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REVIEW ARTICLE

# Comparison of frontostriatal circuits in adolescent nicotine addiction and internet gaming disorder

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**ABSTRACT**

*Background:* Recently, there has been significantly increased participation in online gaming and other addictive behaviors particularly in adolescents. Tendencies to avoid social interaction and become more involved in technology-based activities pose the danger of creating unhealthy addictions. Thus, the presence of relatively immature cognitive control and high risk-taking properties makes adolescence a period of major changes leading to an increased rate of emotional disorders and addiction. *Aims:* The critical roles of frontostriatal circuits in addiction have become the primary focus associated with reward in the striatum and cognitive control in the PFC. Internet gaming disorder (IGD) and nicotine addiction are currently becoming more and more serious. *Methods:* In the light of neuroimaging, the similarity between brain mechanisms causing substance use disorder (SUD) and IGD have been described in previous literature. *Results:* In particular, two distinct brain systems affect the way we act accounting for uncharacteristic neural function in addiction: the affective system comprises of the striatum driven by emotional, reward-related, and internal stimuli, and a cognitive system consisting of the prefrontal cortex (PFC) supporting the ventral affective system's actions via inhibitory control. *Discussion and Conclusion:* Therefore, as a novel concept, we focused on the implication of frontostriatal circuits in nicotine addiction and IGD by reviewing the main findings from our studies compared to those of others. We hope that all of these neuroimaging findings can lead to effective intervention and treatment for addiction especially during this critical period.

**KEYWORDS**

nicotine addiction, internet gaming disorder, frontal cortex, striatum, reward, cognitive control

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## INTRODUCTION

Neurobiology research shows addiction is a disorder that has gradually emerged with a predominant onset in adolescence, which is a time when the still-developing brain is particularly sensitive to the effects of drugs, a factor that contributes to adolescents' greater vulnerability to drug experimentation and addiction (Volkow, Koob, & McLellan, 2016). In particular, we focus on two distinct addictions, nicotine addiction and internet gaming

disorder (IGD), which are defined as the intake of nicotine leading to abnormal patterns of brain activity and inhibition control deficits (Dong et al., 2021) and using Internet games that must result in clinically significant impairment, rather than engaging in sexual Internet sites, online gambling, or any other kind of Internet use (APA, 2013), respectively. According to most recent surveys of nicotine addiction in youth via the Chinese Center for Disease Control and Prevention as of May 2014, junior high school students consisted of 10.6% of Chinese males (Yuan, Yu et al., 2016). In 2020 in the USA, nearly 7 out of 100 middle school students (6.7%) and about 23 out of 100 high school students (23.6%) used tobacco products (Gentzke et al., 2020). IGD has also become a universal mental health disorder with the incidence rate of about 14.1% among Chinese urban adolescents (Yuan, Yu, Cai et al., 2017). In the USA, it was reported that there was a 75% increase in online gaming (Pantling, 2020). In Italy, a 70% rise in Fortnite-gaming-related Internet traffic was reported (Lepido & Rolander, 2020). Steam, a top gaming distributor, stated they had over 20 million active users, the most in its entire existence, while YouTube Gaming and Twitch showed a 10% increase in viewers (Stephen, 2020). According to the ABCD study (www.abcdstudy.org), it can be used to predict the risk and onset of nicotine addiction and IGD.

Common characteristics between brain mechanisms triggering substance use disorder (SUD) and IGD have also been described in previous literature (Kuss et al., 2018; Weinstein & Lejoyeux, 2015, 2020; Weinstein, Livny, & Weizman, 2017; K. Young, 2010; K. S. Young, 1998; Yuan, Qin, Liu, & Tian, 2011). Primarily, two distinct brain systems affect the way we act accounting for uncharacteristic neural function in addiction: the affective system comprises of the striatum driven by emotional, reward-related, and internal stimuli, and a cognitive system consisting of the prefrontal cortex (PFC) supporting the ventral affective system's actions via inhibitory control. The SUD studies showed how frontostriatal circuits were associated with reward in the striatum, cognitive control in the PFC (Volkow, Wang, Fowler, Tomasi, & Telang, 2011; Volkow, Wang, Tomasi, & Baler, 2013; Tomasi & Volkow, 2013), and craving changes in the left dorsolateral prefrontal cortex (DLPFC)-bilateral thalamus (Liu et al., 2021; Zhang et al., 2021). The critical roles of frontostriatal circuits in adolescent addiction have become the primary focus associated with reward in the striatum and cognitive control in the PFC so that early intervention can prevent the onset and development of chronic addiction. Therefore, we focused on the implication of frontostriatal circuits in nicotine addiction and IGD (Fig. 1), and their importance in future treatment as in SUD. It is important to see if the current progress in SUD can be usefully applied in these two addictions as well. The main content included: 1) Dopamine system dysfunction in nicotine addiction and IGD; 2) Structural abnormalities within frontostriatal circuits in nicotine addiction and IGD; 3) Resting state functional abnormalities within frontostriatal circuits in nicotine addiction and IGD; 4) Diffusion tensor imaging (DTI) results; and 5) Activation/functional connectivity during cue tasks.

## NICOTINE ADDICTION AND INTERNET GAMING DISORDER

### Dopamine system dysfunction in nicotine addiction and IGD

Stimulating the dopamine (DA) system is a widespread method for the reinforcement and reward characteristics of drugs (Di Chiara & Imperato, 1988; Koob & Le Moal, 2005). The effects of nicotine, one of the most widely used drugs on the DA system, have been reported in substantial studies (Brody, Mandelkern, London et al., 2006; Livingstone & Wonnacott, 2009; Marshall, Redfern, & Wonnacott, 1997; Singer et al., 2004; Wonnacott, Sidhpura, & Balfour, 2005).

