IN PRESS: CURRENT ADDICTION REPORTS

Neural Underpinnings of Social Contextual Influences on Adolescent Risk Taking

Seh-Joo Kwon, B.S., Caitlin C. Turpyn, Ph.D., Natasha Duell Ph.D., Eva H. Telzer, Ph.D.*

University of North Carolina at Chapel Hill

Keywords: adolescence, parent influence, peer influence, substance use, brain development, fmri

* Corresponding author: Eva H. Telzer (ehtelzer@unc.edu), 235 E. Cameron Avenue, Chapel Hill, NC 27514, 919-962-9720

Abstract

Purpose of review: Adolescence is a developmental period often characterized by heightened risk taking and increased sensitivity to socially salient stimuli. In this report, we discuss how the developing brain serves as both a link between, and a susceptibility factor for, social contextual factors and risk taking in adolescence. **Recent findings:** Neural activity in regions related to affective processing, cognitive control, and social cognition, which continue to develop across the adolescent years, shape the relationship between adolescents' social environment and their risk taking. **Summary:** Examining neural patterns of adolescent brain development enriches our understanding of how adolescents' complex social environment modulates their risk-taking behavior, which may have implications for adolescents' current and future substance use.

Introduction

Substance use rises markedly during adolescence [1]. By twelfth grade, over 50% of adolescents have tried alcohol, about 20% have reported using prescription medicine for non-medical purposes, and approximately 40% have tried cigarettes [2]. The rise in substance use during adolescence poses serious public health concerns and has detrimental implications to adolescents' long-term well-being. Indeed, substance use, misuse, and addiction are among the leading causes of adolescent morbidity and mortality in the United States [3]. Further, initiating substance use during adolescence poses an increased risk for substance addiction and abuse of multiple substances [4, 5]. The long-term consequences of substance use in adolescence are manifold, including risk for mental health, poor academic performance, and neurocognitive problems [5, 6, 7].

One likely reason for the rise in substance use during adolescence is the increased propensity for risk taking that is characteristic of the second decade of life. Cross-national reports of experimental and real-world risk taking (e.g., health-related risks, antisocial risks) have demonstrated increases in risk taking across adolescence such that it peaks during late adolescence [8]. Various biopsychosocial factors are thought to contribute to adolescents' propensity for risk. For instance, puberty is thought to induce key hormonal changes that result in the reorganization of dopaminergic pathways to reward-related brain regions [9]. In effect, adolescents evince a heightened sensitivity to rewards and an increased tendency to seek out exciting, novel experiences [10]. In contrast to the developmental peak in reward-related brain regions is the protracted development of prefrontal brain regions responsible for self-regulation, which continue developing into early adulthood [11]. The developmental mismatch between reward sensitivity and self-regulation is thought to be a key characteristic of risk-taking

propensity in adolescence, placing youth at risk for substance use. Indeed, heightened reward sensitivity during adolescence is associated with substance use initiation during adolescence, and high reward sensitivity coupled with poor self-regulation predicts earlier onset of substance use among adolescents [12, 13]. Together, findings indicate that adolescents' increased propensity for risk taking may be a key contributing factor to the onset of substance use during adolescence and thus studying adolescent risk taking may have implications for substance use.

Given the increased salience and importance of social contexts for adolescent decision-making, the social figures in adolescents' lives have the potential to either amplify or inhibit adolescents' likelihood of risk taking [14]. In the following sections, we provide insights from research on magnetic resonance imaging (MRI) studies that clarify the role of social context on adolescent risk taking. We first explore social and contextual effects on adolescent risk taking. Next, we discuss functional changes that take place in the developing adolescent brain. Following, we review literature linking social context with adolescent brain development and function as they relate to risk-taking behaviors, and discuss how adolescents' social contexts may tune the developing neural systems to confer either vulnerability or protectionagainst risk-taking during adolescence. We end with suggestions for future research.

Social Context of Adolescent Substance Use

Risky behaviors, including substance use, do not occur in a social vacuum. Social information often guides adolescent decision-making, and indeed, most risk taking occurs in a social context [14, 15]. Two of the key social figures shaping adolescents' behaviors include parents and peers. The transition from late childhood to early adolescence parallels a shift from susceptibility to parental influence to susceptibility to peer influence [16]. While parents continue to play an important influence, adolescents spend more time with peers than with

parents and form more supportive and interdependent bonds with their peers [17, 18]. Thus, adolescents tend to be sensitive to, and reinforced by, the norms and behaviors endorsed by their peers (e.g., [19]). Additionally, young adolescents are more likely to conform to their peers' perceptions of risky behaviors than to adults' perceptions [20]. This emphasizes that social norms deemed as high value by their peers are incorporated into adolescents' own set of values, which ultimately guide their future behaviors.

Though adolescents increasingly gain independence from their parents, parents remain integral social agents in their lives, and adolescents continue to seek guidance from their parents [21]. In particular, parents exert important influences on adolescents' decisions, especially when those decisions are related to moral and ethical values, which may help adolescents determine which behaviors are socially acceptable and which are not (e.g., [22]). This is evident with respect to parental modeling of risky behaviors, as adolescents are more likely to partake in the same risky behaviors that their parents engage in [23, 24]. As such, contrary to popular belief that peers have stronger influence over adolescents' behaviors than do parents, parents continue to exert meaningful influence on adolescent risky behaviors.

