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Addiction Research

Impaired Inhibitory Control in Substance Use Disorders: Neurocognitive Mechanisms, Clinical Consequences, and Therapeutic Perspectives

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ABSTRACT

Impaired inhibitory control is increasingly recognized as a hallmark deficit in substance use disorders (SUDs). This executive function impairment contributes to compulsive drug-seeking, maladaptive decision-making, and heightened relapse vulnerability. Neuroimaging, behavioral, and neurochemical evidence implicate dysfunction in prefrontal–striatal circuits, particularly involving the dorsolateral prefrontal cortex (dlPFC), orbitofrontal cortex (OFC), and anterior cingulate cortex (ACC). Drug-induced dysregulation of dopamine and glutamate signaling further disrupts top-down control over subcortical reward and habit systems. This review synthesizes current knowledge on the neurocognitive underpinnings of impaired inhibitory control in SUDs, discusses its role in addiction trajectories, and evaluates therapeutic approaches targeting inhibitory dysfunction. Emerging modalities, including cognitive training, neuromodulation, and pharmacotherapies, hold promise in complementing established behavioral interventions.

Keywords

Substance Use Disorders, Dorsolateral prefrontal cortex (dlPFC), Orbitofrontal cortex (OFC), Anterior cingulate cortex (ACC), Drugs.

Introduction

Substance use disorders are characterized by persistent drug use despite adverse consequences, reflecting a breakdown in self-regulation. A critical aspect of this breakdown is impaired inhibitory control—the capacity to suppress prepotent impulses and inappropriate actions [1]. While drug reward mechanisms have long been the focus of addiction neuroscience, there is growing recognition that executive dysfunction, particularly inhibitory deficits, is central to the transition from voluntary to compulsive use [2].

The Impact of Drug Use on Executive Functions of the Brain

Executive functions are the brain's command-and-control processes, enabling humans to focus, maintain attention, plan activities, make sound and logical decisions, and regulate emotions and adapt to change. The executive functions centers reside primarily in the prefrontal cortex and form continuous connections to deeper brain structures. When functioning properly, these processes enable humans to manage daily activities and pursue long-term goals. Drug use, however, whether involving stimulants, depressants, opioids, or cannabis, can severely disrupt executive functioning, impairing judgment, self-control, and adaptability.

Executive Functions and Their Roles

Executive functions encompass several interrelated skills, including:

- Working memory – holding and manipulating information in the mind.
- Cognitive flexibility – shifting between tasks, perspectives, or problem-solving strategies.
- Inhibitory control – resisting impulses, distractions, or risky behaviors.
- Decision-making – weighing consequences, predicting outcomes, and choosing adaptive actions.

These functions are essential not only for daily cognitive functions and productivity but also for maintaining social relationships and the overall welfare of humans.

Moreover, Inhibitory control encompasses three domains:

- Motor inhibition (suppressing physical responses, e.g., stop-signal tasks),
- Cognitive inhibition (suppressing intrusive thoughts), and
- Behavioral inhibition (suppressing maladaptive actions such as drug-taking).

These crucial domains are mediated by distributed prefrontal–striatal networks and rely heavily on the neurotransmitters dopamine and glutamate.

This article focuses on the Impact of drug use on one Executive Function – the Inhibitory Control. Furthermore, this article reviews the neurocognitive mechanisms underlying impaired inhibitory control in drug use, highlights relevant empirical evidence, and discusses the implications for treatment.

Contemporary Models of Addiction

Contemporary models of addiction (e.g., the incentive-sensitization theory and habit-based frameworks) emphasize that impaired inhibitory control allows maladaptive reward-driven and habitual behaviors to dominate, fueling compulsive drug use [3].

Drug-Induced Impairment of Executive Functions in Substance Use Disorders

Psychotropic drugs directly affect neurotransmitter systems, particularly dopamine and glutamate pathways in the prefrontal cortex. This disruption diminishes inhibitory control, making it harder to resist cravings or risky impulses. For example, cocaine and methamphetamine overstimulate dopamine release, producing short-term euphoria while damaging the brain's reward-regulation circuits. Over time, the ability to "hit the brakes" weakens, fueling compulsive drug-seeking behavior.

Impaired Inhibitory Control: Neurocognitive and Clinical Perspectives

Inhibitory control is a central component of executive functioning, broadly defined as the capacity to suppress inappropriate or maladaptive responses in favor of goal-directed behavior. Neurobiologically, this ability depends on the integrity of the prefrontal cortex (PFC) and its top-down regulation over subcortical structures, including the striatum and amygdala. Impairments in inhibitory control are strongly implicated in the development, maintenance, and relapses of substance use disorders (SUDs) [4].

Habitual vs. Goal-Directed Control Model

While in healthy behavior, humans successfully balance both systems: habits free up mental energy, whereas goal-directed control allows adaptability. In addiction and compulsive disorders, habitual control can dominate the decision-making process. Similarly, in cognitive aging or following brain injury, goal-directed control may weaken, leading to behavior that is overly habit-driven.

