# Neuropsychiatric Aspects of Impulse Control Disorders



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#### **KEYWORDS**

- Attention-deficit/hyperactivity disorder
  Impulse control disorders
- Neurodegenerative disorders Neurodevelopmental disorders Parkinson disease
- Tourette syndrome

#### **KEY POINTS**

- Impulse control disorders (ICDs) are neuropsychiatric conditions characterized by the repeated inability to resist an impulse, drive, or temptation to perform an act that is harmful to the person or others.
- Pathologic gambling, kleptomania, trichotillomania, excoriation (skin picking) disorder, intermittent explosive disorder, pyromania, oppositional defiant, conduct, and antisocial personality disorders are often classified as ICDs, although there is significant variability across classification systems.
- ICDs are relatively common conditions, both as primary disorders and as comorbidities of neurodevelopmental and neurodegenerative disorders.
- In most cases, the exact cause and pathophysiology of ICDs remain largely unknown.
- Treatment of ICDs is often multimodal, including both pharmacotherapy and cognitivebehavioral therapy approaches, based on the individual presentation.

#### INTRODUCTION

Impulsivity is both a personality trait and a clinical construct, defined as a predisposition toward rapid, unplanned reactions to internal or external stimuli without regard to the negative consequences of these reactions to the impulsive individual or to others.<sup>1</sup>

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Impulse control disorders (ICDs) are prevalent and disabling psychiatric disorders, characterized by the repeated inability to resist an impulse, drive, or temptation to perform an act that is harmful to the person or others. ICDs tend to develop early in life, with a chronic, sometimes fluctuating, course. Although the consequences are damaging, carrying out the impulsive act may be experienced as rewarding or may relieve distress, implicating dysfunction of the neural circuitry involved in reward processing and/or behavioral inhibition. Comorbidity with other psychiatric disorders is common, hinting at overlapping neurobiological processes across various diagnostic groups.

Multiple neurotransmitter systems (serotonergic, dopaminergic, adrenergic, and opioidergic) seem to be implicated in the pathophysiology of ICDs. For instance, ICDs, such as pathologic gambling (PG), hypersexuality, compulsive eating and shopping, can develop as adverse effects of dopamine replacement therapy in patients with Parkinson disease (PD).<sup>3</sup> Neuroimaging studies have implicated the ventromedial prefrontal cortex and ventral striatum in the pathophysiology of ICDs.<sup>1</sup> This review focuses on the clinical characteristics and treatment of the main ICDs and discusses their role as comorbidities in neurodevelopmental and neurodegenerative disorders.

# DIAGNOSTIC CLASSIFICATION OF IMPULSE CONTROL DISORDERS

ICDs have traditionally been problematic in terms of psychiatric classification. The Diagnostic and Statistical Manual of Mental Disorders (DSM), Fourth Edition, Text Revision included intermittent explosive disorder (IED), kleptomania, PG, pyromania and trichotillomania, with pathologic skin picking, compulsive sexual behavior (CSB), and compulsive buying (CB), categorized as ICDs not otherwise specified.<sup>4</sup> The DSM-5 introduced a new chapter on Disruptive, Impulse-Control, and Conduct Disorders covering disorders characterized by problems in emotional and behavioral self-control, which encompasses the following clinical entities: oppositional defiant disorder (ODD), IED, conduct disorder (CD), antisocial personality disorder (ASPD), pyromania, and kleptomania.<sup>2</sup> In the DSM-5, PG was reclassified as an addictive disorder, manly based on clinical and biological similarities to substance use disorders.<sup>5</sup> Specifically, PG shares several features with drug addiction, such as the development of euphoria, craving, and tolerance, possibly mediated by similar alterations in the dopaminergic mesolimbic reward system. Although the intent was for DSM-5 to reflect the most up-to-date scientific understanding of PG and addiction, the changes in the classification system have been controversial, because of their impact on prevalence figures, as well as their wider implications on the diagnosis and treatment of PG.<sup>6</sup> Trichotillomania and pathologic skin picking, referred to as Excoriation (Skin Picking) Disorder (ED), were moved into the category of obsessive-compulsive spectrum disorders, mainly because of their ritualistic nature. Finally, CSB and CB were dismissed because of the lack of compelling biological evidence.

# CLINICAL CHARACTERISTICS OF IMPULSE CONTROL DISORDERS Pathologic Gambling

Gambling involves risking something of value in the hopes of obtaining something of greater value. The essential feature of PG is the persistent and recurrent maladaptive gambling that disrupts personal, family, or vocational pursuits. Besides impulsivity, lack of perseverance and suspiciousness may be predictors of disease severity, possibly through emotion dysregulation. The prevalence of PG has been estimated as 0.2% to 1.6% in the general population, with higher prevalence figures in men (2–3:1). The onset is typically in early adolescence, and women seem to progress

more rapidly in disease severity.<sup>11–13</sup> Psychiatric comorbidity is the rule in patients with PG, especially nicotine dependence (60.1%), substance misuse (57.5%), affective disorders (37.9%), and anxiety disorders (37.4%).<sup>14</sup>

# Kleptomania

Kleptomania is defined as a recurrent failure to resist the impulse to steal items not needed for personal use or for their monetary value, with an urge to perform the act that is pleasurable at the moment but later causes significant distress and dysfunction.<sup>2</sup> The value of the stolen items tends to increase over time, suggesting the development of tolerance, akin to that of substance addiction.<sup>15</sup> The overall prevalence has been estimated at 6 per 1000.<sup>16</sup> Kleptomania is more common in women (2:1 in clinical samples), and the mean age of onset is in late adolescence or puberty.<sup>15,17</sup> Lifetime rates of other psychiatric disorders in kleptomania are high, including personality disorders (55.0%), substance misuse (29.0%–50.0%), suicidal behavior (36.0%), affective disorders (27.0%), anxiety disorders (18.0%), and attention-deficit/hyperactivity disorder (ADHD) (15.0%), as well as other ICDs (36.0%), particularly CB (18.0%) and trichotillomania (9.0%).<sup>15,17-19</sup>

