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Brain Plasticity during Adolescence: Effects of Stress, Sleep, Sex and Sounds on Decision Making

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Abstract

Adolescence represents a critical time window of neural plasticity when different regions of the brain are still maturing. This phase of life is associated with risk taking and impulsivity and these behavioral outcomes are expected to be adaptive. Personality traits, stress, sleep deprivation as well as a person's sex influence adolescent risk taking, behavior. The effects of these factors rangefrom the anatomical to the molecular levels. Risk taking behavior is controlled by extensive interactions between the prefrontal cortexes the limbic system and the dopamine signaling system. In adolescent brains, limbic regions mature at a faster rate than the impulse-managing prefrontal regions. As a result, the neurological transformation from childhood to adulthood can create an imbalance in the neural circuitry controllingdecision making and especially risk taking behaviors. Here we discuss the neural basis ofrisk taking in adolescents at the anatomical, physiological and molecular levels and examine how stress and other factors influence the neurodevelopmental process. We postulate that musical sounds processed by some of the same brain regions involved in decision making can impact the developing neural circuits and physiological status into early adulthood.

Keywords: Stress; Sleep; Sex; Decision making; Brain plasticity

Introduction

Research findings over the past two decades have firmly established the plasticity inherent in all brains, including the human brain. In fact, plasticity is the essence of learning and this primary function of neural circuits allows organisms to adapt to their environment. The degree to which neural circuits are modifiable, however, changes over the time course of one's life. The time period during which a system is maximally plastic is called a critical time window, which terminates with the crystallization of a generally irreversible behavioral outcome. In humans, many critical time windows that open and close during brain development are closely associated with the teenage years, also referred to as "adolescence". Although this adolescent period may seem disadvantageous and inconvenient for everyday modern life with its traditional societal rules and norms, it is in fact a naturally selected phase in the development of individuals of many species.

Adolescence is a stage in human development, which represents a prolonged (compared to other species) transition from childhood to adulthood. It is a time when an individual experiences many physiological and associated physical changes in the brain and body. In contrast to adults, adolescents typically have high emotional reactivity, which results from an imbalance between the emotional and control systems [1]. Adolescence allows an individual to acquire skills necessary for independence from the family. This phase of one's life is characterized by novelty and sensation seeking, grouping with similar age groups and conflicts with parents, as a young individual strives to adapt, learning new abilities and indulging in mate selection for reproductive success [2].

Many species go through a distinctive developmental period during which they are vulnerable to disorders and addictions [3]. Rats share a similar pubertal change as humans do during their development [4] and "adolescent mice" show heightened novelty seeking compared to adult mice [5]. In studies on rats, stress and gender or sex were found to have significant impact on risk taking behavior specifically related to forced swims and mazes [4].

Here, we will examine the neurobiological basis of brain plasticity and its behavioral expression during adolescence. We will also investigate the consequences of physiological and social factors that can interfere and interrupt the "normal" developmental process and the associated risk taking behaviors and their impact on decision making as a whole. We will describe the brain regions and mechanisms that partake in developmental plasticity in the teen brain from the viewpoint of decision making and how they are disrupted by chronic stress and sleep deprivation, which ravages the teenage or "teen" brain in most modern societies. We will also briefly discuss the differences in the influence of these agents among males vs. females and finally, how sounds have a potential to prevent and protect the relevant circuitry and synaptic connectivity from going array. By understanding this process, we argue and hope that the negative consequences of risk-taking by adolescents can be averted or minimized, while still allowing creativity and productivity to flourish within a society. This knowledge and understanding can eventually ensure the freedom of all individuals within a progressive society.

Risk taking During Adolescence

From an ontogenetic perspective, decision making first appears to be under emotional/impulsive control (a fast, mostly automatic system), evolving progressively towards a larger involvement of

cognitive function (a slow, deliberate system) [6]. Risk taking is a decision making behavior that varies with age and depends on multiple factors, such as personality correlates, self-regulating processes, and cognitive vs. impulse control [7]. All of these factors are discussed in more detail later. All behaviors can be considered as a sequence of explicit or implicit decisions. Decision making involves approach (motivation), avoidance (anxiety or negative emotion), and willingness to work toward a certain goal (regulation of motivation). Emotion refers to feelings that individual's experience and that influences their physiological status and the direction of their behaviors. Adolescence is typically associated with a lack of impulse control and relatively more risk taking than young children or adults. Their departure from the established norms of society is a natural outcome of brain plasticity that is designed to adapt and improve a population. It allows nature to experiment and ensure that mistakenly adopted behavioral rules and societal expectations are not re-implemented and that a population continues to evolve within a particular historical, geographical and social context.

A 2005 National Youth Risk Behavior Survey suggests that adolescents are more likely to drive under the influence of alcohol, disregard seat belts, use drugs, and take part in unprotected sex [1]. There are over 13,000 adolescent deaths in the United States each year, 70% of them from vehicle crashes, homicide, and suicide. It is commonly assumed that adolescents are unable to properly judge themselves and the danger they may put themselves in. However, studies suggest that adolescents are not "irrational or deficient in their information processing" ability; they have identical risk assessment abilities of a fully-grown adult; they do not believe they are "invulnerable" nor are they "less risk-averse" [8]. In fact, they are prone to overestimating risks, akin to adults. However, a diversion in the trajectory and relative levels of intellectual ability vs. psychological maturity [8] together with lack of experience and knowledge may result in a general lack of impulsivity control and contribute to their inability to manage spur-of-the-moment decision-making behavior.

