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REVIEW

Brain circuitry of compulsivity and impulsivity

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Impulsivity and compulsivity have been considered opposite poles of a continuous spectrum, but their relationship appears to be more complex. Disorders characterized by impulsivity often have features of compulsivity and vice versa. The overlaps of the constructs of compulsivity and impulsivity warrant additional investigation, not only to identify the similarities and differences, but also to examine the implications for prevention and treatment strategies of both compulsive and impulsive behaviors.

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Introduction

Compulsivity and impulsivity are terms reflective of complex neurocircuitries,[1–3] but these terms are used in clinical settings in imprecise and oftentimes contradictory fashions. The American Psychiatric Association defines compulsivity as the performance of repetitive behaviors with the goal of reducing or preventing anxiety or distress, not to provide pleasure or gratification,[4] and obsessive compulsive disorder may be the most representative disorder with compulsive features. On the other hand, impulsivity has been defined as a predisposition toward rapid, unplanned reactions to either internal or external stimuli without regard for negative consequences.[5] Although impulsivity may be seen in a variety of behavioral problems, only certain disorders have been formally classified as impulse control disorders (for example, gambling disorder).[4] To complicate matters further, obsessive compulsive disorder may have elements of impulsivity, and individuals with impulse control disorders may exhibit compulsive behaviors. In fact, both compulsivity and impulsivity are key elements of many psychiatric disorders (for example, substance use disorders, bipolar disorder, personality disorders, and attention deficit hyperactivity disorder).[4,6,7] So, although the domains of impulsivity and compulsivity have been considered by some as being diametrically opposed, the relationship appears to be more intricate. Compulsivity and impulsivity may co-occur simultaneously in the same disorders, at different times within the same disorders, or only in some people meeting the similar diagnostic criteria for the same putative disorder.

This review article discusses the neurobiology of impulsivity and compulsivity, examines the overlap of these constructs in two representative disorders (one for compulsivity [obsessive compulsive disorder] and one for impulsivity [gambling disorder]), and then discusses how knowledge of these constructs may impact the clinical care of individuals struggling with these disorders.

Impulsivity, Compulsivity, and Brain Circuitry

Impulsivity represents a multidimensional construct, and deconstructing impulsivity into its component cognitive processes and their related neurobiological underpinnings should assist in understanding its relationship to compulsivity.[1,3] When one talks of impulsivity, it may refer to problems with response inhibition, hypersensitivity of reward anticipation, or poor planning. Impulsivity may also refer to actions that are risky, prematurely expressed, and poorly conceived.

Three of the most studied domains of impulsivity might be best characterized as motor impulsivity, reward impulsivity, and reflection impulsivity.[1] Motor impulsivity is defined as the inability to suppress prepotent responses, and is most likely due to deficits in mechanism of behavioral inhibition. Two of the most common measures of motor impulsivity are the go/no-go task and the stop signal reaction time task. The stop signal reaction time task is modulated by norepinephrine. Studies have shown deficits in motor impulsivity in a range of psychiatric disorders, including obsessive compulsive disorder and attention deficit hyperactivity disorder. Reward impulsivity refers to the discounting of a larger reward with increasing delay and

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can be measured with the Iowa Gamble Task or the Cambridge Task. Deficits in reward impulsivity have been found in a range of addictive behaviors and may be modulated by dopamine and serotonin jointly in subcortical circuitry. Finally, reflection impulsivity refers to making choices with insufficient information and can be measured with the Reflection Task.[8]

Compulsivity on the other hand refers to a tendency to perform unpleasantly repetitive actions in a habitual or stereotyped fashion in order to prevent a perceived negative consequence, leading to functional impairment. How to best measure compulsivity, however, has been a matter of some debate. Although traditionally used to assess attentional issues, tasks that examine set switching, such as the Wisconsin Card Sorting Test or the Intra-dimensional/Extra-dimensional Shift Paradigm may also be reflective of compulsivity. Dysfunction on these tasks results in perseveration errors and problems shifting attention, two features that are reflective of repetitive behaviors seen in compulsivity problems.[9]