In effect, both peers and parents can have meaningful impacts on adolescents' decisions to engage in substance use. Adolescents are more likely to engage in substance use if their parents or peers engage in substance use, including alcohol, cigarettes, and marijuana use [23, 24, 25, 26]. Longitudinal trends demonstrate that parental alcoholism predicts greater consumption of alcohol in adolescents over time, and peers' initial alcohol use predicts adolescents' alcohol use 3-years later [27, 28]. Therefore, parents and peers are salient social figures who shape adolescent substance use behavior, both concurrently and longitudinally.

In addition to the direct influence of parents' and peers' own substance use, adolescents' social context includes broader influences; for instance, early life experiences are often shaped by the family context (e.g., maternal depression, childhood neglect) while school experiences are often guided by the peer context (e.g., hostile peers). These broader social contexts, beyond the direct parent and peer influences, have implications for adolescent adjustment, including risk-taking and substance use behaviors. This review therefore encompasses a diverse range of social influences to best reflect the complexity of adolescents' social context.

Brain Development in Adolescence

The effect of adolescents' social contexts on their risky decision-making is related, in part, to various changes in brain development, with respect to both structure and function. These neurobiological changes are not only tuned by adolescents' social experiences, but also serve to modulate associations between adolescents' social contexts and their risky behaviors. In particular, adolescence is a period of developmental neuroplasticity, during which the brain is reorganizing and changing with experience in response to environmental and sociocultural inputs [29]. Neurodevelopmental changes occur in regions involved in affective processing (e.g., ventral striatum (VS), amygdala), cognitive control (e.g., ventrolateral prefrontal cortex (vlPFC)), and social cognition (e.g., medial prefrontal cortex (mPFC)) that render adolescents more sensitive to socially salient inputs such as social rewards, and more flexible in their ability to engage in inhibitory control [30, 31, 32].

Such changes in brain function may underlie adolescent risk-taking behavior. For example, adolescents at risk for substance use show elevated VS activation when anticipating rewards and blunted prefrontal activation while engaging in cognitive control [33, 34]. Further, earlier onset of substance use is associated with enhanced coupling between reward and

cognitive control neural systems, positing that reward plays a key role in these adolescents' goal-directed behaviors [35]. Such neural processes may be enhanced or dampened under different social contexts. For instance, risk taking in the presence of peers recruits neural regions involved in reward sensitivity (e.g., VS), whereas in the presence of parents, VS activation is blunted and connectivity between affective and social cognitive regions is enhanced, indicating that the same risky behavior elicits divergent neural activation under different social contexts [36, 37, 38].

Given the relevance of brain development to understanding adolescent risky behaviors, the following sections will focus on recent empirical research that examines the role of adolescent brain development in the relationship between social contextual influences and risky behaviors in youth. We review studies that demonstrate how the brain can serve as both a mechanism (i.e., mediator) or a susceptibility factor (i.e., moderator) of social contextual influences on risky behaviors in adolescence. The mediation model identifies neural functions that serve as a biological mechanism linking social contextual influences to risk-taking behavior, whereas the moderation model identifies neural functions that enhance or blunt the interplay between social contextual influences and risk-taking behavior.

Neural Mechanisms of Social Contextual Influences on Risk Taking

Investigations of the brain as a mediator of social context focuses on how social influences may operate in part through neurobiological mechanisms to impact risky behavior, potentially elucidating how negative social experiences lead to escalated risky behaviors in youth. For instance, adolescents' experiences of chronic peer victimization are associated with greater risky behaviors, both concurrently in an experimental task and longitudinally in real-world antisocial behavior [39]. The relationship between peer victimization and risk taking is mediated by heightened activation in the amygdala during risk taking, suggesting that

chronically victimized youth may become more sensitive to the affective value of high risks, thereby heightening their proclivity to engage in risky and antisocial behaviors [39]. Similarly, hostile school environments, including higher prevalence of delinquent peers at school, are related to adolescents' social deviance, and this relationship is mediated by activation in the subgenual anterior cingulate cortex (subACC), a brain region involved in affective regulation, during social exclusion [40]. The mediating role of the subACC suggests that hostile school environments may make adolescents increasingly sensitive to hostility and more susceptible to future social stimuli, thereby pushing them to affiliate with negative peers and engage in deviant behaviors [40]. Furthermore, negative peer affiliations during adolescence have long-term implications for risk taking during adulthood. For example, negative peer affiliation at age 20 is related to greater delay discounting at age 25 [41]. Delay discounting characterizes a stronger preference for smaller, immediate rewards rather than larger, delayed rewards, and serves as a proxy for risky behaviors. This longitudinal relationship is mediated by resting state frontostriatal functional connectivity, a neural circuit involved in impatience and temporal discounting due to greater reward-driven executive functioning [41, 42]. This finding posits that poor peer relationships during late adolescence may have long-lasting implications for their neurocognitive functions [41]. Together, these findings demonstrate that various types of negative peer experiences are linked to risky behaviors via altered neural activation and functional connectivity.

