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Adolescent Substance Use Risk: A Review of Dopamine and Reward-System Development

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Abstract: ***Adolescence represents a critical developmental period characterized by increased reward sensitivity, risk-taking, and heightened vulnerability to substance and other addictive behaviors. The literature is becoming increasingly clear that the influence of dopamine pathways, associated brain activity related to reward, and other neural mechanisms play a role in susceptibility to substance use during adolescent development. The reviewed articles present both converging and conflicting findings on dopaminergic sensitivity, functional connectivity of reward circuits, the role of stress and social context, and differences in adolescent development compared to younger adults. Overall, the evidence suggests that adolescent vulnerability to substance use emerges from the interaction of neurodevelopmental processes and emotional, social, and environmental factors.***

Keywords: Adolescent Substance Use, Dopamine and Reward System, Neural Mechanisms of Addiction, Mesolimbic Pathway/Ventral Striatum Activation, Neurodevelopment and Risk Taking

1. Introduction

Adolescence is a point in development comprised of biological, cognitive, and psychosocial changes that combine to create behavior and decision making. A major challenge in adolescent development is understanding why young people are at increased risk for substance use; the exact neural explanations are still unclear. This lack of clarity provides reason to consider how neurobiological development, specifically among dopaminergic and reward pathways, may increase risk during a period of development. Research shows that adolescents, not only are they at a greater risk to try a substance, but they are also at a greater risk compared to adults to start a pattern of using a substance (Hamidullah et al., 2020).

Neuroscientific perspectives emphasize that these associated risks are likely related to dopaminergic and reward-related neuroanatomy. In the brain, the adolescent brain shows an imbalance, where subcortical systems which mediate reward response (ventral striatum) undergo development much earlier, while likewise neuroanatomic systems which mediate regulation and control of behavior develop much later (Bjork, 2020; Ernst & Luciana, 2015). This developmental timing likely contributes to greater risk-taking and increased sensitivity to rewards, including potential exposure to drugs.

Recent neuroimaging and longitudinal research add clarification on how changes in dopamine signaling, sensitivity to reward cues, and neural connectivity may drive vulnerability to substance use and related disorders. For example, decreased reward-related activity in the brain is predictive of increases in substance use during the post-adolescent period (Bart et al., 2021). Increased sensitivity in reward-related circuits also predicts increases in substance use (Swartz et al., 2020). Findings further suggest that emotional and social contexts influence these neural processes, highlighting the interaction between neurobiology and environment (Beard et al., 2022).

In this review, the term "dopaminergic sensitivity" is used as an umbrella concept referring to multiple levels of neural explanation rather than direct molecular measurement of dopamine transmission. Specifically, it encompasses (a) mesolimbic reward-system reactivity, particularly within the ventral striatum and associated circuitry, (b) functional and structural characteristics of reward-related networks observed through neuroimaging, and (c) developmental differences in how these systems interact with prefrontal control mechanisms across adolescence. Thus, references to dopaminergic processes throughout this paper reflect converging neural markers of reward function and regulation rather than direct assessments of dopamine release or receptor activity.

The objective of this review is to summarize current findings on dopamine-related reward processing during adolescence and to examine how these neural processes are associated with substance-use risk.

2. Methodology

This review examines peer-reviewed research to better understand neurobiological and psychosocial factors that contribute to adolescents' elevated risk of substance use, with a primary emphasis on dopamine, reward-system functioning, and brain development.

Database Search

To identify areas of research, targeted literature searches of major biomedical and psychological databases (PubMed, Google Scholar, ScienceDirect and SpringerLink) were carried out. We also identified additional papers by tracing citations and references from key reviews. We prioritized neuroscience studies from 2014 to 2024 but included earlier foundational research on reward processing and dopaminergic function in adolescent brain development.

Keywords and Search Terms

A comprehensive combination of keywords and Boolean search strings was developed and tested to identify articles on behavioral, neuroimaging, and molecular aspects of adolescent substance use. The central search terms included.

- *Adolescent Substance Use*
- *Dopamine and Reward System*
- *Neural Mechanisms of Addiction*
- *Mesolimbic Pathway/Ventral Striatum activation*
- *Neurodevelopment and Risk-Taking*
- *Prefrontal Cortex and Inhibitory Control*
- *Functional Connectivity/fMRI*

This approach provided both broad coverage of neurobiological correlates, developmental trajectories, and cognitive-affective driving factors of adolescent substance use susceptibility.