Adolescent brain development

Societies are under constant pressure to adapt to the changing environment (living conditions) as well as to ensure and further improve the chances of survival of the next generation, promoting dominance among competing populations. Decision making by an individual is powered by a reward seeking, punishment-avoiding system that seeks maximum gain and minimum risk. Within this period of rapid change, the behavior of adolescents can be dramatically different from that of other, older individuals for brief and sometimes elongated intervals.

Neurobiologically, several regions of the brain continue to mature during this developmental stage. Of greatest relevance, for the purposes of this selective review, is the time window of a few years when neural connections within the frontal lobe of the human brain and its connections with the amygdala are rapidly modified as they mature, adapting the individual to its social environment. The Triadic model proposed by Monique Ernst provides a useful framework for studying the adolescent brain [9]. This model postulates three neural structures, the prefrontal cortex, the amygdala, and the nucleus accumbens (part of the striatum that plays a big role in reward) that interact to produce adolescent behaviors in different situations (Figure 1). The prefrontal cortex is responsible for executive functions, and the amygdala is particularly associated with emotions of fear and aggression. As we will see later, other brain structures, such as the hippocampus, which regulates memory and the hypothalamus, which maintains the body's homeostasis, are important as well in that they can store information and modulate long-term changes in the brain and body, respectively.

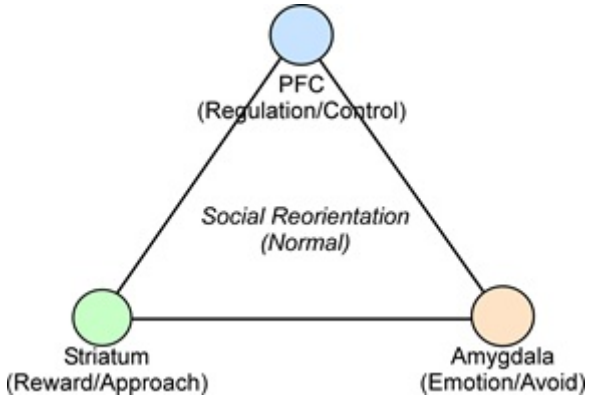

Figure 1: Triadic model showing the relationship between three brain structures involved in making risky decisions. The prefrontal cortex (PFC) has a reciprocal relationship with the stratum and amygdala; the amygdala projects directly to the stratum, whichis chiefly responsible for risk seeking and cognitive impulsivity; the amygdala for emotional intensity and lability. Social reorientation involves interaction among all three structures. Adapted from Ernst, 2014 [9].

The prefrontal cortex (PFC) regulates decision making by interacting with the striatum and amygdala, thereby controlling approach and avoidance behaviors. It fine-tunes motivation, emotion and attitude when choices among complex or ambiguous circumstances are made [10]. The overall direction and level of interaction between these brain structures may change throughout the development of the brain. The nucleus accumbens (NA), located inside the ventral striatum, is involved in predicting reward outcome. The amygdala, which is part of the limbic system, plays a predominant role in emotions. Figure 2 shows the location and spatial relationship of these three structures with other brain regions. The NA and amygdala interact with the PFC to produce behavioral changes in impulsivity and risk-taking [1]. Positive and negative emotions point towards different emotive directions, with positive associated with motivation and approach, and negative associated with avoidance. In the Triadic model, the amygdala is implicated inavoidance because of its stronger association with negative emotions. The amygdala and the striatum both have some level of influence on avoidance and reward processing. The amygdala overall plays a dominant role in avoidance behavior, while the striatum plays a more important role in reward-driven behavior. It is important to note that the three brain regions overlap from neural, psychological, and functional perspectives, creating a complicated relationship between them [10].

Research on the human brain shows that different brain regions have distinct developmental trajectories [6]. During maturation from childhood to adulthood, prefrontal regions partake in a linear increase in cognitive control and regulation [1]. During adolescence, limbic regions are already close to maturation, while prefrontal regions are still developing linearly, making this period most seriously affected by the difference in developmental stages of the two regions. Linear development of the PFC indicates that adolescents, compared to

children, have better analytical ability and can make judgments that reflect the corresponding level of their PFC development in hypothetical scenarios. Protracted development of prefrontal regions alone, however, cannot explain the differences in behavior between adolescents and children because the general trajectory would indicate that children are worse in behaving appropriately due to their underdeveloped prefrontal cortex. However, adolescents are observed to be more impulsive than both adults and young children, contradicting the linear increase in cognitive control.

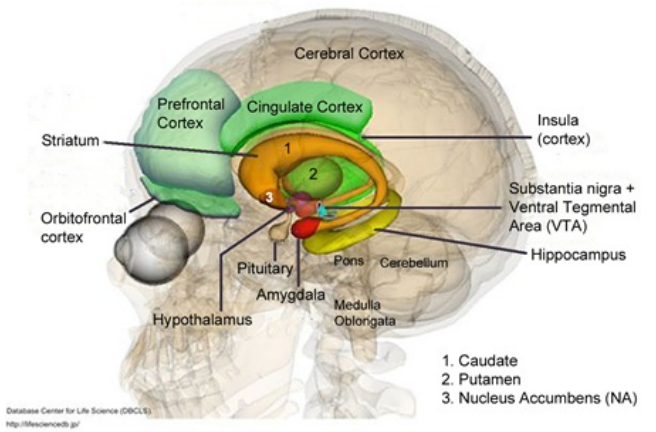

Figure 2: Illustration of the lateral view of the human brain showing key cognitive and emotive structures involved in reward processing and decision-making. Reproduced from the Database Center for Life Science (DBCLS) at http://www.net/cellbiol.net/ste/alpobesity3.php.

