

Addiction, Orexin Dysregulation, and Educational Therapy: A Neurobiological Framework for Intervention in Neurodevelopmental and Psychiatric Disorder Comorbidities

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ABSTRACT

Addiction has been increasingly recognized as a neurodevelopmental and neuropsychiatric disorder rooted in dysregulation of the brain's reward-stress-executive function systems. Central to this neurological dysregulation is the hypothalamic orexin system, which modulates dopamine pathways involved in reward, motivation, and compulsive behavior. This paper explores the role of orexin in addiction and its complex interactions with the hypothalamic-pituitary-adrenal (HPA) axis, prefrontal cortex (PFC), amygdala, and nucleus accumbens. Special emphasis is placed on how orexin dysfunction contributes to addiction vulnerability in individuals, especially young people with psychiatric disorder comorbidities, such as attention deficit-hyperactivity disorder (ADHD) and emotional disturbances (ED). Additionally, this paper proposes educational therapy (EdTx) as a neuroscience-informed, non-pharmacological intervention that directly targets orexin-dopamine-reinforcement circuits. Through structured reinforcement, executive function support, cue exposure, and psychoeducation, EdTx offers a brain-based intervention strategy aligned with developmental frameworks. This integrative approach holds promise for promoting recovery, neuroplastic resilience, and sustained behavioral change in young people with addiction.

Keywords

Addiction Neurology, Educational Therapy (EdTx), Dopamine Reward Circuitry, Neurodevelopmental Disorders, Orexin System.

Introduction

Addiction, especially in the young people population, is a complex and multifactorial condition involving interactions between neural circuitry, psychological vulnerabilities, behavioral patterns, and socio-environmental pressures. Each classification contributes unique mechanisms to the onset, maintenance, and relapse of addictive behaviors, often converging on the neurological dysregulation of the reward system, primarily involving the mesolimbic and mesocortical pathway. According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), addiction is clinically recognized under the umbrella of substance use disorders (SUDs) and, increasingly, certain compulsive behavioral addictions (including gambling,

gaming and internet use). Compulsive behavioral addictions share similar neural substrates with substance use addiction, reinforcing the compulsive maladaptive habits through compulsive reward-seeking and impaired executive functions. The spiritual and existential dimensions of addiction highlight the human drive for purpose, identity, and connection, revealing that chronic addiction may arise from internal voids and unresolved existential crises.

Addiction leads to long-lasting changes in the brain structures and pathways, affecting areas involved in reward, motivation, memory, and decision-making. Neurobiologically, addiction is characterized by imbalances in neurotransmitters (e.g., dopamine, glutamate, GABA, and serotonin) as well as impairments in key brain regions including the prefrontal cortex (PFC), amygdala, hippocampus, hypothalamus, and nucleus accumbens (NAc) [1]. Neurodevelopmental and psychiatric disorder Comorbidities, including ADHD, post-traumatic stress disorder (PTSD),

schizophrenia, anxiety disorder and depression, heighten susceptibility to addiction through emotional dysregulation and cognitive distortions.

The Neurobiology Of Dopamine Reward System Associated With Addiction

Dopamine is synthesized at the ventral tegmental area (VTA) and projected across the brain's reward system including the limbic system via the mesolimbic pathway, and cortical areas via mesocortical pathway (Figure 1) [2]. The reward system is a complex neurobiological network that processes rewarding stimuli, such as seeking food or social interaction, driving motivation, pleasure, and learning. The brain regions involved in the brain reward system include the VTA, NAc, hippocampus, amygdala, hypothalamus and PFC.

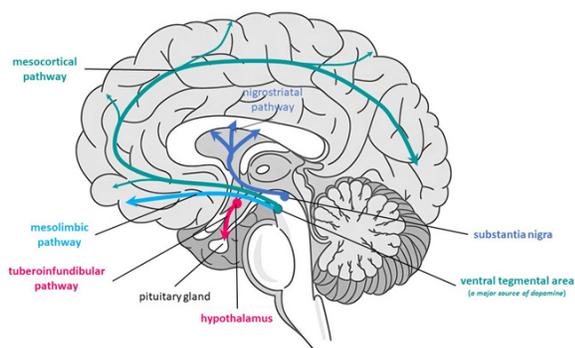


Figure 1: The dopaminergic system and projection pathways.

