including appetitive, physical, emotional, and motivational states—represent action-tendencies. The appetitive feeling of hunger naturally inclines thoughts and action toward eating. A physical feeling of extreme tiredness promotes a powerful urge to rest or go to sleep. A feeling of being cold naturally inclines action toward several types of heat-conserving behaviors such as huddled posture, shivering, or putting on a coat. A feeling of being too warm creates an opposite but equally adaptive range of action-tendencies like seeking shade, decreasing physical activity, and promoting physical postures that aid the body in cooling.

In a similar way, an *emotional* feeling of loneliness can signal (and motivate) behavior to seek social connection and support. A feeling of anger, in a situation of inescapable threat, can evoke automatic tendencies to use aggressive action in ways that can increase the chances of survival.

Some situations can trigger powerful affective signals—high intensity feelings—that can create a compelling action-tendency. Consider for example how the feelings activated in a parent who witnesses a threat to her child can launch heroic (or desperate) action. Consider the set of feelings activated in an adolescent who first falls in love, creating action tendencies—suddenly shifting all priorities and motivations in ways that can seem to make little rational sense.

### ***Rationally Ambiguous Decision-making:***

*In an event that stirred a great deal of local controversy last year, a young man, JM, was handcuffed, held by police and cited for reckless endangerment. His crime: After being told repeatedly by firefighters to back away from the area of roaring flames sweeping through his apartment building, JM crossed the safety line, climbed to the second story balcony of his apartment and entered the burning building.*

*Why did JM defy authorities and enter a building engulfed in flames? To save his dog. The sight of his beloved pet jumping up and down against a glass door in a room filled with smoke was too much, he said. So he climbed to the balcony, used a barbell to smash the window, and threw the dog to safety.*

*The ensuing controversy pitted local pet-lovers, who supported JM's decision to save his dog, against police and fire authorities who argued that JM recklessly placed lives at danger—not only his own life but also firefighters who could have been placed in danger by a sudden “backdraft” of oxygen into the fire. In an interview, the Assistant Fire Chief, was asked what would have happened if JM had done the same thing to save a child from a burning building. “That would be something that would be a split-second decision depending on the circumstances.”*

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*On the morning of September 11, Teresa Foxx dropped off her 15-month-old daughter, Trinity, at the Discovery Learning Center on the plaza level of 5 World Trade Center. While working in a nearby office, Ms. Foxx heard the blast and went outside. She began running toward the daycare center. She started crying. The feeling of needing to get to her daughter took priority over every other thought, consideration, or motivation. When she got to the center, the children were gone—evacuated several blocks away. She finally found her daughter. “I just grabbed her and held her,” she said. “I was still crying, the other parents were still crying, but we all got our children.”*

*After she got home, Ms. Foxx told her husband, “Now I understand why people run into burning buildings.”*

\* \* \*

*When he saw people running toward Bear Creek on Friday afternoon and heard that a 4-year-old boy was drowning in its cold and swollen currents, Abdulkadir Mohamud dashed four blocks, jumped a 3-foot fence and dived in.*

*“I was running past people, tearing my jacket and sweater off,” the 16-year-old Mayo High School student said Saturday. “When I got to the river, there were people just standing there. Then I saw the boy's red jacket.”*

*When asked the following day about his decision to dive into the icy waters, Mohamud said he could not remember his thoughts; he couldn't even remember that the water felt cold. He just knew there was a boy's life in danger.*

*“Some weird stuff happened to me yesterday,” he said.*

*Mohamud said that when he finally reached the little boy, he was completely underwater with his eyes open. His red jacket, caught on a tree branch, was the only thing keeping him from being swept away. Mohamud grabbed the boy with one arm, but he began to slip. “I had to take him with both arms and just [swim] as hard as I could,” he said.*

*When he reached safety, Mohamud pushed the child onto the river bank, but was too exhausted to pull himself from the water and needed help regaining the shore.*

*The little boy required CPR and was admitted to the hospital in critical condition ... Police said they were sure that if not for Mohamud's immediate action the child would have died.*

\* \* \*

*Ronnie Lott, a defensive back with the San Francisco 49ers, crushed the tip of his little finger in a collision with an opponent in a football game near the end of the season. The medical decision was straightforward: Because the mangled digit required surgery to insert a pin in the bone and a full hand cast, Lott would miss the playoffs. Lott—famous among his aggressive NFL peers as a true “warrior” of the game—came up with an alternative approach: he asked the doctors to amputate the damaged fingertip. Lott succeeded with his goal; he played that Sunday with nine and half fingers. His team went on to win the Super Bowl, with Lott playing a pivotal role.*

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### ***Affective Signals: Flexible and Self-Adjusting Motivations***

In contrast to relatively rigid patterns of behavior, such as reflexes or habits, these affective action-tendencies usually promote *flexible* learned behaviors. This can be illustrated by returning to the simple example of appetitive feelings. A feeling of thirst can create a strong action-tendency to find and consume fluids, yet there is great freedom in selecting a specific behavior—such as when, where, and what to drink. When a person experiences a feeling of being cold this action-tendency can promote a wide range of behaviors consistent with the biological goal of seeking warmth. For an individual outside on a winter day this action-tendency could motivate seeking shelter inside, bundling up with warmer clothes, or increasing physical activity; for an individual in an air-conditioned building the same affective signal might lead to adjusting the thermostat.

This flexibility of affective influences is essential. It promotes a *category* of response priority while permitting multiple adaptive modifications in behavior. This allows a natural balance between biologic needs with cognitive goals, while making complex decisions over long periods of time. If, for example, the feeling of a full bladder created an automatic *reflex* to urinate this could result in some extremely awkward social situations. Yet, if people could easily ignore such biological requirements this could lead to physiological damage. Affective signals in the form of strong feelings create an elegant solution to such problems. The feeling of a full bladder creates a motivational shift that is flexible but persistent.

One of the important qualities of these feeling-based action-tendencies is how they can “adjust” across a range of intensities, in adaptive ways. That is, the amplitude of the subjectively-experienced signal (the intensity of the feeling) is often calibrated according to the magnitude of need (the biological or emotional/motivational priority of the goal).

This principle (and its adaptive nature) can be illustrated by considering the range of intensities in the feeling of thirst. As neural systems first detect a slight need for water this gives rise to a subtle sensation—a low-volume signal that gently suggests the desirability of drinking. In many situations one may not consciously notice a subtle feeling of thirst until walking past a water fountain or seeing some “cue” or reminder that brings the affective signal to full awareness.

Even moderate levels of thirst can go relatively unnoticed if one is engaged in an activity—playing a sport or reading a good book. Yet, if one goes very long without water, the sensation becomes stronger and harder to ignore. If salt/water balance in the body becomes severely out of kilter, at the point of becoming seriously dehydrated, these neural systems can give rise to a very intense signal calling for water-seeking behavior. This high-intensity feeling—experienced as a *raging thirst*—creates a *compelling action-tendency*. The motivation to find and drink water can dominate all competing goals and priorities.

In a similar way, a feeling of sleepiness may begin as a slight tug of a sensation at the edge of awareness that gently suggests the desirability of going to bed. However, if one stays awake for days at a time, sleepiness can become amplified into a high-intensity feeling—an action-tendency that begins to dominate every thought and action.

The feeling of fear can range in intensity from a subtle sensation of anxiety that is barely registered in consciousness, to an overwhelming terror that commands every fiber of one’s being—a feeling that

cries for all mental and physical actions to be directed at finding escape from a sudden threat. A feeling of loneliness can occur as the mildest twinge of longing that is barely noticed, yet in other situations, feelings of loneliness can reach a painful intensity that cannot be ignored.

These natural motivational feelings tend to pull at conscious attention and behavior in ways that serve a variety of biological, psychological, and social needs. In many situations, these feelings are activated by well-tuned brain systems that have detected some internal condition or external cue, which requires attention or action. A particular category of need is being “flagged” through the activation of a feeling—a signal calling for and naturally motivating behavior to address this category of priority.

### ***Affective Signals Versus Conscious Decision Making***

These self-adjusting, feeling-based, and flexible action-tendencies are quite adaptive. Without the nudges and pulls from these internal sensations, one might not remember to attend to the full range of changing biological and social needs. These affective brain systems are organized in ways to motivate behaviors to *get* valuable things (like food, water, sex, sleep, social support, and social status) and to *avoid* harm and danger (including environments that are too cold, too hot, painful, as well as detecting and escaping from sources of physical threat).

One of the best ways to illustrate the power and elegance of this adaptive priority shifting system of human affective signals is to perform a thought experiment: consider daily life in its absence. Imagine making every moment-to-moment decision—even very simple things such as when to sleep, eat, drink, or actions to help maintain correct body temperature—*without* the motivational nudge by feelings of tiredness, hunger, thirst, or feeling too warm or cold. Now, extend this one more step and imagine trying to remember to attend to all of these survival priorities *without* the good feelings that follow eating, drinking, resting, or correcting swings in body temperature, and without the bad feelings created if one forgets to do these things. Imagine the burden of having to meet all of these decision-making processes every moment of every day, without the help of the broad range of affective signals that constantly push and pull on behavior.

These affective signals (feelings) create a common mental currency—allowing biological, psychological, and emotional needs to negotiate effectively with each other, *and* with the human brain systems that operate through semantic processing and the pursuit of long-term goals: the thinking, planning, and talking brain. This permits a capacity for balancing priorities over longer intervals of time. For example, if one decides that a long term goal (e.g. writing a grant application) is more important than getting sleep, it is possible to go for days at a time with little or no rest. For a while, one can ignore and/or override the physiological need for sleep. Yet, if one pushes for too long, the feeling of tiredness can become so strong that one will not be able to think about anything but the need for rest. The *feeling* of wanting sleep can become a powerful magnet that prevails over all competing goals and priorities, and in this way diverts behavioral choices toward getting the essential restorative sleep.

A key point—one that becomes even more relevant when considering the affective changes during adolescent development that will be discussed later—is the capacity of these affective systems to create *high-intensity feelings*.

On one hand, the effects on behavior from these powerful affective signals can be quite *adaptive*. They often help shift priorities according to an emerging biological need—a raging thirst, or overwhelming tiredness; they can launch a heroic action to save the life of a child. On the other hand, it is also evident that high-intensity affective signals can contribute to irrational behavior. “Hot-headed” actions fueled by strong emotion can lead to senseless and reckless actions with disregard for long term consequences.

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*From NY Times February 14, 2003:*

*A Texas jury concluded that Dr. Clara Harris acted with “sudden passion” when she murdered her husband by running over him with her Mercedes-Benz, repeatedly, in a hotel parking lot after discovering an extra-marital affair. Because of the mitigating circumstances of her “sudden passion”*

*Dr. Harris may be eligible for parole in ten years. Otherwise, this 45-year-old dentist and mother of 4-year-old twin boys could be facing a 99-year prison sentence.*

\* \* \*

Why does passion alter the legal judgment of an action? The underlying principle—the idea that high-intensity feelings can transiently hijack rational judgment—is as old as civilization. It is evident in literature from all corners of the world. Tales of individuals who behave in unthinking ways under the influence of strong emotions are also found in many traditional myths that predate written stories.

This same principle underlies a long historical interest in strategies for reducing or eliminating passions. Early Greek philosophers championed logic and calm analytic thought. Chinese scholars dating back to Lao Tzu in the 6<sup>th</sup> century B.C. taught methods for detaching from all strong desires. For perhaps as long as our species has been capable of self-reflection, strong emotions have been seen as a natural enemy of reasoning, planning, and disciplined efforts to achieve long term goals.

Yet, the opposite is also true. High-intensity feelings can sometimes sharpen the focus of thinking, planning, and effortful actions leading toward a goal. Intense desires can fuel inspired motivations. Passionate feelings can become linked to disciplined actions in ways that serve the highest forms of human endeavors.

As Aristotle noted long ago in his arguments against pure reason, *thought by itself moves nothing*. Without feelings of desire the human capacity for rational thought would lack any power to act. Aristotle recognized—twenty-two centuries before scientists began using brain-scanning technology to map neural systems of cognition, emotion, and motivation—that all actions leading to higher goals require a *union* of reason and desire.

### ***Adaptive versus Maladaptive Affective Influences: Adolescent Passions***

On one hand, powerful feelings can sometimes undermine logic and responsible considerations about consequences, creating actions that lead toward recklessness and disasters. On the other hand, intense feelings can sometimes help to *focus* all thoughts, efforts, and actions into a well-planned, tenacious pursuit of an inspired goal. As will be discussed in greater detail in Part Two of this review, adolescence (and more specifically the onset of pubertal maturation) appears to be a natural time for igniting passions of both types—risk-taking/reckless adventures as well as inspired goals.