Therefore, the development of other brain regions must contribute to adolescent behavior patterns. In fact, the PFC, the amygdala, and the striatum interact to produce the adolescent patterns of decision making. Because the PFC is relatively underdeveloped in adolescence compared to the amygdala and the striatum, these two regions are able to override the PFC in situations where reward is presented or emotion is involved.

Functional magnetic resonance imaging (fMRI) shows that the gray matter and the white matter of the brain also develop in different ways during adolescence [1]. FMRI studies show a positive correlation between limbic subcortical activity and suboptimal choice behaviors. Since the limbic system is involved in motivation and emotional reactivity and the PFC serves to control it, it is reasonable for adolescents to display behaviors that appear to be less thoughtful.

Among other species, adolescent rats have a larger proportion of neurons in the dorsal striatum than adults, which further suggests that mechanisms of the brain may differentiate an adolescent's behavior from other age groups [11]. In this study, single unit activity was recorded from the striatum of adolescent and adult rats as the subjects learned to associate an action with a reward. The task was performed in a box with holes in one wall and a food bowl placed on the opposite wall. When the center hole lit up and the rat poked its nose into the hole, the light turned off, and simultaneously another light turned on above the food bowl and food was dispensed. After the rat ate the food, this light turned off again. Adolescent rats exhibited more striatal neuron firing during reward anticipation and this activity lasted all the way through the reward period, while in adults, striatal neurons were activated earlier, reflecting improved prediction, but returned to baseline before reward. Also, adults had much larger proportions of inhibited units, whereas adolescents had more activated units that exhibited sustained firing until the animal reached the food bowl [11].

Synaptic mechanisms

A process called "synaptic pruning" effects the development of each of the above brain regions. An overproduction of axons and synapses during puberty and rapid pruning in later adolescence is observed in multiple brain regions [12]. In the process of synapse pruning and myelination of neurons in the adolescent phase, the varying ratesof maturation of emotional regulation and cognitive function may underlie the increased risk and novelty seeking in preadolescent mice [5] and rats of both sexes [13]. Maturation partly implies the completion of extensive pruning of synaptic connectivity. By studying the differences in pruning in different brain regions, researchers have found distinct developmental trajectories of different neural systems. Synaptic pruning studies suggest that subcortical limbic regions (e.g., amygdala, NA) mature earlier than cortical (prefrontal) regions given their less prolonged pruning, meaning that both the amygdala and the NA are relatively more developed during adolescence compared to the PFC. As synaptic connectivity continues to be fine-tuned throughout development, gray matter volume is gradually reduced and white matter volume gradually expands [14]. Thus, structural and physical transformations of the brain, which modify the influence of subcortical activity on cortical (prefrontal cortex) development and cognitive control, can explain the observed cognitive changes. These structural-functional changes both trigger and are influenced by changes in the brain's neurotransmitters.

Dopamine, a neurotransmitter associated with cognition, reward seeking, and certain psychological disorders, is a vital part of decision making in an organism's brain. In particular, the dopamine system in the brain plays an important role in reward seeking. During adolescence, there is a peak in dopamine release and remodeling of the dopamine system, meaning that decisions are more reward-based. Dopamine mainly originates from the striatum, which is connected to the frontal and limbic cortices, where dopamine behaves rather like a signal between "go" - associated with positive outcomes - and "no go" - associated with avoidance of punishment. The balance in the adolescent brain between cortical and subcortical dopamine systems undergoes a transformation so that there are greater levels of dopamine in the cortical areas during adolescence [2]. In nonhuman primates as well, dopamine levels increase in the prefrontal cortex, whose neurons undergo an extended transformation throughout childhood and adolescence, interacting with other circuits in the brain [15].

There are two dopaminergic mechanisms: one involves a slow and gradual release of dopamine via D2 receptors on the striatal neurons, and the other is a series of dopamine firing, signaling both D1 and D2 receptors. D1 receptors have a low affinity to dopamine and allow one to learn to approach rewarding stimuli, whereas D2 receptors have a high affinity to dopamine and allow one to avoid negative outcomes [16]. Another study suggests that, in adolescents, D1 over-expression leads to greater immediate self-satisfaction, and reduces D2 receptors, aggravating hedonistic tendencies [17]. Dopamine receptors, which play an important role in the communication between cortical and subcortical regions, are overproduced in the amygdala and NA during early adolescence [18]. Given the influence of dopamine on

motivation, such a peak can explain the enhanced NA activity to rewards and elevated amygdala activity to emotional stimuli in the adolescent brain. Consequently, the limbic regions of the brain have more control on an individual's behavior during adolescence than the cortical regions.

Stress

Behavioral responses for dealing with stressful situations can vary with age. In some species of bats, the overall strategy to cope with distress changes from seeking help by young bats to problem solving and increased aggression by adults [20]. When approached by a predator or when trapped in a net, young bats invariably vocalize much more than adults to seek help even though their vocalizations can increase the risk of attracting the attention of and revealing their location to predators. With experience, and greater impulsive control, adult bats tend to quietly struggle on their own to extract themselves from being entangled in a net and flap their wings to escape. These different types of strategies likely represent differences in the level of development of the amygdala vs. the frontal cortex, as in human adolescents.

