Addiction and Substance Abuse

Lindquist DH, Addict Subst Abuse. 2026;4(1):11-13.

Commentary

The biphasic model of addiction: integration, application, and limitations

Derick H. Lindquist[1,2,*]

[1]Jindal School of Psychology and Counselling, O.P. Jindal Global University, Sonipat, Haryana, India

[2]E-Cog: Emotion and Cognition Research Centre, O.P. Jindal Global University, Sonipat, Haryana, India

*Author for correspondence: Email: dhlindquist@jgu.edu.in

Received date: June 03, 2026

Accepted date: August 12, 2026

Commentary

The conceptualization of substance addiction is linked to diverse theories, with competing models emphasizing distinct psychological, behavioral, and neurobiological mechanisms [1,2]. As illustrated in **Table 1**, the Biphasic model of addiction proposed by Aggarwal, Naik, and Lindquist [3] offers an integrative framework that systematically organizes addiction processes across five domains: reinforcement, motivation, associative learning, tolerance, and inhibitory control.

Table 1. Biphasic Model of Addiction. Illustrates the phase transition within each of five independent but interactive domains.

Domain	Phase Transition
Reinforcement	Positive → Negative
Motivation	Liking → Wanting/Craving
Associative Learning	Classical → Instrumental
Tolerance	Physiological → Conditioned
Inhibitory Control	Impulsivity → Compulsivity

Each domain captures a specific neurobehavioral transition, which collectively map the gradual shift from casual, voluntary psychoactive drug use to compulsive, pathological drug intake [3]. The model offers a unified foundation that aligns and builds on established theories of addiction, including those focused on the underlying neurocircuitry [4], incentive sensitization [5], and habit learning [6].

Importantly, the model hypothesizes the phase transitions to be dynamic and overlapping rather than sequential. This is a notable strength, as empirical evidence suggests that multiple processes—such as craving, habit formation, and impaired inhibitory control—co-occur across the addiction cycle, from drug use to abuse to addiction [7]. By avoiding rigid staging, the model better reflects the heterogeneity and fluidity observed in clinical populations [8].

Neurobehavioral Adaptations

The Biphasic model effectively links shifts in cognition, emotion, and behavior to experience-dependent alterations in the relevant brain regions and circuits. Early-stage substance use is characterized by the activation of mesocortical and mesolimbic pathways, particularly dopaminergic projections from the ventral tegmental area to the nucleus accumbens [9]. Over time, addictive behavior takes hold as progressive neuroadaptations diminish mesolimbic reward sensitivity, weaken mesocortical executive regulation, and shift behavioral control toward fronto-striatal habit circuitry [10].

With respect to the first domain transition, occasional recreational drug use is driven by positive reinforcement associated with elevated dopamine release in the mesolimbic reward circuit [11]. Continued use diminishes reward sensitivity, reduces responsiveness to natural reinforcers, and contributes to a shift toward negative reinforcement [12]. Substance use becomes increasingly driven by the desire to avoid or alleviate the withdrawal symptoms, dysphoria, or stress that emerge in the absence of the drug [13].

After its first use, an individual likely continues using a specific drug because its immediate effects are experienced as rewarding or pleasurable. This hedonic "liking" is mediated primarily by opioid and endocannabinoid activity, while concurrent dopaminergic signaling reinforces repeated drug use [14]. Chronic drug exposure sensitizes neural systems underlying motivation and incentive salience, increasing the urge to seek out and utilize the drug [15]. Consequently, the subjective pleasure derived from the drug compound decreases over time, with a corresponding increase in wanting or craving [16].

The development of drug-seeking behavior involves two forms of associative learning [17]. In the early stages, classical conditioning—via the amygdala and hippocampus—links environmental cues with the drug's psychological and physiological outcomes [18]. Subsequent exposure, in the absence of the drug, can induce a sense of expectation, incentivizing the individual to pursue further drug use. Commensurately, the neural loci of behavioral control shifts from the ventral striatum, containing the nucleus accumbens, to the dorsal striatum—i.e., from reward-driven behavior to habit-like responding [19]. Instrumental conditioning gradually automates drug-seeking behaviors, which become increasingly habitual and less dependent on conscious decision-making.

As drug use becomes more frequent, progressively larger quantities are required to achieve the same high or level of intoxication. Physiological tolerance reflects homeostatic neuroadaptations, including diminished dopamine release and postsynaptic responsiveness within reward circuitry [20], blunting the drug's pleasurable effects. In addition, conditioned tolerance occurs when the environmental cues associated with drug use evoke anticipatory compensatory responses that counteract the drug's physiological effects [21]. These learned adaptations contribute to escalating drug intake and may help explain the increased risk of overdose when drugs are taken in a novel location—i.e., in the absence of the conditioned compensatory responses that offset the forthcoming drug [22].