This adolescent interval of “igniting passions” is not simply a matter of activating new romantic and sexual feelings at puberty. There are a multitude of emotional and motivational changes that emerge during this period of development. Adolescence is associated with an increased tendency to *seek* strong sensations and intense emotions. It is a time when sex, drugs, loud music, and other high-stimulation experiences often take on great appeal. Adolescence is a period when an appetite for adventure, a predilection for risks, desire for excitement, and inclination toward passionate action, seem to reach naturally high levels.

Although these patterns of emotional changes are evident at least to some degree in most adolescents, it is also important to acknowledge the wide range of individual differences during this period of development. In some adolescents the increased tendency to explore and take risks may be relatively mild and can be easily managed and channeled into healthy pursuits, with little or no reckless behavior or risk-taking. Yet, for many youth, the pubertal stirring of passions—and burgeoning appetite for high-intensity feelings—comes at a terrible cost. Emotionally charged actions often lead to impulsive adolescent behaviors that seem to ignore consequences—and at times, to momentary choices that seem completely outrageous.

### ***What is passion?***

At one level, passion is a strong motivational feeling—an internal sensation that drives behavior toward a goal. It has an appetitive or seeking quality, similar to the way feelings of hunger and thirst are signals

that call for food and water. However, a feeling of passion seems to scream its demands. It is like a ravenous hunger or a raging thirst—it is a *high-intensity action tendency*.

Adolescent passions show a fundamental difference from the food-seeking purpose of hunger or the water-seeking goal of thirst, which are biologically “hard wired” to motivate specific categories of consuming behaviors (eating and drinking). In contrast, the motivational aims of passion are *learned*. These powerful motivational feelings can become aligned toward a diverse range of targets.

Passion can ignite a thousand varieties of inspired action. It can launch heroic pursuits and reckless adventures. It can compel selfless acts of love and monstrous actions of rage. Feelings of passion have primal roots in the same deep brain systems as biologic drives and primitive elements of emotion. Yet, passion intertwines with the highest levels of human endeavor: Passion for ideas and ideals. Passion for beauty. Passion to create music or art. Passion to succeed in a sport, business, or politics. Passion toward that one person, activity, object, or pursuit that inspires transcendent feelings.

Adolescence appears to be a key time in the development of passions—a time when new types of intense feelings are being activated, and these can be sculpted toward specific types of goals and activities. It creates opportunities to forge new types of emotionally-based motivations.

### ***The Development of Acquired Motivations***

A *pattern* of experiences that activate high-intensity positive feelings through effortful, goal-directed, action can lead to the establishment of *new* motivational affinities. An adolescent who has learned to create these desired emotional states by ratcheting-up efforts to achieve a purposeful goal, can gradually develop an “appetite” for this particular activity. This type of emotional learning can sculpt new sources of strong motivational feelings. For example, if a kid works very hard at developing basketball skills and this leads to some exciting, intensely-rewarding moments of success while playing the game, this can create a hunger for—a passion for—the beloved sport.

A key issue centers on the *emotional* roots of the acquired motivation. This is not simply a matter of developing positive thoughts and good associations with a particular sport. It has more to do with the creation of new *motivational feelings*—capable of activating affective signals that begin to pull at behavior in automatic ways—strong feelings that underpin intrinsic motivation.

This kind of acquired motivation is illustrated by adolescents who develop such a “hunger” to play a particular sport that it would take parental effort to *prevent* the youth from working out, practicing, and honing skills related to these goals. It is the kind of motivation captured in the movie, *Bend it like Beckham*, where an Indian girl growing up in England develops, in adolescence, such a passion for playing soccer, that when her parents forbid her to play this sport she resorts to an elaborate scheme of lies and deceptions just to practice.

An acquired motivation can develop qualities similar to the way feelings of hunger create a natural desire to eat food. The affective state of hunger creates motivation to ingest food—such that it takes effort to *refrain* from eating food if it is available. In an analogous way an affective state of passion can create natural desires aligned toward a particular goal or activity. Moreover, just as the process of waiting and working toward the goal of obtaining food can amplify the intensity of hunger (and the enjoyment of eating), so too, can inspired efforts and struggles aimed at a passionate goal lead to a ratcheting-up of motivation, as well as joy.

The emphasis here is *not* on creating *conscious* thoughts or insights about the value of hard work leading to enjoyable rewards. An adolescent who has become convinced (logically) about the virtues of reading classic literature and then uses self-discipline to complete an impressive list of great books is not illustrating a feeling-based acquired motivation. In contrast, a youth who develops a nearly insatiable love for great literature is an example of this type of emotional learning process. A crucial element here is the way that motivational *feelings*—affective signals—become amplified and aligned, building into a natural hunger which, once established, requires little or no conscious effort or rational arguments.

There are many versions of this process of ratcheting-up high-intensity motivational feelings aimed at a particular kind of goal or pursuit. An adolescent can discover passion through the effortful pursuit of literature, art, music, or academic achievements. Similar types of strong motivational feelings can become linked to an activity like teaching, caring for the sick, working to serve the poor through a humanitarian organization, or in the form of a religious calling.

A key issue is that there is something about *adolescence*—rooted in brain changes that begin during pubertal maturation—which seems to promote the development of new types of hungers or acquired passions at this point of life. This seems to be, at least in part, related to the natural inclination toward activating high-intensity feelings at puberty.

These emotional changes at adolescence—a developmental period of igniting passions—can create unique vulnerabilities as well as opportunities. The pubertal brain seems to be primed for this kind of emotional-motivational learning. This type of learning has less to do with words and concepts, and more to do with developing strong *feelings* of motivation directed at higher pursuits. Adolescence appears to be a natural time for sculpting these high-intensity feelings into specific patterns. This can lead to vulnerabilities toward destructive passions—drugs, alcohol, risk-taking and reckless behavior; it can also lead to opportunities for healthy, positive passions—high intensity motivations aimed at literature, art, music, science, sports, serving others, reaching toward goals of higher purpose.

### **Brief Summary of Key Points Regarding Affective Influences**

The “value” of a particular goal or choice, at a particular time, for a particular person—be it obtaining food, water, money, success, trying to save the life of a dog, protecting one’s child from harm, impressing one’s peers with a daring action, achieving an athletic victory, swimming to Antarctica, or risking everything to pursue the object of desire after falling in love—is inherently intertwined with one’s *feelings* about the goal or object. It is directly related to these fast automatic affective signals of personal salience. These are based in *emotional* evaluations that work through neural systems in deep central areas of frontal cortex and interconnections to limbic regions of the brain that underpin affective appraisals—evaluations that occur quickly and automatically, and do not require thoughts in the forms of words, sentences, or consciously weighed considerations about the risks and benefits.

These signals operate through fast neural connections that link to an intricate web of affective systems (including drives, appetites, and biologically-based motivations). These systems, as well as connections between them, are sculpted by both heritable or genetic variation in brain structure and function as well as individual emotional experiences in childhood and adolescence. The strength and speed of these neural connections are further shaped by *learned* fears, desires, and passions. These emotional brain systems are capable of activating specific action tendencies, and at times, intense feelings of motivation. These affective signals contribute in important ways to much of what is often called “impulsive”, reckless, or emotionally influenced behavior.

Several specific lines of investigation are emerging to help inform our understanding of these affective influences (see [1, 2, 3, 4]. Although this paper is emphasizing a cognitive and affective neuroscience approach to these questions, there are also a wide range of studies in psychology, developmental psychology, and the social sciences addressing questions and mechanisms of emotional influences. These include some elegant studies in affective influences on perception, attention, memory, and judgment, as well as many direct measures of behavior (for a broader review see Loewenstein and Lerner[5] Slovic [6]and Dolan [7].

**PART TWO:**  
**PUBERTY, BRAIN MATURATION, AND THE DEVELOPMENT OF**  
**DECISION MAKING CAPACITIES IN ADOLESCENCE:**  
**A CONCEPTUAL FRAMEWORK FOCUSING ON**  
**BRAIN/BEHAVIOR/SOCIAL-CONTEXT *INTERACTIONS***

There is an emerging body of evidence that adolescence is a period of malleability, or developmental plasticity in some neural systems that underpin behavior, emotions, and decision making. Patterns of neural connection among and between systems of emotion, motivation, and cognitive processes related to the pursuit of long-term goals appear to undergo a natural reorganization during adolescence [8]. One important component, as will be described in this review, focuses on a set of changes in motivational and emotional systems that are activated in association with the onset of puberty. These pubertal changes in affect contribute to the development of sexual and romantic interests, but also appear to influence other emotional processes and tendencies—in ways that may be important to understanding some aspects of risk-taking, sensation-seeking, and some types of reckless decisions in adolescence.

Before describing several areas of research that are advancing knowledge of adolescent brain development, this review will begin by considering the background and significance of focusing on these neurobehavioral changes, and placing them into a conceptual framework for understanding adolescence as a developmental period.

***The Health Paradox of Adolescence:***

***Examining the Neurobehavioral Underpinnings of Risk-taking, Sensation-seeking, and the Slow Maturation of Cognitive Control***

Adolescence represents one of the healthiest periods of the life span with respect to physical health, yet paradoxically overall morbidity and mortality rates *increase* 200% between mid-childhood and late adolescence [9, 10]. This increase in serious health problems in adolescence is primarily related to *difficulties with the control of emotions and behavior*. Rates of accidents, suicide, homicide, depression, alcohol and substance use, HIV, Hepatitis C, unwanted pregnancies, anorexia, and bulimia all rise sharply in this developmental period [10, 11]. This wide range of behavioral and emotional difficulties must be considered within a framework of normal development.

Broadly speaking, adolescence is a transition from “child” status (requiring parent/adult monitoring of behavior) toward autonomous control of behavior in productive, socially-responsible “adult” ways. However, the emergence of competent self-control of behavior and emotions is a slow, gradual process that continues to develop through the *late* teen-age years and into the 20s. In contrast, the emergence of pubertal influences on emotion and motivation usually occurs in *early* adolescence—with the most tumultuous developments of puberty typically occurring by age 11-12 in girls and age 12-13 in boys.

This period of pubertal maturation is a time of dramatic changes: rapid physical growth, the onset of sexual maturation, the activation of new drives and motivations, and a wide array of affective changes and challenges that include increased self-consciousness, social anxieties, igniting romantic interests, academic pressures, and attempts to balance desire for immediate gratification with an understanding of the importance of long-term goals and consequences. These dramatic changes *create challenges in the integration of cognitive and emotional processes—in ways that place demand on* the functional neural circuits that are critical for mediating arousal, orientation, attention, and affect (e.g. limbic regions) as well as regulating and integrating these drives in the generation of long-term goal-directed behaviors (e.g. prefrontal regions).

Competence in self-control of behavior emerges slowly. Brain imaging studies have shown that cortical development is continuing well into early adulthood [12]. Thus, these dramatic pubertal changes at age 11-13 are often occurring as much as a decade before the development of competent

self-control. This interval—several years between the onset of sexual maturation and the attainment of adult levels of regulatory competence—is a time of great risk for a variety of clinically significant problems in the control of behavior and emotions: high rates of affective disorders, health problems related to risky behavior, and adolescent-onset substance use disorders.

Moreover, many adult problems, such as substance use disorders, typically have onsets in adolescence or young adulthood. Approximately three-fourths of adult tobacco users in the U.S. begin smoking between the ages of 11 and 17, with 60 percent starting by age 14. Fifty percent of illicit drug abuse in adults with substance use disorders begins between the ages of 15 and 18, and initiation is rare after the age of 20. Earlier substance use also predicts greater addiction severity and morbidity. Clinical data also indicate that adolescence is a period of heightened vulnerability, often demonstrating a steeper trajectory toward abuse and dependence than adults.

Thus, adolescence is a crucial time in the setting the trajectory for many types of health behaviors and problems. There is a need to understand how individual, cognitive, and neurobiological factors interact with social conditions and experiences in producing trajectories that lead some individuals in a progression toward serious problems, while others do not.

Individual differences in affective experiences—especially those involving motivation, sensation-seeking, judgment and decision-making—and the neural systems that underpin these processes, appear to be particularly important candidates for influencing vulnerability to a wide range of risk taking, and problem behavior including drug abuse and addiction.

Many significant changes impacting adolescent development involve *interactions* between biologic and social/cultural influences [13]. Changes in sleep during adolescence represent an example to illustrate these interactions. Biologic changes in sleep regulation at puberty interact with adolescent social and school schedules in ways that lead to erratic sleep patterns, less sleep on school nights, and high rates of sleep deprivation in adolescence [14]. Daytime tiredness and irritability from insufficient sleep may interact with other affective changes in adolescence including the well-documented increases in mood lability and sensation-seeking in early adolescence.