Imaging studies in humans show that stress causes the volume of the medial PFC (mPFC) to decrease, meaning that this region of the brain is less active after stress exposure. In contrast, the striatum (both dorsolateral and dorsomedial striatum) becomes more active when an organism is experiencing stress [3,21]. Thus, the striatum starts to exert greater control relative to the PFC, preventing one to make effective decisions under novel conditions (Figure 3A). Furthermore, the normal balance in the level of the excitatory neurotransmitter glutamate and the inhibitory neurotransmitter gamma-amino- butyric acid (GABA) is reduced in prefrontal cortex during adolescence, while input from another neurotransmitter, dopamine, peaks in prefrontal cortex during adolescence. This imbalance can accentuate the effects of stress [19]. Stress also has an effect on the dopamine system, which leads to more reward-biased decisions in stressed individuals [5,17]. Based on the scope and scale of stress, adolescence can be considered a more challenging developmental period than childhood and even adulthood.

Stress responsiveness can be transmitted across generations via both genetic and epigenetic mechanisms, such as maternal care, which can lead to changes in the expression of estrogen receptor (ERα) in the medial preoptic area [4,23]. Mouse pups raised for 5 weeks in individual cages, mimicking separation from parents and family members and social isolation in humans, show significant behavioral deficits [24]. In a recent study [25], investigators asked the question whether "sub-optimal" levels of exposure to environmental stressors during adolescence might serve as a risk factor for adult behavioral deficits when combined with one or more appropriate genetic risks. They raised wild type and transgenic schizophrenia-prone mice for only 3 weeks in isolation and discovered robust deficits in all stress-sensitive behavioral tests. They traced the cause of these effects to alteration in neurotransmission. They observed elevated expression of D2 receptors in the frontal cortex, but not in the NA. Their data demonstrated a glucocorticoid-induced, projection-specific epigenetic modification in the dopamine neuronsThis resultedfrom a significant increase in DNA methylation in the Th (Tyroxine hydroxylase) gene in neurons projecting from the ventral tegmental area (reward center in the brainstem) to the frontal cortex. These results suggest that isolation stress during adolescence can elicit molecular, neurochemical, and behavioral deficits when combined with an appropriate genetic predisposition [25].

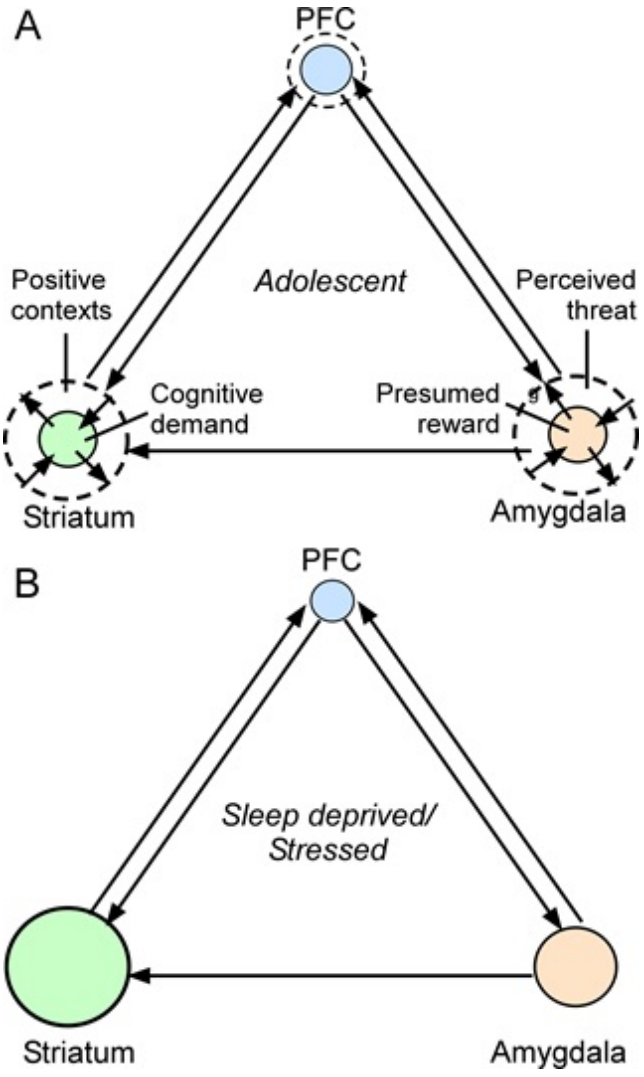

Figure 3: Functional connectivity between the striatum, amygdala and the PFC during A. adolescence and B. during sleep deprived and stressed conditions. The striatum-centered network shows a hyper-responsive peak in adolescence in positive contexts, but can show reduced functionality during cognitive demands. Similarly, the amygdala-centered network can become hyper-responsive to threat in adolescents, but hyporesponsive in a reward context. Sleep deprived and stressful conditions mimic and exacerbate imbalances in decision making circuits and may also lead to long-term physiological disturbances. Dashed circles show the uppers bounds of activity in each adapted from Ernst, 2014 [9].