Emerging evidence also reveals that aspects of the family context may influence youth's risky behavior via altered neural patterns. For example, high family conflict is associated with longitudinal increases in risk taking, which is mediated by longitudinal increases in vlPFC activity during cognitive control [43]. Longitudinal increases in vlPFC activation is thought to be

a phenotype that characterizes heightened susceptibility to risk taking, suggesting that poor family dynamics place adolescents at risk for heightened risk-taking behavior via changes in the cognitive control system [44]. Similarly, high family conflict is associated with longitudinal increases in real-life risk taking, which is mediated by longitudinal increases in functional coupling between the anterior insula (AI) and VS when making safe decisions during risk taking under maternal presence [45]. This demonstrates that poor family relationships may lead to a dysregulated integration of reward information from the VS by AI, which in turn, may lead to heighted risk-taking behavior [45, 46].

Simultaneously, more positive family relationships serve to reduce adolescent risk taking via changes in neural processing. For example, greater positive parent-child relationship quality is linked to longitudinal declines in risk-taking behavior, which is mediated by longitudinal declines in VS activation during risk taking [47]. This suggests that risk taking is a less rewarding or salient experience for adolescents within a positive family environment, and thus positive interactions with family members may serve as a protective factor against risky behavior by reducing the reward value of engaging in such behavior [47]. One aspect of the family environment that is often understudied is the important role of siblings on adolescent risky behavior. Indeed, sibling relationships have unique implications on adolescent adjustment such that greater closeness among siblings is linked to lower externalizing symptoms, which is mediated by stronger AI activation during safe decision making [48]. Given the insula's role in integrating affective signals, this finding indicates that positive sibling relationships may enhance the affective salience of safe choices that may mitigate externalizing behaviors [48]. In sum, positive and negative family contexts can differentially shape adolescents' risky behaviors over

time, which may be guided by changes in neural development in brain regions involved in cognitive control and reward value.

Other social contextual factors that stem from family and caretaking environments, including early life stressors and childhood adversity, also relate to risk taking via modulated brain activation. Greater childhood adversity (e.g., emotional neglect from a caretaker) is related to higher externalizing symptoms in early adolescence, which is associated with later substance use such as alcohol and marijuana [49]. This relationship is mediated by greater ACC activation during cognitive control, which posits that childhood adversity may dysregulate ACC functioning, a region that is critical for inhibitory processing and conflict monitoring [49]. Similar patterns emerge later in development as well. For example, adolescents who experience more stressful life events (e.g., injury or death in family) are more likely to form alcohol dependence later in life [50]. This relationship is mediated by reduced mPFC activation during reward anticipation and receipt, indicating that social stressors during adolescence may disrupt reward circuitry, thereby placing youth at higher risk for substance use [50]. Together, alterations in affective and cognitive control neural regions may link experiences of social stressors to later risky behaviors across development. In summary, social influence from family and peer contexts can determine how adolescents make risky decisions via dysregulated neural development.

Neurobiological Susceptibility to Social Contextual Influences on Risk Taking

The above evidence highlights the potential for social experiences to shape developing neural circuitry, potentially creating vulnerability for health-compromising or antisocial risk behaviors. In addition to such direct influences, a promising theoretical framework, neurobiological susceptibility to social context (also referred to as differential susceptibility theory and biological sensitivity to context), also highlights that individual differences in neural

endophenotypes, such as heightened reward sensitivity, may leave some youth more susceptible to the influence of their social environment [51, 52, 53]. That is, social environmental factors may influence youth non-uniformly, such that susceptible endophenotypes may render youth vulnerable to the influence of family and peer contexts, whereas less susceptible endophenotypes are not influenced by the social context. Moreover, consistent with differential susceptibility theory, these effects may occur in a "for better or for worse" fashion, such that the same youth who suffer most in harsh social environments could thrive most in supportive ones [54]. In other words, this theory emphasizes that positive social context may, in fact, be an opportunity for positive adjustment for youth at risk.

Most studies investigating susceptibility to the social environment have assessed the effects of the caregiving environment on youth adjustment as a function of genes or other biological factors (e.g., vasovagal response, [53, 55, 56]). This work has documented interactions between genetic factors associated with neurotransmitters (e.g., dopamine) and parenting quality in predicting youth outcomes such as substance use and externalizing psychopathology (e.g., [57, 58]). For example, findings suggest that youth with less efficient dopamine-related genetic polymorphisms are more susceptible to both positive and negative caregiving environments, with these youth showing poorer outcomes in contexts of adversity but profiting the most from support [55].

Although these studies provide initial evidence of susceptibility patterns in adolescent youth, neural indices, such as brain function and structure, may also represent optimal endophenotypic markers of susceptibility to social influence, as neural measures offer a summation of intrinsic biological factors (e.g., genomic expression) and may shed light on specific cognitive, affective, and social processes involved [51]. Indeed, a small handful of

studies have applied such models to predict psychosocial outcomes in adolescents, with the majority of this initial work assessing internalizing presentations such as depressive symptoms [59, 60, 61, 62, 63]. Like risk-taking behavior, depression sharply increases during the adolescent period and often co-occurs with risk behaviors such as substance use [64]. One study observed that greater functional sensitivity to social exclusion in affective salience regions, such as the AI and dorsal ACC, predicted lower levels of depressive symptoms when adolescents reported having supportive parent-adolescent relationships, but predicted higher levels of depressive symptoms when adolescents reported having conflictual relationships with their parents [60]. Further, adolescents with lower neural responsivity to social exclusion were resilient, with these youth exhibiting low or average levels of depressive symptoms. This work stresses that individual differences in neurobiological susceptibility during the adolescent period may dictate the extent to which social influence, particularly salient social influences such as the parent-adolescent relationship, may influence behavioral outcomes during this time.