# Trichotillomania

In trichotillomania, a build-up of tension results in recurrent hair pulling with noticeable hair loss, followed by relief, gratification, or pleasure.<sup>2</sup> The mean age of onset is 12 to 13 years.<sup>20</sup> The lifetime prevalence of trichotillomania has been reported to be 0.5% to 4.0% in the United States, and this condition is significantly more common in women (93.2%), with men usually having a later onset and greater functional impairment.<sup>21–23</sup> The most commonly affected body areas are the scalp and eyebrows (56.4%).<sup>24</sup> Subjects reported an elevated lifetime prevalence of affective disorders (51.8%), anxiety disorders (8.9%–32.0%), obsessive-compulsive disorder (OCD) (8.3%–30.4%), and substance misuse (15.0%–20.0%).<sup>25–28</sup>

### Excoriation (Skin Picking) Disorder

ED is defined as recurrent skin picking resulting in skin lesions despite repeated attempts to decrease or stop that behavior.<sup>2</sup> It has been suggested that both ED and trichotillomania can belong to a group of body-focused repetitive behaviors.<sup>27</sup> The reported prevalence of ED is 4.0% in college students and 0.2% to 5.4% in the general population.<sup>29,30</sup> Skin picking is more common in women, and the face is the most common site of excoriation, although any body part can be involved.<sup>31</sup> Individuals with ED often present with comorbid psychiatric conditions, especially substance misuse (38.0%), affective disorders (28.6%–36.4%), and OCD (15.2%–19.0%).<sup>25,27,32</sup> The association between ED and organic disorders is rare, despite occasional case reports of ED in patients with neurodegenerative disorders, such as frontotemporal dementia (FTD).<sup>33</sup>

# Intermittent Explosive Disorder

IED is characterized by brief (<30 minutes) outbursts of aggression that result in serious assaultive acts or destruction of property, out of proportion to precipitating stressors.<sup>2</sup> Prevalence figures vary between 4.0% and 7.0%, and IED usually manifests in adolescence, with an earlier onset and possibly higher prevalence in men.<sup>34</sup> Psychiatric comorbidities are frequently reported: these include affective (11.0%–93.0%) and anxiety disorders (48.0%–58.1%), substance misuse (35.1%–48.0%), ADHD (19.6%), suicide attempts (12.5%), and nonlethal self-injurious behaviors (7.4%). Moreover, about 25.0% of patients with IED have a previous history of CD

or ODD.<sup>34</sup> Among organic conditions, aggressive behaviors have been associated most strongly with traumatic brain injury (TBI).<sup>35</sup>

# **Pyromania**

Pyromania is characterized by multiple episodes of deliberate and purposeful fire setting without external reward, preceded by tension or affective arousal and commonly followed by a feeling of relief.<sup>2</sup> The prevalence and long-term course of pyromania are poorly described, because this is a relatively rare condition. The mean age of onset has been estimated as 18 years, with a significantly higher prevalence in men (8:1).<sup>36</sup> Pyromania is associated with affective disorders (14.0%–91.9%), anxiety disorders (33.3%), substance misuse (33.3%), kleptomania (23.8%), PG (9.5%), IED (9.5%), and trichotillomania (4.8%).<sup>32,36</sup>

# Oppositional Defiant, Conduct, and Antisocial Personality Disorders

ODD and CD relate to challenging or disruptive behavior exhibited by children and adolescents that go beyond what is expected in this population and lead to significant distress or functional impairment. The symptoms of ODD are grouped into 3 types: angry/irritable mood, argumentative/defiant behavior, and vindictiveness.<sup>2</sup> Oppositional behaviors often manifest in the home setting and with adults the youth knows well.<sup>37</sup> Like children with ODD, those with CD may have an issue with controlling their temper; however, they also violate the rights of others, including aggression toward people and/or animals, destruction of property, deceitfulness, theft, and serious violation of rules.<sup>38</sup> CD can appear as early as in the preschool years, with ODD as a common premorbid condition that may progress to CD: the 2 disorders share common risk factors and genetic backgrounds. 39 ASPD refers to a persistent impairment in self and interpersonal functioning associated with the pathologic personality traits of antagonism and disinhibition.<sup>2</sup> Although ASPD and psychopathy are similar and are highly comorbid with each other, strictly speaking, they are not synonymous: psychopathy is theorized as a disorder of personality and affective deficits, whereas the diagnosis of ASPD is primarily behaviorally based.<sup>40</sup>

ASPD is typically an outcome of CD rather than ODD, because individuals with ASPD often engage in repetitive irresponsible, delinquent, and criminal behavior. <sup>41</sup> Prevalence rates have been reported for ODD (1.0%–11.0%), CD (2.0%–10.0%), and ASPD (1.0%–4.0%). <sup>2,42</sup> Studies of the comorbidity rates for ODD have shown that 14.0% to 40.0% of patients also have ADHD, and 9.0% to 50.0% have an anxiety or affective disorder. <sup>43</sup> Youth with both ODD and ADHD have a poorer prognosis and are at increased risk of transitioning to CD. <sup>2</sup> Among youths with serious emotional or behavioral disorders, adolescents with CD have the highest risk for problem alcohol and substance misuse. <sup>44</sup> A strong relationship between CD, academic failure, and learning disabilities has also been identified. <sup>45</sup>

# Compulsive Buying and Compulsive Sexual Behavior

CB and CSB are not formally recognized by the *DSM-5*. CB is characterized by preoccupation with buying unneeded items or more than one can afford, and shopping for longer durations of time than originally intended, resulting in marked distress or interference with social and occupational functioning.<sup>46,47</sup> Purchased items typically do not get used, are given away, or are returned.<sup>48</sup> CSB is characterized by nonparaphilic, impulsive, recurrent, and intense sexual fantasies resulting in significant distress or functional impairment.<sup>49</sup> The estimated prevalence of CB in the United States is 5.8%, and most patients are women (80%–95%).<sup>50</sup> Comorbid conditions include affective (21%–100%), anxiety (41%–80%), and substance misuse (21%– 46%) disorders, as well as other ICDs (21%–40%).<sup>32,48,51</sup> The prevalence of CSB remains uncertain, with estimated figures of 5% to 6% in the US population.<sup>52</sup> Individuals with CSB usually present with other comorbid disorders, including affective disorders (71.6%), substance misuse (40.8%), anxiety disorders (38.3%), and ADHD (35.8%).<sup>53</sup>