Many, stress-induced changes in the brain are reversible [26]. Brain regions in subjects tested after exposure to prolonged stress and retested after a 6-week stress-free period recovered from structural changes caused by stress. This suggests that even after somewhat chronic stress, the adult brain is able to return to its original state if given time to relax after stress exposure. However, the adolescent brain,

which is undergoing continuous intrinsic changes, also permanently incorporate the effects of stress during its pruning and wiring phase.

Sleep deprivation

The effects of stress are aggravated by sleep deprivation. Studies have shown that the adolescent brain is programmed to have unique sleep patterns. However, adolescents are often sleep deprived due to a mismatch between the shift in their internal rhythm and external rules that make them wake up earlier than they should. During the teenage years, melatonin that impacts the biological clock is produced about three hours later in the sleep cycle than in children or adults. At the end of puberty, a teenager's circadian rhythm moves back gradually [27]. Most of the studies on sleep deprivation and decision making involve sleep deprivation for over 24 hours.

The PFC, a brain region crucial in the process of decision making, is especially vulnerable to sleep loss [28]. In an experiment using the Iowa Gambling Task (IGT), subjects displayed impaired ability to make decisions based on experience of reward and punishment after 49 hours of sleep deprivation [20]. The IGT is a paradigm that mimics real-world decision making under risk in a lab setting [30]. In the IGT, subjects are provided four decks of cards that represent high reward, low reward, high punishment or low punishment. The IGT is set in a way that choosing the high reward and punishment side results in overall loss, while choosing the low reward and punishment side results in overall gain. During the study, subjects gradually learn to take low risk so that they can gain, but individuals with lesions in the ventromedial prefrontal cortex (vmPFC) learn poorly compared to others. In another experiment, researchers hypothesized that sleep deprivation reduces glucose metabolism within the PFC, and sleep deprived subjects would show a deficit in decision making similar to that of patients with damaged vmPFC [31]. They found sleep loss induced atrophy in the mPFC and hypertrophy of the dorsolateral and dorsomedial striatum (DLS and DMS, respectively) (Figure 3B).

Sleep deprivation is also found to have an influence on subcortical regions, such as the NA. By adopting a modified version of the IGT and scanning the brains of participants in the experiment, it was shown that sleep deprivation leads to increased activation in the NA [32]. The NA is typically more active when making riskier choices in both states (with and without sleep deprivation). Therefore, elevated NA activity with sleep deprivation implies less thoughtful and enhanced risk taking behavior. Therefore, not getting enough sleep can cause adolescents to lose creativity when dealing with tasks and prevents learning based on experience.

In mice, sleep deprivation (SD) was shown to trigger changes in intrinsic neural properties in the PFC. It caused opposite changes at synaptic and membrane levels, with a decrease in synaptic output, as seen in changes in miniature excitatory postsynaptic currents (mEPSCs), and increase in membrane excitability, which is reflected through action potential firing frequency [33]. Although these intrinsic changes counteract each other so that the overall the effects appear to cancel out, such changes are likely to have some negative influences on PFC neurons as there is a shift in the input/output activity of PFC neurons. In summary, risky decision making in adolescence is caused by the uneven pace of development of different brain regions, which are exacerbated both by increased levels of stress and sleep deprivation.

Sex differences

Sex differences exist in multiple brain regions, especially those involved in the processing of cognitive and emotive signals [34]. Sex hormones interact extensively with developing neural circuits and can lead to major structural changes within different brain regions, including the development of corticostriatal patterns of lateralization [35]. Males generally exhibit greater risk taking behavior than females because of differences in the neurotransmitter and hormonal milieu that accentuate small structural differences. Accordingly, stressful situations seem to have opposite effect on male and female risk taking. In a stressed state, the male brain triggers the release of testosterone, which increases aggression, whereas the female brain releases oxytocin, which has calming effects. FMRI activity scans showed that women had greater activation in the amygdala, ventromedial prefrontal cortex and anterior cingulate, but men had much greater activation in the dorsolateral PFC and insula. Due to this difference, stress is more likely to activate the emotional networks in decision making in women, and in the medial prefrontal regions in males, increasing strategic processing rather than risk avoidance or somatic cues. As a result, under acute stress, the contrast between women and men brain activity is heightened [36].

Cognitive factors play an important role in differentiating males and females based on their tendency to assess injury-risk in different settings. In one study [38], participantsof ages 6 to 10 were recruited and presented with pictures from low risk (an example would be a person riding a bicycle with safety gear) to high risk (person riding a bicycle with one hand, carrying a bag, without a helmet). Then, they were asked how much they were engaged in the activity. It was found that girls perceived the “evidence” of possible risk in a situation more than boys. Boys had a tendency to assume that possible risk did not have implications for them. They may engage in risk-taking activity more than girls, even if they have seen a peer get injured from the activity [38].

Respiratory sensations are an essential interoceptive experience, which includes a sensory dimension, a strong affective component, and a strong motivational drive to homeostatically regulate the internal state [39]. Therefore, activities Therefore, activities such as breathing are carefully monitored by relevant brain regions [40]. In one study, scientists explored the neurological sex-related differences in the presence of aversive respiratory stimulus by having participants rate the level of difficulty of breathing on a computer while they breathed normally or with a respiratory load [41]. They propose and present evidence indicating that men are more sensitive than woman to hedonistic rewards and sensation seeking. Sex differences were observed in the insula activity level after the termination of the respiratory load that acted as the aversive stimulus. Men especially reported the highest perceived unpleasantness, and showed the strongest activation of the reward system in the brain. This finding indicates that in men, the more aversive the stimulus, the greater the reward system activation after the termination of the stimulus [41]. Although these studies were not conducted with adolescents, these differences may emerge from a pre-existing bias in the teen brain.