The classical conditioning theory by Ivan Pavlov, the Nobel Prize winning Russian psychologist, claims that a novel external cue could be associated with a rewarding experience relevant to an individual [3, 4]. As the process of association with the rewarding experience is repeated and becomes predictable, these external cues become conditioned and learned triggers [5]. The learned triggers are encoded by the amygdala (emotional salience), hippocampus (contextual memory) [6], and PFC (decision-making). Once the individual encounter the same external cue again, the PFC, amygdala and hippocampus send concurrent signals to various brain regions (Figure 2) that coordinate the reward and addiction system [2]. The functions of each brain region and their effects of chronic addiction is shown in Table 1 [1, 7-13].

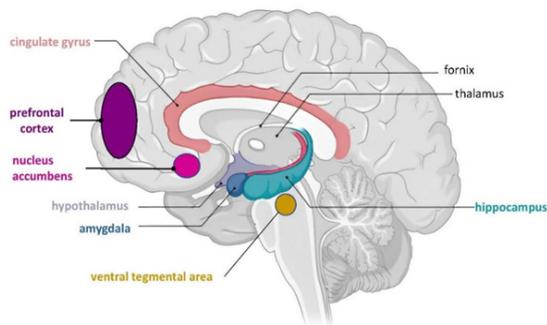


Figure 2: Regions associated with the brain's reward system.

Table 1: Functions of the Brain Regions and Their Effects of Chronic Addiction.

Brain regions	Functions	Effect of Chronic Addiction
Amygdala	Emotion/fear processing; assigns emotional significance to stimuli (e.g., linking cues to rewards or threats).	Hyperreactivity to stress and withdrawal cues, amplifying negative emotional states (anxiety, dysphoria). Drives substance use to avoid discomfort (<i>negative reinforcement</i>).
Hippocampus	Encodes contextual/spatial memories; consolidates learned associations (e.g., linking environments to drug rewards).	Strengthened, maladaptive cue-reward memories. Triggers cravings in contexts associated with past use, increasing relapse risk.
Hypothalamus	Regulates homeostasis (hunger, sleep) and motivated behaviors; integrates hormonal/autonomic responses.	Dysregulated stress hormones (e.g., cortisol) and arousal systems (e.g., orexin). Increases cravings and compulsive drug-seeking to restore "balance."
Nucleus accumbens (NAc)	Reward processing and reinforcement; integrates dopamine signals to drive motivation.	Downregulated dopamine D2 receptors, reducing sensitivity to natural rewards. Prioritizes addictive substances/behaviors as the primary source of reward.
Ventral tegmental area (VTA)	Produces and releases dopamine to the NAc and prefrontal cortex; central to reward signalling.	Overactivation causes excessive dopamine surges during drug use. Chronic use leads to dopamine depletion, worsening cravings and withdrawal.
Prefrontal cortex	Executive functions (decision-making, impulse control); regulates limbic-driven urges.	Impaired regulation of limbic activity (weakened inhibition). Loss of impulse control and foresight, making cravings harder to resist.

Ventral Tegmental Area (VTA)

The VTA is a primary source of dopaminergic neurons where they stretch their axons to multiple brain regions, including the NAc, PFC, amygdala, and hippocampus. It plays a central role in the initiation of reward signalling and reinforcement learning. When VTA receives the glutamatergic reward stimuli signals from the PFC, hypothalamus and amygdala, it projects back dopaminergic signals through both the mesolimbic pathways (to the NAc, hippocampus and amygdala) and the mesocortical pathways (PFC) to drive motivated and reward seeking behaviors, in their bidirectional communication. These pathways are critical in the experience of pleasure and reinforcement of learning.

Nucleus Accumbens

The NAc, a central component of the brain's reward system, serves as a crucial integration of excitatory glutamatergic stimuli signals from PFC (cognition and control), amygdala (emotion memory) and hippocampus (contextual memory) to drive motivated behaviours. It also receives the modulatory dopaminergic signals from the VTA to coordinate the complex interplay of factors that underlie reward-seeking behavior and its dysregulated conditions such as addiction [14]. These converging signals allow the NAc to assess the salience and value of rewarding stimuli, facilitating the initiation and reinforcement of goal-directed actions¹⁴ that lead

to positive outcomes. The NAc is involved in the transition from goal-directed actions to habitual behaviors, particularly in the context of addiction. Over time, control over behaviour shifts from the ventral striatum (including the NAc) to the dorsal striatum, leading to more automatic and compulsive actions [15]. The NAc undergoes neuroplastic changes in response to chronic exposure to addictive substances. These changes include alterations in gene expression and synaptic strength, which contribute to the development and persistence of addictive behaviors.