Although most work in this domain has focused on internalizing symptoms, the differential susceptibility framework may be equally relevant for understanding the interplay between the social environment and brain functions on risk taking. Indeed, one study documented individual differences in neurobiological susceptibility to peer influence in predicting adolescent risk behavior. Specifically, adolescents' VS activity during the anticipation of social rewards and during the avoidance of social punishments marked a pattern of neurobiological susceptibility to peer influence [65]. Whereas negative perceived peer norms were associated with higher levels of risk behavior for youth with high VS sensitivity, youth with low VS sensitivity were resilient and exhibited lower levels of risk behavior regardless of peer norms. This study provides initial evidence of adolescent neurobiological susceptibility to social context, particularly for the

association between peer influences and emerging risk-taking, underscoring the promise of this framework for characterizing social and neural vulnerabilities. Together, this research suggests that neurobiological sensitivity may identify adolescents who are most at risk within negative social contexts and that redirecting or enhancing their social environment may have optimal consequences for positive developmental trajectories.

Future Directions

In this review, we discuss how the developing brain can serve as a mediator and moderator of the link between social contextual influences and adolescent risk taking. These two bodies of work have largely been conducted separately, with little consideration of how neurodevelopment can serve as both a mediator and a moderator. It is possible that relatively earlier social contextual influences tune the developing brain, heightening neurobiological sensitivity for some (e.g., those exposed to high family conflict develop increases in functional coupling between the AI and VS), which results in later risk taking and substance use (i.e., mediational pathway) [45]. This earlier tuning of the brain and heightened neurobiological sensitivity may then serve to modulate later social contexts, making some youth even more susceptible to the influence of their social environment, whereas other youth who are less neurobiologically sensitive are resilient to their social context (i.e., moderational pathway; see Figure 1). Future research that utilizes longitudinal designs is key to unpacking the complex ways that the brain and social context interact which will allow us to examine the unfolding of these mediational and moderational pathways over time.

Future research should also carefully assess the developmental timing of social contextual influences in order to identify whether neural mediators and moderators function differently at different developmental periods. For instance, mediation may be amplified during

sensitive periods of development when the brain is particularly tuned to the social environment. Indeed, stressors have an undue influence on brain development during early developmental periods. For instance, socioeconomic stressors in childhood predict altered neural processing in adulthood, even if there has been a change in SES later in life, suggesting that childhood may be a sensitive period during which social stressors tune the brain in ways that are not recoverable later in life [66, 67]. Moreover, some neural regions may be more or less susceptible to social contextual influences at different developmental periods based on the timing of their structural and functional development. For instance, the amygdala is an early developing brain region that may be particularly susceptible to input from the environment early in life, whereas prefrontal regions develop later in adolescence and therefore may be more susceptible during adolescence (see [68]). Thus, tuning of the brain may occur in a region-specific manner, which may have differential consequences for later behavioral and adjustment outcomes. Future research should examine how social influences during individual periods within development (i.e., infancy versus childhood versus adolescence) result in differential outcomes on brain development and subsequent adjustment in adolescence and adulthood.

Finally, future research should utilize experimental designs as well as randomized control trials to capture causal pathways to inform interventions. Significant behavioral and neuroimaging research that has implemented experimental designs has shown that adolescents are sensitive to both positive and negative social contexts. For instance, relative to older individuals, younger adolescents change their own attitudes after being exposed to prosocial as well as risky norms, and heightened neurobiological sensitivity to peers and parents results in both risky and prosocial behaviors, depending on the social norms being modeled [21, 36, 37, 69, 70]. To date, differential susceptibility models have largely been correlational. Experimental

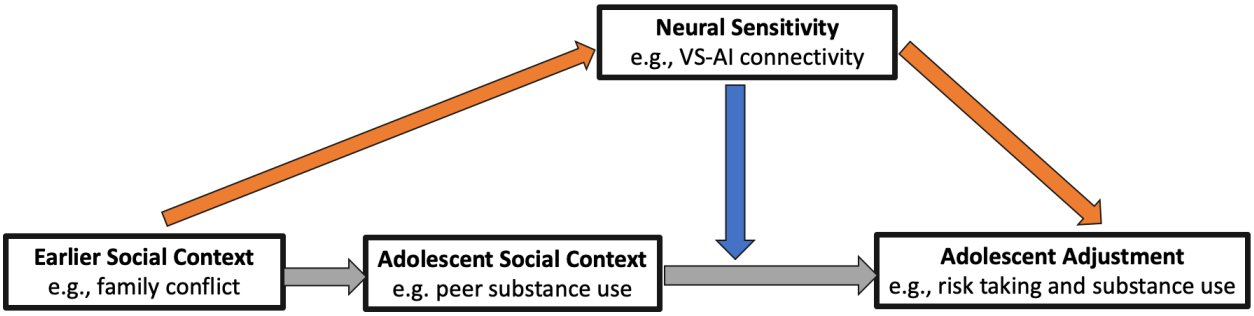
designs are important in order to identify whether the same adolescent high in susceptibility who is exposed to maladaptive social inputs and suffers will benefit when exposed to adaptive social inputs. Experimental designs can therefore identify how susceptible youth will respond to different social contexts, which will be important for implementing interventions targeted at decreasing adolescent risk taking. Indeed, randomized controlled trials have shown than youth with enhanced genetic sensitivity to context (e.g., risk allele of the D4 receptor) benefit the most from interventions that focus on improving their social context (e.g., [71]).