Finally, positron emission tomography (PET) of male and female brains shows differences in the rate of serotonin synthesis. In this imaging study, tryptophan levels were measured from brain scans taken before and after the depletion of plasma tryptophan since tryptophan is needed for serotonin synthesis. Lack of serotonin, which normally has a calming effect, may raise the threshold for arousal and expected stimulation. Thus, adolescent males may engage in more risk-

taking behavior because their plasma tryptophan depletion rate is higher than in females.

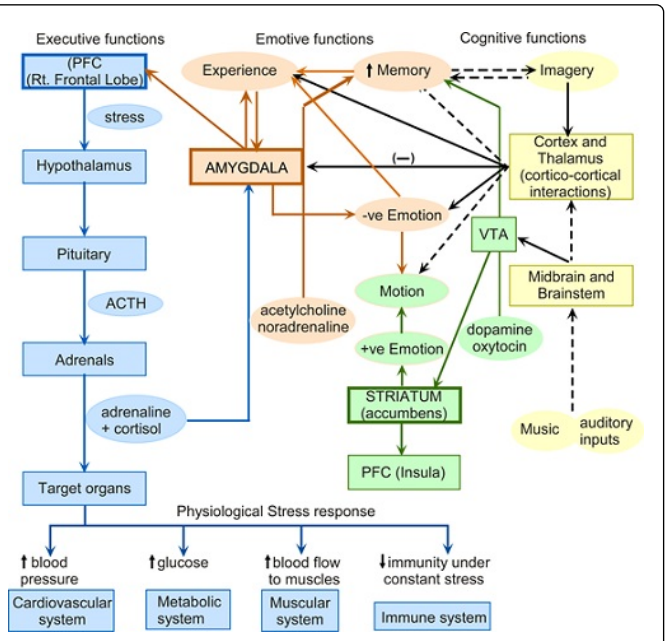

Figure 4: Flow chart showing the involvement of the structures belonging to the triadic model (thick rectangular boundaries) in the processing, representation, storage and recall of musical sounds. The perceptual/cognitive functions depend upon sensory processing structures, which projects to those are processing emotive information. The stored and incoming information from the amygdala can influence executive brain regions and the hypothalamic pituitary axis to trigger the physiological stress response in the body. Striatal and cortical representations can suppress and modify these experiences and potentially produce changes, lasting into early adulthood that modify risk taking behaviors. Solid lines indicate direct projections/effects and dashed lines indicate more complex indirect pathways/effects.

Sounds

Like most bodily structures, the form and functional efficiency of the brain is greatly determined by the genetic make-up and gene expression during key developmental periods. Unlike other organs, however, brain cells and their connections can be greatly influenced by extra-bodily information via sensory inputs, which can change the strength and patterns of synaptic connectivity. In the context of stress and anxiety, an imbalance between physiological states is a key distinctive characteristic of adolescent behavior, as noted above.

Vocal output, with its modulation patterns, can both soothe [21] and heighten anxiety in conspecifics from a distance [43-45]. Responses to the sounds of laughing and crying have also been reported for the amygdala and insula using fMRI in humans [46,47]. Thus, vocalizations can be used to rapidly modify one's own mental and physiological state. Music, a rhythmic patterning of sound, is specifically designed to influence the mental and physiological state of an individual (see Figure 4). Similar effects can also be elicited by other sensory inputs, such as touch and olfaction [48], although these modalities require close contact or take longer times to process their physiological effects. The flow chart in Figure 4 shows how sound can provide rapid input of large amounts of semantic as well as emotive information to specific brain circuits that are part of the prefrontal, amygdala and striatal circuitry constituting the triadic model (discussed earlier)of adolescent decision-making circuitry.

Merely listening to conversational sounds and participating in a conversation with others can lead to release of oxytocin [49], which is well established as being important for bonding in animals, including humans [50,51]. Although in humans, it is frequently artificially created; music also exists in nature and is produced by many species, such as songbirds, frogs, bats and even some species of insects. The evening chatter in many vocal species, e.g. birds, bats and primates may have the same effect and therefore is important for social bonding. Neurons in both the prefrontal cortex and the basolateral amygdala also respond to these species-specific social calls [52]. Oxytocin has been shown to be closely associated with the auditory system throughout the brain of bat species [53,54], which are highly vocal and social, living in tightly clustered colonies in caves or hanging in trees in close proximity to each other. Functional and effective connectivity analyses shows that listening to music strongly modulates activity in a network of mesolimbic structures involved in reward processing including the NA and the ventral tegmental area as well as the hypothalamus and insula, which are thought to be involved in regulating autonomic and physiological responses to rewarding and emotional stimuli [55]. Activation of the accumbens is also associated with release of dopamine, signaling pleasure and making the experience rewarding [28-34].

These observations taken together suggest that plasticity within the fronto-amygdalar and fronto-striatal connectome is especially amenable to changes produced by sound inputs and oxytocin release during the teenage years. This is consistent with the extensive preference for and dependence on pop music among teenagers. Oxytocin can fixate incoming sensory information into long-term memories [50,51]. Thus sounds and especially music have the ability to influence the same neural circuits that are also being modified by changes in the hormonal milieu of the adolescent brain. In this way, sounds can produce everlasting changes in the executive-emotive neural circuitry that is extremely plastic during adolescent years. The neural mechanisms of how this may happen are not yet known. This same neural circuitry together with the neurotransmitters associated with it, as shown earlier, is a key substrate of decision making in later years of one's life as well [51-55].