#### TREATMENT OF IMPULSE CONTROL DISORDERS

Pharmacologic treatments for primary ICDs have been relatively understudied. There are no Food and Drug Administration–approved medications for any individual ICD. Serotonergic antidepressants may be useful for some of the ICDs (IED, ED, CB, and CSB), whereas there is more robust evidence for the use of opioid antagonists for the management of PG and kleptomania. \*\*N-acetyl cysteine is a promising agent for the treatment of patients with PG and trichotillomania. \*\*54\* Atypical antipsychotics are unlikely to offer significant benefits, and data on mood stabilizers are far too limited at the moment for their use to be recommended, unless a diagnosis of comorbid bipolar affective disorder has been established. Finally, cognitive behavioral therapy (CBT) appears to be particularly useful in the management of kleptomania, CB, and PG. \*\*55\*

# IMPULSE CONTROL DISORDERS IN NEURODEVELOPMENTAL AND NEURODEGENERATIVE DISORDERS

Attention-Deficit/Hyperactivity Disorder

ADHD is characterized by inattentive, hyperactive, and impulsive behaviors, associated with elevated levels of impulsivity as measured by poor performance on a variety of tasks requiring attentional ability and/or behavioral inhibition.<sup>56</sup> The neural correlates of ADHD converge on the prefrontal cortex, ventral regions of the frontal lobes, and subcortical structures within the basal ganglia.<sup>57</sup> These areas have consistently been linked to deficits in a variety of inhibitory processes and are known to be implicated in the development of impulsive behaviors. Furthermore, there seems to be a differential contribution of the various frontostriatal loops to different aspects of behavioral disinhibition and impulsivity. Specifically, dysfunction in the prefrontal cortex and striatal systems could mediate loss of inhibitory control in 1 subgroup of ADHD patients, and abnormal activity within areas involved in reward-learning and regulation of affect such as the nucleus accumbens and the amygdala could be implicated in avoidance of delay in another subgroup. It has been shown that about two-thirds of patients with ADHD have at least 1 ICD, the most common being IED (29.6%), followed by CB (23.4%), PG (7.4%), kleptomania and CSB (2.4%), and trichotillomania (1.2%).58 Studies looking at psychiatric comorbidities in patients with known ICDs have also shown high prevalence rates for ADHD. In particular, ADHD was diagnosed in 20% to 25% of patients seeking treatment of PG.59-61 In a large sample of nontreatment-seeking gamblers in the United States, 20.3% screened positive for ADHD and only 7.3% of those subjects had ever received a formal diagnosis, suggesting that this disorder might remain unrecognized in adults who gamble. 62

Psychostimulants, the first-line pharmacotherapy for ADHD, have been shown to reduce several measures of impulsivity in this patient population. A similar improvement in inhibitory control has been achieved with atomoxetine, and nonpharmacologic treatments, such as neurofeedback, have also been associated with a reduction in measures of impulsivity. However, studies looking at the relationship between psychostimulant treatment and substance misuse in patients with ADHD often report contradicting results, with some studies showing an increased risk for substance

misuse, and other studies suggesting a reduced risk or no change in risk. <sup>66</sup> Only anecdotal evidence is currently available regarding treatment outcomes for comorbid ICDs in patients with ADHD. For example, patients with PG and ADHD features were reported to have benefited from treatment with bupropion in 1 open-label study, <sup>67</sup> and a patient with ADHD and skin picking disorder improved with methylphenidate. <sup>68</sup>

# **Tourette Syndrome**

Tourette syndrome (TS) is a neurodevelopmental disorder characterized by the presence of multiple motor and phonic tics. <sup>69</sup> Most patients with TS present with comorbid psychiatric disorders. <sup>70,71</sup> About 50% of children diagnosed with ADHD have been shown to have a comorbid tic disorder, whereas ADHD-related symptoms have been reported in 35% to 90% of children with TS. <sup>72</sup> Several studies have shown that most cognitive impairment found in patients with TS can be linked to comorbidity with ADHD or OCD, whereas patients with uncomplicated TS tend to perform similarly to healthy controls in most cognitive domains. <sup>73</sup> There is the possibility that TS is associated with deficits in inhibitory functioning regardless of the presence of comorbid ADHD, although these impairments may only be apparent on particular measures. Specifically, deficit in inhibitory functions has been linked to dysfunction at the level of the anterior cingulate pathways, and neurobiological changes in this region have been associated with TS. <sup>74,75</sup>

Overall, neuropsychological changes related to impulsivity appear to be subtle in patients with TS, whereas antisocial behaviors, inappropriate sexual activity, nonobscene socially inappropriate behaviors, and self-injurious behaviors have consistently been reported in this population.<sup>70,71</sup> There is sparse literature available on the prevalence of specific ICDs in patients with TS, but it has been reported that as much as 74.2% of patients present with at least 1 ICD. 76,77 IED has been reported in 16.0% of patients with TS, and temper tantrums and rage attacks were found in 34.8% to 64.0% children with TS. 76,78,79 The frequency of these comorbid symptoms, in particular, rage attacks, was found to be increased when ADHD was present, and even more so when both ADHD and OCD were present.  $^{78}$  Trichotillomania has been reported in 2.6% to 3.0% of patients with TS, a prevalence figure that was found to be independent from the presence of comorbid ADHD. 72,80 Trichotillomania has also been reported to be more prevalent in female (12%) than male (2%) patients.81 CSB has been observed in 2.0% to 4.3% of patients with TS and has been linked to comorbid ADHD and adult age. 76,80 Prevalence rates have also been reported for CB (13%), compulsive computer use (7%), kleptomania (4%), and pyromania (3%).<sup>76</sup> Little is known about the treatment of ICDs in patients with TS and other chronic tic disorders: both alpha-2 agonists and antidopaminergic medications might prove beneficial for impulsive behaviors, in addition to their known anti-tic effects.<sup>82</sup>