These examples of affective changes (and their interactions) have relevance to substance use and other types of risky and reckless behavior. For example, sleep deprivation and tiredness can make psychoactive stimulants more appealing and rewarding (including caffeine and nicotine as well as illicit stimulants) and irritability can increase motivation to use mood-altering substances. These examples have direct relevance for the heuristic model because *mood lability, increased sensation-seeking, and biological changes in sleep regulation are among the adolescent changes that are most directly associated with pubertal maturation.*

### ***Structural Changes in Brain Maturation in Adolescence***

A surge of recent research has identified a series of structural changes in the brain that occur during childhood and adolescence [15-19]. Spatial and temporal patterns of normative changes in gray and white matter tissues observed thus far are consistent with the known cellular maturational changes that occur between childhood and adolescence (i.e., myelination, synaptic pruning), as well as cognitive and behavioral changes. For example, recent findings have suggested that maturation of frontal lobe gray and white matter accelerates during adolescence [15, 16], paralleling the increased effectiveness of executive functions (i.e., response inhibition) that are not yet fully developed by adolescence [20]. In contrast, it appears that the parietal cortical regions that underlie sensory and perceptual functions may develop earlier in childhood [16]. Most studies to date, however, have been open to the criticism that they are not longitudinal. Cross-sectional samples are not sufficient to validate “change” in brain structure during maturation, because of the difficulty of assembling comparable cohorts at different ages. Nonetheless, there has been a strong inclination to attribute differences between subjects primarily to differences in age.

Despite the enormous progress in documenting late changes in several brain structures—and excitement about the implications of this work—what is now needed is to apply this type of advanced image analysis techniques to MRI data from *longitudinal* developmental cohorts. In addition, as will

argued repeatedly in this review, it is essential that these studies include measures of *puberty*, to elucidate the contributions of both puberty-dependent vs. puberty-independent developmental changes in the structural maturation of neural circuits (and to link to *functional neuroimaging studies* indicating changes in reward processing, affect, and cognitive control, as will be discussed in a later section).

### ***Puberty, Pubertal Timing, and Adolescent Brain Maturation***

Despite the widely held notion that the brain “changes” at puberty, there is a surprising dearth of neuroscience data that specifically refer to the links between brain development and pubertal maturation. As a consequence, this section will draw on other areas of neuroscience that frame our understanding of maturational changes more specific to the interval surrounding pubertal development. This includes general aspects of brain development, contextual effects on brain development, and a discussion of what is known about changes in brain function in specific brain regions during adolescence.

It is important to note at the outset that not all brain development in adolescence is closely linked to processes of pubertal maturation. One limitation of extant views of adolescent development, and of psychopathology in adolescence in particular, is that “biology” has been used as an explanatory construct without sufficient attention paid to the fact that biological change in adolescence is multi-systemic, and that even pubertal change itself is not a unitary phenomenon. Thus, it is important to distinguish between aspects of brain development and function that are closely tied to puberty and those that appear to take place relatively independent of pubertal maturation (i.e., which follow a different timetable and which are influenced by other aspects of aging and or experience). Moreover, even within puberty, some aspects of brain development may be particularly heavily influenced by specific facets of puberty but unrelated to others (e.g., those which are closely linked to changes along the hypothalamic-pituitary-adrenal [HPA] axis versus those that are closely linked to changes along the hypothalamic-pituitary-gonadal [HPG] axis).

There are several reasons to focus on puberty-specific changes in neural systems that may influence decision-making. Such focus can lead to the identification of specific aspects of brain maturation linked to a rise in reproductive hormones; it points to a set of biologically based changes that occur *early* in adolescence (as opposed to other maturational changes in adolescent cognitive development that occur in late adolescence); and highlight important questions about the consequences of recent historical changes in pubertal timing.

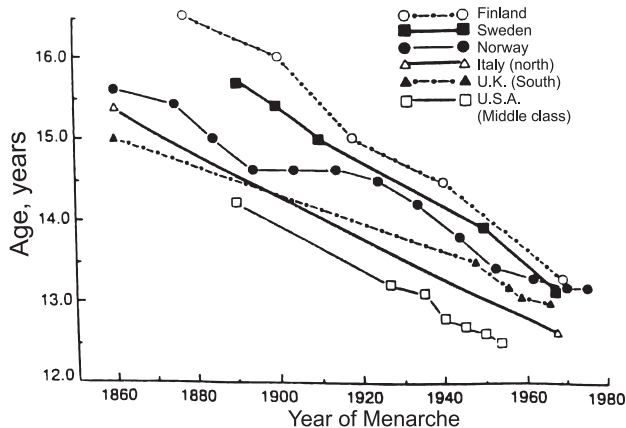
### ***Early Activation of Limbic Drives vs. Gradual Emergence of Cognitive Self-Control:***

Questions about emotional and motivational changes during adolescent development and their influences on decision-making represent issues of great clinical and social policy significance, yet there has been surprisingly little work aimed at understanding neural circuits that underpin these changes. Part of the problem relates to pragmatic and methodological challenges in performing neurobehavioral studies during this developmental period. Several domains of development are changing *simultaneously* during adolescence—including rapid physical growth, primary and secondary sexual maturation, cognitive development, the maturation of emotional skills, and an array of social and cultural influences that show great variability across this interval of time. It is also essential to point out that few studies have been designed in ways to specifically address the impact of pubertal maturation on cognitive and behavioral development and the relevant developing neural systems. First of all, it is important to note that a large number of the most influential studies of adolescent cognitive and emotional development have contained no measures of puberty at all. Second, the majority of those studies that have included pubertal measures have relied on self-report questionnaires, which at best, are rough approximations of the specific physiological changes of interest. Third, even among the studies that have obtained objective measures of puberty, it has been difficult to disentangle age effects from pubertal maturation, because in most samples these two are closely correlated with each other (and age is measured with greater precision than categories of pubertal stage).

However, there have been a few studies that have utilized cross-sequential or longitudinal designs with measures of reproductive hormones, such as the Great Smoky Mountain Study (GSMS) [21], where several puberty-specific findings have emerged, including strong evidence for a direct link between puberty and risk for affective disorders [22-25]. Another example of a study design that allows disentanglement of puberty-specific effects is illustrated by Martin et al.[26]. They selected 208 children in a narrow age range (11-14 years of age) and examined the influence of pubertal maturation on sensation-seeking as well as nicotine, alcohol, and marijuana use. Within this narrow age range they found that while sensation-seeking did *not* correlate with age, it did correlate with pubertal maturation—boys and girls with more advanced pubertal development had higher ratings of sensation seeking ( $r^2 = .45$  in females and  $r^2 = .27$  in males) and greater drug use. They concluded: “this study clearly demonstrates that pubertal stage, regardless of age, is associated with drug use risk” [26].

### Historical Changes in Pubertal Timing:

Within this framework emphasizing the importance puberty-specific effects on brain development and affective function, it is important to consider the role of historical changes in pubertal timing. The adolescent transition has undergone significant transformation in recent human history. Physical/sexual maturation has been occurring at much earlier ages in industrialized societies, particularly among girls. In a comprehensive review, an anthropologist who has studied puberty across the world concludes: “The past 150 years have witnessed a quiet revolution in human development that still sweeps across the globe today: children nearly everywhere are growing faster, reaching reproductive and physical maturity at earlier ages, and achieving larger adult sizes than perhaps ever in human history” [27].



**Figure 1. Change in ages of menarche from 1860-1960 in Finland, Sweden, Norway, Italy, U.K., and USA**

The fact that children are now growing more rapidly and beginning to develop sexually at younger ages, raises several questions about the maturation of neurobehavioral systems involved with reproductive behavior, biological drives, emotions, and the development of regulatory control. While some of these affective changes are directly influenced by early puberty, it is unclear to what degree other aspects of cognitive development have accelerated on a parallel trajectory. Regions in prefrontal cortex (PFC) that underpin some types of cognitive-executive functions mature slowly, with some functional changes continuing well into late adolescence/adulthood [28-30]. Some performance

measures of cognitive ability continue to mature into early adulthood and these cognitive improvements *correlate more strongly with age and experience* than with pubertal development [31]. To date, the strongest evidence for puberty-specific influences on development are in the domain of romantic interest and sexual motivation [32, 33]. There is also evidence that *some changes in emotional intensity and reactivity are more closely linked to pubertal maturation* rather than age, including measures of parent-adolescent conflict [34-36]. Developmental changes in sleep and circadian regulation also appear to be linked to pubertal maturation [14]. There is also evidence that risk-taking, sensation-seeking, and novelty-seeking tendencies are correlated more strongly with puberty than age [13, 20, 37].

One *heuristic model* [38] posits this recent historical shift toward earlier timing of puberty directly affects *some components* of emotional, motivational, and cognitive development (particularly those related to sexual and romantic interest, sensation-seeking, and affectively “hot” cognition) whereas other aspects of cognitive development occur slowly and continue long after puberty is over. Thus, many adolescents in modern society experience several years with relative physical maturity (including

adult-like bodies as well as post-pubertal activation of brain circuits involved in reproductive drives and related affect) before the completion of neurocognitive development necessary for *competent skills in self-control over behavior and emotions*. This has led to a metaphor for considering the recent historical advancement of puberty as creating a situation of *starting the engines with an unskilled driver*.

This earlier increase in the intensity of affective influences relative to the development of adult cognitive skills may be particularly salient in some individuals (such as those with heritable difference impacting the development of limbic-prefrontal dynamics) and in some social contexts (stressful environments that increase the emotional challenges) in ways that create increased vulnerability to affective influences on decision-making.

Another set of factors to be considered in young adolescents is the way in which they are often dealing with increasingly more difficult “decision-making” and challenges to self-control—in complex environments that activate many arousing but conflicting feelings and desires. They must often navigate complex ambiguities. The range of behavioral options available to adolescents in modern society—ranging from choosing among alternative sources of entertainment to choosing among alternative educational or vocational pathways—has increased dramatically in contemporary industrialized society. Thus, today’s adolescents face more decisions, and more complicated decisions, than their counterparts did in previous eras. These changes are reflected in higher rates of adverse experiences that are thought to interact with maturation in cognitive capacities to precipitate episodes of depression in vulnerable individuals.

Also, there has been an historical shift toward increased behavioral autonomy among teenagers, such that external constraints on their behavior (in the form of parental and adult supervision) are diminishing and in some cases absent. Changes in patterns of parental employment, in rates of divorce and separation, and in patterns of residential mobility, which have led to disruptions in community ties, have decreased the amount of time that young people spend in the company of parents, adult neighbors, and members of the extended family. As a consequence, today’s adolescents have fewer resources on which to draw in the task of regulating new emotions and drives. These contextual changes may exacerbate special vulnerability of adolescents to emotional and behavioral problems.

This review will argue that disjunctions in biology, cognitive capability, and contextual demands in adolescence create vulnerabilities for certain types of emotional and behavioral difficulties, in particular, those that involve the regulation of affect (e.g., depression, social anxiety), appetitive and reward motivation (e.g., substance abuse and dependence, eating disorders), and impulsivity (e.g., antisocial behavior, excessive risk-taking).

This framework is relevant to the study of a wide range of behavioral and emotional health problems—including internalizing, externalizing, and addictive disorders as well as common problems that have an onset in adolescence. A key aspect of progress in these areas must focus on understanding changes in affective systems, including arousal and motivation, the development of regulatory competence, and the ways in which this competence may be compromised or strengthened by the interplay among biology, cognition, and context.

It is important to recognize that the affective changes—the increased intensity and duration of emotion and the increased strength of at least some appetitive drives at puberty—create new regulatory challenges, particularly with respect to self-regulation in the face of high-intensity emotions and motivation, and in the midst of emotional conflicts. During adolescence, there is a shift in regulatory capability away from regulation that is assisted by external agents, such as parents, toward regulation that is primarily internal, cognitive in nature, and involving higher-order executive functioning as well as a broader range of self-regulatory skills that support the ability to execute rational choices.

The type of integrated executive function that is needed (and assembled) during the adolescent transition is in fact a collaboration of a number of specific cognitive and motivational developments, particularly in planning, monitoring, evaluating, and reflecting. Together, these can be thought of as an “executive suite” that comes increasingly, but gradually, under conscious control during adolescence [39]. Because the maturation of regulatory systems relevant to the modulation of emotion and motivation is not driven directly by pubertal development and is still taking place during late

adolescence, however, adolescents are relatively more vulnerable than children (whose levels of arousal and motivation are lower) or adults (whose regulatory capabilities are stronger) to extremes in affective and drive states, which may leave them more susceptible to behavioral and emotional problems—difficulties in self-control that create regulatory problems.