Summary

Decision making behavior is multifactorial and takes different trajectories starting with adolescence when genetic and environmental (perceptual and socioemotional) inputs blend together within developing neural circuits. These trajectories are the outcome of individual variation in neurotransmitters, hormones, sex, personality dispositions and/or situational factors. They also result from changes in both the relative volume of different brain structures and their wiring. As yet, we do not fully understand how exactly these factors interact at the cellular and molecular levels to bring about long-term behavioral changes and the extent to which they are reversible. We are only now beginning to make an effort to incorporate individual differences, many of which crystallize during adolescence, into personalized treatments. We stand the best chance of understanding the developmental and neural origins of individual differences at the cellular and synaptic levels by studying very simple nervous systems, as

are present in the brains of a worm, a fruitfly or a zebrafish - organisms whose connectome and/or genome has been completely mapped. With this cellular and molecular level understanding, it may even be possible to intervene and correct extremely abnormal neural adolescent circuitry and behaviors.

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References

1. Casey BJ, Jones RM, Hare TA (2008) The adolescent brain. Ann N Y Acad Sci 1124: 111-126.
2. Spear LP (2000) The adolescent brain and age-related behavioral manifestations. Neurosci Biobehav Rev 24: 417-463.
3. Schramm NL, Walker QD, Caster JM, Kuhn CM (2009) Are adolescents more vulnerable to drug addiction than adults? Evidence from animal models. Psychopharmacology 206:1–21.
4. Primus RJ, Kellogg CK (1989) Pubertal-related changes influence the development of environment-related social interaction in the male rat. Dev Psychobiol 22: 633–643.
5. Adriani W, Chiarotti F, Laviola G (1998) Elevated novelty seeking and peculiar d-amphetamine sensitization in periadolescent mice compared with adult mice. Behav Neurosci 112: 1152-1166.
6. Ernst M, Paulus MP (2005) Neurobiology of decision making: a selective review from a neurocognitive and clinical perspective. Biol Psychiatry 58: 597-604.
7. McGhee RL, Ehrler DJ, Buckhalt JA, Phillips C (2012) The Relation between Five-Factor Personality Traits and Risk-Taking Behavior in Preadolescents.
8. Steinberg L (2008) A Social Neuroscience Perspective on Adolescent Risk-Taking. Dev Rev 28: 78-106.
9. Ernst M (2014) The triadic model perspective for the study of adolescent motivated behavior. Brain and Cognition 89: 104–111.
10. Pribram KH (2006) What makes humanity humane. J Biomed Discov Collab 1: 14.
11. Sturman DA, Moghaddam B (2012) Striatum processes reward differently in adolescents versus adults. Proceedings of the National Academy of Sciences 109: 1719–1724.
12. Crews F, He J, Hodge C (2007) Adolescent cortical development: a critical period of vulnerability for addiction. Pharmacol Biochem Behav 86: 189–199.
13. Toledo-Rodriguez M, Sandi C (2011) Stress during Adolescence Increases Novelty Seeking and Risk-Taking Behavior in Male and Female Rats. Front Behav Neurosci 5: 17–17.
14. Squeglia LM, Jacobus J, Tapert SF (2009) The influence of substance use on adolescent brain development. Clin EEG Neurosci 40 :31–38.
15. Rosenberg DR, Lewis DA (1995) Postnatal maturation of the dopaminergic innervation of monkey prefrontal and motor cortices: a tyrosine hydroxylase immunohistochemical analysis. J Comp Neurol 358 :383–400.
16. Clark CA, Dagher A (2014) The role of dopamine in risk taking: a specific look at Parkinson's disease and gambling. Front Behav Neurosci 8: 196–196.
17. Sonntag KC (2014) Viral over-expression of D1 dopamine receptors in the prefrontal cortex increase high-risk behaviors in adults: comparison with adolescents. Psychopharmacology 231: 1615–1626.
18. Crews F, He J, Hodge C (2007) Adolescent cortical development: a critical period of vulnerability for addiction. Pharmacol Biochem Behav 86: 189–199.
19. Lewis D (1997) Development of the Prefrontal Cortex during Adolescence: Insights into Vulnerable Neural Circuits in Schizophrenia. Neuropsychopharmacology 16: 385–398.
20. Huang X, Kanwal JS, Jiang T, et al (2015) Situational and Age-Dependent Decision Making during Life Threatening Distress in Myotis macrodactylus. PLoS ONE 10: e0132817.
21. Galvan A, Rahdar A (2013) The neurobiological effects of stress on adolescent decision making. Neuroscience 249: 223–231.
22. de Kloet ER, Rots NY, Cools AR (1996) Brain-corticosteroid hormone dialogue: slow and persistent. Cell Mol Neurobiol 16: 345-356.
23. Champagne FA, Curley JP (2005) How social experiences influence the brain. Current Opinion in Neurobiology 15:704–709.
24. Niwa M, Matsumoto Y, Mouri A, Ozaki N, Nabeshima T (2011) Vulnerability in early life to changes in the rearing environment plays a crucial role in the aetiopathology of psychiatric disorders. International Journal of Neuropsychopharmacology 14: 459–477.
25. Niwa M, Jaaro-Peled H, Tankou S, Seshadri S, Hikida T, et al. (2013) Adolescent stress-induced epigenetic control of dopaminergic neurons via glucocorticoids. Science 339: 335-339.
26. Soares JM (2012) Stress-induced changes in human decision-making are reversible. Transl Psychiatry 2: e131.
27. Carskadon MA, Acebo C, Jenni OG (2004) Regulation of adolescent sleep: implications for behavior. Ann N Y Acad Sci 1021: 276–291.
28. Horne J (2012) Working throughout the night: Beyond "sleepiness" – impairments to critical decision making. Neurosci Biobehav Rev 36: 2226–2231.
29. Killgore WDS, Balkin TJ, Wesensten NJ (2006) Impaired decision making following 49 h of sleep deprivation. Journal of Sleep Research 15: 7–13.
30. Orsini CA, Moorman DE, Young JW, Setlow B, Floresco SB (2015) Neural mechanisms regulating different forms of risk-related decision-making: Insights from animal models. Neurosci Biobehav Rev.
31. Thomas M (2000) Neural basis of alertness and cognitive performance impairments during sleepiness. I. Effects of 24 h of sleep deprivation on waking human regional brain activity. Journal of Sleep Research 9: 335–352.
32. Venkatraman V, Chuah YML, Huettel SA, Chee MWL (2007) Sleep deprivation elevates expectation of gains and attenuates response to losses following risky decisions. Sleep 30: 603–609.
33. Winters BD, Huang YH, Dong Y, Krueger JM (2011) Sleep loss alters synaptic and intrinsic neuronal properties in mouse prefrontal cortex. Brain Research 1420: 1–7.
34. Juraska JM (1991) Sex differences in "cognitive" regions of the rat brain. Psychoneuroendocrinology 16: 105–109.
35. Cahill L (2006) Why sex matters for neuroscience. Nat Rev Neurosci 7: 477–484.
36. Lighthall NR, Mather M, Gorlick MA (2009) Acute stress increases sex differences in risk seeking in the balloon analogue risk task. PLoS ONE 4: e6002.
37. Baker SP, O'Neill B, Ginsburg M, Li G (1992) The injury fact book 2nd ed.
38. Morrongiello BA, Rennie H (1998) Why do boys engage in more risk taking than girls? The role of attributions, beliefs, and risk appraisals. J Pediatr Psychol 23: 33–43.
39. Leupoldt Von A, Riedel F, Dahme B (2006) The impact of emotions on the perception of dyspnea in pediatric asthma. Psychophysiology 43: 641–644.
40. Craig ADB (2009) How do you feel—now? The anterior insula and human awareness. Nat Rev Neurosci 10: 59–70.
41. Galli G, Shukla A, Simmons AN, Davenport PW, Paulus MP (2013) Sex differences in the neural processing of aversive interoceptive events: the benefit of relief. PLoS ONE 8: e84044.
42. Nishizawa S (1997) Differences between males and females in rates of serotonin synthesis in human brain. Proceedings of the National Academy of Sciences 94: 5308–5313.