According to Skinner [16], behaviors are shaped and maintained by their consequences through reinforcement. Behaviors followed by rewarding outcomes are more likely to be repeated and vice versa. In his operant conditioning understanding, when the VTA releases dopamine, the dopaminergic signaling of the mesolimbic and mesocortical pathways reinforces the association between the behavior and the reward, increasing the likelihood of the behavior being repeated [17]. In this feedback loop, the PFC, amygdala and hippocampus assess the value of actions and guide future behaviour based on past experiences. Operant conditioning plays a pivotal role in the development and maintenance of addiction and compulsive behaviors by reinforcing actions through their consequences. During the initial stages of addiction, substances or compulsive behaviors massively increase dopamine release in the NAc projected from the VTA. This reward signal in turn strengthens associations between the addictive substances or compulsive behaviors and pleasure. Over time, external environmental cues activate the amygdala and hippocampus, triggering cravings via the conditioned learning even in the absence of the substance itself [18].

With repeated exposure, these external environmental cues induce transition in behavior from flexible goal-driven actions at the NAc to automatic rigid habits with increasing involvement of the dorsolateral striatum, a region associated with automated, stimulus-response habits [18]. At the core of this shift is dopamine dysregulation where addictive substances flood the brain with dopamine. The brain adapts by reducing dopamine receptors (especially D2 receptors) at the NAc, dulling responses to natural rewards like food or social interaction, leading to tolerance (needing more of the substance to feel the same effect) and anhedonia (inability to enjoy everyday activities) [18]. The brain eventually becomes dependent on the substance just to function normally.

As the hippocampus encodes powerful memories linking substance to specific environmental triggers, these triggers could spark intense cravings years after quitting. While the amygdala becomes hypersensitive to stress and withdrawal, driving users to seek the substance not necessary for pleasure, but to avoid negative emotions such as anxiety or pain. This shift from “*chasing a euphoria*” to “*avoiding pain*” is called “*negative reinforcement*”, a key mechanism sustaining addiction. This explains why addicts continue substance use even when the reward diminishes as the behavior becomes ingrained, like a reflex triggered by cues (e.g., people, places, or emotions linked to substance use). These compounded changes weaken the PFC in decision-making. Thus, chronic addiction reduces PFC activity and impair impulse control

and judgment. Even when individual is aware of the harm, addicts struggle to resist urges because cravings which are overridden by the hyperactive brain limbic regions [19].

Hypothalamus

Another critical brain region associated with addiction, the hypothalamus, is responsible for integrating internal physiological signals and orchestrating appropriate responses to maintain body’s homeostasis [20]. These responses include essential functions such as thirst, hunger, sleep, temperature regulation, circadian rhythm, sexual behavior, blood pressure and its pH level, glucose level, heart rate, and emotional responses (Figure 3) [20]. The key function of homeostasis is to maintain a stable and balanced internal environment in the body despite external changes. This stability and balance are crucial for the optimal functioning of cells, tissues, and organs, and it enables the body to sustain life and maintain well-being. An imbalanced body’s internal condition could lead to illness and diseases (e.g., diabetes, dehydration, acidosis, hypoxia).

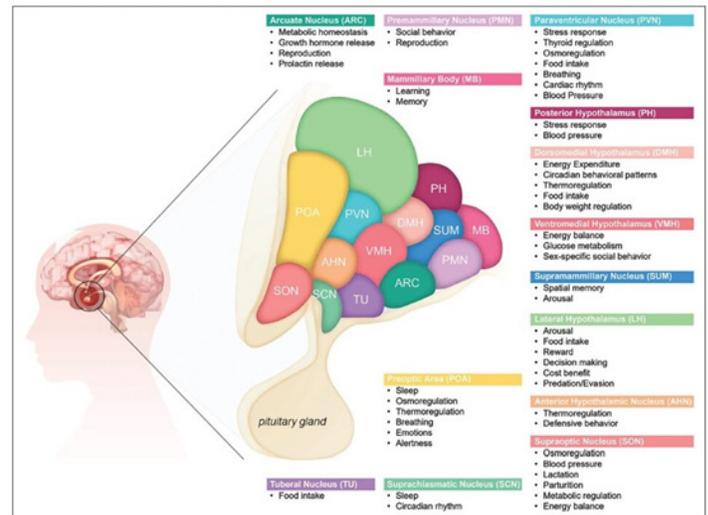


Figure 3: Functional map of the hypothalamus, depicting distinct subparts (nuclei) and their associated functions.