### Parkinson Disease

PD is the second most common neurodegenerative disorder after Alzheimer disease and is characterized by the motor symptoms of tremor, bradykinesia, and rigidity. Over the last few years, interest has gathered around the nonmotor symptoms of PD, and there is now ample evidence that cognition and emotion are also impaired, with psychiatric symptoms being present in more than 60% of patients with PD.<sup>83</sup> ICDs are clinically relevant nonmotor manifestations, as it has been reported that as many as 20% of patients with PD present with an ICD.<sup>84</sup> The most commonly reported ICDs are PG (3.9%–5.30%), CSB (3.5%–9.7%), binge eating (4.3%–10.5%), and CB (4.6%–6.5%).<sup>85</sup> Crucially, there seems to be no increased risk for the development of ICDs or related reward-seeking behaviors in patients with PD in the absence of

dopamine replacement therapy. <sup>86</sup> Risk factors for the development of ICDs in patients with PD encompass male gender, higher disease severity and earlier age of onset, novelty-seeking personality traits, and family history of ICDs. <sup>87</sup> Therefore, the development of ICDs in patients with PD can be linked to 3 distinct but possibly interacting processes: disease process, premorbid susceptibility to impulsivity, and dopaminergic treatment. Studies looking at the neuropsychologic performance of drug-naïve, nondemented patients with PD have yielded inconsistent results. <sup>88</sup> Historically, the emergence of impulsivity in PD has been attributed to neuronal dopaminergic degeneration, facilitating the development of ICDs in patients receiving dopamine replacement therapies. In patients with PD and ICDs, a diminished striatal D2/D3 receptor level and an increase in mesolimbic dopaminergic tone have been documented. <sup>89,90</sup> Dopamine replacement therapy acts at the level of a depleted dorsal striatum and a relatively intact ventral striatum: this can affect the function of the lateral orbitofrontal cortex, the rostral cingulate cortex, the amygdala, and the external pallidum, resulting in impaired inhibitory response and impulse control. <sup>84,85,91</sup>

The management ICDs in patients with PD typically involves dose reduction or discontinuation of dopamine agonists. When doing so, the risk of increasing motor symptoms and inducing dopamine agonist withdrawal syndrome must be taken into account. <sup>92,93</sup> A double-blind randomized controlled trial looking at the effect of amantadine in 17 patients with PD and PG showed a significant reduction in PG behavior in the patient group. <sup>94</sup> Another trial on 45 patients with PD and ICDs treated with nurseled CBT revealed a statistically significant decrease in impulsive behaviors. <sup>95</sup>

# Frontotemporal Dementia

FTD is a neurodegenerative condition characterized by selective involvement of the frontal lobe and anterior temporal lobe, resulting in profound alterations in behavior and social conduct, in the context of relative preservation of perception, spatial skills, praxis, and memory. 96,97 The behavioral variant of FTD can be associated with cognitive and personality impairment, leading to antisocial behavior (including kleptomania), as well as specific ICDs. 33,98 Importantly, behavioral problems are often the earliest manifestations of the behavioral variant of FTD. 99 Compared with PD, relatively little is known about the prevalence and clinical characteristics of ICDs in FTD; however, several case reports suggested a possible link between the behavioral variant of FTD and PG. 100-105 Because abnormal functioning of the orbitofrontal cortex appears to be implicated in the pathophysiology of gambling behavior, FTD could be considered in the differential diagnosis of a new-onset gambling behavior in adults if there are changes of personality and other more "typical" features of FTD. In summary, this literature provides additional evidence that FTD should be considered in the differential diagnosis of late-onset PG and raises the possibility that it could be appropriate to broaden the behavioral criteria for FTD toward psychiatric symptoms in the early phase of the disease. Clearly, additional research is needed to further clarify the relationship between ICDs and regional brain involvement in patients with FTD. Likewise, the management of ICDs in patients with FTD is an area that deserves further investigation in order to establish evidence-based treatment approaches.

### IMPULSE CONTROL DISORDERS IN TRAUMATIC BRAIN INJURY

TBI is a relatively common injury characterized by a change in brain function after an external blow to the head and is associated with psychological distress, substance abuse, risk-taking behaviors, and ICDs.<sup>106</sup> There is evidence suggesting that TBI could be a risk factor for the later development of changes in brain structure and

function. 107 Specifically, several studies have shown evidence of long-term brain changes and accumulation of pathologic biomarkers (eg, amyloid and tau proteins) related to a history of moderate to severe TBI. These findings have led to the suggestion that patients with moderate to severe injuries have an increased risk of developing neurodegenerative disorders. 107 Reports on long-term brain changes in patients with milder forms of TBI have been mixed, because they are often complicated by factors related to injury exposure and complications, including the development of substance abuse and psychiatric conditions. Overall, it appears that most subjects who sustain a TBI of milder severity do not experience worse outcomes with aging. Chronic traumatic encephalopathy, although often described in terms of a neurodegenerative disorder, remains a neuropathologic condition that is poorly understood. Future research is needed to clarify the significance of pathologic findings in chronic traumatic encephalopathy and to determine whether such changes can explain any clinical symptoms, including psychiatric manifestations and ICDs.