Although both impulsivity and compulsivity may reflect failures of response inhibition or top-down cognitive control, they also differ in aspects of response inhibition: compulsivity relates to an inability to terminate action, whereas impulsivity refers to problems initiating actions.[2] Dissection of the components of impulsivity and compulsivity may be important in better understanding how the two constructs relate to each other and how they both relate to the clinical presentation of behavioral difficulties.[10]

Neural substrates of impulsivity

Although most research on impulsivity has examined the neural substrates of response inhibition, cortical as well as subcortical mechanisms may be implicated in a variety of impulsive elements. One key component of impulsive choice is an overactive reward drive, and reward has been consistently associated with increased activity of the ventral striatum and the medical prefrontal cortex.[11] Earlier research suggested that selections of immediate reward are associated with disproportionately increased signal activity in the ventral striatum, and medial prefrontal and medial orbitofrontal cortices. Choice of a delayed option, on the other hand, has been associated with higher activity in the lateral prefrontal cortex and orbitofrontal cortex. More recent research however has suggested that that the ventral striatum and medial frontal cortex track the subjective value of all rewards, regardless of whether the immediate reward or delayed reward is chosen.[12,13] The right inferior frontal gyrus and its associated networks may also have an important role in top-down response control, given that malfunction of this area is associated with impulsive behaviors.[14,15]

Thus, distinct but inter-related neurocircuits may be relevant to the many facets of impulsivity. One such circuit could be characterized as a ventral striatal loop involving the ventral medial prefrontal cortex, the subgenual cingulated cortex, and the nucleus accumbens/ventral striatum. This circuit is involved in discounting of reward. A separate neural circuit may underlie motor inhibitory deficits, as reflected by stop signal inhibition deficits, and includes the ventrolateral prefrontal cortex, the anterior cingulate, and the presupplementary motor and their link to the caudate nucleus and putamen.

Neural substrates of compulsivity

Circuits implicated in compulsivity include the circuits of reversal learning (the dorsolateral prefrontal cortex, the lateral orbital frontal cortex, and the caudate nucleus) and habit learning (the supplementary motor area, the premotor cortex, and the putamen). Neurobiological models of obsessive compulsive disorder propose aberrations in frontal–striatal–thalamic–cortical loops in its pathogenesis including abnormalities of the anterior cingulate cortex, orbitofrontal cortex, thalamus, and basal ganglia.[16,17] Hyperactivity of the orbitofrontal–subcortical loops caused by a disruption in the balance of activity through the opposing basal ganglia pathways (ie, excessive direct pathway activation) is hypothesized to give rise to obsessive compulsive disorder symptoms.[18]

Functional neuroimaging studies have consistently reported greater brain activity in the anterior cingulate in adults with obsessive compulsive disorder during symptom provocation[19,20] and during executive functioning tasks.[21] Altered functional connectivity of the anterior cingulate in adults and pediatric obsessive compulsive disorder patients has also been demonstrated[22,23] (although with opposite results between children and adults in some studies[24]).

Impulsivity and Compulsivity Overlap

Although compulsivity and impulsivity are distinguished by their involvement with different aspects of response control, most probably mediated by related but distinct neural circuitry linked with motivational and decisional processes (this circuitry involves the basal ganglia, their limbic cortical inputs, and top-down control from cortical prefrontal circuitry),[2] there may be important overlap between these constructs. Additionally, goal-directed behavior, which is mediated by a desire for the consequences, may become habit over time (controlled by external stimuli via stimulus–response associations that occur due to behavioral repetition).[1,25]

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One important related area of research concerning the potential overlap of impulsive and compulsive behaviors is the field of Parkinson's research. Parkinson's disease is characterized by dopaminergic neuronal loss and is often treated with dopamine replacement therapies. These medications have been hypothesized to result in impulsivity (for example, gambling disorder) in some vulnerable patients.[26] Although less reported than the impulsive behaviors, punding (a stereotyped, repetitive, purposeless behavior that could be best characterized as a compulsion) has also been reported as resulting from dopamine agonist therapy in Parkinson's disease.[27] Thus, these behaviors in Parkinson's disease offer a clinically relevant and scientifically informative model for investigating dopaminergic influences in both compulsivity and impulsivity.