Regulatory problems may result either from inadequate regulatory capacities, from poorly or incompletely developed regulatory capacities, or from an excessive challenge—particularly with respect to regulating the strong affective experiences of adolescence. Bringing the potent and novel affective and motivational systems into an integrated, functioning system is a lengthy and effortful process, which requires complex skills as well as knowledge and capacities. Thus, emotional and behavioral disorders may result from under-regulation (e.g., where the under-regulation of anger may lead to conduct problems) or inappropriate regulation (e.g., where the over-regulation of sadness by rumination may lead to the development of depressive disorder).

Thus, while many individuals may experience emotions and drives whose intensity and duration exceeds their regulatory competence, those adolescents who enjoy supportive home, peer, school, and neighborhood contexts are buffered from the ill effects of the emotion-cognition disjunction. In addition, their transition to an internal, consciously controlled regulatory system is more effectively scaffolded compared with individuals lacking in such support. Conversely, individuals whose environments do not provide sufficient support, control, and predictability are relatively more vulnerable to the development of psychopathology.

In this view, the adolescent is not merely the passive recipient of contextual support, however. Context is a resource that is both provided by outside agents (such as parents or teachers) and also actively recruited by adolescents. An important, yet remarkably understudied question, is how individuals develop the capacity to identify, enlist, and employ sources of contextual support during times of stress as a means of protection against the development of emotional and behavioral difficulty. In this regard, “resilience” in the face of adversity may reflect in part the ability to engage contextual resources in the service of self-protection.

### ***Contextual Effects on Brain Development***

Discussions of brain development in adolescence and its implications for understanding behavioral and emotional problems, must acknowledge not only the importance of normative maturational processes during this time but the role of the social context and environment in shaping patterns of growth and maturation. Brain development appears to be more plastic and susceptible to environmental influence in adolescence than had been previously thought. Indeed, current neuroscience research on contextual influences suggests that environmental factors might conceivably profoundly affect brain development in adolescence and that neurodevelopmental processes are affected on varying time scales. Thus, one of the reasons for the heightened vulnerability of individuals during adolescence to various forms of problems could lie in the vulnerability of the adolescent brain to contextual influence. More specifically, if a key element of pubertal maturation is associated with sensation-seeking and an increased “appetite” for high-intensity emotional experiences, then it is clear that some social environments may permit these motivational changes to accelerate into destructive spirals of behavior.

There are interesting neurobiological elements to these processes. In terms of effects that persist across the life span, some contextual factors produce permanent change in neural circuitry by affecting developmental processes. One of the best-understood effects in this area derives from the work by Meaney and colleagues, revealing an effect of handling manipulations on rodent pups prior to adolescence [40, 41]. Contextual manipulations early in development permanently alter the rat’s physiological response to various stressors by affecting the sensitivity of feedback regulation in limbic brain regions, including the hippocampus and ventral prefrontal region. The precise developmental period during which these effects can occur has not been established. Interestingly, however, it appears that an enriched social and learning environment during the peripubertal period in rats is capable of reversing many of the adverse effects of early maternal separation [42] and that these experiences later in development influence some, but not all of the brain systems impacted by the early handling and separation paradigms.

Other work, examining contextual effects on synaptic plasticity in the rodent cerebral cortex, emphasizes the need for research on contextual effects on prefrontal and limbic regions in adolescence. In work on plasticity in the cortex, contextual manipulations exert effects on dendrite patterns in adult animals, and these effects vary as a function of developmental stage [43, 44]. Contextual factors appear to produce particularly robust long-term changes in dendrites when they operate during periods of high synapse formation. This is important, because some regions of the brain may undergo particularly marked synapse formation in adolescence [45], and as a result, the development of these brain regions may be particularly susceptible to the effects of context. This emphasizes the need to extend work exemplified in the studies from Meaney and colleagues through the adolescent period.

Beyond such long-term neurodevelopmental effects, other studies demonstrate contextual effects on neural function that operate over days-to-weeks. Such intermediate effects are elucidated in a particularly compelling fashion through studies examining the response, following contextual manipulations, in the hippocampus, a part of the brain in the temporal lobe involved in memory. Specifically, relatively brief periods of stress alter dendrite patterns in one group of neurons as well as survival rates for another group of newly generated neurons. Interestingly, less extreme contextual manipulations, such as learning experiences, can exert comparable effects. Both monoamines and neurohormones are central regulators of these processes. As a result, changes in the functioning of monoamine and neurohormonal systems during puberty may alter the response of neural systems, including the hippocampus, to contextual effects operating on an intermediate time-scale.

Finally, contextual factors exert acute effects on functioning in neural circuits. Because these effects are at least partially mediated by systems that undergo robust developmental changes during adolescence, acute contextual effects on neural function may change with the initiation of puberty.

For example, hormonal systems that signal the onset of puberty have robust effects on functional aspects of neural systems in animals that appear relevant for human cognitive functioning. A series of neuroimaging studies among adults demonstrates a robust effect of sex hormones on executive tasks that engage prefrontal regions [46, 47]. Given the particularly high levels of steroid hormone receptors in medial temporal regions, changes in the hormonal milieu during adolescence may also affect performance on tasks that engage these regions.

Similarly, autonomic systems that mature during puberty affect functional aspects of neural systems in animals. For example, emotional modulation of mnemonic functions results from the acute peripherally-mediated effects of stress on the noradrenergic system that, in turn, affects a neural circuit involving the basolateral amygdala and hippocampus [48]. Sensitivity of the noradrenergic system to stress, as reflected in peripheral measures, appears to increase during the pubertal years [49].

Finally, contextual factors may exert unique acute effects on brain function during adolescence due to interactions between changes in hormonal or autonomic systems and the underlying brain regions on which they act. For example, executive functions mediated by dorsal prefrontal regions are modulated by dopamine input to this region [50]. Stress effects on prefrontal function may change during adolescence due to developmental changes in the dopamine system as well as in prefrontal targets [51]. These changes may be particularly observable during adolescence, in light of the key modulatory role for the dopamine system in prefrontal functions [52, 53]. Hence, changes in the hormonal, autonomic, and monoamine milieu during adolescence may alter the brain's response to acute stress.

### **Candidate Systems for Advancing Understanding of Specific Neurobehavioral Changes Relevant to Adolescent Decision Making**

As discussed in Part One of this review, emotions are brain states associated with rewards and punishments, that form part of a larger set of affective systems. The affective signals from these systems must be capable of interpreting and responding to complex stimuli and activating appropriate affective states in the context of resolving environmental and/or behavioral uncertainty or ambiguity in facilitating goal directed actions.

### *The amygdala, prefrontal cortex, serotonin and emotional behavior*

The generation and regulation of affective states (and signals) involve a complex set of functional interactions between interconnected brain structures including the amygdala, extended amygdala/ventral striatum, hippocampus and several neocortical regions particularly areas of the ventral, medial and orbitofrontal cortices (see reviews [2, 54, 55]). Areas of the anterior cingulate cortex also are involved, especially in situations of response conflict and/or error detection in relation to an affective state [56]. The amygdala is typically recognized as a key structure for integrating the perception of biologically salient (e.g., rewarding/punishing or familiar/unfamiliar) stimuli and orchestrating some aspects of an organism's response to these stimuli. Through its principal connections, as well as top-down regulation from the prefrontal cortex and negative feedback from output structures, the amygdala is centrally involved in fear/threat behaviors. Moreover, through its interconnectedness with distributed cortical and subcortical brain regions the amygdala is also uniquely situated to regulate other motivated behaviors (e.g. positive or rewarding) and generate a range of responses to biologically salient stimuli and contingencies. In addition, recent work has implicated the cerebellum as playing a crucial role in these complex affective circuits.

### *Pubertal Maturation and Affective Development*

In contrast to most measures of cognitive development, which seem to correlate more closely with age and experience rather than the timing of pubertal maturation, there is evidence for a specific link between pubertal maturation and developmental changes in various aspects of arousal, motivation, and emotion. For example there is evidence that pubertal development directly influences the development of romantic interest and sexual motivation [33, 57]. There is also evidence that some changes in emotional intensity and reactivity are more closely linked to pubertal maturation rather than to age, such as measures of parent-adolescent conflict [8]. Some cognitive skills related to human face-processing have also shown intriguing alterations in mid-adolescent development—an apparent *decrement* in face processing skills that is associated with sexual maturation (measured by Tanner staging by physical examinations) rather than age or grade level [58]. A parallel finding has been reported for voice recognition [59].

There is also evidence that the increase in sensation-seeking, risk-taking, and some proclivity toward reckless behavior is influenced by puberty. For example, in a recent study by Martin et al (2002) where sensation-seeking and risk behaviors were examined in a large group of young adolescents aged 11 to 14, there was no significant correlation between age and sensation-seeking, but a significant correlation between sensation-seeking and pubertal stage among both boys and girls [26]. There is also evidence in animal and human studies supporting a link between increasing levels of reproductive hormones and sensitivity to social status [60, 61], which is consistent with the link between puberty and risk-taking, since at least some theories of adolescent risk-taking (e.g., [62]) suggest that at least some of this behavior is done in the service of enhancing one's standing with peers. There is evidence, as well, that adolescent girls prefer and find more attractive dominant and aggressive boys, although this preference appears to wane as girls mature out of adolescence [63].

### *The Role of Neocortical Brain Regions in Regulating Limbic Drives*

A convergence of evidence from multiple fields and experimental frameworks has provided compelling evidence for the role of the prefrontal cortex in regulating and integrating our emotional experiences. Studies of patients with well-circumscribed brain lesions have substantiated the role of the amygdala in the perceptual and autonomic processing of emotional stimuli and that of the prefrontal cortex in the appraisal and adaptive manipulation of these same stimuli [4, 64, 65]. These findings have been bolstered by work in murine models illustrating a critical role for prefrontal inhibition of amygdala circuits in facilitating the extinction of conditioned fear responses [66-68]. Functional neuroimaging studies of emotion processing and inhibitory control have also revealed an important modulatory role of the prefrontal cortex, especially in the right hemisphere, on amygdala responses. Specifically, a series of imaging studies have revealed that engagement of the prefrontal cortex, through a variety of cognitive tasks, results in the modulation, and possibly inhibition, of the

amygdala[69-75]. In an early study, Hariri et al. implicated the right prefrontal cortex in modulating the response of the amygdala during cognitive evaluation of stimuli representing social threat[70]. In an ensuing study, this amygdala attenuation was associated with a corresponding attenuation of autonomic reactivity as measured by changes in skin conductance [76]. The results of these studies suggest that the dynamic interactions of the amygdala and prefrontal cortex may be critical in regulating emotional behavior [71].

### *Amygdala-Prefrontal Dynamics - Implications for Affective Influences on Decision Making*

Alterations in the functional dynamics of the amygdala and prefrontal cortex have been documented in affective disorders [73]. Drevets et al.[77] were the first to demonstrate such dysfunction, finding relatively diminished prefrontal and heightened amygdala glucose metabolism in subjects with major depression using PET. Subsequently, other investigators, using both PET and fMRI, have replicated the finding of relative amygdala hyperresponsivity in depression [78-81]. Furthermore, abnormal activity in the amygdala has been linked with symptom severity and morbidity in depression and anxiety [77, 79, 82]. Similarly, abnormal prefrontal function including diminished regional cerebral blood flow has been repeatedly documented in depression[80, 83, 84]. Most recently, Siegle et al.[75] have used fMRI to demonstrate that abnormally prolonged amygdala activation in response to emotional words in depression is associated with concurrent failure to engage the prefrontal cortex, resulting in an inability to inhibit the amygdala. Thus, imbalances in the functional interactions of the amygdala and prefrontal cortex appear to play a critical role on the pathophysiology of affective disorders.

It is critical to examine shifts in these functional dynamics during *adolescent development* because this is a period of particular vulnerability for mood and anxiety disorders, with a significant rise in prevalence of these conditions[23, 24, 85-93], and significant implications regarding vulnerability to affective influences during this period of development. Our group has already demonstrated that there are developmental shifts during adolescence in the response specificity of the amygdala to facial expressions that may be relevant for the emergence of affective disorders [94, 95]. Although there appear to be several contributing factors to these shifts, there is strong evidence implicating a central role of *puberty*[23, 24, 85, 86]. Moreover, there is evidence suggesting that puberty directly affects *some neural components* of emotional, motivational, and cognitive behavior (particularly those related to sexual and romantic interest and social cognition subserved by limbic brain regions) whereas development of systems mediating higher cognitive functions (particularly those related to behavioral inhibition, complex planning and execution subserved by the prefrontal cortex) occur slowly, continue well beyond pubertal maturation, and occur relatively independent of pubertal timing.