43. Kato Y (2014) Vocalizations associated with anxiety and fear in the common marmoset (Callithrix jacchus). Behavioural Brain Research 275: 43–52.
44. Seltzer LJ, Ziegler TE, Pollak SD (2010) Social vocalizations can release oxytocin in humans. Proceedings of the Royal Society B: Biological Sciences 277: 2661–2666.
45. Sander K, Scheich H (2001) Auditory perception of laughing and crying activates human amygdala regardless of attentional state. Brain Res Cogn Brain Res 12: 181-198.
46. Sander K, Scheich H (2005) Left auditory cortex and amygdala, but right insula dominance for human laughing and crying. J Cogn Neurosci 17: 1519-1531.
47. Uvnäs-Moberg K, Handlin L, Petersson M (2014) Self-soothing behaviors with particular reference to oxytocin release induced by non-noxious sensory stimulation. Front Psychol 5: 1529.
48. Feldman R (2012) Oxytocin and social affiliation in humans. Horm Behav 61: 380-391.
49. Debiec J (2005) Peptides of love and fear: vasopressin and oxytocin modulate the integration of information in the amygdala. Bioessays 27: 869-873.
50. Insel TR, Winslow JT, Wang Z, Young LJ (1998) Oxytocin, vasopressin, and the neuroendocrine basis of pair bond formation. Adv Exp Med Biol 449: 215–224.
51. Grandjean D, Sander D, Pourtois G, Schwartz S, Seghier ML, et al. (2005) The voices of wrath: brain responses to angry prosody in meaningless speech. Nat Neurosci 8: 145-146.
52. Naumann RT, Kanwal JS (2011) Basolateral amygdala responds robustly to social calls: spiking characteristics of single unit activity. J Neurophysiol 105: 2389–2404.
53. Rao PDP, Kanwal JS (2004) Oxytocin and vasopressin immunoreactivity within the forebrain and limbic-related areas in the mustached bat, Pteronotus parnellii. Brain Behav Evol 63: 151–168.
54. Kanwal JS, Rao PDP (2002) Oxytocin within auditory nuclei: a neuromodulatory function in sensory processing? Neuroreport 13: 2193–2197.
55. Menon V, Levitin DJ (2005) The rewards of music listening: response and physiological connectivity of the mesolimbic system. Neuroimage 28: 175–184.