A Targeted Review of the Neurobiology and Genetics of Behavioural Addictions: An Emerging Area of Research

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This review summarizes neurobiological and genetic findings in behavioural addictions, draws parallels with findings pertaining to substance use disorders, and offers suggestions for future research. Articles concerning brain function, neurotransmitter activity, and family history and (or) genetic findings for behavioural addictions involving gambling, Internet use, video game playing, shopping, kleptomania, and sexual activity were reviewed. Behavioural addictions involve dysfunction in several brain regions, particularly the frontal cortex and striatum. Findings from imaging studies incorporating cognitive tasks have arguably been more consistent than cue-induction studies. Early results suggest white and grey matter differences. Neurochemical findings suggest roles for dopaminergic and serotonergic systems, but results from clinical trials seem more equivocal. While limited, family history and genetic data support heritability for pathological gambling and that people with behavioural addictions are more likely to have a close family member with some form of psychopathology. Parallels exist between neurobiological and genetic and family history findings in substance and nonsubstance addictions, suggesting that compulsive engagement in these behaviours may constitute addictions. To date, findings are limited, particularly for shopping, kleptomania, and sexual behaviour. Genetic understandings are at an early stage. Future research directions are offered.
Classes of behaviours having hedonic qualities (at least initially), including gambling, shopping, sexual behaviours, internet use, and video game play may lead to compulsive engagement among a minority of people. At excessive levels, these behaviours are considered “impulse control disorders not elsewhere classified” in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. However, they may also be considered nonsubstance or behavioural addictions. As gambling, shopping, sex, gaming, and Internet use are normative behaviours, it may be challenging to differentiate between normal and excessive participation. Further challenges may stem from greater heterogeneity in the syndromes of behavioural addictions, complicating their categorization. Mechanisms underlying behavioural (compared with substance) addictions are relatively poorly understood, in part because animal models that have facilitated insight into SUDs are less straightforward or advanced for behavioural addictions.

Behavioural addictions share important elements with substance addictions. These include impaired control over engagement, continued engagement despite negative consequences, and urges or cravings. Behavioural and substance addictions frequently co-occur, and there are similarities in the progression of the disorders (for example, high rates of the conditions in adolescents and young adults, negative reinforcement motivations, and a telescoping phenomenon observed in females). Behavioral addictions have a broader range of possible targets of addictions, including the dopaminergic system, which is involved in the mesolimbic and mesocortical DA pathways. DA levels that are either too high or too low are suboptimal and may lead to impulsive and risk-taking acts, including excessive substance use. Natural rewards and abused substances appear to induce cross-sensitization, brain function, and neurochemistry. Cross-sensitization involves neuroadaptations in which repeated exposure to one drug leads to a more robust response to another. Regarding nonsubstance addictions, exposure to a substance of abuse can lead to sensitization to a natural reward and vice versa. The extent to which these findings extend to behaviours such as gambling warrants additional investigation. All drugs of abuse affect the brain’s reward circuit, with the mesolimbic DA pathway being of particular importance. This pathway includes dopaminergic neurons extending from the ventral tegmental area to the NAc. DA levels that are either too high or too low are suboptimal and may lead to impulsive and risk-taking acts, including excessive substance use. Natural rewards and abused substances appear to induce similar activity in reward circuitry and connected regions, including the amygdala, hippocampus, and frontal cortex.

Genetic and family history findings, albeit limited, suggest heritability in multiple brain areas and neurotransmitter systems. Behavioural addictions are characterized by dysfunction involving cross-sensitization, brain function, and neurochemistry. Cross-sensitization involves neuroadaptations in which repeated exposure to one drug leads to a more robust response to another. Regarding nonsubstance addictions, exposure to a substance of abuse can lead to sensitization to a natural reward and vice versa. The extent to which these findings extend to behaviours such as gambling warrants additional investigation. All drugs of abuse affect the brain’s reward circuit, with the mesolimbic DA pathway being of particular importance. This pathway includes dopaminergic neurons extending from the ventral tegmental area to the NAc. DA levels that are either too high or too low are suboptimal and may lead to impulsive and risk-taking acts, including excessive substance use. Natural rewards and abused substances appear to induce similar activity in reward circuitry and connected regions, including the amygdala, hippocampus, and frontal cortex.