Understanding the neurobiological and cognitive overlap between compulsivity and impulsivity may lead to more effective treatments for both compulsive as well as impulsive disorders. For example, use of exposure therapies (classically used for the treatment of compulsive behaviors) for impulsive disorders such as gambling disorder has recently demonstrated promise.[28]

Gambling Disorder

Gambling disorder (http://www.DSM5.org) is characterized by persistent and recurrent maladaptive patterns of gambling behavior, and is associated with impaired functioning, reduced quality of life, and high rates of bankruptcy, divorce, and incarceration.[29] Gambling disorder usually begins in early adulthood, with males tending to start at an earlier age.[30]

The behaviors that characterize gambling disorder (eg, chasing losses, preoccupation with gambling, inability to stop) are impulsive[31] in that they are often premature, poorly thought out, risky, and result in deleterious long-term outcomes.[32] Developmentally, impulsive behavior that underlies problematic gambling tends to initiate during late adolescence or early adulthood.[31]

Neurocognitive data support the idea that gambling disorder is an impulsive behavior. Objective brain-based measurable traits, or endophenotypes, that deconstruct top-level phenotypes into meaningful markers more proximally related to the etiology are important to understand the neurobiology of behaviors such as compulsivity and impulsivity, their relationship with each other, and their relationship to the syndrome-based psychiatric conditions used on an individual clinical level.[33] Deficits in aspects of inhibition, working memory, planning, cognitive flexibility, and time management/estimation have been reported in individuals with gambling disorder compared to healthy volunteers[34,35] (though other studies have found contrary findings[36]). Individuals with gambling disorder also discounted delayed rewards to a greater extent than controls on a task in which they selected between small, immediate, and larger distal hypothetical rewards.[37] One neuroimaging study on inhibition in pathological gambling reported decreased activation in the ventrolateral prefrontal cortex compared to healthy controls using the color–word Stroop task.[38]

In addition to impulsivity, gambling disorder is associated with many features of compulsivity.[39] Gambling disorder is characterized by the repetitive behavior of gambling and impaired inhibition of the behavior. People with gambling disorder often have specific "lucky" rituals associated with their gambling—for example, wearing certain clothes when gambling or gambling on particular slot machines.[39] As with obsessive compulsive disorder, the "compulsive" behavior of gambling is often triggered by aversive or stressful stimuli.[29]

Assessing compulsivity in gambling disorder has the potential to clarify the role of compulsivity in many other impulsive disorders. Although many studies have assessed impulsivity and related constructs in gambling disorder, relatively few have explored the construct of compulsivity. In one study, gamblers scored higher than normal controls on a measure of compulsivity (the Padua Inventory).[40] Other studies suggest heightened compulsivity, particularly response perseveration, in gambling disorder.[41] Compared to control subjects, people with gambling disorder have demonstrated greater response perseveration on a card-playing task (which was characterized as a measure of compulsivity, although it also comprised elements of risky decision making).[42] In addition, individuals with gambling disorder have demonstrated more total errors than control subjects on the intradimensional/extradimensional set-shifting (IDED) task that measures cognitive flexibility, which is a construct reflective of compulsivity.[43] Similar findings on this task have been reported in obsessive compulsive disorder.[44]

A recent study attempting to understand the compulsive and impulsive dimensions of gambling disorder examined 38 subjects with the general Padua Inventory before and after 12 weeks of treatment with paroxetine.[45] The Padua Inventory measures obsessions and compulsions and contains four factors: (1) impaired control over mental activities, which assesses ruminations and exaggerated doubts; (2) fear of contamination; (3) checking; and (4) impaired control over motor activities. (Scores on the Padua Inventory have demonstrated high correlations with the Maudsley Obsessional Compulsive Questionnaire and the Leyton Obsessional Compulsive Inventory[46]).