Inclusion and Exclusion Criteria

Studies were included if they:

- Explicitly examined neural or dopaminergic processes associated with adolescent substance use, reward sensitivity, or risk-taking.
- Used human adolescent samples (approximately ages 12–20) or directly compared adolescents and adults to probe developmental differences.
- Were primary empirical articles (neuroimaging, longitudinal, or behavioral) or systematic/narrative reviews published in peer-reviewed journals.
- Fell within the 2014–2024 timeframe, with select earlier work retained for theoretical and methodological grounding.

Studies were excluded if they:

- Focused solely on adults without a developmental comparison.
- Relied exclusively on animal models without clear translational relevance to human adolescence.
- Addressed topics outside neural or dopaminergic mechanisms (e.g., purely sociological or policy-only discussions).
- Were non-peer-reviewed, purely theoretical commentaries, or lacked adequate methodological detail.

A total of 17 studies published in peer-reviewed journals were chosen for review that directly examined dopaminergic function and reward processing and/or neural mechanisms relevant to adolescent substance use. These studies were given priority due to their empirical richness, use

of human adolescent samples, and methodological variety (neuroimaging, longitudinal, or behavioral studies). Together, these studies provide the representation of current understanding (2014-2024) of adolescent vulnerability from a neurobiological perspective.

To clearly organize the evidence, the studies selected for review were grouped into seven interrelated themes that encapsulate fundamental core aspects of adolescent vulnerability to substance use. Together, these findings illustrate how heightened reward sensitivity, ongoing maturation of regulatory control systems, and individual developmental timing interact to produce a distinct neurodevelopmental risk profile for substance use during adolescence.

The major thematic domains identified in the literature are summarized in Table 1.

Table 1: Core Thematic Domains of Adolescent Substance Use Vulnerability

Sl. No	Thematic Domain	Description
1	Dopamine and Reward-System Development	Developmental changes in dopaminergic function, reward reactivity, and regulatory control
2	Emotion, Stress, and Social Context	Influence of mood, stress exposure, and peer environment on neural risk pathways
3	Network and Structural Markers	Functional connectivity and morphometric indicators of vulnerability
4	Genetic and Individual Differences	Genetic polymorphisms, sex differences, and individual traits shaping neural risk
5	Early Life Stress and Affective Processing	Impact of early adversity and affect-related neural responses on later substance use

Across all five themes, the literature indicates that dopaminergic and reward-related neural systems are consistently related to vulnerability to substance use in adolescence; however, the direction and nature of those relationships differ based on the population being studied. Conflicting patterns across studies may be due to differences in task designs, measurement, and
the characteristics of the populations being studied. Future research may strive for more

consistency in methodology, use larger longitudinal cohorts, and include genetic, social, and emotional moderators, to clarify how brain development in adolescence manifests into behavioral vulnerabilities.

3. Review of Literature (ROL)

Dopamine and Reward-System Development in Adolescence

The literature consistently shows that adolescence represents a period of transformed dopaminergic function in the mesolimbic reward pathway, with increased sensitivity to rewarding stimuli. Corongiu et al. (2020), Ernst and Luciana (2015), and Thorpe et al. (2019) noted changes in the expression and transmission of dopamine receptors that distinguish adolescents from adults as more reactive to these stimuli. Similarly, Baker et al. (2018) linked dopaminergic polymorphisms to altered orbitofrontal–striatal activity related to an increased risk of alcohol misuse, and Urošević et al. (2014) showed structural correlates such as regional volumes that interact with reward sensitivity to predict substance initiation. These studies share a focus on dopamine's importance but differ in their emphasis on molecular versus structural and functional aspects. For example, Baker et al. (2018) and Thorpe et al., (2019) place more emphasis on molecular influences or receptor levels, while Ernst and Luciana (2015) and Urošević et al. (2014) studies on structural and functional correlates at the systems level. This disparity draws on different methodological approaches and demonstrates the need for more integrative multimodal investigations that simultaneously expand understanding of the genetic, receptor level, structure, and function (Adindu et al., 2024).

A major debate concerns whether lower or higher neural activity in reward circuits predicts substance use. Bart et al. (2021) demonstrate that decreased reward-related brain function predicts an increase in substance use over time, which aligns with a "reward deficiency" model. On the other hand, Swartz et al. (2020) show that increased ventral striatal activation predicts increases in alcohol use, suggesting a "reward hypersensitivity" pathway. Bjork (2020), among other reviews, attempts to reconcile these conflicting findings by emphasizing the role of task differences (monetary vs. social rewards), a person's developmental timing, and the type of substance outcome being measured. Despite the contradiction, a clear agreement is present: reward circuit activity predicts later substance use, independent of the direction. The disagreement about direction of reward circuit activity in prediction of later substance use probably reflects the multiple and heterogeneity of methods, including reward paradigms, characteristics of a baseline sample, and how the data were analyzed. This highlights the need for more standardized tasks, and longitudinal multimodal designs, to settle the dispute.