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Table 1 Overview of brain function and neuroimaging results for 6 types of behavioural addiction, along with similarities to, and differences from, key results in SUDs, with a focus on frontostriatal findings

<table>
<thead>
<tr>
<th>Key results</th>
<th>Comparisons with key results in SUDs</th>
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<tbody>
<tr>
<td><strong>Frontal areas and striatum</strong></td>
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<tr>
<td>Gambling</td>
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<tr>
<td>- <strong>D2-like DA receptor PET Studies:</strong> Do not support between-group differences from control subjects in striatal binding</td>
<td>- Between-group differences observed in substance-dependent and control subjects in striatal binding</td>
</tr>
<tr>
<td>- <strong>Cue-induction:</strong> Difference from control subjects in frontal cortical areas and striatum but precise nature of differences seemingly inconsistent</td>
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</tr>
<tr>
<td>- <strong>Cognitive tasks:</strong> Reduced frontal activity in most studies; typically reduced ventral striatal activity in PG groups; stronger ventral striatal activity in less severe groups, compared with control subjects</td>
<td>- Most findings suggest reduced activity in frontal areas, similar findings of reduced ventral striatal activity, compared with control subjects, but also findings suggest increased activity and negative findings</td>
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<tr>
<td>White matter</td>
<td></td>
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<tr>
<td>Poor integrity in multiple regions, including corpus callosum</td>
<td>Poor white matter integrity in multiple regions, including corpus callosum</td>
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<tr>
<td>Internet use</td>
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<tr>
<td>Frontal areas and striatum</td>
<td></td>
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<tr>
<td>- <strong>D2-like DA receptor PET studies:</strong> reduced D2-like receptor availability in dorsal striatum, no differences in ventral striatum</td>
<td>- Between-group differences observed in substance-dependent and control subjects in striatal binding, particularly in dorsal striatum</td>
</tr>
<tr>
<td>- <strong>Resting state:</strong> Increased regional homogeneity in multiple regions including frontal areas and ACC</td>
<td>- No findings using the same regional homogeneity method were located</td>
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<tr>
<td>White and grey matter</td>
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<tr>
<td>Poor white matter integrity and decreased grey matter volumes in multiple regions.</td>
<td>Poor white matter integrity and decreased grey matter volumes in SUDs</td>
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<tr>
<td>Video game playing</td>
<td></td>
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<td>Frontal areas and striatum</td>
<td></td>
</tr>
<tr>
<td>- <strong>Resting state:</strong> Increased metabolism in middle orbitofrontal gyrus, reduced metabolism in left precentral gyrus, increased metabolism in left caudate</td>
<td>- Reduced activity at resting state typically found in frontal areas, but some exceptions; reduced ventral striatal activity and increased dorsal activity typically found</td>
</tr>
<tr>
<td>- <strong>Cue induction:</strong> Increased activity, compared with control subjects, in multiple frontal areas, including OFC, dIPFC; increased activity in NAc and right caudate, compared with control subjects</td>
<td>- Differences from control subjects in frontal areas and ventral striatum but precise nature of differences inconsistent; evidence of increased dorsal activity, compared with control subjects</td>
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<tr>
<td>Other regions</td>
<td></td>
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<tr>
<td>Increased activity in ACC in response to cues, decreased activation in loss trials of risk and reward task; increased activity in insula</td>
<td>Increased activity in ACC in response to cues, also implicated in risky decision making in SUD; increased activity in insula</td>
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<tr>
<td>Grey matter</td>
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<tr>
<td>Increased volume in left thalamus; decreased volume in multiple regions; for example, inferior temporal gyri</td>
<td>Decreased grey matter volume in SUDs in multiple regions; for example, OFC and cerebellum</td>
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<tr>
<td>Shopping</td>
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<td>Striatum</td>
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<tr>
<td>Increased activity in ventral striatum upon product presentation</td>
<td>Dysfunction in ventral striatum but precise nature of dysfunction differs per task</td>
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<tr>
<td>Other regions</td>
<td></td>
</tr>
<tr>
<td>Reduced activity in insula and ACC during price presentation, ACC activated during decision phase</td>
<td>Insula activated in response to substance cues; proposed role for ACC activity in risky decision making in SUDs</td>
</tr>
<tr>
<td>Kleptomania</td>
<td></td>
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<tr>
<td>White matter</td>
<td></td>
</tr>
<tr>
<td>Poor integrity in ventral-medial-frontal regions</td>
<td>Poor white matter integrity in SUDs</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
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<tr>
<td>White matter</td>
<td></td>
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<tr>
<td>Higher integrity in lower superior frontal region</td>
<td>Poor white matter integrity in SUDs</td>
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Table 2 Overview of neurotransmitter system involvement in 6 types of behavioural addiction, along with similarities to, and differences from, key results in SUDs