Goal-Directed Behavior Control

In the Goal-Directed Behavioral Control Model, actions are chosen based on their expected outcomes and are modified in response to changes that affect possible outcomes. Goal-directed behavior relies on a model-based system — the brain holds an internal "map" of actions geared toward outcomes, and decisions are flexible. Goal-directed behavior is based on multiple neural circuits and strongly tied to the prefrontal cortex and dorsomedial striatum.

Habitual Behavior Control

In the Habitual Behavior Control Model, actions are driven not by evaluating current goals, but rather by learned stimulus–response associations. Once habits are formed, they are triggered automatically and often persist even if the outcome is no longer valuable. The mechanism of Habitual Behavior Control relies on a model-free system when behavior is guided by past reinforcement rather than real-time evaluation. Neural circuits development is linked to the dorsolateral striatum and procedural memory systems.

Chronic drug use biases control toward the dorsal striatum, promoting stimulus–response habits over flexible, goal-directed action [5]. This transition reduces the ability to inhibit drug-seeking once habits are established, proving the Striatal system's contributions to habitual behavior.

Drug-Induced Shift from Goal-Directed to Habitual Behavior

The impairment of inhibitory control in addiction reflects a broader shift from goal-directed to habitual behavior. Neuroimaging evidence presented by Everitt & Robbins shows increased reliance on dorsal striatal circuits (habit learning) at the expense of PFC-mediated goal-directed control as substance use progresses [5].

Neurochemical Dysregulation of Inhibitory Control Prefrontal Cortex Dysfunction

The dorsolateral prefrontal cortex (dlPFC), ventrolateral prefrontal cortex (vlPFC), and orbitofrontal cortex (OFC) are critical for inhibitory control. Chronic drug exposure produces both structural (reduced gray matter volume) and functional (diminished activation) alterations in these regions. Functional MRI studies demonstrate hypoactivation of the anterior cingulate cortex (ACC)

and lateral PFC during inhibitory control tasks in cocaine- and alcohol-dependent individuals fMRI findings show with attenuated activation of the right inferior frontal gyrus (rIFG) during response inhibition tasks [6]. Additionally, structural MRI studies by Connoly et al. demonstrated reduced gray matter volume in the dlPFC and OFC of chronic cocaine and alcohol users [7].

Anterior Cingulate Cortex (ACC) and Error Monitoring

The ACC supports conflict monitoring and adaptive adjustments. Drug users exhibit diminished ACC activation during inhibitory tasks, impairing error detection and behavioral correction [8].

Dopaminergic Dysregulation

Dopamine (DA) signaling in the mesocorticolimbic system plays a dual role: encoding reward salience and modulating executive control. Reduced striatal D2 receptor availability in addicted individuals correlates with poor inhibitory task performance [8]. Furthermore, Glutamate Dysregulation caused by glutamatergic projections from the PFC to the nucleus accumbens weakens top-down inhibitory signaling [9].

Drug-induced DA surges overstimulate the ventral striatum while attenuating D2 receptor availability in the PFC. This imbalance weakens top-down inhibitory processes, thereby facilitating compulsive drug-seeking [10].

Empirical Evidence

Behavioral Paradigms

Pertaining to Go/No-Go Tasks, individuals with SUDs (particularly among cocaine and heroin users) exhibit a higher rate of commission errors, indicating diminished response ability caused by reduced capacity to inhibit prepotent responses [11].

Regarding Delay Discounting Tasks, drug users display steep temporal discounting, indicative of impaired capacity to suppress immediate rewards in favor of long-term benefits [12].

In relation to Stop-Signal Tasks (SST), prolonged stop-signal reaction times (SSRTs) in cocaine, methamphetamine, and alcohol users suggest slowed inhibitory processing and impaired motor inhibition [13].

Neuroimaging Evidence

Cannabis

Adolescence represents a critical window of neurodevelopment, characterized by the ongoing maturation of the prefrontal cortex (PFC) and the refinement of executive functions, such as inhibitory control. Early substance exposure disproportionately impacts inhibitory control, increasing vulnerability to lifelong SUD [14].

Cannabis use during this sensitive period has been consistently associated with persistent deficits in inhibitory regulation and atypical trajectories of PFC development. Neuroimaging studies demonstrate that early cannabis exposure disrupts synaptic pruning, myelination, and functional connectivity within prefrontal–striatal circuits, processes essential for the maturation of top-down control mechanisms. Cannabis use, particularly during adolescence, has been linked to persistent deficits in inhibitory control and abnormal PFC maturation with lasting inhibitory deficits [15].