Another recurring theme is that adolescents are more susceptible to substance use owing to a developmental imbalance between rapidly developing subcortical reward systems and the slower development of prefrontal control systems (Ernst & Luciana, 2015; Corongiu et al., 2020). Heitzeg et al. (2015) point out that a mixture of inhibitory-control deficits and reward reactivity is a risk-marking combination, while Bjork (2020) argues that the same neural marker can have different implications dependent on developmental stage. Though there is agreement surrounding the developmental imbalance model, literature does vary in whether changes in phasic dopamine signalling (Ernst & Luciana, 2015; Corongiu et al., 2020) or prefrontal control maturation (Heitzeg et al., 2015) are more important. A significant gap is that we still do not have longitudinal imaging studies with repeated measures across early, mid-, and late adolescence to tease apart normative developmental changes of a lot of youth from potentially pathological trajectories.

Emotion Regulation, Stress, and Social Context

The reward circuitry is not static, rather it is an important component of interconnected emotional and social processes that affect risk. Kirsch et al. (2020) demonstrate that stress in early life changes dopamine function which contributes to risk in later substance use and Smith et al. (2024) show that mood symptom trajectories, especially in people at risk for bipolar disorder, predict substance use in the future. Beard et al. (2022) present systematic evidence that social influences, especially those in peer-related contexts, substantially modulate reward processing and substance use outcomes. While these studies demonstrate consistency in a moderator role of context, they differ in mechanisms; independent pathways of mood disorders (Smith et al., 2024), HPA-axis and dopaminergic changes related to early life stress (Kirsch et al., 2020), and peer influence on reward valuation (Beard et al., 2022). The drawback is consideration of concurrent variables in longitudinal neuroimaging studies. Most imaging studies focus primarily on reward activation without taking into consideration moderators such as stress, mood, and peer context.

Network or Structural Markers of Developmental Risks:

Network-level investigations offer further understanding of risk pathways. For example, Huntley and colleagues (2019) demonstrated that a connection between the ventral striatum and the hippocampus was predictive of substance initiation, and Urošević and collaborators (2014) studied how regional volumes and sensitivity to reward predicted initiation. Combined, these studies also describe interactions between inhibitory-control networks and reward networks that may promote risk (Heitzeg et al., 2015). Although useful, these studies demonstrate the predictive value of structural measures and connectivity but differ in focus, i.e., morphometry (Urošević et al., 2014) and functional connectivity (Huntley et al., 2019). Integrative studies that combine structural, functional, and connectivity measures are still limited, suggesting a methodological gap in the field (Adindu et al., 2024).

Genetic and Individual Differences in Neural Risk Markers

Individual differences are increasingly recognized as important moderators of risk. Chaplin et al. (2023) identify sex differences in reward- and emotion-related neural responses, showing distinct predictive pathways for males and females. Baker et al. (2018) highlight the role of dopaminergic polymorphisms in shaping orbitofrontal–striatal activity and alcohol misuse, while Smith et al. (2024) emphasize the unique vulnerability of adolescents at risk for bipolar disorder. The literature agrees that individual differences matter but has not consistently tested moderators such as sex, genetic variability, or comorbid psychopathology across studies. Chaplin et al. (2023) and Baker et al. (2018) are exceptions, but most imaging studies either ignore or underpower these analyses. This lack of systematic attention to moderators constitutes a significant gap in understanding.

Early Life Stress, Affective Processing, and Substance Use

Several studies converge on early life stress as a pathway to substance use risk. Kirsch et al. (2020) review evidence that stress alters dopaminergic signalling, while Gonçalves et al. (2022) show that affect-related neural activity predicts substance use in adolescents. Compared to reward-only models, these findings highlight how environmental and developmental experiences shape neurobiology in ways that influence vulnerability. A key gap in this area is the lack of longitudinal studies that simultaneously track early life stress, neural changes, and later substance outcomes. Most work is cross-sectional or relies on retrospective stress measures, limiting causal inference. Finally, multiple reviews synthesize findings across the field. Ernst and Luciana (2015) and Heitzeg et al. (2015) emphasize inhibitory-control and reward markers as risk factors. More recent reviews (Gonçalves et al., 2022; Beard et al., 2022; Adindu et al., 2024) emphasize interactions between reward systems, affect, social context and genetics. Adindu et al. (2024) call for the need for large-scale, multimodal longitudinal studies that integrate across these factors.