<table>
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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Gambling</strong></td>
<td></td>
</tr>
<tr>
<td>Dopamine</td>
<td>Data suggest reduced numbers of D2-like receptors in SUDs, compared with control subjects; substance use has been related to release in some studies but also individual differences; some clinical trial findings with antagonists positive, while others negative, with limited clinical utility demonstrated</td>
</tr>
<tr>
<td>Serotonin</td>
<td>Neurochemical studies suggest differential function; some clinical trial results with SRIs have been positive, while others negative, suggesting possible individual differences in activity</td>
</tr>
<tr>
<td>Opioids</td>
<td>Multiple positive clinical findings suggest role for opioidergic systems, particularly for opiates and alcohol</td>
</tr>
<tr>
<td>Glutamate</td>
<td>Preliminary positive clinical findings suggest it may have a role, particularly in impulsive and compulsive behaviours</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>Elevated during use of some substances, particularly cocaine</td>
</tr>
<tr>
<td>Internet use</td>
<td></td>
</tr>
<tr>
<td>Dopamine</td>
<td>Low levels of DA transporter expression in striatum in some studies though higher levels in other studies</td>
</tr>
<tr>
<td>Video game playing</td>
<td>Evidence suggests differences in dopaminergic activity between substance-dependent subjects and control subjects</td>
</tr>
<tr>
<td>Shopping</td>
<td>Clinical results with SRIs have been positive in some studies and negative in others</td>
</tr>
<tr>
<td>Kleptomania</td>
<td>Neurochemical studies suggest differences from control subjects in serotonergic function; clinical results inconclusive and suggest possible individual differences</td>
</tr>
<tr>
<td>Sex</td>
<td>Clinical results with SRIs have been positive in some studies and negative in others</td>
</tr>
</tbody>
</table>

**Notes:**
- DA = dopamine
- PG = pathological gambling
- SRIs = serotonin receptor antagonists
- SUDs = substance use disorders
suggestions for future research. Epidemiologic and clinical findings are addressed briefly; however, several recent reviews and an edited volume have addressed these topics. We excluded studies involving only participants who were healthy or had Parkinson disease. While Parkinson disease studies provide a useful model for behavioural addictions, the extent to which these findings apply to the larger population of patients without Parkinson disease is uncertain (see Leeman and Potenza and Leeman et al).

Methods

Literature searches were conducted in May 2012 using MEDLINE and Google Scholar. Each search was conducted using a general search term (neuro*, MRI, PET, imaging, and genet*) and a search term for one of the following behavioural addictions (search terms in parentheses): gambling (gambi*), shopping (compulsive shopping, shopping addict*, compulsive buying), kleptomania (kleptomania, steal), sexual behaviour (compulsive sex*, sex addict*), internet (Internet addict*, compulsive Internet) and video game play (video gam*). Given space limitations and the multiple topics reviewed, data deemed most relevant are covered.