Impulsivity has been commonly described in persons with TBI. <sup>108,109</sup> A multidimensional model of impulsivity encompassing 4 dimensions (urgency of reactions, lack of premeditation, lack of perseverance, and sensation seeking) has been confirmed in patients with TBI. <sup>110–112</sup> Moreover, specific impulsivity dimensions have been related to different behavioral disorders and/or psychopathologic states, including ICDs. For example, significant correlations have been reported between the urgency dimension of impulsivity and a tendency to CB in patients with moderate to severe TBI. <sup>111</sup> These findings illustrate the existing relationships between the different types of problematic behaviors and the potential implications of common psychological mechanisms in the various behavioral changes in patients with TBI. <sup>113</sup>

In addition to sparse evidence on hypersexuality, <sup>114</sup> multiple clinical observations have suggested that TBI can be associated with PG. <sup>115–117</sup> Moreover, it has been found that problem gamblers may be characterized by increased aggressiveness, risk-taking behaviors, and impulsivity in comparison to the general population, which are characteristics that have been observed among those who have experienced TBI. <sup>118</sup> Thus, it is possible that increased aggressiveness, impulsivity, and risk taking that can result from TBI might predispose individuals to problem gambling, although there is insufficient evidence to determine if there is a causal relationship. Further research is needed also to determine the potential implications of the link between TBI and moderate to severe problem gambling in terms of prevention and treatment.

# **SUMMARY**

Although their first description dates back to over a century ago, ICDs have received relatively little attention from researchers and clinicians for decades. In the last few years, however, there has been an increase in the amount of research and clinical information on these fairly common and debilitating disorders. The nosologic reorganization brought about by the *DSM-5* and the upcoming ICD-11 reflects the growing understanding of the underlying neurocognitive and biological processes governing different types of impulsive behaviors, although controversy persists. <sup>119</sup> Research over the past decade has shown that impulsivity is linked to 2 or more dissociable domains, for example, a failure of motor or cognitive inhibitory control, and a failure of the reward valuation system. These components may relate to specific aspects of psychiatric practice in terms of behavior prediction and understanding of interaction between genetic and environmental factors. <sup>120</sup> Undeniably, a significant amount of work remains to be done; however, sustained and directed research efforts will help

develop more accurate diagnostic protocols and more targeted treatment strategies for patients with ICDs.

### DISCLOSURE

The authors have nothing to disclose.

#### REFERENCES

- 1. Grant JE, Potenza MN. The Oxford handbook of impulse control disorders. Oxford (United Kingdom): Oxford University Press; 2011.
- American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Fifth Edition (DSM-5). Arlington (VA): American Psychiatric Publishing; 2013.
- 3. Probst CC, van Eimeren T. The functional anatomy of impulse control disorders. Curr Neurol Neurosci Rep 2013;13(10):386.
- American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Fourth Edition (DSM-IV). Washington, DC: American Psychiatric Publishing; 1994.
- Potenza MN. Should addictive disorders include non-substance-related conditions? Addiction 2006;101(Suppl):142–51.
- Agrawal A, Heath AC, Lynskey MT. DSM-IV to DSM-5: the impact of proposed revisions on diagnosis of alcohol use disorders. Addiction 2011;106:1935–43.
- Stein DJ, Grant JE, Franklin ME, et al. Trichotillomania (hair pulling disorder), skin picking disorder, and stereotypic movement disorder: toward DSM-V. Depress Anxiety 2010;27(6):611–26.
- 8. Rogier G, Beomonte Zobel S, Velotti P. Pathological personality facets and emotion (dys)regulation in gambling disorder. Scand J Psychol 2019. https://doi.org/10.1111/sjop.12579.
- 9. Shaffer HJ, Hall MN, Vander Bilt J. Estimating the prevalence of disordered gambling behavior in the United States and Canada: a research synthesis. Am J Public Health 1999;89(9):1369–76.
- 10. Petry NM, Stinson FS, Grant BF. Comorbidity of DSM-IV pathological gambling and other psychiatric disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry 2005;66(5):564–74.
- 11. Rosenthal RJ. Pathological gambling. Psychiatr Ann 1992;22(2):72-8.
- 12. Ladouceur R, Dube D, Bujold A. Prevalence of pathological gambling and related problems among college students in the Quebec metropolitan area. Can J Psychiatry 1994;39(5):289–93.
- 13. Volberg RA. The prevalence and demographics of pathological gamblers: implications for public health. Am J Public Health 1994;84(2):237–41.
- 14. Lorains FK, Cowlishaw S, Thomas SA. Prevalence of comorbid disorders in problem and pathological gambling: systematic review and meta-analysis of population surveys. Addiction 2011;106(3):490–8.
- 15. Grant JE. Family history and psychiatric comorbidity in persons with kleptomania. Compr Psychiatry 2003;44(6):437–41.
- **16.** Goldman MJ. Kleptomania: making sense of the nonsensical. Am J Psychiatry 1991;148(8):986–96.
- 17. Presta S, Marazziti D, Dell'Osso L, et al. Kleptomania: clinical features and comorbidity in an Italian sample. Compr Psychiatry 2002;43(1):7–12.
- **18.** McElroy SL, Pope HG Jr, Hudson JI, et al. Kleptomania: a report of 20 cases. Am J Psychiatry 1991;148(5):652–7.