Conclusion

In summary, adolescents undergo a multitude of changes including heightened risk-taking behavior, resulting in substance use engagement. Parallel with this behavior is changes in youth's social environment and neurobiological transformations. Thus, adolescent risky behaviors are often accompanied by various social inputs from their parents and peers and are modulated by the brain in complex, interacting ways. In this review, we discuss two ways in which the developing brain modulates social contextual influences on risk taking: first, we highlight the brain as a mechanism (i.e., mediator) that links social influence and risk taking; and second, we describe the brain as a susceptibility factor (i.e., moderator) that differentiates the non-uniform effects of social influence on risk taking. These two models emphasize the key role of neurobiological development in understanding adolescent risk taking in a social context; specifically, neural changes in regions involved in affective processing, cognitive control, and social cognition contribute to and modulate adolescent risk taking, which demonstrate the need to understand neurodevelopment that uniquely characterizes adolescence in order to help unpack the complexity of adolescent development. Substance use during adolescence has damaging consequences on youth's immediate and long-term well-being and adjustment, and thus

understanding the neural underpinnings may elucidate ways to direct youth towards positive developmental trajectories.

Figure 1. Brain development as a mediator between social influence and risk-taking behavior (orange arrows; e.g., [45]), and as a moderator on the effect of social influence on risk-taking behavior (blue arrow; e.g., [65]).



Disclosure

The authors declare no conflicts of interests.

Human and Animal Rights

All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

References

Recent papers of particular interest have been highlighted as:

* Of importance

** Of major importance

1. Richmond-Rakerd LS, Slutske WS, Wood PK. Age of initiation and substance use progression: A multivariate latent growth analysis. Psychol Addict Behav 2017:31(6):664–675. Doi: 10.1037/adb0000304
2. Johnston LD, O'Malley PM, Bachman JG, Schulenberg JE, Miech RA. Monitoring the Future national survey results on drug use, 1975-2013: Volume 1, Secondary school students. Ann Arbor, MI: Institute for Social Research, University of Michigan: 2014
3. Institute of Medicine and National Research Council. U.S. Health in International Perspective: Shorter Lives, Poorer Health. (S. H. Woolf & L. Aron, Eds.). Washington, DC: The National Academies Press: 2013
4. Lopez-Quintero C, Pérez de los Cobos J, Hasin DS, Okuda M, Wang S, Grant BF, Blanco C. Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: Results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Drug Alcohol Depend 2013:115(1–2):120–130. Doi: 10.1016/j.drugalcdep.2010.11.004
5. Center for Behavioral Health Statistics and Quality. The TEDS Report: Age of substance use initiation among treatment admissions aged 18 to 30. Rockville, MD: Substance Abuse and Mental Health Services Administration: 2014

6. Cox RG, Zhang L, Johnson WD, Bender DR. Academic performance and substance use: Findings from a state survey of public high school students. J School Health 2007:77(3):109–115. Doi: 10.1111/j.1746-1561.2007.00179.x
7. Brook JS, Stimmel MA, Zhang C, Brook DW. The association between earlier marijuana use and subsequent academic achievement and health problems: A longitudinal study. Am J Addict 2008:17(2):155–160. Doi: 10.1080/10550490701860930
8. Duell N, Steinberg L, Icenogle G, Chein J, Chaudhary N, Di Giunta L, et al. Age patterns in risk taking across the world. J Youth Adolesc 2018:47(5):1052–1072. Doi: 10.1007/s10964-017-0752-y
9. Blakemore SJ, Burnett S, Dahl RE. The role of puberty in the developing adolescent brain. Hum Brain Mapp 2010:31(6):926–933. Doi: 10.1002/hbm.21052
10. Steinberg L, Icenogle G, Shulman EP, Breiner K, Chein J, Bacchini D, et al. Around the world, adolescence is a time of heightened sensation seeking and immature self-regulation. Dev Sci 2018:21(2). Doi: 10.1111/desc.12532
11. Casey BJ. Beyond simple models of self-control to circuit-based accounts of adolescent behavior. Annu Rev Psychol 2015:66(1):295–319. Doi: 10.1146/annurev-psych-010814-015156
12. Urošević S, Collins P, Muetzel R, Schissel A, Lim KO, Luciana M. Effects of reward sensitivity and regional brain volumes on substance use initiation in adolescence. Soc Cogn Affect Neurosci 2015:10:106–113. Doi: 10.1093/scan/nsu022
13. Kim-Spoon J, Deater-Deckard K, Holmes C, Lee J, Chiu P, King-Casas B. Behavioral and neural inhibitory control moderates the effects of reward sensitivity on adolescent

substance use. Neuropsychologia 2016:9:318–326. Doi: 10.1016/j.neuropsychologia.2016.08.028