Pathological Gambling

Neurobiological responses to cue-induction and behavioural tasks assessing cognitive control, simulated gambling, impulse control, risk and (or) reward decision making, and reward processing have been reported in PG. Findings demonstrating similarities and differences between PG and substance addictions have recently been reviewed. Most neuroimaging studies have implicated PFC areas and the striatum. Tasks related to cognitive control, reward processing, gambling (gambl*), shopping (compulsive shopping, shopping addict*, compulsive buying), kleptomania (kleptomania, steal), sexual behaviour (compulsive sex*, sex addict*), internet (Internet addict*, compulsive Internet) and video game play (video gam*). Given space limitations and the multiple topics reviewed, data deemed most relevant are covered.

Brain Function in PG

Most neuroimaging studies have implicated PFC areas and the striatum, as well as other regions. Generally, findings regarding brain function underlying cognitive tasks have been more consistent than cue-induction findings. 

Cue-induction studies suggest dysfunction in frontal areas, although the precise nature of the dysfunction is unclear. In cue-exposure tasks, PG (compared with control) participants have shown reduced activation in vIPFC and vmPFC, although other cue-presentation studies in problem gamblers and PG have shown increased frontal activations. Apparent differences in findings across studies may relate to task design and analytic approaches. Studies with imaging conducted during cognitive tasks have more consistently shown decreased activity in frontal areas, such as the vmPFC in PG, although increased frontal activation in problem gambling and PG has also been reported.

Multiple studies implicate the striatum in PG. Decreased ventral striatal glucose metabolism and increased metabolism in the dorsal striatum at resting state have been found among PG patients with comorbid bipolar disorder. However, in PET studies at resting state, no significant differences have been found between PG and healthy control subjects in D2-like receptor or 5-HT 1B receptor availability in the ventral and dorsal striata, although in the latter case, receptor availability correlated with problem gambling severity in ventral striatum and (or) pallidum. In fMRI studies during gambling-cue exposure, decreased activation has been observed in the ventral and dorsal striatum in subjects with PG (compared with control subjects); however, there have also been negative results in the ventral striatum in PG and (or) mixed problem gambling and PG groups who may have different biological responses. Findings from Linnet et al suggest individual differences, with the PG sample divided about evenly between subjects who showed and did not show elevated DA release in the ventral striatum during the Iowa Gambling Task. Limited findings with tasks related to impulsivity (for instance, stop signal tasks) have not shown significant differences in striatal activation between subjects with PG and control subjects.

Regarding other brain regions, subjects with PG (compared with control subjects) differ in ACC activity following gambling-cue exposure. Relatively diminished activity in the insula in PG during cue presentation and reward processing has been reported. Relatively poor white matter integrity has been related to impulsivity and has been found among people with PG, compared with control subjects, in areas including the corpus collosum. Negative results have been found for white and grey matter volume differences between subjects with PG and control subjects.

In summary, most imaging findings in people with PG have implicated PFC areas and the striatum. Tasks related to risk and reward, gambling, and cognitive control typically show reduced activity in people with PG in frontal areas and ventral striatum more consistently. Early results suggest reduced insula activity and poor white matter integrity in people with PG.

Neurotransmitter Activity in PG

Most findings relate to DA and 5-HT, although other neurotransmitters have been implicated. While DA dysfunction has been hypothesized for people with PG, findings have been less conclusive. Data suggest...
Table 3 Overview of genetic results for 6 types of behavioural addiction, along with similarities to, and differences from, key results in SUDs