Together, these reviews emphasize two consistent points we have noted: (1) the predictive value of neural reward systems

for substance-use outcomes, and (2) the heterogeneity of the findings demonstrates the need for agreed, integrative methodologies.

4. Critical Analysis

The studies analyzed suggest that dopamine and reward circuitry are critical to adolescent vulnerability to substance use. The evidence regarding dopamine and reward circuitry comes from a variety of neuroimaging, MRI, functional connectivity, and genetic studies. For example, Baker et al. (2018) and Thorpe et al. (2019) provided multimodal evidence for these mechanisms. Moreover, a longitudinal study such as Swartz et al. (2020), Bart et al. (2021), and Smith et al. (2024) demonstrate that neural markers can predict substance use vulnerability. As a result of this work, we are now beginning to incorporate environmental moderators such as stress, mood disorders, social context, and sex differences as moderators of such neural vulnerabilities. Collectively, these studies have underscored the importance of context-dependent and environment-based moderators of adolescent risk.

Despite the advances in this work, the current literature indicates some notable limitations. One significant limitation is the heterogeneity of task paradigms and, therefore, outcome measures, primarily around reward-related neural activity studies. Reward tasks can include monetary, social, affective, and drug cues, hence the variability in reward-related literature is significant with both activation rosettes and general activation patterns across reward circuitry. Many neuroimaging and genetic studies continue to use small samples with little diversity or are also financially limited, or from a similar demographic. Consequently, the larger picture of the work becomes difficult to generalize to the population at large. Although some studies assess moderators such as stress, mood, or social factors, few have examined these within the same longitudinal cohort as structural, functional, and connectivity assessments, limiting knowledge of the full complexity of the risk pathways. The use of cross-sectional designs and shorter follow-up periods in some studies limits causal inference, further compounded by inconsistent consideration of sex, genetic polymorphisms, and comorbid psychopathology account leads to less interpretability of predictive models for adolescent substance use.

Despite these drawbacks, this is a clear advance in the field, as it provides a more mechanistic understanding of vulnerability to substance use in adolescence. These studies build on previous evidence from molecular, structural, functional, and connectivity studies to show how reward circuitry interacts with environmental and individual factors to push the study of their neurophysiology further than a solely behavioral explanation. Reward-related neural measures combined with contextual moderators such as those mentioned above appear to be good candidates for early developmental biomarkers of risk for substance use and could serve as potential targets for intervention. Furthermore, studies that inform mechanisms for neural and psychosocial vulnerabilities also inform prevention strategies that enhance inhibiting control, moderated stress regulation capacity or tailoring of interventions based on sex and genetic profiles.

Future research could benefit from creating longitudinal multimodal studies that test and assess structural, functional, connectivity, and genetic metrics over early, mid, and late periods of adolescence to clarify developmental trajectories and causal mechanisms. By standardizing reward paradigms or comparing multiple tasks in the same experiment, further inconsistencies related to patterns of neural activation will be clarified. Attaching both environmental and individual moderators into one framework will provide a realistic characterization of risk, while combining neural measures with translational research focused on prevention or intervention outcomes is crucial. Lastly, including distal social and cultural diversity in samples will guarantee that results apply beyond Western populations and account for social and peer contexts.

5. Conclusion

Across studies, disruptions in dopamine function and circuitry as it pertains to reward represented a significant, consistent mechanism associated with risk during adolescence. Neuroimaging and connectivity studies demonstrated that both hypo- and hyperactivation in reward circuitry predicted substance use trajectories and therefore, it is imperative we consider the paradigms to which tasks reflect real-world behaviour (timing of development) and across individual differences. Further, emotional and social moderators (mood symptoms, early life stress, peer context) also shape developed neural vulnerability suggesting that risk is not solely biologically determined. Developmental comparisons suggest that the adolescent readiness and reactivity is a risk phenotype due to their increased reward sensitivity balanced with underactive prefrontal control and reflects a unique window of risk relative to adulthood. Despite the literature's confidence in these mechanisms, methodological inconsistencies, limited sample diversity, and insufficient integration of various behavioral moderators confound the evidence. Future efforts should increase comprehensiveness of previous literature with longitudinal multimodal designs combining structural, functional, genetic, and environmental/social variables to assist in developing reliable markers of risk and to inform targeted prevention strategies. This body of work expands contemporary understandings of a neurodevelopmental basis of adolescent substance-use risk and highlights a pathway for future integrative integration. These findings are especially relevant for informing early prevention strategies, guiding neurodevelopmentally informed interventions, and shaping public-health approaches aimed at reducing adolescent substance-use risk during this critical developmental window.

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