14. •• Blakemore SJ. The social brain in adolescence. Nat Rev Neurosci 2008:9(4):267–277. Doi:10.1038/nrn2353 **This paper reviews changes in the social brain (network of brain regions involved in other-oriented processes) during adolescence.**
15. •• Steinberg L. A social neuroscience perspective on adolescent risk-taking. Dev Rev 2008:28(1):78–106. Doi:10.1016/j.dr.2007.08.002 **This paper reviews changes in risk-taking behavior across adolescence and its association with the developing brain.**
16. Utech DA, Hoving KL. Parents and peers as competing influences in the decisions of children of differing ages. J Soc Psychol 1969:78(2):267–274. Doi: 10.1080/00224545.1969.9922366
17. Furman W, Buhrmester D. Age and sex differences in perceptions of networks of personal relationships. Child Dev 1992:63(1):103. Doi: 10.2307/1130905
18. Larson RW, Moneta G, Richards MH, Holmbeck G, Duckett E. Changes in adolescents' daily interactions with their families from ages 10 to 18: Disengagement and transformation. Dev Psychol 1996:32(4):744–754. Doi: 10.1037/0012-1649.32.4.744
19. van Hoorn J, van Dijk E, Meuwese R, Rieffe C, Crone EA. Peer influence on prosocial behavior in adolescence. J Res Adolesc 2016:26(1):90–100. Doi:10.1111/jora.12173
20. Knoll LJ, Leung JT, Foulkes L, Blakemore SJ. Age-related differences in social influence on risk perception depend on the direction of influence. J Adolesc 2017:60:53–63. Doi: 10.1016/j.adolescence.2017.07.002
21. Nickerson AB, Nagle RJ. Parent and peer attachment in late childhood and early adolescence. J Early Adolesc 2005:25(2):223–249. Doi: 10.1177/0272431604274174

22. Speicher B. Family patterns of moral judgment during adolescence and early adulthood. Dev Psychol 1994:30(5):624–632. Doi: 10.1037/0012-1649.30.5.624

23. Hoffmann JP, Cerbone FG. Parental substance use disorder and the risk of adolescent drug abuse: an event history analysis. Drug Alcohol Depend 2002:66(3):255–264. Doi: 10.1016/s0376-8716(02)00005-4

24. Windle M. Effect of parental drinking on adolescents. Alcohol Health Res World 1996:20(3):181–184.

25. Robalino JD, Macy M. Peer effects on adolescent smoking: Are popular teens more influential? PLOS ONE 2018:13(7):e0189360. Doi: 10.1371/journal.pone.0189360

26. Tucker JS, de la Haye K, Kennedy DP, Green HD, Pollard MS. Peer influence on marijuana use in different types of friendships. J Adolesc Health 2014:54(1):67–73. Doi: 10.1016/j.jadohealth.2013.07.025

27. Chassin L, Curran PJ, Hussong AM, Colder CR. The relation of parent alcoholism to adolescent substance use: A longitudinal follow-up study. J Abnorm Psychol 1996:105(1):70–80. Doi: 10.1037/0021-843X.105.1.70

28. Curran PJ, Stice E, Chassin L. The relation between adolescent alcohol use and peer alcohol use: a longitudinal random coefficients model. J Consult Clin Psychol 1997:65(1):130–140. Doi: 10.1037//0022-006x.65.1.130

29. Galván A. Insights about adolescent behavior, plasticity, and policy from neuroscience research. Neuron 2014: 83 262–265. Doi: 10.1016/j.neuron.2015.06.027

30. Pfeifer JH, Masten CL, Moore WE, Oswald TM, Mazziotta JC, Iacoboni M, Dapretto M. Entering adolescence: Resistance to peer influence, risky behavior, and neural changes in emotion reactivity. Neuron 2011:69(5):1029–1036. Doi: 10.1016/j.neuron.2011.02.019

31. Galván A. The teenage brain. Curr Dir Psychol Sci 2013:22(2):88–93. Doi: 10.1177/0963721413480859

32. Crone EA, Dahl RE. Understanding adolescence as a period of social-affective engagement and goal flexibility. Nat Rev Neurosci 2012:13(9):636–650. Doi: 10.1038/nrn3313

33. Stice E, Yokum S. Brain reward region responsivity of adolescents with and without parental substance use disorders. Psychol Addict Behav 2014:28(3):805–815. Doi: 10.1037/a0034460

34. Rømer Thomsen K, Blom Osterland T, Hesse M, Feldstein Ewing SW. The intersection between response inhibition and substance use among adolescents. Addict Behav 2018:78:228–230. Doi: 10.1016/j.addbeh.2017.11.043

35. Weissman DG, Schriber RA, Fassbender C, Atherton O, Krafft C, Robins RW, et al. Earlier adolescent substance use onset predicts stronger connectivity between reward and cognitive control brain networks. Dev Cogn Neurosci 2015:16:121–129. Doi: 10.1016/j.dcn.2015.07.002

36. Chein JM, Albert D, O'Brien L, Uckert K, Steinberg L. Peers increase adolescent risk taking by enhancing activity in the brain's reward circuitry. Dev Sci 2011:14(2):F1–10. Doi: 10.1111/j.1467-7687.2010.01035.x

37. Telzer EH, Ichien NT, Qu Y. Mothers know best: redirecting adolescent reward sensitivity toward safe behavior during risk taking. Soc Cogn Affect Neurosci 2015:10(10):1383–1391. Doi: 10.1093/scan/nsv026

38. van Hoorn J, McCormick EM, Rogers CR, Ivory SL, Telzer EH. Differential effect of parent and peer presence on neural correlates of risk taking in adolescence. Soc Cogn Affect Neurosci 2018:13(9):945–955. Doi: 10.1093/scan/nsy071