<table>
<thead>
<tr>
<th>Key results</th>
<th>Comparisons with key results in SUDs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gambling</strong></td>
<td>SUDs highly heritable, equivalent heritability between males and females</td>
</tr>
<tr>
<td>Behaviour genetics</td>
<td>PG highly heritable, equivalent heritability between males and females</td>
</tr>
<tr>
<td>Molecular</td>
<td>Small, additive effects across genes; associations with polymorphisms of DA receptor genes, but also negative findings; also preliminary findings associating 5-HTT and MAOA polymorphisms; no GWASs to date for PG or other behavioural addictions</td>
</tr>
<tr>
<td>Internet use</td>
<td>Findings associating 5-HTT to SUDs</td>
</tr>
<tr>
<td>Molecular</td>
<td>Harm-avoidant subgroup showed over-expression of SS-5-HTTLPR in preliminary studies</td>
</tr>
<tr>
<td>Video game playing</td>
<td>Some findings linking SUDs to Taq1A polymorphism but negative findings as well; COMT has been linked to nicotine dependence and the low activity variant has been associated with early onset alcoholism</td>
</tr>
<tr>
<td>Molecular</td>
<td>Taq1A polymorphism of DRD2 receptor gene and low-activity COMT alleles more prevalent in compulsive video game players in preliminary studies</td>
</tr>
<tr>
<td>Shopping</td>
<td>People with SUDs likely to have close family members with various psychopathology</td>
</tr>
<tr>
<td>Behaviour genetics</td>
<td>Compulsive shoppers likely to have close family members with various psychopathology</td>
</tr>
<tr>
<td>Molecular</td>
<td>No evidence of abnormality in two 5-HTT polymorphisms that were investigated</td>
</tr>
<tr>
<td>Kleptomania</td>
<td>People with SUDs likely to have close family members with various psychopathology</td>
</tr>
<tr>
<td>Behaviour genetics</td>
<td>Kleptomaniacs likely to have close family members with various psychopathology</td>
</tr>
<tr>
<td>Sex</td>
<td>People with SUDs more likely to have first-degree relatives with SUDs</td>
</tr>
<tr>
<td>Behaviour genetics</td>
<td>Relation to parental history of sexual compulsion, more likely to have first-degree relatives with SUDs</td>
</tr>
<tr>
<td><strong>COMT</strong> = catechol-O-methyltransferase; <strong>GWAS</strong> = genome-wide association study; <strong>MAOA</strong> = monoamine oxidase A; <strong>SS</strong> = short form</td>
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</table>

individual differences in PG and control groups in DA release during the Iowa Gambling Task but no baseline between-group differences regarding D2-like receptor availability. Although PG and control groups showed similar DA release during slot machine task performance, DA release correlated with problem gambling severity in PG.56 Amphetamine administration increased motivations to gamble among problem gamblers.57 The D2-like antagonist haloperidol has also been associated with increased gambling motivations in PG,58 although individual differences appear important.59 Individual differences may explain negative clinical trial findings with D2-like antagonist drugs.60,61

Findings from neurochemical studies with varied methods suggest differences in serotonergic function between subjects with PG and control subjects.18,62-67 Clinical trial findings involving SRIs and a 5-HT2 receptor antagonist have been negative or mixed though.60,61,68-72 While neurochemical studies indicate serotonergic dysfunction in people with PG, mixed clinical findings suggest important individual differences.

Regarding other neurotransmitters, multiple positive clinical trial findings with opiate antagonists73-76 (see Toneatto et al77 for negative results) suggest opioidergic involvement in people with PG. Preliminary evidence of efficacy for medications that alter glutamate neurotransmission78,79 suggest that glutamate may contribute to impulsive and compulsive behaviours and treatment outcome in people with PG.79 Elevated levels of adrenergic agents and their metabolites have been observed in people with PG.80,81 Norepinephrine levels increase in problem gamblers during
Family History and Genetics in PG
Twin studies suggest that genetic factors may contribute more than environmental factors to gambling problems. PG heritability estimates range from 50% to 60%, with increasing genetic contributions seen with greater problem gambling severity. Molecular studies find small, additive effects across multiple genes. Associations between PG and genetic variants related to DA transmission (for example, DRD2) have been found (but see Lim et al for negative results). A variant in the 5-HTTLPR has been associated with PG in males and monoamine oxidase A among males with severe PG. These studies have multiple limitations related to sample size, sample characterization, and analytic approaches, and these factors may relate to inconsistencies in replication.

Compulsive Internet Use

Brain Function in Compulsive Internet Use
In a resting-state fMRI study, increased regional homogeneity was found among compulsive Internet users in frontal areas (for example, superior frontal gyrus) and other regions (for example, parahippocampus). Increased regional homogeneity may reflect greater synchronization among these regions. Given that many of the implicated regions are components of the reward circuit, these findings intimate enhanced sensitivity to reward among compulsive Internet users.