Hypothalamic-Pituitary- Adrenal Axis

The stress response system mediated by the hypothalamic-pituitary-adrenal (HPA) axis is highly associated with addiction and is frequently dysregulated in psychiatric conditions (depression, PTSD, anxiety disorders, bipolar disorder, psychosis and schizophrenia) [2]. When the body encounters a stressor, the amygdala processes the threat and activates the paraventricular nucleus (PVN) of the hypothalamus (Figure 3) [20]. In response, the hypothalamus releases corticotropin-releasing factor (CRF), which stimulates the anterior pituitary gland to secrete adrenocorticotropic hormone (ACTH). ACTH then signals the adrenal cortex (part of the adrenal gland) to produce cortisol, the primary glucocorticoid involved in the stress response [21]. Cortisol plays a key role in regulating the longer-term phase of the stress response by mobilizing energy reserves, modulating inflammation, and influencing memory and emotional processing.

Chronic overactivation or dysregulation of the HPA axis can impair mood regulation, cognition, and lead to structural and functional brain changes, particularly in the hippocampus, PFC, and amygdala (Table 2) [21-23].

Table 2: Functional differences of acute and chronic stress.

Feature / Function	Acute Stress (Fight-or-Flight)	Chronic Stress
Primary System Activated First	SAM system (Sympathetic-Adrenal-Medullary)	HPA axis (Hypothalamic-Pituitary-Adrenal) — chronically engaged
Hormone responsible for rapid fight-or-flight	Adrenaline (epinephrine) and Noradrenaline from adrenal medulla	Cortisol from adrenal cortex is not responsible for immediate fight-or-flight
HPA Hormone Cascade	Begins after SAM: CRF → ACTH → Cortisol (~15–30 min delay)	Continuously elevated or dysregulated cortisol due to prolonged activation
Purpose of Adrenaline	↑ Heart rate, ↑ BP, ↑ breathing, ↑ glucose, pupil dilation — immediate survival	Minimal role once stress becomes chronic
Purpose of Cortisol	Supports prolonged energy needs, modulates inflammation, helps recovery post-stress	Chronic high levels → hippocampal atrophy, immune suppression, mood dysregulation
Onset Timing	Seconds (adrenaline), minutes (cortisol starts rising after ~15–20 min)	Hours → days → months
Endocrine Glands Involved	- Adrenal medulla (SAM) - Adrenal cortex (HPA)	Adrenal cortex (persistent cortisol output)
Neurotransmitters Increased	Dopamine, norepinephrine, glutamate, serotonin (transient)	↓ Dopamine, ↓ Serotonin, ↑ Glutamate (neurotoxicity), ↓ GABA
Brain Area Response	Amygdala = threat detection PFC = initial decision-making	Amygdala hypertrophy, PFC atrophy, hippocampus atrophy

Orexin System at the Lateral Hypothalamus

The lateral hypothalamus (LH), a nucleus of the hypothalamus, regulates our sleep-wake cycle and arousal, hunger and feeding behaviours, most importantly modulating our reward-seeking behaviour aligned with our needs and environmental context. For instance, in the situation when an individual is hungry, orexinergic neurons at the LH become more active and modulates the brain reward system [24]. These orexinergic neurons at the LH project orexin (which are neuropeptides), activate the synthesis of the dopamine at the VTA and enhance the release of these dopamine projected from the VTA at the NAc (Figure 4) [25]. As a result, the salience of rewarding stimuli is amplified, influencing the initiation and execution of goal-directed actions. Various studies have shown that the orexin level is also elevated by the CRF when an individual faces dysregulated HPA axis resulted from chronic stress common seen in psychiatric disorders. This elevation influences the individual to initiate and execute goal-directed actions, including substance use or compulsive behaviors as coping mechanisms for stress. It is critical to recognize that these relationships are complex and bidirectional, with multiple systems and factors influencing each other [14-24].