39. • Telzer EH, Miernicki ME, Rudolph KD. Chronic peer victimization heightens neural sensitivity to risk taking. Dev Psychopathol 2018:30(1):13–26. Doi: 10.1017/S0954579417000438 **This empirical paper provides evidence that chronically victimized girls take more risks, where this relationship is mediated by alterations in affective processing, cognitive control, and social cognition brain regions.**

40. • Schriber RA, Rogers CR, Ferrer E, Conger RD, Robins RW, Hastings PD, Guyer AE. Do hostile school environments promote social deviance by shaping neural responses to social exclusion? J Res Adolesc 2018:28(1):103–120. Doi: 10.1111/jora.12340 **This empirical paper shows that delinquent peer behaviors are associated with greater conduct and defiant disorders in youths, where this relationship is mediated by greater affective processing.**

41. • Holmes C, Owens M, Beach SRH, McCormick M, Hallowell E., Clark US et al. Peer influence, frontostriatal connectivity, and delay discounting in African American emerging adults. Brain Imaging Behav 2020:14(1):155–163. Doi: 10.1007/s11682-018-9977-y **This empirical paper shows that cortico-subcortical functional coupling at rest links peer affiliation and longitudinal impulsive decision making.**

42. van den Bos W, Rodriguez CA, Schweitzer JB, McClure SM. Adolescent impatience decreases with increased frontostriatal connectivity. P Natl Acad Sci USA 2015:112(29):E3765–E3774. Doi: 10.1073/pnas.1423095112

43. McCormick EM, Qu Y, Telzer EH. Adolescent neurodevelopment of cognitive control and risk-taking in negative family contexts. NeuroImage 2016:124(Pt A):989–996. Doi: 10.1016/j.neuroimage.2015.09.063

44. Qu Y, Galván A, Fuligni AJ, Lieberman MD, Telzer EH. (2015). Longitudinal changes in prefrontal cortex activation underlie declines in adolescent risk taking. J Neurosci 2015: 35(32):11308–11314. Doi: 10.1523/JNEUROSCI.1553-15.2015

45. • Guassi Moreira JF, Telzer EH. Family conflict is associated with longitudinal changes in insular-striatal functional connectivity during adolescent risk taking under maternal influence. Dev Sci 2018:21(5):e12632. Doi: 10.1111/desc.12632 **This empirical paper provides evidence that negative family context is associated with a longitudinal increase in risk taking, where this relationship is mediated by poor integration of reward values.**

46. van Duijvenvoorde AC, Op de Macks ZA, Overgaauw S, Gunter Moore B, Dahl RE, Crone EA. A cross-sectional and longitudinal analysis of reward-related brain activation: Effects of age, pubertal stage, and reward sensitivity. Brain Cogn 2014:89:3–14. Doi: 10.1016/j.bandc.2013.10.005

47. Qu Y, Fuligni AJ, Galván A, Telzer EH. Buffering effect of positive parent-child relationships on adolescent risk taking: A longitudinal neuroimaging investigation. Dev Cogn Neurosci 2015:15:26–34. Doi: 10.1016/j.dcn.2015.08.005

48. • Rogers CR, McCormick EM, van Hoorn J, Ivory SL, Telzer EH. Neural correlates of sibling closeness and association with externalizing behavior in adolescence. Soc Cogn Affect Neurosci 2018:13(9):977–988. Doi: 10.1093/scan/nsy063 **This empirical paper**

identifies siblings as salient social figures who modulate adolescent risky behaviors, where this relationship is mediated by affective processing.

49. • Fava NM, Trucco EM, Martz ME, Cope LM, Jester JM, Zucker RA, et al. Childhood adversity, externalizing behavior, and substance use in adolescence: Mediating effects of anterior cingulate cortex activation during inhibitory errors. Dev Psychopathol 2019:31(4):1439–1450. Doi: 10.1017/S0954579418001025 **This empirical paper demonstrates the lasting effect of childhood social deprivation on disinhibited behaviors, where this relationship is linked via affective dysregulation.**
50. Casement MD, Shaw DS, Sitnick SL, Musselman SC, Forbes EE. Life stress in adolescence predicts early adult reward-related brain function and alcohol dependence. Soc Cogn Affect Neurosci 2015:10(3):416–423. Doi: 10.1093/scan/nsu061
51. Schriber RA, Guyer AE. Adolescent neurobiological susceptibility to social context. Dev Cogn Neurosci 2016::19:1–18. Doi: 10.1016/j.dcn.2015.12.009
52. Belsky J. Differential susceptibility to rearing influences: An evolutionary hypothesis and some evidence. In B. Ellis & D. Bjorklund (Eds.), Origins of the social mind: Evolutionary psychology and child development. New York, NY: Guildford; 2005:p.139–163
53. Boyce WT, Ellis BJ. Biological sensitivity to context: An evolutionary–developmental theory of the origins and functions of stress reactivity. Dev Psychopathol 2005:17:271–301. Doi: 10.1017/S0954579405050145
54. Belsky J, Bakermans-Kranenburg MJ, van IJzendoorn MH. For better and for worse: Differential susceptibility to environmental influences. Curr Dir Psychol Sci 2007:16:300–304. Doi: 10.1111/j.1467-8721.2007.00525.x

55. Bakermans-Kranenburg MJ, van Ijzendoorn MH. Differential susceptibility to rearing environment depending on dopamine-related genes: New evidence and a meta-analysis. Dev Psychopathol 2011:23: 39–52. Doi: 10.1017/S0954579410000635