In a small, resting-state fMRI and PET study, reduced D2-like receptor availability was found in the dorsal striatum, with negative correlations between binding potential in this region and self-reported Internet addiction measures. No evidence of dysfunction in the ventral striatum was found.

Regarding other brain regions, the ACC was implicated in the aforementioned study of increased resting-state regional homogeneity among compulsive Internet users. Poor white matter integrity and grey matter density and volume differences have been seen in compulsive Internet users (compared with control subjects). Using DTI, lower FA in OFC, corpus callosum, and cingulum was seen in compulsive Internet users (compared with control subjects). Using MRI, lower grey matter density was found in regions tied to emotion regulation, including the ACC, posterior cingulate, insula, and lingual gyrus. In a separate study, reduced FA values were found in the parahippocampal gyrus, and decreased volume observed in the cerebellum, OFC, dIPFC and ACC. Regional grey matter volumes correlated inversely with duration of Internet addiction. These findings intimate that compulsive Internet use may induce grey matter reductions or that people with low grey matter volumes may be predisposed to Internet addiction.

In summary, early findings suggest regional homogeneity in frontal areas, reduced D2-like receptor availability in the dorsal striatum, poor white matter integrity, and grey matter density and volume differences affecting regions implicated in reward and emotion processing.

Neurotransmitter Activity in Compulsive Internet Use
In a small single photon emission computed tomography (commonly referred to as SPECT) study, the DA transporter appeared to be expressed at lower levels in the striatum among young adult males with compulsive Internet use, compared with control subjects. Regarding clinical trial results, there have been no controlled pharmacotherapy studies.

Family History and Genetics in Internet Use
Harm-avoidant, problem Internet users more frequently carried the short allele of a variant in the promoter region of the gene coding for the 5-HTTLPR, an allele also common among depressed patients.

Compulsive Video Gaming
We have separated findings concerning video gaming from those pertaining to Internet use. However, neurobiological research on compulsive video gaming typically involves web-based games; thus video game findings cannot be separated clearly from Internet findings.

Brain Function in Compulsive Video Gaming
Using resting-state PET, increased metabolism was found in the middle orbitofrontal gyrus, which may reflect compensatory cognitive processing. Reduced metabolism was found in the precentral gyrus, which may reflect insensitivity to negative consequences. In cue-exposure studies, greater pre- and postcue changes indicative of increased activity were observed in compulsive Internet users (compared with control subjects) in the OFC, medial frontal cortex, and dIPFC. In a subsequent study, greater pre- and postcue changes were observed in the dIPFC among current compulsive players, compared with control subjects. Pre- and posttreatment fMRI during cue induction was incorporated into an open-label bupropion trial. Similar to other studies, stronger activity was found in the dIPFC (compared with control subjects), with dIPFC activity declining after the 6-week treatment period. In an fMRI study tied to a computer-based guessing task involving monetary wins and losses, greater activation in the OFC was found on win trials among compulsive Internet users, attributed to higher reward sensitivity.
Regarding striatal activity, increased metabolism was found in the left caudate. Greater activity postcue induction was found in the right NAc and right caudate in compulsive game-players, compared with control subjects, during fMRI.

The ACC and insula have also been implicated in compulsive video gaming. In a cue-induction fMRI study, greater activity postcue was found in the ACC among compulsive gamers. During a reward processing guessing task, decreased ACC activation was found during loss trials in compulsive video gamers (compared with control subjects), suggesting hyposensitivity to loss. Increased activity in the insula was found at rest. Compulsive game-players demonstrated increased volume in the thalamus but decreased volume in the inferior temporal, right middle, and left inferior occipital gyri.

In summary, findings in samples of predominantly young male compulsive game-players suggest increased activity at rest, to cues and during reward processing in frontal areas, the striatum and other regions, and reduced sensitivity to loss outcomes. Findings of increased activity seem to run counter to multiple PG study findings. Areas implicated in compulsive video gaming appear to contribute to reward processing, impulse control, and memory.