### *Serotonergic Neurotransmission and Affect Regulation*

The functional dynamics of the amygdala and prefrontal cortex underlying affect regulation may also be sensitive to variation in monoamine neurotransmission. Converging evidence from animal and human studies has revealed that serotonin (5-HT) is a critical neurotransmitter in the generation and regulation of emotional behavior [96]. Importantly, the amygdala is densely innervated by serotonergic neurons and 5-HT receptors are abundant throughout amygdala subnuclei [97]. Thus, the activity of the amygdala may be uniquely sensitive to alterations in serotonergic neurotransmission and any resulting variability in amygdala excitability is likely to contribute to *individual differences* in affect regulation.

For example, a common regulatory variant (5-HTTLPR) in the human serotonin transporter (5-HTT) gene, resulting in altered transcription and transporter availability, has been associated with vulnerability for affective disorders, including anxiety and depression. A recent functional magnetic resonance imaging (fMRI) study suggested that this association may be mediated by 5-HTTLPR effects on the response bias of the human amygdala [98]. This original finding of 5-HTTLPR short (S) allele driven amygdala hyper-reactivity has now been replicated in a large independent cohort of healthy subjects[99]. Furthermore, the short allele has also been associated in normal individuals with diminished functional coupling of the amygdala and subgenual prefrontal cortex, a key affective

regulatory circuit [100]. Moreover, the degree of positive coupling between these reciprocally connected structures, likely reflecting cortical integration of affective arousal mediated by the amygdala towards goal-directed behaviors, significantly predicts individual difference in affective temperament. Thus, genetically driven variation affecting the integrity of this neural circuit likely reflects a predictive biological marker of vulnerability for mood and affective disorders. However, a shift toward pathology will likely reflect the effects of additional genetic and environmental factors on these brain regions. For example, Caspi et al (2003) have demonstrated that the 5-HTTLPR short allele increases risk for developing depression as well as the severity of depressive episodes but only in individuals experiencing significant stressful life events (e.g. unemployment, poor medical health, bad relationships) [101].

### *Implications for the Emergence of Gender Differences at Puberty*

The adolescent increase in affective disorders is particularly steep in girls, resulting in a 2:1 female/male preponderance of these disorders that continues through adulthood. Further potentiation of 5-HT neurotransmission associated with the 5-HTTLPR S allele by the sharp rise in estrogen during puberty may contribute to this bias. Bethea et al. have demonstrated that both estrogen and progesterone can produce down regulation of both the 5-HTT and 5-HT<sub>1A</sub> auto receptor, leading to decreased reuptake and inhibitory feedback and, subsequently, increased 5-HT neurotransmission [102]. This suggests that gender differences in the effects of the 5-HTTLPR on amygdala-prefrontal function may emerge during the pubertal transition and the maturation of gonadal steroid systems. Thus, developing estrogen x 5-HTTLPR interactions on amygdala-prefrontal function may play a critical role in the manifest female bias in the occurrence and severity of affective disorders and provide a unique biological pathway by which at-risk individuals can be identified and meaningful interventions implemented.

### ***Reward Systems, Dopamine, and Pubertal Maturation***

#### *Central Role of the Striatum in Reward*

Neurophysiological and lesion studies in animals have implicated the striatum as a major component in motivated behavior and reward-related processing [103]. For example, dorsal and ventral striatal neurons are affected by the expectation and actual delivery of a reward. Converging data indicates that lesions to the ventral striatum affect motivated behavior. Functional neuroimaging studies have similarly revealed that differential striatal activity may reflect sensitivity to positive, neutral, and negative outcomes as well as differences in reinforcement cues, or differences in the behavioral relevance of these reinforcement cues, or a sensitivity to both factors [103-105].

#### *Contributions of the Prefrontal Cortex to Reward*

It is also likely that reward-related responses in the dorsal and ventral striatum are influenced by projections from prefrontal cortex [106]. The dorsal striatum receives extensive projections from dorsolateral prefrontal cortex, as well as other surrounding prefrontal and frontal regions. The ventral striatum receives extensive projections from ventral frontal (orbitofrontal, ventromedial, and ventrolateral) cortex. Thus, the prefrontal cortex may provide contextual modulation of the reward-related responses in the striatum (see ref [107]).

#### *Dopaminergic Neurotransmission and Reward*

The reward-related responses in the dorsal and ventral striatum may reflect the influence of dopamine neurons located in the substantia nigra and the ventral tegmental area (VTA) [108, 109]. These neurons have extensive direct projections to the dorsal and ventral striatum. In addition, they project to cortical areas, including dorsolateral prefrontal cortex and ventral frontal cortex. The dopaminergic

synapses between these ascending brainstem projections and cortical and striatal neurons are major targets for drugs of abuse [110]. Single-unit recording studies conducted in the substantia nigra and VTA have shown that neurons in these areas fire at unexpected rewards, and they can be conditioned to fire to the earliest predictor of a reward [111]. Taken together, such experimental evidence strongly implicates the striatum, the midbrain dopamine system, and the frontal cortex in a core neural circuitry that mediates reward-related processing.

### *Developmental Effects*

Our research group in Pittsburgh has demonstrated that the response of the dorsal striatum during the processing of positive and negative feedback in children and adolescents is significantly less robust than that observed in adults, suggesting that evaluation of the relationship between actions and consequences is not fully developed by this time point [112]. In addition to these intriguing preliminary developmental data, additional experimental work is needed to understand how developmental shifts in the responsivity of the dorsal and ventral striatum 1) reflect puberty-dependent and independent phenomena, 2) are influenced by genetic and environmental influences on dopamine neurotransmission, 3) contribute to changes in reward-seeking, risk-taking and decision making and 4) contribute to individual differences in vulnerability for substance use disorders during adolescence.

### SUMMARY

Affective influences as highlighted above are relevant in many day-to-day “decisions” that are made at the level of “gut-feelings” regarding what to do in a particular situation (rather than deliberate thoughts about outcome probabilities or risk value). These gut-feelings appear to be the products of affective systems in the brain that are performing computations that are largely outside conscious awareness (except for the feelings they evoke) [113, 114]. How these feelings develop, become calibrated during maturation, and how the strengths of fears versus desires are influenced by particular types of experiences at particular points in development, are only beginning to be studied within the framework of affective neuroscience [115]. It does, however, appear that puberty and sexual maturation have important influences on at least some aspects of affective influences on behavior through new drives, motivations, and intensity of feelings, as well as new experiences that evoke strong feelings (such as developing romantic involvement) [31, 32, 116, 117].

### *A Neuroscience Perspective on Cognitive Development in Adolescence*

Until recently, much of the work on adolescent cognitive development was devoted to a search for a core mechanism that could account parsimoniously for the broad change in adolescent thinking that are observed at a more general level [39]. After nearly 50 years of searching, what has emerged instead is the necessity of an integrated account. What lies at the core of adolescent cognitive development is not likely to be any single device that drives it. Rather, it is the attainment of a more fully conscious, self-directed, and self-regulating mind that characterizes the adolescent transition. One perspective on how this is achieved focuses principally through the assembly of an advanced “executive suite” of capabilities [118], rather than through specific advancement in any one of the constituent elements. This represents a major shift in prevailing views of cognition, going beyond the search for underlying elements that are formed and operate largely outside awareness.

The plausibility of such an integrative account has been substantially enhanced by recent major advances in the neurosciences (e.g., [12, 119-126]), in comparative neuroanatomy across closely related primate species that illuminate core issues of human cognitive evolution [127-129], and in a deepened understanding of the critical role of culture and context in the shaping of cognitive and brain development [42, 127]. Much of the underlying action is focused on specific developments in the prefrontal cortex, but with an equally significant role for rapidly expanding linkages to the whole brain [121, 127, 130]. This complex process of assembly is supported by increasingly rapid connectivity (through continued myelination of nerve fibers), particularly in communication among different brain

regions, and by significant and localized synaptic pruning especially in frontal areas that are crucial to executive functioning [12, 19, 124, 125]

### ***Studies on the development of response inhibition and neurocognitive maturation of behavioral control***

Voluntary response suppression, also known as response inhibition, underlies goal-directed executive behavior through stopping planned or pre-potent responses and filtering distracters. Response inhibition is an executive process [106] that is considered central to the emergence of adult-level cognitive control of behavior [131]. Developmental studies indicate that response inhibition improves throughout childhood [132-140] and does not mature until adolescence [141-144]. These studies indicate that children and adolescents *can* suppress responses, but are unable to do so in a consistent manner, suggesting a mature brain circuitry supporting response suppression, but immature processes that support sustaining a state of cognitive control. Since impaired response inhibition has been reported for patients with lesions in frontal cortex [145], it has been suggested that late integration of frontal brain processes determined by a biologic timeline may play a primary role in the development of voluntary response suppression. Single-cell studies in non-human primates indicate that response planning and preparation are primary to response inhibition and underscore the importance of efficient top-down modulation of reflexive acts [146, 147]. Thus, response inhibition tasks such as the visual antisaccade may be effective for investigating the development of cognitive control and the transition to adult-level cognition. Moreover, these measures of inhibitory control can be used to evaluate the integrity of underlying neural circuits examined with functional and structural MRI as well as explore the functional impact of genetically driven variation on these systems.

The antisaccade task has been used by Luna and colleagues to characterize developmental improvements in voluntary response suppression in 245 8-30 year old healthy subjects. Subjects fixated a central stimulus for 3 to 5 seconds, after which a peripheral stimulus appeared for 1.5 seconds at one of three locations, 8, 16, or 24 degrees, to the left or right of center fixation. Subjects were not to look at the light, but were to move their eyes immediately to the mirror location. There were no developmental improvements in saccade velocity or accuracy in fixating the location of the visual stimulus, indicating that basic sensorimotor function is in place by 8 years of age. Subjects demonstrated significant decreases until mid-adolescence in the proportion of trials where they erroneously made saccades to the visual target indicating continued improvements in voluntary response suppression. Change-point analyses show that these developmental improvements stabilize by 15 years of age, suggesting that the circuitry underlying the cognitive/voluntary suppression of a prepotent response is not mature until late adolescence [148].

### ***Studies of Neurocognitive Development of Performance or Action Monitoring and Decision Making***

Several research groups have been examining the neural underpinnings of action monitoring (and/or error detection)—fast automatic neural processes that are an essential component to many types of decision learning. An outstanding review and set of empirical studies on the development of these systems is provided in the dissertation and published manuscripts of Eveline Crone, Ph. D [149]. For example, in one study this group examined the effects of cognitive and behavioural disinhibition on real life decision-making in three different age groups (young adults, 15-16 year-olds and 12-13 year-olds). The Disinhibition-scale of Zuckerman's Sensation Seeking Scale was used to differentiate between low vs. high in cognitive disinhibition and the Matching Familiar Figures Test was used to obtain an index of behavioural inhibition. All participants completed two versions of an experimental analogue of the Iowa Card Gambling Task. In the standard version rewards were placed up front and punishments were delayed and this schedule was reversed in the other version. The results showed impaired performance of cognitively disinhibited individuals but only on the standard task, not on the reversed gambling task. Performance increased with age on both tasks. Behavioral inhibition failed to influence performance on both versions of the gambling task. These findings were interpreted to suggest that (1) real-life decision-making is intact in cognitively disinhibited individuals, and (2) the

age-related increase in real life decision-making cannot be attributed to developmental changes in cognitive disinhibition.

Crone, Van der Molen, and colleagues have placed this line of work within a framework of developmental cognitive neuroscience, and hypotheses about regional brain maturation [149].

Another exciting link to this line of investigation has been the use of evoked potential (ERP) studies of neural mechanisms of action monitoring, focusing on a specific component called error-related negativity (ERN). Error-related negativity (ERN) is a sharp negative response-locked event-related potential (ERP) that appears to be generated in the anterior cingulate cortex (ACC) and reflects action-monitoring processes. It is usually followed by the P<sub>E</sub>, a component thought to reflect error awareness. There is evidence for late maturational changes in these systems. This includes ERN studies from [150] and from our research group in Pittsburgh [151]. This line of investigation appears to be very promising in elucidating specific developmental changes in neural systems that contribute directly to decision making processes in adolescence—especially the capacity of the brain to incorporate fast monitoring processes that may facilitate learning and adjusting action according to errors.

### ***Do Affective Influences Contribute to Adolescent “Deficiencies” in Decision-Making Capacity?***

It is well established that reasoning capabilities increase through childhood into adolescence and that preadolescents and younger teens differ substantially from adults in their cognitive abilities [39]. These basic improvements in reasoning are complemented by increases in specific and general knowledge gained through education and experience and by improvements in basic information-processing skills, including attention, short- and long-term memory, and organization [152].