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At baseline, gambling symptom severity was associated with features of both impulsivity and compulsivity (specifically factors 1 and 4 of the Padua Inventory), which is consistent with prior research.[40] During treatment, overall scores on measures of impulsivity and compulsivity diminished, with significant decreases seen in factor 1 of the Padua Inventory (impaired control over mental activities, which arguably could be characterized as an impulsivity scale) and the impulsiveness subscales of the Eysenck Impulsivity Questionnaire.[45] Factor 1 of the Padua Inventory was significantly correlated with the Eysenck Impulsivity Questionnaire and the Yale Brown Obsessive Compulsive Scale Modified for Pathological Gambling.[45] Thus, compulsivity and impulsivity in gambling disorder interact in a complex fashion and may be difficult to disentangle clinically. Compulsivity or impulsivity (or specific aspects of each) might represent treatment targets for gambling disorder.

Although pathogenesis is arguably the most valid indicator of whether disorders are related, there has only been a sparse amount of research on possible neurobiological correlates of gambling disorder. The evidence suggests a different pathology from that seen in classically compulsive disorders, such as obsessive compulsive disorder (for a review, please see van Holst *et al.*[35]). A functional magnetic resonance imaging study of gambling urges in male pathological gamblers suggests that gambling disorder has neural features (relatively decreased activation within cortical, basal ganglionic, and thalamic brain regions in PG subjects as compared to control ones)[47] that are distinct from the brain activation pattern observed in cue provocation studies of obsessive compulsive disorder (relatively increased cortico–basal–ganglionic–thalamic activity).[18] More recent neuroimaging research has demonstrated that problem gamblers also show hyporesponsiveness of the dorsomedial prefrontal cortex compared to healthy controls during successful as well as failed response inhibition,[48] and gamblers demonstrate a hypoactive reward system.[49,50]

Obsessive Compulsive Disorder

Traditionally, obsessive-compulsive disorder is the classic representative disorder of compulsivity. Obsessive compulsive disorder is characterized by anxiety-evoking obsessions and repetitive behaviors designed to neutralize the anxiety provoking thoughts. Individuals with obsessive compulsive disorder score high on measures of harm avoidance.[1,51]

Functional imaging studies have identified abnormalities in the basal ganglia (especially caudate), the cingulate cortex, and the orbitofrontal cortex of individuals with obsessive compulsive disorder.[52] Thus, the neurobiology of obsessive compulsive disorder has been conceptualized in terms of lateral orbitofrontal loop dysfunction.[53]

Various neurocognitive deficits have been identified across several domains in obsessive compulsive disorder, including memory, set-shifting, response inhibition, and attentional processing. There is direct evidence for response inhibition failures, as indexed by go/no-go and oculomotor tasks, in which there is a need to inhibit prepotent motor responses,[53] and inhibition as a cognitive function has been associated with neural substrates including the dorsolateral prefrontal cortex, the inferior frontal cortex, and the orbitofrontal cortex.[54] Set-shifting is classically regarded as a distinct cognitive function from inhibition, and some have argued that the dorsolateral prefrontal cortex is important in set-shifting, whereas the orbitofrontal cortex is more important in response inhibition.[9] Research has demonstrated set-shifting deficits in obsessive compulsive disorder.[55] Set-shifting not only requires the ability to adopt a new rule or attend to a different stimulus dimension, but also the inhibition of responding to the previously acquired rule.

In addition to the more classic example of set-shifting as a compulsivity domain, individuals with obsessive compulsive disorder have also demonstrated elevated impulsivity. Subjects with obsessive compulsive disorder have exhibited significantly elevated scores of cognitive impulsiveness using the Barratt Impulsiveness Scale.[56] In addition, cognitive–attentional impulsiveness was associated with aggressive obsessions and checking, but not washing.[56] This suggests that certain subtypes of obsessive compulsive subjects may have more impulsive features.