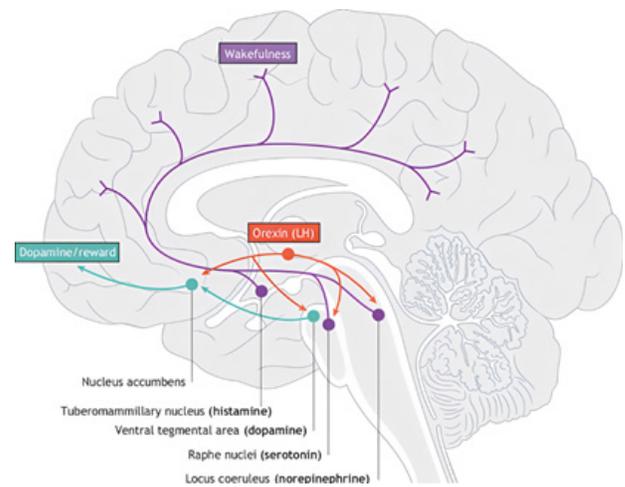


Figure 4: Orexin signaling pathway.

Psychiatric Disorders and their Association with Substance Use Disorders

The relationship between psychiatric disorders and SUDs represents one of the most significant challenges in modern mental health care (Table 3) [26-33]. Current research consistently demonstrates remarkably high rates of psychiatric disorder comorbidities conditions with addiction, revealing complex bidirectional relationships that substantially complicate treatment approaches and worsen clinical outcomes. These findings underscore the critical need for multimodally treatment that address both psychiatric symptoms and SUDs simultaneously, as traditional sequential or parallel treatment approaches often prove inadequate for this highly vulnerable population especially young people.

Table 3: Estimated prevalence of psychiatric disorder comorbidities with substance use disorders.

Condition	Estimated Prevalence of Co-occurring SUD (%)
ADHD	21%
Schizophrenia	40%
Bipolar Disorder	40%
Major Depression	24%
Anxiety Disorders	33% - 45%
PTSD	20% - 60%
OCD	21% - 36%
OCD	18-24%

The adolescent brain continues developing and undergo extensive remodeling until the mid-20s, particularly in the PFC that regulates executive functions and the limbic system that is associated with emotional regulation. The protective myelin sheaths around nerve fibers are still forming during adolescence. The brain naturally prunes unused neural connections during adolescence. Substance use during this period can disrupt normal developmental processes, increasing vulnerability to mood disorders, anxiety, and other psychiatric conditions. Substances can interfere with this process, potentially leading to long-term alterations in brain circuits associated with psychiatric disorders [34-36].

ADHD and Altered Reward System

Studies have shown the PFC of young people with ADHD linked to delays in brain maturation are often smaller in size. The underdevelopment of the PFC resulted in impairment in executive functioning skills and symptoms of inattention, hyperactive, impulsivity and difficulty in delaying gratification, making it harder to these population to manage cravings and resist addictive behaviours [37]. The dysregulation of the brain's reward circuitry commonly seen in ADHD young people, causes a lower level of dopamine being released in areas like the PFC and NAc. This dysregulation hyperactivates the homeostatic nature of the hypothalamic orexin system at the LH to release orexin neuropeptides to modulate the synthesis of dopamine at the VTA in response to rewarding stimuli and release them at the PFC and the NAc via the dopaminergic pathways [38].

As a result, the role of orexin system in increasing dopamine release from the VTA to the NAc can cause the reward circuitry to become hyperactive resulting in enhanced craving, poor inhibition and engage in behaviors that provide immediate gratification. Many individuals with ADHD self-medicate using substances like alcohol, nicotine, or stimulants to provide short-term relief from their emotional distress, stress, or difficulty regulating attention. The immediate pleasurable effects from substances or compulsive behaviors in ADHD individuals create a positive feedback loop where the orexin system and dopamine release reinforce the addiction, making it difficult to break free from the cycle [39].

Psychiatric Disorders and Addiction Risk

Individuals with emotional dysregulation or psychiatric disorders often experience elevated stress levels. This alters the functioning of the HPA axis and affects the orexin system. Chronic stress, in particular, can lead to hyperactivation of the orexin system, making individuals more susceptible to impulsive decisions, reward-seeking behaviors, and even addiction [14]. Acute stress activates the orexin system to project orexin to both raphe nuclei and locus coeruleus in modulating synthesis and projection of serotonin and norepinephrine respectively that promote adaptive mood regulation, arousal alertness and stress responsiveness, aiding in immediate responses to challenges. In contrast, chronic stress can dysregulate the orexin system. This leads to exacerbation of reward dysregulation, promoting maladaptive coping strategies like substance abuse [41-43].