By mid-adolescence, it appears that capacities for understanding and reasoning in making decisions roughly approximate those of adults [153]. However, as argued by Steinberg and colleagues, there is good reason to question whether age differences in decision making disappear by mid-adolescence, particularly as capacities may be manifested in the real-world settings in which choices about criminal activity are made [154]. Laboratory studies that are the basis of asserting that adolescents' reasoning ability is equivalent to that of adults are only modestly useful in understanding how youths compare with adults in making choices that have salience to their lives or that are presented in stressful, unstructured settings in which decision makers must rely on personal experience, knowledge, and intuition [155, 156].

In typical laboratory studies of decision making, individual adolescents are presented with hypothetical dilemmas under conditions of low emotional arousal and then asked to explain their decisions in words (rather than actions). In the real world, however, adolescents' decisions are not hypothetical, they are generally made under conditions of emotional arousal (whether negative or positive), and they usually are made in groups—situations that activate emotions and affective signals that influence behavior.

One example of an important affective component in adolescent decision-making priorities may be reflected by the observations of higher levels of sensation-seeking among adolescents (compared to adults). According to Arnett [157-159], sensation-seeking is one of the developmental contributors to risk behaviors, and is more likely to emerge during adolescence than any other time period. In a study of 1,053 Danish youth (12-20 years of age), sensation-seeking was found to be related to most types of risk behaviors (e.g., sex without contraception, marijuana use, cigarette smoking) [157]. Thus, the positive thrill associated with risk-taking sometimes has greater influence on behavioral choices than the cognitive understanding of possible negative consequences associated with the particular behavior. In similar ways the affective component of peer pressure, fears of being rejected, and the desire to be popular can sharply impact rational choice among adolescents.

Thus, the “decision” to engage in a specific behavior with long-term health consequences—such as smoking a cigarette, ingesting a drug or alcohol, or engaging in unprotected sex—cannot be completely understood within the framework of “cool” cognitive processes. “Cool” cognition refers to thinking processes under conditions of low emotion and/or arousal; while “hot” cognition refers to thinking under conditions of strong emotion or high arousal that may be more important for

understanding risky choices in many real life situations. There has been increasing evidence that neural systems that underpin “hot” cognition may involve different processes, including more ventral prefrontal as well as limbic structures [160]. Developmental research groups, including our NIMH-funded ADAPT research network on adolescent affect regulation (R24MH067346) have emphasized the increasing importance of these “hot” cognitive influences at puberty in relation to developmental psychopathology (see [161]). There is clear need to examine these developmental questions within an affective neuroscience framework. In particular, it will be important to examine the development of these affective and “hot” cognition systems, in relation to the development of inhibitory control and decision-making under “cool” or low-emotion situations.

Studies using the Experience Sampling Method, in which individuals are paged several times each day and asked to report on their emotions and activities, indicate that adolescents have more rapid and more extreme mood swings (both positive and negative) than adults, which may lead them to act more impulsively [162]. Taken together, these findings indicate that adolescents may have more difficulty regulating their moods, impulses, and behaviors than do adults. This broader range of difficulties in self-regulation of affect and behavior may represent a framework for understanding what are often called deficiencies in “decision making”.

First, patterns of individual differences in how cognition, emotion, and behavior become integrated during adolescence may well have a long reach with respect not only to the development of psychopathology but also to normative habits of mind [116] that influence trajectories of competence and coping. Second, as already noted, the pubertal influences on many hormonal and neuroendocrine systems are dramatic [23, 24], entailing the cascading reorganization of body and brain systems. Third, recent evidence from animal models has demonstrated the partial reversibility of damage acquired during early development, at both the behavioral and the physiological levels, as a function of enriched environments during puberty [42]. In combination, this evidence points strongly toward both enduring (but not limitless) neural plasticity and the critical role of developmental experience in shaping future developmental trajectories in cognition and behavior [126, 163].

### ***Romantic relationships***

Another change evident over the past twenty years is the increasing attention to romantic relationships as contexts for adolescent development [36, 164, 165]). Romantic relationships emerge in adolescence, though they may remain exploratory until early adulthood. These special peer relationships, spurred by new motivational systems, pubertal processes, and a culture promoting adolescent sexuality and romance, offer a new realm of possibilities for adolescents to experience emotional extremes of happiness, excitement, disappointment, and despair. Romantic feelings appear to be powerful activators of behavior; concomitantly, romantic relationships appear to be powerful regulators of arousal and affect [32, 164, 166].

As noted earlier, early maturation is a risk factor for a variety of problems; for some girls, this risk appears to be mediated by romantic relationships with older boys [36]. Break-ups of romantic relationships also may trigger great distress in adolescents [166]. At the same time, there has been speculation that the formation of romantic relationships may improve behavior among antisocial males, perhaps through differential time with deviant peers. Recent work based on sexual selection theory also suggests that peer group dominance among males and relational aggression among females are related over time to dating popularity in young adolescents [63]. Though still limited, the growing literature on romantic relationships in adolescence suggests that these relationships may play complex roles in social development and the regulation of affect, with positive and negative ramifications.

### ***Media and Virtual Contexts***

While many of the traditional “contexts” of adolescence development—involving family, peers, school, neighborhoods, and work—readily fit an embedded systems model of development, as proposed by Bronfenbrenner and others, other elements of context in adolescents’ lives do not fit so neatly [167]. Yet these experiences may play an enormous and growing role in adolescent

development. In particular, music, movies, and television, as well as the new virtual worlds of electronic games, websites, and Internet chat rooms saturate the lives of many adolescents many hours a day, penetrating most other contexts of interaction.

The “media diet” [168] of American teenagers reflects a rapidly changing and increasingly individualized context for learning, self-regulation, victimization, friendship formation, sex, violence, illegal activity, and self-discovery, among other processes. Teenagers clearly utilize music, phones, movies, games, chat rooms, instant messaging, e-mail, and other electronic media to meet all kinds of needs. Increasingly these media can be tailored to individual desires, so that adolescents can fine tune their own experiences. Concomitantly, the same strategies can be utilized by marketers to recruit teenagers as consumers, often with the promise of happiness or sex appeal through consumption of food or drugs, or the purchase of goods and services. The role of these transactions in the development of avoidance of psychopathology, misery, antisocial behavior, or risk-taking behavior is only beginning to be considered, as concern grows about the unmonitored interactions of adolescents through these media on violence, depression, self-injury behavior, substance use, and many other problems or risky behaviors.

### IN SUMMARY:

Pubertal maturation and adolescent development are associated with complex changes in affective systems impacting emotion, motivation, sensation-seeking, and emotional influences on decision-making. Adolescence, and more specifically pubertal maturation, represents a developmental period where there is a sharp increase in rates of behavioral and emotional health problems—especially risky behavior and sensation seeking. A barrier to developing more effective interventions (and ultimately better prevention) is the lack of understanding how normative changes in affective and motivational neurobehavioral systems interact with genetic and environmental factors to bias adolescent tendencies toward risk-taking and sensation-seeking, and, in an extended fashion, to substance use, abuse, and dependence in youth. Progress in developing more effective early intervention and prevention strategies will benefit from a stronger foundation of knowledge about these normal developmental changes and their variants.

Developing and refining a more integrated heuristic model of affective and other implicit and procedurally learned influences on behavior and decision making, appears crucial. There is also a need to empirically test key features of these conceptual models which can provide valuable contributions toward these goals and significantly impact the health and well being of youth.

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## REFERENCES

1. Davidson, R.J., D.C. Jackson, and N.H. Kalin, *Emotion, plasticity, context, and regulation: perspectives from affective neuroscience*. Psychol Bull, 2000. 126(6): p. 890-909.
2. Rolls, E.T., *The brain and emotion*. 1999, New York: Oxford University Press.
3. LeDoux, J.E., *Emotion circuits in the brain*. Annu Rev Neurosci, 2000. 23: p. 155-84.
4. Damasio, A.R., *Descartes' error and the future of human life*. Sci Am, 1994. 271(4): p. 144.
5. Lerner, J.S., D.A. Small, and G. Loewenstein, *Heart strings and purse strings: Carryover effects of emotions on economic decisions*. Psychol Sci, 2004. 15(5): p. 337-41.
6. Slovic, P., et al., *The affect heuristic*, in *Heuristics and biases: The psychology of intuitive judgment*, T. Gilovich, D. Griffin, and D. Kahneman, Editors. 2002, Cambridge University Press: Cambridge. p. 534-547.
7. Dolan, R.J., *Emotion, cognition, and behavior*. Science, 2002. 298(5596): p. 1191-4.
8. Dahl, R.E., *Adolescent brain development: a period of vulnerabilities and opportunities. Keynote address*. Ann N Y Acad Sci, 2004. 1021: p. 1-22.
9. Resnick, M.D., et al., *Protecting adolescents from harm. Findings from the National Longitudinal Study on Adolescent Health*. Jama, 1997. 278(10): p. 823-32.
10. Ozer, E.M., et al., *Provider self-efficacy and the screening of adolescents for risky health behaviors*. J Adolesc Health, 2004. 35(2): p. 101-7.
11. Force, R.C., *An outcome measure for postdischarge follow-up of residential treatment*. Psychiatr Serv, 1996. 47(5): p. 481-2.
12. Giedd, J.N., et al., *Brain development during childhood and adolescence: a longitudinal MRI study*. Nat Neurosci, 1999. 2(10): p. 861-3.
13. Dahl, R.E. *Adolescent Brain Development*. in *Annals of the New York Academy of Sciences*. 2004.
14. Carskadon, M.A., *Adolescent sleep patterns: biological, social, and psychological influences*. 1999, New York: Cambridge University Press.
15. Giedd, J., *Brain development, IX: human brain growth*. Am J Psychiatry, 1999. 156(1): p. 4.
16. Sowell, E.R., et al., *In vivo evidence for post-adolescent brain maturation in frontal and striatal regions*. Nat Neurosci, 1999. 2(10): p. 859-61.
17. Courchesne, E., et al., *Normal brain development and aging: quantitative analysis at in vivo MR imaging in healthy volunteers*. Radiology, 2000. 216(3): p. 672-82.
18. Thompson, P.M., et al., *Growth patterns in the developing brain detected by using continuum mechanical tensor maps*. Nature, 2000. 404(6774): p. 190-3.
19. Sowell, E.R., et al., *Mapping continued brain growth and gray matter density reduction in dorsal frontal cortex: Inverse relationships during postadolescent brain maturation*. J Neurosci, 2001. 21(22): p. 8819-29.
20. Spear, L.P., *The adolescent brain and age-related behavioral manifestations*. Neurosci Biobehav Rev, 2000. 24(4): p. 417-63.
21. Costello, E.J., et al., *The Great Smoky Mountains Study of Youth. Goals, design, methods, and the prevalence of DSM-III-R disorders*. Arch Gen Psychiatry, 1996. 53(12): p. 1129-36.
22. Angold, A., *Adolescent depression, cortisol and DHEA*. Psychol Med, 2003. 33(4): p. 573-81.