- 19. Baylé FJ, Caci H, Millet B, et al. Psychopathology and comorbidity of psychiatric disorders in patients with kleptomania. Am J Psychiatry 2003;160(8):1509–13.
- 20. Christenson GA. Trichotillomania: from prevalence to comorbidity. Psychiatr Times 1995;12(9):44–8.
- 21. Christenson GA, Pyle RL, Mitchell JE. Estimated lifetime prevalence of trichotillomania in college students. J Clin Psychiatry 1991;52(10):415–7.
- 22. Cohen LJ, Stein DJ, Simeon D, et al. Clinical profile, comorbidity, and treatment history in 123 hair pullers: a survey study. J Clin Psychiatry 1995;56(7):319–26.
- 23. Grant JE, Christenson GA. Examination of gender in pathologic grooming behaviors. Psychiatr Q 2007;78(4):259–67.
- 24. Woods DW, Flessner CA, Franklin ME, et al. The Trichotillomania Impact Project (TIP): exploring phenomenology, functional impairment, and treatment utilization. J Clin Psychiatry 2006;67(12):1877–88.
- 25. Lochner C, Simeon D, Niehaus DJ, et al. Trichotillomania and skin picking: a phenomenological comparison. Depress Anx 2002;15(2):83–6.
- 26. Woods D, Miltenberger R. Tic disorders, trichotillomania, and other repetitive behavior disorders: behavioral approaches to analysis and treatment. New York: Springer Science & Business Media; 2007.
- 27. Odlaug BL, Grant JE. Trichotillomania and pathologic skin picking: clinical comparison with an examination of comorbidity. Ann Clin Psychiatry 2008;20(2): 57–63.
- 28. Bohne A, Wilhelm S, Keuthen NJ, et al. Skin picking in German students: prevalence, phenomenology, and associated characteristics. Behav Modif 2002; 26(3):320–39.
- 29. Keuthen NJ, Deckersbach T, Wilhelm S, et al. Repetitive skin-picking in a student population and comparison with a sample of self-injurious skin-pickers. Psychosomatics 2000;41(3):210–5.
- 30. Keuthen NJ, Koran LM, Aboujaoude E, et al. The prevalence of pathologic skin picking in US adults. Compr Psychiatry 2010;51(2):183–6.
- 31. Odlaug BL, Grant JE. Clinical characteristics and medical complications of pathologic skin picking. Gen Hosp Psychiatry 2008;30(1):61–6.
- 32. Grant JE. Impulse control disorders: a clinician's guide to understanding and treating behavioral addictions. New York: Norton & Company; 2008.
- 33. Pompanin S, Jelcic N, Cecchin D, et al. Impulse control disorders in frontotemporal dementia: spectrum of symptoms and response to treatment. Gen Hosp Psychiatry 2014;36(6):760.e5-7.
- 34. Coccaro EF, Posternak MA, Zimmerman M. Prevalence and features of intermittent explosive disorder in a clinical setting. J Clin Psychiatry 2005;66(10): 1221–7.
- 35. Ferguson SD1, Coccaro EF. History of mild to moderate traumatic brain injury and aggression in physically healthy participants with and without personality disorder. J Pers Disord 2009;23(3):230–9.
- 36. Grant JE, Won SK. Clinical characteristics and psychiatric comorbidity of pyromania. J Clin Psychiatry 2007;68(11):1717–22.
- 37. Gathright M, Tyler D. Disruptive behaviors in children and adolescents. Fayette-ville (NC): Psychiatric Research Institute (University of Arkansas); 2012.
- 38. Murphy M, Cowan R, Sederer L. Disorders of childhood and adolescence. Malden (MA): Blackwell Science; 2001.
- 39. Rowe R, Costello EJ, Angold A, et al. Developmental pathways in oppositional defiant disorder and conduct disorder. J Abnorm Psychol 2010;119(4):726–38.

- Werner KB, Few LR, Bucholz KK. Epidemiology, comorbidity, and behavioral genetics of antisocial personality disorder and psychopathy. Psychiatr Ann 2015; 45(4):195–9.
- 41. Glenn AL, Johnson AK, Raine A. Antisocial personality disorder: a current review. Curr Psychiatry Rep 2013;15(12):427.
- 42. Lenzenweger MF, Lane MC, Loranger AW, et al. DSM-IV personality disorders in the National Comorbidity Survey Replication. Biol Psychiatry 2007;62(6):553–64.
- 43. Riley M, Ahmed S, Locke A. Common questions about oppositional defiant disorder. Am Fam Physician 2016;93(7):586–91.
- 44. Bukstein OG. Disruptive behavior disorders and substance use disorders in adolescents. J Psychoactive Drugs 2000;32(1):67–79.
- 45. Frick PJ, Kamphaus RW, Lahey BB, et al. Academic underachievement and the disruptive behavior disorders. J Consult Clin Psychol 1991;59(2):289–94.
- 46. McElroy SL, Keck PE Jr, Pope HG Jr, et al. Compulsive buying: a report of 20 cases. J Clin Psychiatry 1994;55(6):242-8.
- 47. Schreiber L, Odlaug BL, Grant JE. Impulse control disorders: updated review of clinical characteristics and pharmacological management. Front Psychiatry 2011;2:1.
- 48. Schlosser S, Black DW, Repertinger S, et al. Compulsive buying. Demography, phenomenology, and comorbidity in 46 subjects. Gen Hosp Psychiatry 1994; 16(3):205–12.
- 49. Kafka MP. Hypersexual disorder: a proposed diagnosis for DSM-V. Arch Sex Behav 2010;39(2):377–400.
- 50. Koran LM, Faber RJ, Aboujaoude E, et al. Estimated prevalence of compulsive buying behavior in the United States. Am J Psychiatry 2006;163(10):1806–12.
- 51. Christenson GA, Faber RJ, de Zwaan M, et al. Compulsive buying: descriptive characteristics and psychiatric comorbidity. J Clin Psychiatry 1994;55(1):5–11.
- 52. Coleman E. Compulsive sexual behavior: new concepts and treatments. J Psychol Human Sex 1991;4(2):37–52.
- 53. Kafka MP, Hennen J. A DSM-IV Axis I comorbidity study of males (n = 120) with paraphilias and paraphilia-related disorders. Sex Abuse 2002;14(4):349–66.
- Deepmala, Slattery J, Kumar N, et al. Clinical trials of N-acetylcysteine in psychiatry and neurology: a systematic review. Neurosci Biobehav Rev 2015;55: 294–321.
- 55. Hodgins DC, Peden N. Tratamento cognitivo e comportamental para transtornos do controle de impulsos. Braz J Psychiatry 2007;30(Suppl 1):31–40.
- 56. Solanto MV. Dopamine dysfunction in AD/HD: integrating clinical and basic neuroscience research. Behav Brain Res 2002;130(1–2):65–71.
- 57. Castellanos FX, Tannock R. Neuroscience of attention-deficit/hyperactivity disorder: the search for endophenotypes. Nat Rev Neurosci 2002;3(8):617–28.
- 58. Porteret R, Bouchez J, Baylé FJ, et al. ADH/D and impulsiveness: prevalence of impulse control disorders and other comorbidities, in 81 adults with attention deficit/hyperactivity disorder (ADH/D)]. Encephale 2016;42(2):130–7.
- 59. Grall-Bronnec M, Wainstein L, Augy J, et al. Attention deficit hyperactivity disorder among pathological and at-risk gamblers seeking treatment: a hidden disorder. Eur Addict Res 2011;17(5):231–40.
- Waluk OR, Youssef GJ, Dowling NA. The relationship between problem gambling and attention deficit hyperactivity disorder. J Gambl Stud 2016; 32(2):591–604.
- 61. Mak C, Tan KK, Guo S. ADHD symptoms in pathological and problem gamblers in Singapore. Int J Environ Res Public Health 2018;15(7):E1307.