Addiction substances disrupt normal neurotransmitters' functions by enhancing their release, blocking reuptake, or mimicking their effects at receptors of dopamine, serotonin and endorphins (see Table 4) [44-50]. These actions create intense reward signals, reinforcing drug-seeking behaviour. The orexin system, as discussed previously, amplifies these effects by enhancing arousal and cue-driven responses in the neurotransmitters' pathway. Addiction significantly disrupts sleep-wake regulation which is associated with dysfunctional orexinergic signalling. Its dysregulation, especially commonly seen in psychiatric disorders, may lead to excessive daytime arousal, insomnia, or disrupted sleep patterns [51]. This imbalance can result in restlessness and

Table 4: Substance use affecting the mechanism of brain neurons contributing to addiction.

Substance	Neuro-transmitter /Receptor Affected	Mechanism of Action	Contribution to Addiction
Nicotine (cigarettes)	Dopamine	Activates nAChRs on VTA dopamine neurons, increasing dopamine in NAc; chronic use desensitizes β 2-nAChRs, reducing GABA inhibition.	Dopamine surges reinforce reward-seeking; desensitization maintains craving.
	Serotonin	Triggers serotonin release in cortex and limbic areas.	Mood modulation enhances reinforcing effects.
	Endorphins	Indirectly increases endorphins via nAChR activation.	Euphoria reinforces use.
	Nicotinic Receptors	Direct agonist of nAChRs, stimulating neurotransmitter release.	Repeated stimulation contributes to dependence.
Alcohol	Dopamine	Increases dopamine in NAc via indirect GABA/glutamate modulation in VTA.	Reward-driven behaviour due to dopamine increase.
	Serotonin	Enhances serotonin release; interacts with 5-HT1B and others.	Mood changes facilitate dependence.
	Endorphins	Stimulates endorphin release, binds opioid receptors.	Euphoria reinforces drinking behaviour.
	Opioid Receptors	Indirectly activates opioid receptors via endorphin release.	Pain relief and mood elevation increase risk of use.
	NMDA Receptors	Blocks NMDA receptors, leads to hyperexcitability in withdrawal.	Withdrawal symptoms reinforce continued use.
Opioids (e.g., Morphine, Heroin)	Dopamine	Inhibits GABAergic VTA neurons via μ -opioid receptor, increasing dopamine in NAc.	Euphoria and reward drive compulsive use.
	Endorphins	μ -opioid receptor agonists mimic endorphins causing euphoria and analgesia.	High euphoria leads to dependence; endogenous suppression.
	Pain Receptors	Directly activates μ -opioid receptors, blocking pain signals.	Strong reinforcement via analgesia and pleasure.
Cocaine	Dopamine	Blocks DAT, increasing synaptic dopamine.	Reward amplification promotes compulsive use.
	Serotonin	Blocks serotonin reuptake, raising synaptic levels.	Mood elevation enhances compulsive behaviour.
	Nicotinic Receptors	No direct interaction; indirect effects via dopamine.	Minimal direct impact on addiction.
Amphetamines (e.g., Methamphetamine)	Dopamine	Reverses DAT, causes non-vesicular dopamine release; also inhibits reuptake.	Massive dopamine surge reinforces use; neurotoxicity risk.
	Serotonin	Increases serotonin release and inhibits reuptake.	Mood effects and toxicity contribute to addiction.
	Nicotinic Receptors	Indirect cholinergic modulation of dopamine neurons.	Indirectly supports dopamine-related addiction.
Cannabis (THC)	Dopamine	CB1 activation inhibits GABA, indirectly increasing dopamine in NAc.	Reward enhancement through dopamine increase.
	Endorphins	Indirect effects via CB1 and endogenous opioids (anandamide-like).	Euphoria supports continued use.
	Pain Receptors	Modulates pain via CB1 and possibly opioid cross-talk.	Pain relief adds to reinforcing properties.

a craving for stimulation, potentially contributing to impulsivity and addictive tendencies. While this connection is plausible, direct evidence linking orexin dysregulation in psychological disorders to addiction is limited and merits further exploration.

Educational Therapy as a Neuroscience-Informed Non-Pharmacological Intervention for Addiction

Young people commonly develop dependencies on substances such as alcohol, cannabis, and nicotine, along with compulsive behaviors involving gambling, excessive online activity, social media engagement, and video gaming. These problematic patterns often stem from social influences, environmental factors, and efforts to manage emotional difficulties or underlying psychological issues [52].