23. Angold, A., et al., *Pubertal changes in hormone levels and depression in girls*. *Psychol Med*, 1999. 29(5): p. 1043-53.
24. Angold, A., E.J. Costello, and C.M. Worthman, *Puberty and depression: the roles of age, pubertal status and pubertal timing*. *Psychol Med*, 1998. 28(1): p. 51-61.
25. Angold, A., et al., *Depression scale scores in 8-17-year-olds: effects of age and gender*. *J Child Psychol Psychiatry*, 2002. 43(8): p. 1052-63.
26. Martin, C.A., et al., *Sensation seeking, puberty, and nicotine, alcohol, and marijuana use in adolescence*. *J Am Acad Child Adolesc Psychiatry*, 2002. 41(12): p. 1495-502.
27. Worthman, C., *Epidemiology of human development*, in *Hormones, Health, and Behavior: A Socio-Ecological and Lifespan Perspective*, C. Panter-Brick and C. Worthman, Editors. 1999, Cambridge University Press: New York. p. 63-70.
28. Jernigan, T.L. and E.R. Sowell, *Magnetic resonance imaging studies of developing brain*, in *Neurodevelopment and Adult Psychopathology*, M.S. Keshvan and R.M. Murray, Editors. 1997, Cambridge University Press: Cambridge. p. 63-70.
29. Sowell, E.R. and T.L. Jernigan, *Further MRI evidence of late brain maturation: Limbic volume increases and changing asymmetries during childhood and adolescence*. *Developmental Neurophysiology*, 1998. 14(4): p. 599-617.
30. Lewis, D.A., *Development of the prefrontal cortex during adolescence: insights into vulnerable neural circuits in schizophrenia*. *Neuropsychopharmacology*, 1997. 16(6): p. 385-98.
31. Keating, D. and J. Shapka. *Pubertal change, cognitive change, and the development of psychopathology in adolescence: summary of current work*. in *MacArthur Foundation Research Network on Psychopathology and Development*. 1999.
32. Richards, M.H., et al., *Developmental patterns and gender differences in the experience of peer companionship during adolescence*. *Child Dev*, 1998. 69(1): p. 154-63.
33. Udry, J.R., *Hormonal and social determinants of adolescent sexual initiation*, in *Adolescence and puberty*, J. Bancroft, Editor. 1987, Oxford University Press: New York. p. 70-87.
34. Steinberg, L., *Reciprocal relation between parent-child distance and pubertal maturation*. *Developmental Psychology*, 1988. 24(1): p. 122-128.
35. Steinberg, L., *Pubertal maturation and parent-adolescent distance: An evolutionary perspective*, in *Advances in Adolescent Development*, G. Adams, R. Montemayor, and T. Gullotta, Editors. 1989, Sage: Beverly Hills.
36. Steinberg, L. and A.S. Morris, *Adolescent development*. *Annu Rev Psychol*, 2001. 52: p. 83-110.
37. Steinberg, L., *Adolescence*. Fifth ed. 1999, New York: McGraw-Hill College.
38. Steinberg, L., et al., *The Study of Developmental Psychopathology in Adolescence: Integrating Affective Neuroscience with the Study of Context*. *Development and Psychopathology*, In Press.
39. Keating, D.P., *Cognitive and brain development*, in *Handbook of Adolescent Psychology*, R.J. Lerner and L.D. Steinberg, Editors. 2004, Wiley and Sons: New York.
40. Liu, G., et al., *Molecular and cellular aspects of allergic conjunctivitis*. *Chem Immunol*, 1999. 73: p. 39-58.
41. Meaney, M.J., et al., *Effect of neonatal handling on age-related impairments associated with the hippocampus*. *Science*, 1988. 239(4841 Pt 1): p. 766-8.
42. Francis, D.D., et al., *Environmental enrichment reverses the effects of maternal separation on stress reactivity*. *J Neurosci*, 2002. 22(18): p. 7840-3.

43. Greenough, W.T., J.R. Larson, and G.S. Withers, *Effects of unilateral and bilateral training in a reaching task on dendritic branching of neurons in the rat motor-sensory forelimb cortex*. Behav Neural Biol, 1985. 44(2): p. 301-14.
44. Kolb, B., *Synaptic plasticity and the organization of behaviour after early and late brain injury*. Can J Exp Psychol, 1999. 53(1): p. 62-76.
45. Lewis, D.A., et al., *Postnatal development of prefrontal inhibitory circuits and the pathophysiology of cognitive dysfunction in schizophrenia*. Ann N Y Acad Sci, 2004. 1021: p. 64-76.
46. Berman, K.F., et al., *Modulation of cognition-specific cortical activity by gonadal steroids: a positron-emission tomography study in women*. Proc Natl Acad Sci U S A, 1997. 94(16): p. 8836-41.
47. Shaywitz, S.E., et al., *Effect of estrogen on brain activation patterns in postmenopausal women during working memory tasks*. Jama, 1999. 281(13): p. 1197-202.
48. Roozendaal, C., et al., *Clinical significance of anti-neutrophil cytoplasmic antibodies (ANCA) in autoimmune liver diseases*. J Hepatol, 2000. 32(5): p. 734-41.
49. Galanter, C.A., et al., *Changes in autonomic regulation with age: implications for psychopharmacologic treatments in children and adolescents*. J Child Adolesc Psychopharmacol, 1999. 9(4): p. 257-65.
50. Arnsten, A.F., et al., *Noradrenergic influences on prefrontal cortical cognitive function: opposing actions at postjunctional alpha 1 versus alpha 2-adrenergic receptors*. Adv Pharmacol, 1998. 42: p. 764-7.
51. Rosenberg, D.R. and D.A. Lewis, *Postnatal maturation of the dopaminergic innervation of monkey prefrontal and motor cortices: a tyrosine hydroxylase immunohistochemical analysis*. J Comp Neurol, 1995. 358(3): p. 383-400.
52. Cohen, R.M., et al., *The brain metabolic patterns of clozapine- and fluphenazine-treated female patients with schizophrenia: evidence of a sex effect*. Neuropsychopharmacology, 1999. 21(5): p. 632-40.
53. Cohen, Y.E. and C.M. Wessinger, *Who goes there?* Neuron, 1999. 24(4): p. 769-71.
54. Davidson, R.J., et al., *Depression: perspectives from affective neuroscience*. Annu Rev Psychol, 2002. 53: p. 545-74.
55. Drevets, W.C., *Neuroimaging abnormalities in the orbital and medial prefrontal cortex and amygdala in mood disorders: Implications for a neural circuitry-based approach to major depression*. Biol Psychiatry, 2000.
56. Carter, C.S., et al., *Anterior cingulate cortex, error detection, and the online monitoring of performance*. Science, 1998. 280(5364): p. 747-9.
57. Neeman, J., J. Hubbard, and A. Masten, *The changing importance of romantic relationship involvement to competence from late childhood to late adolescence*. Development and Psychopathology, 1995. 7: p. 727-750.
58. Diamond, R., S. Carey, and K. Back, *Genetic influences on the development of spatial skills during early adolescence*. Cognition, 1983. 13: p. 167-185.
59. Mann, V., R. Diamond, and S. Carey, *Development of voice recognition: Parallels with face recognition*. Journal of Experimental Child Psychology, 1979. 27: p. 153-165.
60. Book, A., K. Starzyk, and V. Qunisey, *The relationship between testosterone and aggression: A meta-analysis*. Aggression & Violent Behavior, 2001. 6: p. 579-599.
61. Josephs, R.A., et al., *Status, testosterone, and human intellectual performance: Stereotype threat as status concern*. Psychological Science, 2003. 14: p. 158-163.
62. Moffitt, T.E., *Adolescence-limited and life-course-persistent antisocial behavior: a developmental taxonomy*. Psychol Rev, 1993. 100(4): p. 674-701.

63. Pellegrini, A.D. and J.D. Long, *A sexual selection theory longitudinal analysis of sexual segregation and integration in early adolescence*. *J Exp Child Psychol*, 2003. 85(3): p. 257-78.
64. Bechara, A., et al., *Different contributions of the human amygdala and ventromedial prefrontal cortex to decision-making*. *J Neurosci*, 1999. 19(13): p. 5473-81.
65. Damasio, A.R., *The somatic marker hypothesis and the possible functions of the prefrontal cortex*. *Philos Trans R Soc Lond B Biol Sci*, 1996. 351(1346): p. 1413-20.
66. Rosenkranz, J.A., H. Moore, and A.A. Grace, *The prefrontal cortex regulates lateral amygdala neuronal plasticity and responses to previously conditioned stimuli*. *J Neurosci*, 2003. 23(35): p. 11054-64.
67. Garcia, R., *Postextinction of conditioned fear: between two CS-related memories*. *Learn Mem*, 2002. 9(6): p. 361-3.
68. Quirk, G.J., et al., *Stimulation of medial prefrontal cortex decreases the responsiveness of central amygdala output neurons*. *J Neurosci*, 2003. 23(25): p. 8800-7.
69. Beauregard, M., J. Levesque, and P. Bourgouin, *Neural correlates of conscious self-regulation of emotion*. *J Neurosci*, 2001. 21(18): p. RC165.
70. Hariri, A.R., S.Y. Bookheimer, and J.C. Mazziotta, *Modulating emotional responses: effects of a neocortical network on the limbic system*. *Neuroreport*, 2000. 11(1): p. 43-8.
71. Hariri, A.R., et al., *Brain-derived neurotrophic factor val66met polymorphism affects human memory-related hippocampal activity and predicts memory performance*. *J Neurosci*, 2003. 23(17): p. 6690-4.
72. Keightley, M.L., et al., *An fMRI study investigating cognitive modulation of brain regions associated with emotional processing of visual stimuli*. *Neuropsychologia*, 2003. 41(5): p. 585-96.
73. Lange, K., et al., *Task instructions modulate neural responses to fearful facial expressions*. *Biol Psychiatry*, 2003. 53(3): p. 226-32.
74. Narumoto, J., et al., *Brain regions involved in verbal or non-verbal aspects of facial emotion recognition*. *Neuroreport*, 2000. 11(11): p. 2571-6.
75. Siegle, G.J., et al., *Can't shake that feeling: event-related fMRI assessment of sustained amygdala activity in response to emotional information in depressed individuals*. *Biol Psychiatry*, 2002. 51(9): p. 693-707.
76. Kapler, E.S., et al. *Correlated attenuation of amygdala and autonomic processes: a simultaneous fMRI and SCR study*. in *Society for Neuroscience*. 2001. New Orleans.
77. Drevets, W.C., et al., *A functional anatomical study of unipolar depression*. *J Neurosci*, 1992. 12(9): p. 3628-41.
78. Drevets, W.C., et al., *PET imaging of serotonin 1A receptor binding in depression*. *Biol Psychiatry*, 1999. 46(10): p. 1375-87.
79. Abercrombie, H.C., et al., *Metabolic rate in the right amygdala predicts negative affect in depressed patients*. *Neuroreport*, 1998. 9(14): p. 3301-7.
80. Mayberg, H.S., et al., *Paralimbic hypoperfusion in unipolar depression*. *J Nucl Med*, 1994. 35(6): p. 929-34.
81. Sheline, Y.I., et al., *Increased amygdala response to masked emotional faces in depressed subjects resolves with antidepressant treatment: an fMRI study*. *Biol Psychiatry*, 2001. 50(9): p. 651-8.
82. Dougherty, D. and S.L. Rauch, *Neuroimaging and neurobiological models of depression*. *Harv Rev Psychiatry*, 1997. 5(3): p. 138-59.
83. Baxter, L.R., Jr., et al., *Reduction of prefrontal cortex glucose metabolism common to three types of depression*. *Arch Gen Psychiatry*, 1989. 46(3): p. 243-50.

84. Bench, C.J., et al., *Regional cerebral blood flow in depression measured by positron emission tomography: the relationship with clinical dimensions*. *Psychol Med*, 1993. 23(3): p. 579-90.
85. Hayward, C., et al., *Pubertal stage and panic attack history in sixth- and seventh-grade girls*. *Am J Psychiatry*, 1992. 149(9): p. 1239-43.
86. Hayward, C., et al., *Predictors of panic attacks in adolescents*. *J Am Acad Child Adolesc Psychiatry*, 2000. 39(2): p. 207-14.
87. Hayward, C., et al., *Cognitive-behavioral group therapy for social phobia in female adolescents: results of a pilot study*. *J Am Acad Child Adolesc Psychiatry*, 2000. 39(6): p. 721-6.
88. Pine, D.S., et al., *Psychiatric symptoms in adolescence as predictors of obesity in early adulthood: a longitudinal study*. *Am J Public Health*, 1997. 87(8): p. 1303-10.
89. Pine, D.S., et al., *The risk for early-adulthood anxiety and depressive disorders in adolescents with anxiety and depressive disorders*. *Arch Gen Psychiatry*, 1998. 55(1): p. 56-64.
90. Weissman, M.M., et al., *The cross-national epidemiology of panic disorder*. *Arch Gen Psychiatry*, 1997. 54(4): p. 305-9.
91. Eaton, Y.M., M.L. Mitchell, and J.M. Jolley, *Gender differences in the development of relationships during late adolescence*. *Adolescence*, 1991. 26(103): p. 565-8.
92. Gurley, D., et al., *Discriminating depression and anxiety in youth: a role for diagnostic criteria*. *J Affect Disord*, 1996. 39(3): p. 191-200.
93. Klein, D.N., et al., *Family study of early-onset dysthymia. Mood and personality disorders in relatives of outpatients with dysthymia and episodic major depression and normal controls*. *Arch Gen Psychiatry*, 1995. 52(6): p. 487-96.
94. Thomas, K.M., et al., *Amygdala response to fearful faces in anxious and depressed children*. *Arch Gen Psychiatry*, 2001. 58(11): p. 1057-63.
95. Thomas, K.M., et al., *Amygdala response to facial expressions in children and adults*. *Biol Psychiatry*, 2001. 49(4): p. 309-16.
96. Lucki, I., *The spectrum of behaviors influenced by serotonin*. *Biol Psychiatry*, 1998. 44(3): p. 151-62.
97. Azmitia, E.C. and P.J. Gannon, *The primate serotonergic system: a review of human and animal studies and a report on Macaca fascicularis*. *Adv Neurol*, 1986. 43: p. 407-68.
98. Hariri, A.R., et al., *Dextroamphetamine modulates the response of the human amygdala*. *Neuropsychopharmacology*, 2002. 27(6): p. 1036-40.
99. Hariri, A.R., et al., *A susceptibility gene for affective disorders and the response of the human amygdala*. *Arch Gen Psychiatry*, 2004. in press.
100. Heinz, A., M. Smolka, and D. Braus, *Amygdala activation, prefrontal metabolism and the serotonin transporter*. *Biol Psychiatry*, 2004. 55(8(S1)): p. 43.
101. Caspi, A., et al., *Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene*. *Science*, 2003. 301(5631): p. 386-9.
102. Bethea, C.L., et al., *Diverse actions of ovarian steroids in the serotonin neural system*. *Front Neuroendocrinol*, 2002. 23(1): p. 41-100.
103. Schultz, W., P. Dayan, and P.R. Montague, *A neural substrate of prediction and reward*. *Science*, 1997. 275(5306): p. 1593-9.
104. Schultz, W., *Multiple reward signals in the brain*. *Nat Rev Neurosci*, 2000. 1(3): p. 199-207.
105. Berridge, K.C. and T.E. Robinson, *Parsing reward*. *Trends Neurosci*, 2003. 26(9): p. 507-13.
106. Fuster, J.M., *The Prefrontal Cortex*. Third ed. 1997, Philadelphia: Lippincott-Raven.