- 62. Chamberlain SR, Ioannidis K, Leppink EW, et al. ADHD symptoms in non-treatment seeking young adults: relationship with other forms of impulsivity. CNS Spectr 2017;22(1):22–30.
- **63.** Aron AR, Dowson JH, Sahakian BJ, et al. Methylphenidate improves response inhibition in adults with attention-deficit/hyperactivity disorder. Biol Psychiatry 2003;54(12):1465–8.
- 64. Chamberlain SR, Del Campo N, Dowson J, et al. Atomoxetine improved response inhibition in adults with attention deficit/hyperactivity disorder. Biol Psychiatry 2007;62(9):977–84.
- 65. Arns M, de Ridder S, Strehl U, et al. Efficacy of neurofeedback treatment in ADHD: the effects on inattention, impulsivity and hyperactivity: a meta-analysis. Clin EEG Neurosci 2009;40(3):180–9.
- 66. Kollins SH. ADHD, substance use disorders, and psychostimulant treatment: current literature and treatment guidelines. J Atten Disord 2007;12(2):115–25.
- 67. Black DW. An open-label trial of bupropion in the treatment of pathologic gambling. J Clin Psychopharmacol 2004;24(1):108–10.
- 68. Bernardes C, Mattos P, Nazar BP. Skin picking disorder comorbid with ADHD successfully treated with methylphenidate. Rev Bras Psiguiatria 2018;40(1):111.
- 69. Martino D, Madhusudan N, Zis P, et al. An introduction to the clinical phenomenology of Tourette syndrome. Int Rev Neurobiol 2013;112:1–33.
- 70. Cavanna AE. Gilles de la Tourette syndrome as a paradigmatic neuropsychiatric disorder. CNS Spectr 2018;23(3):213–8.
- 71. Cavanna AE. The neuropsychiatry of Gilles de la Tourette syndrome: the état de l'art. Rev Neurol 2018:174(9):621–7.
- 72. Erenberg G. The relationship between tourette syndrome, attention deficit hyperactivity disorder, and stimulant medication: a critical review. Semin Pediatr Neurol 2005;12(4):217–21.
- 73. Eddy CM, Rizzo R, Cavanna AE. Neuropsychological aspects of Tourette syndrome: a review. J Psychosom Res 2009;67(6):503–13.
- 74. Peterson BS, Staib L, Scahill L, et al. Regional brain and ventricular volumes in Tourette syndrome. Arch Gen Psychiatry 2001;58(5):427–40.
- 75. Nathaniel-James DA, Frith CD. The role of the dorsolateral prefrontal cortex: evidence from the effects of contextual constraint in a sentence completion task. Neuroimage 2002;16(4):1094–102.
- **76.** Frank MC, Piedad J, Rickards H, et al. The role of impulse control disorders in Tourette syndrome: an exploratory study. J Neurol Sci 2011;310(1–2):276–8.
- 77. Wright A, Rickards H, Cavanna AE. Impulse-control disorders in Gilles de la Tourette syndrome. J Neuropsychiatry Clin Neurosci 2012;24(1):16–27.
- 78. Champion LM, Fulton WA, Shady GA. Tourette syndrome and social functioning in a Canadian population. Neurosci Biobehav Rev 1988;12(3–4):255–7.
- 79. Mol Debes NMM, Hjalgrim H, Skov L. Validation of the presence of comorbidities in a Danish clinical cohort of children with Tourette syndrome. J Child Neurol 2008;23(9):1017–27.
- Freeman RD. Tic disorders and ADHD: answers from a world-wide clinical dataset on Tourette syndrome. Eur Child Adolesc Psychiatry 2007;16(Suppl 1): 15–23
- 81. Janik P, Kalbarczyk A, Sitek M. Clinical analysis of Gilles de la Tourette syndrome based on 126 cases. Neurol Neurochir Pol 2007;41(5):381–7.
- 82. Cavanna AE. Pharmacological treatment of tics. Cambridge (United Kingdom): Cambridge University Press; 2020.