Cocaine

Cocaine dependence is associated with volumetric reductions in the inferior frontal gyrus and hypoactivation of the prefrontal cortex during inhibitory processes. Wiers et al. demonstrated that cocaine-dependent individuals exhibit reduced inferior frontal gyrus (IFG) volume and prefrontal cortical hypoactivity during inhibitory control tasks [16]. Additionally, Kaufman et al. discovered that cocaine-dependent study participants exhibit reduced PFC and ACC activation during inhibitory control paradigms, with deficits correlating to relapse risk [17]. These findings were further supported by Brewer et al., who demonstrated that diminished functional connectivity between the ACC and dlPFC predicts relapse [18].

Alcohol

Alcohol use disorder has been linked to reduced gray matter density in the inferior frontal gyrus, a region essential for inhibitory regulation and a key element supporting inhibitory control. Wiers et al. using neuroimaging evidence indicateindicate that alcohol use disorder is associated with structural reductions in the inferior frontal gyrus, a cortical hub for stopping behavior [19].

Clinical Implications

A growing body of evidence demonstrates that diverse substances of abuse converge on prefrontal systems that support inhibitory control. Cannabis use during adolescence has been associated with disrupted prefrontal cortex (PFC) maturation, including alterations in synaptic pruning and myelination, leading to persistent inhibitory control deficits that can extend into adulthood. Studies by Wiers et al. reported that cocaine-dependent individuals exhibit structural and functional impairments in inhibitory circuitry, characterized by reduced inferior frontal gyrus (IFG) volume and PFC hypoactivity during inhibitory control tasks [20]. Parallel findings, also by Wier et al., have been observed in alcohol use disorder, where diminished gray matter density in the IFG—a cortical region critical for stopping behavior—has been documented [21]. Collectively, these results suggest that substance use, particularly when initiated during vulnerable developmental periods, compromises the structural integrity and functional responsiveness of prefrontal networks, thereby weakening inhibitory control and biasing behavior toward habitual, stimulus-driven responding.

Relapse Vulnerability

Impaired inhibitory control is a predictor of poor treatment outcomes. For instance, greater deficits on SST performance are associated with higher relapse rates among cocaine users [22]. These findings suggest inhibitory dysfunction is not merely a correlate but a mechanistic driver of continued drug use.

Conclusion

Impaired inhibitory control represents a hallmark neurocognitive deficit in substance use disorders, underpinned by PFC dysfunction,

dopaminergic dysregulation, and maladaptive striatal learning. These impairments contribute to compulsive drug-seeking, increased relapse vulnerability, and resistance to treatment. Addressing inhibitory dysfunction-through cognitive training, pharmacotherapy, and neuromodulation-represents a promising frontier in addiction medicine.

References

1. Barkley RA. Executive functions: What they are, how they work, and why they evolved. Guilford Press. 2012.
2. Everitt BJ, Robbins TW. Drug addiction: updating actions to habits to compulsions. Annu Rev Psychol. 2016; 67: 23-50.
3. Goldstein RZ, Volkow ND. Dysfunction of the prefrontal cortex in addiction: neuroimaging findings and clinical implications. Nat Rev Neurosci. 2011; 12: 652-669.
4. Sjoerds Z. *Deficits in inhibitory control in alcohol dependence: Evidence from event-related fMRI.* PLoS ONE. 2014; 9: e114089.
5. Connolly CG. Disrupted prefrontal connectivity in cocaine addiction. Biological Psychiatry. 2013; 73: 595-602.
6. Volkow ND, Gene-Jack Wang, Joanna S Fowler, et al. Addiction: decreased reward sensitivity and increased expectation sensitivity conspire to overwhelm the brain's control circuit. Bioessays. 2010; 32: 748-755.
7. Kalivas PW, Volkow ND. New medications for drug addiction. Nat Rev Neuroscience. 2011; 12: 652-669.
8. Smith DG. Deficits in inhibitory control in substance use disorders. Drug Alcohol Depend. 2014; 134: 31-39.
9. Bickel WK. Temporal discounting as a measure of executive function in addiction research. Psychological Science. 2012; 23: 232-239.
10. Li CSR. Impaired stop signal response inhibition in chronic cocaine users. NeuroImage. 2008; 39: 786-796.
11. Casey BJ, Rebecca M Jones, Todd A Hare, et al. The adolescent brain. Ann N Y Acad Sci. 2008; 1124: 111-126.
12. Meier MH, Avshalom Caspi, Antony Ambler, et al. Persistent cannabis users show neuropsychological decline from childhood to midlife. PNAS. 2012; 109: E2657-E2664.
13. Wiers CE. *Inhibitory control in alcohol dependence: neural and behavioral findings.* Alcoholism: Clinical and Experimental Research. 2015; 39: 531-538.
14. Kaufman JN. Cocaine administration decreases functional connectivity of the ACC during cognitive control. NeuroImage. 2003; 19: 510-514.
15. Brewer JA. Drug dependence and stopping: evidence for impaired response inhibition. Exp Clin Psychopharmacology. 2008; 16: 219-228.