While pharmacological interventions have demonstrated significant efficacy in treating SUDs, no single therapeutic method is effective for all individuals struggling with addiction. Typically, treatment involves combining multiple therapeutic approaches to address substance abuse and addiction. The treatment process breaks the pattern of addictive behavior and usually requires extended, comprehensive intervention [53]. Studies suggest that non-pharmacological interventions (NPIs) may offer superior long-term outcomes, particularly when addressing the complex interplay between addiction and psychiatric comorbidities [54].

The concept of addiction was initially conceptualized in this paper with consideration for its implications in educational therapy (EdTx for short), which offers neuroscience-informed non-pharmacological interventions (NPIs) to addiction. EdTx is a structured approach that utilizes individualized teaching strategies to help individuals understand their addiction, develop coping skills, and build cognitive and emotional tools for long-term recovery. Educational therapists work alongside schools and families to establish accommodations through individualized educational plans (IEPs), supportive technologies, and adaptable teaching methods that are customized to each individual's evolving cognitive and neurological needs, extending support beyond solely medical interventions and behavioral approaches [55].

EdTx *“has been officially recognized by the World Health Organization (WHO) and classified under the procedural code 93.82 since 1986 in the WHO's International Classification of Diseases (ICD) 9th Edition-Clinical Modifications, Volume 3”* [55,56]. While medical professionals including psychiatrists and allied professionals (e.g., psychologists) refer to either ICD or the latest edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM) published by the American Psychiatric Association, the educational therapists also refer to The Educator's Diagnostic Manual of Disabilities and Disorders (EDM) [57], which relies on a five-level coding system for most descriptive identification of a child with a disability based on the 13 disability categories listed in the Individuals with Disabilities Education Act (IDEA); PL No. 108-446, enacted in 2004.

Psychoeducational therapy (PsyEdTx), a branch of EdTx,

proves particularly effective for adolescent addiction because it addresses the neurological immaturity through education and skill-building. PsyEdTx is a structured therapeutic approach that combines psychotherapy or talk therapy, including cognitive behaviour therapy (CBT), Cue Exposure Therapy (CET) and mindfulness-based strategies with educational components to help individuals understand their mental health conditions, behaviors, or life challenges [58]. The educational component covers triggers, warning signs, and the cycle of addiction, helping them recognize patterns in their own behavior. This awareness is crucial for developing self-monitoring skills and early intervention strategies [59]. Psychoeducational therapy can be delivered in individual or group settings and is commonly used to address addiction, mood disorders, anxiety, ADHD, eating disorders, and chronic medical conditions. It's particularly effective when clients need to understand complex conditions, learn new coping skills, or when family members require education about supporting their loved one's recovery. The approach complements other therapeutic methods and often serves as a foundation for more intensive psychological interventions.

Addiction was seen as a moral failing [60], but not today anymore. It has been accepted as a neurobiological disorder rooted in dysfunctions of the brain's stress-reward-executive functioning systems [61]. This evolving understanding has catalyzed a shift toward NPIs that directly target the neural pathways implicated in compulsive substance use. Among these, EdTx stands out as a uniquely positioned, evidence-based approach that combines neurodevelopmental rehabilitation, behavioral scaffolding, and psychoeducation. Far from being a purely academic support, EdTx operates at the intersection of learning science and brain-based mental health, offering a critical contribution to comprehensive addiction treatment [59].

Targeting the Orexin-Dopamine-Reinforcement Circuit

At the core of addiction lies the dysregulation of the orexin (hypocretin) system and dopamine-based reward circuitry. Together they reinforce compulsive substance use in response to environmental cues. EdTx can mitigate these maladaptive reinforcement patterns with the following strategies, e.g., (i) Substituting addictive cues with structured, positive reinforcements (e.g., token economies, praise, or task-based goal rewards), strategies used in EdTx help to activate dopamine release and orexin-mediated motivation, without the neurotoxic effects of substances; (ii) Creating predictable routines and structured environments, and, in turn, EdTx can help to decrease cognitive overload and emotional reactivity; both of which heighten vulnerability to addiction relapse; and (iii) Supporting the internalization of new reward patterns, EdTx enables individuals with addiction to gradually shift from externally reinforced behaviors to intrinsically motivated options. Research studies show that these structured reinforcement strategies applied in EdTx help to recondition the orexin-dopamine system, fostering neuroplastic recovery and adaptive habit formation [62,63].