56. Belsky J, Pluess M. Beyond diathesis stress: Differential susceptibility to environmental influences. Psychol Bull 2009:135:885–908. Doi:10.1037/a0017376

57. Brody GH, Chen YF, Beach SR, Kogan SM, Yu T, DiClemente RJ, et al. Differential sensitivity to prevention programming: A dopaminergic polymorphism-enhanced prevention effect on protective parenting and adolescent substance use. Health Psychol 2014:33:182–191. Doi: 10.1037/a0031253

58. Bakermans-Kranenburg MJ, van Ijzendoorn MH. Gene-environment interaction of the dopamine D4 receptor (DRD4) and observed maternal insensitivity predicting externalizing behavior in preschoolers. Dev Psychobiol 2006:48:406–409. Doi: 10.1002/dev.20152

59. • Deane C, Vijayakumar N, Allen NB, Schwartz O, Simmons JG, Bousman CA, et al. Parenting x brain development interactions as predictors of adolescent depressive symptoms and well-being: Differential susceptibility or diathesis-stress? Dev Psychopathol 2019:32(1):139–150. Doi: 10.1017/S0954579418001475 **This empirical paper found that individual differences in adolescents' neural structure, namely reduced frontal cortical thinning, moderated the influence of maternal behavior on adolescent well-being in a manner consistent with differential susceptibility.**

60. • Rudolph KD, Davis MM, Modi HH, Fowler C, Kim Y, Telzer EH. Differential susceptibility to parenting in adolescent girls: Moderation by neural sensitivity to social cues. J Res Adolesc 2020:30:177–191. Doi: 10.1111/jora.12458 **This empirical paper**

provides evidence that functional brain responses in social-affective salience regions may mark differential susceptibility to parent-child relationship quality in the prediction of adolescent depressive symptoms.

61. Schriber RA, Anbari Z, Robins RW, Conger RD, Hastings PD, Guyer AE. Hippocampal volume as an amplifier of the effect of social context on adolescent depression. Clin Psychol Sci 2017:5:632–649. Doi: 10.1177/2167702617699277
62. • Whittle S, Yap MB, Sheeber L, Dudgeon P, Yücel M, Pantelis C, et al. Hippocampal volume and sensitivity to maternal aggressive behavior: A prospective study of adolescent depressive symptoms. Dev Psychopathol 2011:23:115–129 Doi: 10.1017/S0954579410000684 **This empirical paper found that adolescent girls' larger hippocampal volume represented a marker of susceptibility to maternal aggressive behavior in prospectively predicting depressive symptoms.**
63. Yap MB, Whittle S, Yücel M, Sheeber L, Pantelis C, Simmons JG, Allen NB. Interaction of parenting experiences and brain structure in the prediction of depressive symptoms in adolescents. Arch Gen Psychiatry 2008:65:1377–1385. Doi: 10.1001/archpsyc.65.12.1377
64. O'Neil KA, Conner BT, Kendall PC. Internalizing disorders and substance use disorders in youth: Comorbidity, risk, temporal order, and implications for intervention. Clin Psychol Rev 2011:31:104–112. Doi: 10.1016/j.cpr.2010.08.002
65. • Telzer EH, Jorgensen NA, Prinstein MJ, Lindquist KL. Neurobiological sensitivity to social rewards and punishments moderates relationship between peer norms and adolescent risk taking. Child Dev in press. **This empirical paper identifies a pattern of neurobiological susceptibility to peer influence, finding that ventral striatum**

sensitivity to social rewards and punishments moderated the association between negative perceived peer norms and adolescent risk behaviors.

66. Javanbakht A, King AP, Evans GW, Swain JE, Angstadt M, Phan KL, Liberzon I. Childhood poverty predicts adult amygdala and frontal activity and connectivity in response to emotional faces. Front Behav Neurosci 2015:9:154. Doi: 10.3389/fnbeh.2015.00154
67. Kim P, Evans GW, Angstadt M, Ho SS, Sripada, CS, Swain JE, et al. (2013). Effects of childhood poverty and chronic stress on emotion regulatory brain function in adulthood. P Natl Acad Sci USA 2013:110(46): 18442–18447. Doi:10.1073/pnas.1308240110
68. Tottenham N, Galván A. Stress and the adolescent brain: Amygdala-prefrontal cortex circuitry and ventral striatum as developmental targets. Neurosci Biobehav Rev 2016:70:217–227. Doi: 10.1016/j.neubiorev.2016.07.030
69. van Hoorn J, van Dijk E, Meuwese R, Rieffe C, Crone EA. Peer influence on prosocial behavior in adolescence. J Res Adolesc 2016:26(1):90–100. Doi: 10.1111/jora.12173
70. Foulkes L, Leung JT, Fuhrmann D, Knoll LJ, Blakemore SJ. Age differences in prosocial influence effect. Dev Sci 2018:21(6):e12666. Doi:10.1111/desc.12666
71. Bakermans-Kranenburg MJ, van Ijzendoorn MH, Pijman FT, Mesman J, Juffer F. Experimental evidence for differential susceptibility: Dopamine D4 receptor polymorphism (DRD4 VNTR) moderates intervention effects on toddlers' externalizing behavior in a randomized controlled trial. Dev Psychol 2008:44(1):293–300. Doi: 10.1037/0012-1649.44.1.293