Lastly, the Biphasic model describes a transition in inhibitory control. As drug use transitions toward abuse, the development of hypofrontality impairs executive control and increases vulnerability to impulsive behavior [23]. Immediate gratification increasingly drives behavior despite clear and mounting adverse consequences. Chronic exposure further disrupts executive-control networks dependent on mesocortical and fronto-striatal pathways [24]. Diminished top-down neural control, combined with heightened responsiveness to drug-related cues, fosters compulsive behavior tied to drug seeking and taking [25]—a defining feature of advanced addiction.

Clinical and Translational Implications

Clinically, the Biphasic model has clear implications for phase-specific interventions. It closely aligns, for instance, with precision psychiatry approaches that seek to match treatment strategies to the neurobiological and behavioral mechanisms responsible for addiction [26].

To that end, treatment for individuals in the earlier stages of problematic drug use may benefit from targeting positive reinforcement processes through contingency management or behavioral activation approaches [27]. Late-stage addictive behavior, alternatively, may require strategies that address negative reinforcement, withdrawal, craving, or compulsive responding [28], including pharmacotherapy and relapse prevention approaches.

Associative learning processes are also a critical target for intervention. Cue-exposure therapies, extinction-based approaches, and mindfulness interventions may help weaken conditioned or instrumental (habitual) responding and reduce relapse vulnerability [29]. Similarly, conditioned tolerance underscores the importance of contextual factors in relapse prevention and overdose education.

Finally, deficits in inhibitory control suggest the importance of interventions aimed at strengthening prefrontal-mediated executive functioning. Cognitive remediation, emotion regulation training, problem-solving interventions, and emerging neuromodulation techniques may enhance cortical function and connectivity, thereby improving top-down regulatory control over behavior [30].

Limitations and Future Directions

Despite the Biphasic model's conceptual strengths, several limitations warrant consideration. First, it is primarily integrative rather than mechanistically novel. Most of the proposed phases are well-established in the literature, with the model primarily providing conceptual synthesis. Second, empirical validation remains limited. Experimental and longitudinal studies are needed to determine whether the proposed phase transitions can be reliably identified and whether they predict treatment outcomes or relapse trajectories.

Third, the model does not account for individual differences, such as genetic vulnerability, early-life stress, trauma exposure, or comorbid psychiatric conditions [31]. Incorporation of these moderators will enhance the model's explanatory power and clinical relevance. Fourth, owing to similarities in the behavioral and neural mechanisms underlying substance and non-substance addictions [32], Aggarwal *et al*. [3] proposed that the model may also apply to the latter. This extension remains speculative and requires empirical validation.

Conclusions

The Biphasic model represents a significant step toward conceptual integration in the addiction sciences. Its emphasis on dynamic phase transitions, underlying neural circuitry, and behavioral expression offers both conceptual clarity and translational utility. By organizing complex neurobehavioral adaptations into a coherent, phase-specific framework, it provides a useful perspective through which to view the transition from early, voluntary drug use to uncontrollable, compulsive addictive behavior. Following empirical validation, the model has the potential to inform personalized approaches to addiction assessment, treatment, and prevention.

References

1. Ferrer-Pérez C, Montagud-Romero S, Blanco-Gandía MC. Neurobiological theories of addiction: a comprehensive review. Psychoactives. 2024 Jan 23;3(1):35–47.
2. Ray LA, Grodin EN. Clinical Neuroscience of Addiction: What Clinical Psychologists Need to Know and Why. Annu Rev Clin Psychol. 2021 May 7;17:465–93.

3. Aggarwal D, Naik J, Lindquist DH. Biphasic model of addiction: neurobehavioral adaptations. Curr Behav Neurosci Rep. 2025 Nov 20;12(1):25.

4. Koob GF, Volkow ND. Neurocircuitry of addiction. Neuropsychopharmacology. 2010 Jan;35(1):217–38.

5. Robinson TE, Berridge KC. Review. The incentive sensitization theory of addiction: some current issues. Philos Trans R Soc Lond B Biol Sci. 2008 Oct 12;363(1507):3137–46.

6. Everitt BJ, Robbins TW. Drug Addiction: Updating Actions to Habits to Compulsions Ten Years On. Annu Rev Psychol. 2016;67:23–50.

7. Volkow ND, Koob GF, McLellan AT. Neurobiologic Advances from the Brain Disease Model of Addiction. N Engl J Med. 2016 Jan 28;374(4):363–71.

8. Carroll KM. The profound heterogeneity of substance use disorders: Implications for treatment development. Curr Dir Psychol Sci. 2021 Aug;30(4):358–64.