Furthermore, some have postulated that with progression and chronicity, certain obsessive compulsive behaviors may become more "impulsive," may take on a hedonic quality, and may be associated with a greater involvement of ventral striatal circuits.[57] Research has shown that clinical factors associated with chronicity are linked to an impulsive subtype in obsessive compulsive disorder. It has also been suggested that compulsions may often be performed automatically, in the absence of obsessional or anxiety symptoms, and may be driven by either positive or negative reinforcement.[3,58] Some individuals with obsessive compulsive disorder display an increase in positive affect in anticipation of the realization of compulsions,[58] raising the possibility that at least in a subset of individuals, compulsions may take on hedonic value. Impulsivity has been linked to a ventral striatal cerebral loop, and deep brain stimulation of the ventral striatum (nucleus accumbens) has been shown to improve obsessive-compulsive symptoms[59] (although perhaps not changing cognition[60]).

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Treatment Implications and Future Directions

Originally there was a suggestion that impulsive disorders, like obsessive compulsive disorder, may demonstrate a preferential response to serotonin reuptake inhibitors (SRIs). Data from double-blind randomized pharmacotherapy trials of SRIs in the treatment of a variety of impulsive disorders, however, have been inconclusive.[61,62]

Glutamatergic agents, such as N-acetyl cysteine and memantine, however, may be able to treat both compulsive and impulsive behaviors. Impulsive behaviors such as gambling disorder have shown early promise when treated with N-acetyl cysteine and memantine (both agents have also shown promise in the treatment of obsessive compulsive disorder).[61] Glutamate is the primary neurotransmitter within cortico–striatal–thalamic circuits, with the majority of axon terminals in the striatum being glutamatergic. Increasing evidence has demonstrated an association between obsessive compulsive disorder and disruption of glutamate neurotransmission within these circuits.[63] Glutamate agents may also present a potentially useful option for compulsivity, as in the case of obsessive compulsive disorder.[64]

Given the role of dopamine in reward processing, as well as the potential adjunctive role of dopamine antagonists in obsessive compulsive disorder, the potential effectiveness of dopaminergic agents may also reflect the neural commonality of compulsivity and impulsivity. The treatment studies of dopamine antagonists in the treatment of pathological gambling, however, have demonstrated no benefit compared to placebo.[61] Whether dopamine antagonists targeting the D1 receptor or dopamine agonists working in the prefrontal cortex would benefit both impulsive and compulsive behaviors remains unknown, but is potentially worthy of study.

The role of noradrenaline reuptake inhibitors may also be worth further research. Given their potential to modulate prefrontal inhibitory processes,[8] noradrenaline reuptake inhibitors may be effective agents in the treatment of impulsivity and compulsive behavior.[65] Research supports their use in the treatment of attention deficit hyperactivity disorder, a classic disorder of impulsivity, and their role in the treatment of obsessive compulsive disorder is being re-examined.[66]

Additionally, cognitive and behavioral treatments that address the compulsive aspect of an impulsive disorder such as gambling disorder have shown early benefit.[29] In fact, use of exposure and response prevention treatment, traditionally used for obsessive compulsive disorder,[67] has also demonstrated promise for impulsive behaviors such as gambling disorder.[28,68] (In vivo exposures, as opposed to imaginal exposures, have resulted in less convincing outcomes.[69,70]) The extent to which measures of compulsivity and impulsivity, rather than diagnostic categories, may be used to match specific treatments with specific individuals, or be used to assess or predict treatment outcome, remains to be examined.

Multiple areas of research are deserving of future attention. Relationships between impulsivity and compulsivity are inadequately understood and should be examined further.[2,45] Subsequent work is needed to define clearly and to fractionate the heterogeneous concept of compulsivity,[1,2] along similar lines of work conducted in the impulsivity literature.[3] Neuroimaging research in humans and animals to identify the neurochemistry and brain function underlying impulsivity and compulsivity are needed. Finally, the constructs of compulsivity and impulsivity warrant additional investigation, not only to identify the similarities and differences, but also to examine the implications for prevention and treatment strategies.

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