**Neurotransmitter Activity in Compulsive Video Gaming**

A role for dopaminergic dysfunction has been proposed. Genetic findings reported below are consistent with dopaminergic contributions to compulsive video game playing.

**Family History and Genetics in Compulsive Video Gaming**

Limited molecular genetic research has been performed. Allelic variants of the DRD2 Taq1A1 allele that have been associated with altered DA signalling have been suggested to contribute to compulsive video gaming. Amongst male gamers, the Taq1A1 allele was related to higher self-reported reward dependence. Variants of the gene encoding catechol-O-methyltransferase that have been implicated in DA transmission and addictions have also been reported to be more prevalent among compulsive gamers.

**Compulsive Shopping**

**Brain Function in Compulsive Shopping**

In a recent study, compulsive shoppers and healthy control subjects were compared on a multi-phase purchasing task during fMRI. During an initial product presentation phase, compulsive shoppers showed stronger activity in the NAc than the control subjects. During a subsequent price presentation phase, compulsive shoppers showed less activation of the insula and ACC than the control subjects, the latter of which was activated more strongly by compulsive buyers during the concluding decision phase.

**Neurotransmitter Activity in Compulsive Shopping**

Favourable results were seen with citalopram in a small open-label trial. A subsequent small trial, beginning with an open-label period followed by double-blind, placebo-controlled administration among responders, yielded additional positive results for citalopram. These findings provided tentative support for possible serotonergic dysfunction in compulsive shopping. However, negative results with other SRIs (for example, fluvoxamine, escitalopram) raise questions about the clinical utility of SRIs for compulsive shopping.

**Family History and Genetics in Compulsive Shopping**

Limited data suggest that compulsive shoppers are more likely to have close family members with psychopathology. No differences were seen in the frequencies of two 5-HTT gene polymorphisms in people with and without compulsive shopping.

**Kleptomania**

**Brain Function in Kleptomania**

Relatively poor white matter integrity in ventromedial PFC regions was seen in kleptomania.

**Neurotransmitter Activity in Kleptomania**

Findings regarding serotonergic dysfunction have been inconsistent. Lower numbers of platelet-derived 5-HTTs have been reported in kleptomania, suggesting serotonergic dysfunction; however, negative findings from a small double-blind, placebo-controlled clinical trial involving open-label responders were reported for escitalopram. Positive results in a small double-blind trial of naltrexone suggest possible opioidergic involvement.

**Family History and Genetics in Kleptomania**

Similar to compulsive shopping, limited findings indicate familial links to various psychopathologies.

**Compulsive Sexual Behaviour**

**Brain Function in CSB**

Studies of sexual compulsivity have been limited. In a DTI study, people with sexual compulsivity had relatively low superior frontal region mean diffusivity, compared with control subjects. These findings did not follow patterns of results from studies of other behavioural addictions.
Neurotransmitter Activity in CSB

Positive results for citalopram in a double-blind placebo controlled study of CSB in homosexual and bisexual men suggest possible serotonergic dysfunction.139

Family History and Genetics in CSB

Limited findings suggest a high proportion of people with CSB had a parent with a similar condition.131 Findings indicate tendencies for sexually compulsive people to have first-degree relatives with SUDs.131

Similarities and Differences With SUD Findings

Neurobiological findings in the behavioural addictions remain scant, and data are particularly sparse for compulsive shopping, kleptomania, and CSBs. However, available data provide evidence of underlying neurobiological impairment overall, which parallels SUD findings. Tables 1, 2, and 3 contain information comparing behavioural addictions with SUDs.