Executive Function Rehabilitation and ADHD

Many individuals with addiction, particularly those with co-occurring ADHD, exhibit underactivity in the PFC, which is essential for executive functions (e.g., inhibition, planning, and self-monitoring). EdTx directly addresses these deficits by applying the following strategies, e.g., (i) Breaking down goals into manageable objectives that articulate specific steps, EdTx helps to pace the tasks, and provide attention scaffolds to enhance working memory and task persistence; (ii) Teaching delayed gratification and frustration tolerance, EdTx offers crucial skills that can help to reduce impulsivity and mitigate orexin-driven cravings; and (iii) Rebuilding tolerance for discomfort (e.g., boredom and anxiety), EdTx can help to prevent triggers that lead to substance use, especially in ADHD-affected individuals. By improving executive functioning skills, EdTx can help to restore the top-down PFC regulation over limbic impulses, reducing cue-reactivity and compulsive behavior [64].

Cue Exposure and Adaptive Habit Replacement

Addiction is perpetuated through cue-conditioned responses: emotional and/or environmental triggers that automatically elicit cravings. PsyEdTx disrupts these triggers through the following strategies, e.g., (i) Applying visual schedules, timers, and predictable cues to support attentional control and also reduce emotional reactivity; (ii) Instructing adaptive cue-response alternatives (e.g., using mindfulness or structured breaks instead of stimulants before tasks) in order to break the loop of compulsive responses mediated by the orexin system; and (iii) Self-monitoring is promoted to strengthen metacognitive awareness and also to support long-term behavioral change. These PsyEdTx techniques align with established CET and CBT models, targeting to rewire harmful associations as well as to reinforce resilience to high-risk triggers [65-67].

Psychoeducation, Compassion, and Brain-Based Insight

A foundational component of EdTx is psychoeducation, which can empower individuals with knowledge that their behaviors are the result of neurobiological dysfunctions, not moral weakness. This shift in understanding of addiction can help to facilitate, e.g., (i) A reduction in shame and improvement in self-compassion, which, in turn, can enhance motivation to engage in addiction treatment and sustain recovery; (ii) A greater insight into emotional-behavioral triggers (e.g., trauma or stress) that often activate the HPA axis and orexin system; and (iii) A sense of agency and hope by reframing addiction as a condition to be managed through consistent learning, therapeutic practice, and brain rewiring. By demystifying the process of addiction, psychoeducation within the field of EdTx can help normalize relapse as a neurological setback (not a personal failure), and also promote sustainable recovery [68].

Integration of Mindfulness-Based Learning

Some psychoeducational therapists incorporate mindfulness-based strategies that further support neurobiological regulation. These can include the following strategies, e.g., (i) Reduction in orexin and HPA axis overactivation, lowering reactivity to stress and substance-

related cues; (ii) Strengthening the PFC and downregulation of amygdala activity by enhancing emotion regulation; and (iii) Teaching non-reactive awareness to interrupt the automatic cycle of craving and relapse. Both mindfulness-based relapse prevention (MBRP) and mindfulness-based cognitive therapy (MBCT) have shown the ability to restore emotional balance and self-regulation by calming the stress-response circuitry [69-71].

Conclusion

Addiction is not a moral failing or conscious choice. Instead, it is a neurobiological disorder driven by dysregulation in the reward-stress-executive function systems within the brain, especially within the orexin-dopamine circuitry. The neuro-circuits responsible for motivation, self-control, and emotional regulation are hijacked in this neurological disruption, creating a persistent cycle of craving and compulsion. Moreover, genetic vulnerabilities, environmental stressors, neurodevelopmental and psychiatric comorbidities further amplify susceptibility by impairing PFC regulation and enhancing cue reactivity. Hence, to break this cycle, individuals with addiction need tools to manage stress, triggers and impulsivity in order to restore neural balance.

Notably, young people with dual diagnoses show markedly improved outcomes when receiving integrated NPIs that simultaneously address underlying psychiatric disorder comorbidities, compared to pharmacotherapy only approaches which often fail to address these fundamental contributing factors. As a neuroscience-informed NPIs, EdTx directly targets these mechanisms in the cycle of craving and compulsion by normalizing dopamine and orexin signaling, supporting HPA axis regulation, and reinforcing adaptive learning through structured routines, executive function rehabilitation, psychoeducation, and mindfulness strategies. Far from being a secondary support, EdTx also offers mechanistically targeted, evidence-based pathways for brain rewiring as well as its long-term recovery.

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