- 83. Schrag A. Psychiatric aspects of Parkinson's disease: an update. J Neurol 2004; 251(7):795–804.
- 84. Weintraub D, Claassen DO. Impulse control and related disorders in Parkinson's disease. In: Chaudhuri KR, Titova N, editors. Nonmotor Parkinson's: the hidden face. Cambridge (MA): Academic Press; 2017. p. 679–717.
- 85. Gatto EM, Aldinio V. Impulse control disorders in Parkinson's disease: a brief and comprehensive review. Front Neurol 2019;10:351.
- **86.** Smith KM, Xie SX, Weintraub D. Incident impulse control disorder symptoms and dopamine transporter imaging in Parkinson disease. J Neurol Neurosurg Psychiatry 2016;87(8):864–70.
- 87. Leeman R, Potenza MN. Impulse control disorders in Parkinson's disease: clinical characteristics and implications. Neuropsychiatry 2011;1(2):133–47.
- 88. Antonelli F, Ray N, Strafella AP. Impulsivity and Parkinson's disease: more than just disinhibition. J Neurol Sci 2011;310(1–2):202–7.
- 89. van Oosten RV, Verheij MMM, Cools AR. Bilateral nigral 6-hydroxydopamine lesions increase the amount of extracellular dopamine in the nucleus accumbens. Exp Neurol 2005;191(1):24–32.
- 90. Houeto JL, Magnard R, Dalley JW, et al. Trait impulsivity and anhedonia: two gateways for the development of impulse control disorders in Parkinson's disease? Front Psychiatry 2016;7:91.
- 91. Cossu G, Rinaldi R, Colosimo C. The rise and fall of impulse control behavior disorders. Parkinsonism Relat Dis 2018;46(Suppl 1):24–9.
- 92. Mamikonyan E, Siderowf AD, Duda JE, et al. Long-term follow-up of impulse control disorders in Parkinson's disease. Mov Disord 2008;23(1):75–80.
- 93. Tanwani P, Fernie BA, Nikčević AV, et al. A systematic review of treatments for impulse control disorders and related behaviours in Parkinson's disease. Psychiatry Res 2015;225(3):402–6.
- 94. Thomas A, Bonanni L, Gambi F, et al. Pathological gambling in Parkinson disease is reduced by amantadine. Ann Neurol 2010;68(3):400–4.
- 95. Okai D, Askey-Jones S, Samuel M, et al. Trial of CBT for impulse control behaviors affecting Parkinson patients and their caregivers. Neurology 2013;80(9): 792–9.
- 96. Miller B, Llibre Guerra JJ. Frontotemporal dementia. Handb Clin Neurol 2019; 165:33–45.
- 97. Weder ND, Aziz R, Wilkins K, et al. Frontotemporal dementias: a review. Ann Gen Psychiatry 2007;6:15.
- 98. Birkhoff JM, Garberi C, Re L. The behavioral variant of frontotemporal dementia: an analysis of the literature and a case report. Int J Law Psychiatry 2016;47: 157–63.
- 99. Mendez MF, Perryman KM. Neuropsychiatric features of frontotemporal dementia: evaluation of consensus criteria and review. J Neuropsychiatry Clin Neurosci 2002;14:424–9.
- Lo Coco D, Nacci P. Frontotemporal dementia presenting with pathological gambling. J Neuropsychiatry Clin Neurosci 2004;16:117–8.
- 101. Nakaaki S, Murata Y, Sato J, et al. Impairment of decision-making cognition in a case of frontotemporal lobar degeneration (FTLD) presenting with pathologic gambling and hoarding as the initial symptoms. Cogn Behav Neurol 2007;20: 121–5.
- 102. Manes FF, Torralva T, Roca M, et al. Frontotemporal dementia presenting as pathological gambling. Nat Rev Neurol 2010;6(6):347–52.

- Ozel-Kizil E, Sakarya A, Arica B, et al. A case of frontotemporal dementia with amyotrophic lateral sclerosis presenting with pathological gambling. J Clin Neurol 2013;9(2):133–7.
- 104. Cimminella F, Ambra FI, Vitaliano S, et al. Early-onset frontotemporal dementia presenting with pathological gambling. Acta Neurol Belg 2015;115(4):759–61.
- 105. Tondo G, De Marchi F, Terazzi E, et al. Frontotemporal dementia presenting as gambling disorder: when a psychiatric condition is the clue to a neurodegenerative disease. Cogn Behav Neurol 2017;30(2):62–7.
- 106. Kim E. Agitation, aggression, and disinhibition syndromes after traumatic brain injury. NeuroRehabilitation 2002;17(4):297–310.
- 107. LoBue C, Munro C, Schaffert J, et al. Traumatic brain injury and risk of long-term brain changes, accumulation of pathological markers, and developing dementia: a review. J Alzheimers Dis 2019;70(3):629–54.
- 108. Bechara A, Van Der Linden M. Decision-making and impulse control after frontal lobe injuries (research support, NIH, extramural review). Curr Opin Neurol 2005; 18:734–9.
- 109. McAllister TW. Neurobehavioral sequelae of traumatic brain injury: evaluation and management. World Psychiatry 2008;7:3–10.
- 110. Rochat L, Beni C, Billieux J, et al. Assessment of impulsivity after moderate to severe traumatic brain injury. Neuropsychol Rehabil 2010;20:778–97.
- 111. Rochat L, Beni C, Billieux J, et al. How impulsivity relates to compulsive buying and the burden perceived by caregivers after moderate-to-severe traumatic brain injury. Psychopathology 2011;44:158–64.
- 112. Rochat L, Beni C, Annoni JM, et al. How inhibition relates to impulsivity after moderate to severe traumatic brain injury. J Int Neuropsychol Soc 2013;19: 890–8.
- 113. Arnould A, Dromer E, Rochat L, et al. Neurobehavioral and self-awareness changes after traumatic brain injury: towards new multidimensional approaches. Ann Phys Rehabil Med 2016;59(1):18–22.
- 114. Kaufman KR, Schineller TM, Tobia A, et al. Hypersexuality after self-inflicted nail gun penetrating traumatic brain injury and neurosurgery: case analysis with literature review. Ann Clin Psychiatry 2015;27(1):65–8.
- 115. Guercio JM, Johnson T, Dixon MR. Behavioral treatment for pathological gambling in persons with acquired brain injury. J Appl Behav Anal 2012; 45(3):485–95.
- Hodgins DC, Holub A. Components of impulsivity in gambling disorder. Int J Ment Health Addict 2015;13(6):699–711.
- 117. Whiting SW, Potenza MN, Park CL, et al. Investigating veterans' pre-, peri-, and post-deployment experiences as potential risk factors for problem gambling. J Behav Addict 2016;5(2):213–20.
- 118. Turner NE, McDonald AJ, Ialomiteanu AR, et al. Moderate to severe gambling problems and traumatic brain injury: a population-based study. Psychiatry Res 2019;272:692–7.
- 119. Grant JE, Atmaca M, Fineberg NA, et al. Impulse control disorders and "behavioural addictions" in the ICD-11. World Psychiatry 2014;13(2):125–7.
- 120. Potenza MN, Taylor JR. Found in translation: understanding impulsivity and related constructs through integrative preclinical and clinical research. Biol Psychiatry 2009;66(8):714–6.