107. Schultz, W., L. Tremblay, and J.R. Hollerman, *Reward prediction in primate basal ganglia and frontal cortex*. *Neuropharmacology*, 1998. 37(4-5): p. 421-9.
108. Schultz, W., *Getting formal with dopamine and reward*. *Neuron*, 2002. 36(2): p. 241-63.
109. Schultz, W., *Dopamine neurons and their role in reward mechanisms*. *Curr Opin Neurobiol*, 1997. 7(2): p. 191-7.
110. Volkow, N.D., et al., *Role of dopamine in the therapeutic and reinforcing effects of methylphenidate in humans: results from imaging studies*. *Eur Neuropsychopharmacol*, 2002. 12(6): p. 557-66.
111. Schultz, W. and A. Dickinson, *Neuronal coding of prediction errors*. *Annu Rev Neurosci*, 2000. 23: p. 473-500.
112. May, J.C., et al., *Event-related functional magnetic resonance imaging of reward-related brain circuitry in children and adolescents*. *Biol Psychiatry*, 2004. 55(4): p. 359-66.
113. Bechara, A., H. Damasio, and A.R. Damasio, *Role of the amygdala in decision-making*. *Ann N Y Acad Sci*, 2003. 985: p. 356-69.
114. Damasio, A.R., et al., *Subcortical and cortical brain activity during the feeling of self-generated emotions*. *Nat Neurosci*, 2000. 3(10): p. 1049-56.
115. Dahl, R.E., *Affect Regulation, Brain Development, and Behavioral/Emotional Health in Adolescence*. *CNS Spectrums*, 2001. 6(1): p. 60-72.
116. Keating, D.P. and D.K. Sasse, *Cognitive socialization in adolescence: Critical period for a critical habit of mind*, in *Psychosocial development during adolescence: Progress in developmental contextualism*, T.P. Gullota, Editor. 1996, Sage: Thousand Oaks. p. 232-258.
117. Pine, D.S., J. Grun, and E. Zarahn, *Cortical brain regions engaged by masked emotional faces in adolescents and adults: An fMRI study*. *Emotion*, In Press.
118. Donald, M., et al., *Prevalence of adverse life events, depression and suicidal thoughts and behaviour among a community sample of young people aged 15-24 years*. *Aust N Z J Public Health*, 2001. 25(5): p. 426-32.
119. Casey, B.J., J.N. Giedd, and K.M. Thomas, *Structural and functional brain development and its relation to cognitive development*. *Biol Psychol*, 2000. 54(1-3): p. 241-57.
120. Johnson, M.H., *Functional brain development in humans*. *Nat Rev Neurosci*, 2001. 2(7): p. 475-83.
121. Luna, B., et al., *Maturation of widely distributed brain function subserves cognitive development*. *Neuroimage*, 2001. 13(5): p. 786-93.
122. Paus, T., *Imaging the brain before, during, and after transcranial magnetic stimulation*. *Neuropsychologia*, 1999. 37(2): p. 219-24.
123. Sowell, E.R., et al., *Improved memory functioning and frontal lobe maturation between childhood and adolescence: a structural MRI study*. *J Int Neuropsychol Soc*, 2001. 7(3): p. 312-22.
124. Sowell, E.R., et al., *Development of cortical and subcortical brain structures in childhood and adolescence: a structural MRI study*. *Dev Med Child Neurol*, 2002. 44(1): p. 4-16.
125. Steingard, R.J., et al., *Smaller frontal lobe white matter volumes in depressed adolescents*. *Biol Psychiatry*, 2002. 52(5): p. 413-7.
126. Nelson, C.A., *Neural plasticity and human development*. *Current Directions in Psychological Science*, 1999. 8: p. 42-45.
127. Donald, A. and L. Van Til, *Evaluating screening tests for dementia and cognitive impairment in a heterogeneous population in the presence of verification bias*. *Int Psychogeriatr*, 2001. 13 Supp 1: p. 203-14.
128. Rilling, J.K. and T.R. Insel, *The primate neocortex in comparative perspective using magnetic resonance imaging*. *J Hum Evol*, 1999. 37(2): p. 191-223.

129. Rilling, J.K. and T.R. Insel, *Differential expansion of neural projection systems in primate brain evolution*. *Neuroreport*, 1999. 10(7): p. 1453-9.
130. Newman, J. and A.A. Grace, *Binding across time: the selective gating of frontal and hippocampal systems modulating working memory and attentional states*. *Conscious Cogn*, 1999. 8(2): p. 196-212.
131. Bjorklund, A. and S.B. Dunnett, *Cognitive function. Acetylcholine revisited*. *Nature*, 1995. 375(6531): p. 446.
132. Paus, T., et al., *Oculomotor and electrophysiological signs of distractibility in schizophrenics*. *Act Nerv Super (Praha)*, 1990. 32(2): p. 147-8.
133. Levin, B. and S. Pinker, *Introduction to special issue of Cognition on lexical and conceptual semantics*. *Cognition*, 1991. 41(1-3): p. 1-7.
134. Luciana, M. and C.A. Nelson, *The functional emergence of prefrontally-guided working memory systems in four- to eight-year-old children*. *Neuropsychologia*, 1998. 36(3): p. 273-93.
135. Luciana, M., P.F. Collins, and R.A. Depue, *Opposing roles for dopamine and serotonin in the modulation of human spatial working memory functions*. *Cereb Cortex*, 1998. 8(3): p. 218-26.
136. Wise, L., J.A. Sutton, and P.D. Gibbons, *Decrement in Stroop interference time with age*. *Perceptual and Motor Skills*, 1975. 41: p. 149-150.
137. Tipper, S.P., et al., *Mechanisms of attention: a developmental study*. *J Exp Child Psychol*, 1989. 48(3): p. 353-78.
138. Ridderinkhof, K.R. and G.D. Logan, *A study of adaptive behavior: effects of age and irrelevant information on the ability to inhibit one's actions*. *Acta Psychologica*, 1999. 101: p. 315-337.
139. Ridderinkhof, K.R., et al., *Sources of interference from irrelevant information: a developmental study*. *J Exp Child Psychol*, 1997. 65(3): p. 315-41.
140. Williams, B.R., et al., *Development of inhibitory control across the life span*. *Dev Psychol*, 1999. 35(1): p. 205-13.
141. Fischer, B., M. Biscaldi, and S. Gezeck, *On the development of voluntary and reflexive components in human saccade generation*. *Brain Res*, 1997. 754(1-2): p. 285-97.
142. Klein, C. and F. Foerster, *Development of prosaccade and antisaccade task performance in participants aged 6 to 26 years*. *Psychophysiology*, 2001. 38(2): p. 179-89.
143. Munoz, D.P., et al., *Age-related performance of human subjects on saccadic eye movement tasks*. *Exp Brain Res*, 1998. 121(4): p. 391-400.
144. Fukushima, J., T. Hatta, and K. Fukushima, *Development of voluntary control of saccadic eye movements. I. Age-related changes in normal children*. *Brain Dev*, 2000. 22(3): p. 173-80.
145. Guitton, D., H.A. Buchtel, and R.M. Douglas, *Frontal lobe lesions in man cause difficulties in suppressing reflexive glances and in generating goal-directed saccades*. *Exp Brain Res*, 1985. 58(3): p. 455-72.
146. Everling, S., et al., *Role of primate superior colliculus in preparation and execution of anti-saccades and pro-saccades*. *J Neurosci*, 1999. 19(7): p. 2740-54.
147. Everling, S. and D.P. Munoz, *Neuronal correlates for preparatory set associated with pro-saccades and anti-saccades in the primate frontal eye field*. *J Neurosci*, 2000. 20(1): p. 387-400.
148. Luna, B. and J.A. Sweeney. *Development in cognitive and sensorimotor systems from late childhood to adulthood*. in *30th Annual meeting of the Society for Neuroscience*. 2000.

149. Crone, E., I. Vendel, and M.W. van der Molen, *Decision-making in disinhibited adolescents and adults: Insensitivity to future consequences or driven by immediate reward?* In press.
150. Davies, P.L., S.J. Segalowitz, and W.J. Gavin, *Development of error-monitoring event-related potentials in adolescents*. *Ann N Y Acad Sci*, 2004. 1021: p. 324-8.
151. Ladouceur, C.D., R.E. Dahl, and C.S. Carter, *ERP correlates of action monitoring in adolescence*. *Ann N Y Acad Sci*, 2004. 1021: p. 329-36.
152. Siegler, R.S. and P. Lemaire, *Older and younger adults' strategy choices in multiplication: testing predictions of ASCM using the choice/no-choice method*. *J Exp Psychol Gen*, 1997. 126(1): p. 71-92.
153. Furby, A., et al., *Motor evoked potentials to magnetic stimulation: technical considerations and normative data from 50 subjects*. *J Neurol*, 1992. 239(3): p. 152-6.
154. Cauffman, E. and L. Steinberg, *The cognitive and affective influences on adolescent decision-making*. *Temple Law Review*, 1995. 68: p. 1763-1789.
155. Cauffman, E. and L. Steinberg, *(Im)maturity of judgment in adolescence: why adolescents may be less culpable than adults*. *Behav Sci Law*, 2000. 18(6): p. 741-60.
156. Steinberg, L., *Is decision-making the right framework for the study of adolescent risk-taking?*, in *Reducing adolescent risk: Toward an integrated approach*, D. Romer, Editor. 2003, Sage: Thousand Oaks. p. 18-24.
157. Arnett, J. and L. Balle-Jensen, *Cultural bases of risk behavior: Danish adolescents*. *Child Dev*, 1993. 64(6): p. 1842-55.
158. Arnett, J., *Reckless behavior in adolescence: A developmental perspective*. *Developmental Review*, 1992. 12: p. 339-373.
159. Arnett, J., *Sensation seeking: A new conceptualizing and a new scale*. *Personality and Individual Differences*, 1994. 16: p. 1842-1855.
160. Goel, V. and R.J. Dolan, *Reciprocal neural response within lateral and ventral medial prefrontal cortex during hot and cold reasoning*. *Neuroimage*, 2003. 20(4): p. 2314-21.
161. Steinberg, L., *Risk taking in adolescence: what changes, and why?* *Ann N Y Acad Sci*, 2004. 1021: p. 51-8.
162. Larson, R., M. Csikszentmihalyi, and R. Graef, *Mood variability and the psychosocial adjustment of adolescents*. *Journal of Youth & Adolescence [Peer Reviewed Journal]*, 1980. 9(6): p. 469-490.
163. Nelson, C.A., et al., *An integrative, multidisciplinary approach to the study of brain-behavior relations in the context of typical and atypical development*. *Dev Psychopathol*, 2002. 14(3): p. 499-520.
164. Furman, W., B.B. Brown, and C. Feiring, *The development of romantic relationships in adolescence*. 1999, New York: Cambridge University Press.
165. Collins, W.A. and B. Laursen, *Relationships as developmental contexts: The Minnesota Symposia on Child Psychology*. Vol. 30. 1999, Mahweh: Erlbaum.
166. Larson, R.W., G.L. Clore, and G.A. Wood, *The emotions of romantic relationships: Do they wreak havoc on adolescents?*, in *The development of romantic relationships in adolescence*, W. Furman, B.B. Brown, and C. Feiring, Editors. 1999, Cambridge University Press: New York. p. 19-49.
167. Bronfenbrenner, U., *The ecology of human development: Experiments by nature and design*. 1979, Cambridge: Harvard University Press.
168. Brown, J.D., *Adolescents' sexual media diets*. *J Adolesc Health*, 2000. 27(2 Suppl): p. 35-40.