Findings of poorer white matter integrity have perhaps been the most complementary between SUDs122,133 and behavioural addictions53,54,99,101,122 (but see Miner et al129 for seemingly conflicting results). Cognitive task results in SUDs50,51,134,135 and PG40,50,51,136 have suggested reduced activity in frontal areas. Findings involving aspects of risk and reward decision-making (including reward processing), but arguably less so from response-impulsivity tasks, have tended to show reduced ventral–striatal activity in PG138,48 and SUDs137–140 although there have been seemingly opposing results.41,141,142 Findings have tended to show increased activity in the dorsal striatum in behavioural addictions43,48 and SUDs.143,144

Evidence regarding neurotransmitter activity in behavioural addictions and SUDs has tended to be complementary. Neurochemical evidence has suggested reduced DA transporter and D2-like receptor availability at rest98,102,145,146 and DA release during activity related to addictive behaviour,147,148 although there have been seemingly conflicting results at resting state in PG44,45 and SUDs.149 and individual differences seem relevant to DA release.44,45,150 Neurochemical findings suggest differential serotonergic function, compared with control subjects, among people with behavioural addictions62–66,124 and SUDs.151–153 Clinical results with DA antagonists60,61,154–156 and medications targeting 5-HT systems (primarily SRIs68–72,157–159) have demonstrated negative or mixed findings in people with behavioural addictions and SUDs. Clinical results involving opioid antagonists have tended to be positive for both types of conditions.80,45,73–76,126,160–162 Limited results with pharmacologic probes suggest a role for glutamatergic activity in people with PG78,79 and SUDs.163,164 Neurochemical and clinical findings suggest a possible role for noradrenergic activity in people with PG80–83 and SUDs.165–167 Genetic (especially molecular) and family history evidence is limited for behavioural addictions. However, available evidence suggests substantial heritability for PG.15,84 For other behavioural addictions, there is evidence suggesting familial risk across psychiatric conditions.91,110,119,120,127,28,131 SUDs appear highly heritable as well.27,168 Evidence from cue-induction and resting-state imaging studies have been less clear and seemingly more conflicting. Resting-state and cue-induction findings in compulsive video gaming have suggested increased activity across multiple brain regions.166–168 There have been seemingly conflicting results in problem gambling–PG and SUD cue-induction studies for both ventral striatal (gambling23, SUD7,143,144,170) and frontal activity.171,172 Differences across studies in participant characteristics and other methodological details may contribute to these differing results.171,172 In addition, declines in DA release in response to drug consumption as dependence worsens173 may also lead to heterogeneity in ventral–striatal activity across participants in SUD studies.

In summary, data suggest neurobiological dysfunction in behavioural addictions and SUDs. Some of the more complementary results have involved white matter integrity, brain function during cognitive task performance, neurotransmitter activity, and overall heritability.

Conclusions and Future Research

Research on the neurobiology and genetics of behavioural addictions has accelerated in recent years, particularly in PG, compulsive Internet use, and compulsive video gaming. Gaps in knowledge remain, and research on other behavioural addictions has been limited. Existing research suggests parallels between behavioural addictions and SUDs. Additional genetic research, particularly molecular, would be valuable in delineating similarities and differences among individual behavioural addictions and between behavioural addictions and SUDs. Neuroimaging has begun to provide insight regarding similarities and differences. Additional research is needed, incorporating a broader variety of cognitive tasks.174 While conventional approaches have been valuable, alternative analytic methods, such as computational modelling,175 may further illustrate parallels with SUDs.

Research testing medications and therapies indicated for SUDs has only begun. Studies involving individuals with co-occurring behavioural and substance addictions could enhance our understanding of addiction and advance treatment development. Females are often excluded from or underrepresented in behavioural addiction studies, particularly in existing genetic studies and research on
compulsive video gaming. Future studies should include females and examine the extent to which various phenomena pertaining to behavioural addictions apply to both sexes.

Given that behavioural addictions, particularly those relating to gambling, Internet use, and video gaming, appear relevant to adolescents and young adults, longitudinal studies would be valuable. Epidemiologic data are limited for behavioural addictions, with the possible exception of PG. National and international studies assessing prevalence of multiple behavioural addictions would enhance our knowledge regarding the extent to which these conditions affect people across the lifespan. Uniformly agreed-on diagnostic criteria and assessment instruments would facilitate comparisons across studies.

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