9. Wise RA, Robble MA. Dopamine and Addiction. Annu Rev Psychol. 2020 Jan 4;71:79–106.

10. Koob GF, Kandel DB, Baler RD, Volkow ND. Neurobiology of addiction. In: Tasman A, Riba MB, Alarcón RD, Alfonso CA, Kanba S, Lecic-Tosevski D, et al., editors. Tasman's Psychiatry. Cham, Switzerland: Springer, Cham; 2023. p. 1–51.

11. Everitt BJ, Robbins TW. Neural systems of reinforcement for drug addiction: from actions to habits to compulsion. Nat Neurosci. 2005 Nov;8(11):1481–9.

12. Koob GF. Negative reinforcement in drug addiction: the darkness within. Curr Opin Neurobiol. 2013 Aug;23(4):559–63.

13. George O. Negative reinforcement mechanisms in addiction. In: Torregrossa M, editor. Neural mechanisms of addiction. Cambridge, MA: Academic Press; 2019.p. 179–88.

14. Volkow ND, Wise RA, Baler R. The dopamine motive system: implications for drug and food addiction. Nat Rev Neurosci. 2017 Nov 16;18(12):741–52.

15. Berridge KC, Robinson TE. Liking, wanting, and the incentive-sensitization theory of addiction. Am Psychol. 2016 Nov;71(8):670–9.

16. Nguyen D, Naffziger EE, Berridge KC. Positive Affect: Nature and brain bases of liking and wanting. Curr Opin Behav Sci. 2021 Jun;39:72–8.

17. Hyman SE, Malenka RC, Nestler EJ. Neural mechanisms of addiction: the role of reward-related learning and memory. Annu Rev Neurosci. 2006;29:565–98.

18. Kutlu MG, Gould TJ. Effects of drugs of abuse on hippocampal plasticity and hippocampus-dependent learning and memory: contributions to development and maintenance of addiction. Learn Mem. 2016 Sep 15;23(10):515–33.

19. Everitt BJ, Robbins TW. From the ventral to the dorsal striatum: devolving views of their roles in drug addiction. Neurosci Biobehav Rev. 2013 Nov;37(9 Pt A):1946–54.

20. Melis M, Spiga S, Diana M. The dopamine hypothesis of drug addiction: hypodopaminergic state. Int Rev Neurobiol. 2005;63:101–54.

21. Siegel S. Drug tolerance, drug addiction, and drug anticipation. Current Directions in psychological science. 2005 Dec;14(6):296–300.

22. Siegel S. Pavlovian conditioning and drug overdose: When tolerance fails. Addiction Research & Theory. 2001 Jan 1;9(5):503–13.

23. Crews FT, Boettiger CA. Impulsivity, frontal lobes and risk for addiction. Pharmacol Biochem Behav. 2009 Sep;93(3):237–47.

24. Feltenstein MW, See RE, Fuchs RA. Neural Substrates and Circuits of Drug Addiction. Cold Spring Harb Perspect Med. 2021 Apr 1;11(4):a039628.

25. Volkow ND, Wang GJ, Fowler JS, Tomasi D, Telang F, Baler R. Addiction: decreased reward sensitivity and increased expectation sensitivity conspire to overwhelm the brain's control circuit. Bioessays. 2010 Sep;32(9):748–55.

26. Fernandes BS, Williams LM, Steiner J, Leboyer M, Carvalho AF, Berk M. The new field of 'precision psychiatry'. BMC Med. 2017 Apr 13;15(1):80.

27. Schlund MW, Magee S, Hudgins CD. Human avoidance and approach learning: evidence for overlapping neural systems and experiential avoidance modulation of avoidance neurocircuitry. Behav Brain Res. 2011 Dec 1;225(2):437–48.

28. McCarthy DE, Curtin JJ, Piper ME, Baker TB. Negative reinforcement: Possible clinical implications of an integrative model. In: Kassel JD, editor. Substance abuse and emotion. Washington, DC: American Psychological Association; 2010. p. 15–42.

29. Rosenthal A, Ebrahimi C, Wedemeyer F, Romanczuk-Seiferth N, Beck A. The Treatment of Substance Use Disorders: Recent Developments and New Perspectives. Neuropsychobiology. 2022;81(5):451–72.

30. Soleimani G, Joutsa J, Moussawi K, Siddiqi SH, Kuplicki R, Bikson M, et al. Converging Evidence for Frontopolar Cortex as a Target for Neuromodulation in Addiction Treatment. Am J Psychiatry. 2024 Feb 1;181(2):100–14.

31. George O, Koob GF. Individual differences in the neuropsychopathology of addiction. Dialogues Clin Neurosci. 2017 Sep;19(3):217–29.

32. Yohn SE, Galbraith J, Calipari ES, Conn PJ. Shared Behavioral and Neurocircuitry Disruptions in Drug Addiction, Obesity, and Binge Eating Disorder: Focus on Group I mGluRs in the Mesolimbic Dopamine Pathway. ACS Chem Neurosci. 2019 May 15;10(5):2125–43.