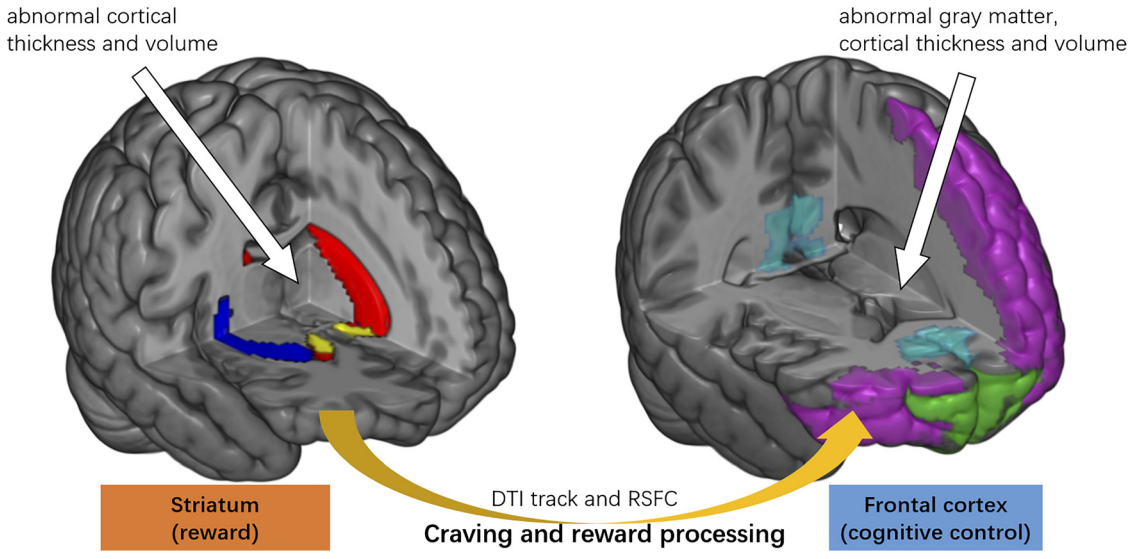


*Fig. 1.* The frontostriatal circuits in nicotine addiction and internet gaming disorder

Clinical evidence validated that IGD patients had symptoms as those with SUD (Petry & O'Brien, 2013; K. Young, 2010). The similarities between the brain mechanisms of SUD and IGD were depicted in other literature (Kuss et al., 2018; Meng, Deng, Wang, Guo, & Li, 2015; Weinstein & Lejoyeux, 2015, 2020; Weinstein, Livny, & Weizman, 2017; Yuan, Qin, Liu, & Tian, 2011), which were related to the DA system (Volkow et al., 2011).

***Nicotine-induced and playing games-induced DA release in the striatum.*** Significantly higher dihydroxyphenylalanine (DOPA) uptake in the putamen and the caudate of nicotine addicts than in those of controls has been reported, suggesting that nicotine addiction is associated with increased DA activation in basal ganglia (Salokangas et al., 2000). In addition, there is a study reporting that nicotine addicts who smoked one cigarette during positron emission tomography (PET) scanning had a decrease in $^{[11C]}$raclopride binding potential in the left ventral caudate/nucleus accumbens (NAc) and left ventral putamen than those who experienced the same experimental process but did not smoke any cigarettes, thus supporting the findings that nicotine addiction caused DA release (Brody et al., 2004). Furthermore, a study reported that DA system genotype variability explained a significant proportion of the inter-individual variability in nicotine addiction-induced DA release and indicated that its release had a genetic predisposition (Brody, Mandelkern, Olmstead et al., 2006). The striatum can be divided into the dorsal and ventral striatum. The dorsal striatum receives input from motor, sensory, and premotor areas. The ventral striatum receives afferent input from the orbitofrontal cortex (OFC), amygdala, hippocampus, and anterior cingulate. Internet game playing can increase the levels of extracellular DA in the ventral striatum, which is induced by a behavioral task (Koepp et al., 1998). On the basis of these anatomical connections, the changes in the ventral striatum may be related to affective components of the task, whereas dorsal striatal DA release may be related to sensorimotor coordination and response selection. Hence, these areas can be important targets for therapeutic approaches.

***DA transporter findings.*** DA transporters take up free DA from the synaptic cleft and carry it to the axonal bouton. The removal rate of DA is one of the main mechanisms to maintain a constant dopaminergic milieu. The concentration of transporters in the region reflects that of the DA nervous system (Mulvihill, 2019). A previous study reported that there was less dopamine transporter (DAT) binding in the striatum, left posterior putamen, and right anterior putamen in nicotine addicts (Leroy et al., 2012). Another study investigated whether striatal DAT levels were altered in individuals with IGD (Hou et al., 2012). Single photon emission computed tomography (SPECT) scanning was done on 5 IGD males and 9 controls and the results displayed that DAT expression was decreased in the striatum, which shared anomalies with other addictions (Hou et al., 2012).

***DA D2/D3 receptor findings.*** Low dorsal striatal D2 receptor availability has been measured in patients dependent on alcohol, heroin, cocaine, and amphetamines during either consumption or early abstinence. To determine the relationship between nicotine dependence and the levels of dopaminergic receptor availability in the striatum, one study was done. Results showed decreased D2/D3 availability of receptors in the bilateral putamen in nicotine-addicted patients who were heavy smokers (Fehr et al., 2008). Attachment of 11C-labeled raclopride (RAC) to DA D2 receptors is responsive to DA levels. Microdialysis studies of non-human primates indicate that a 1% decrease in striatal RAC binding reflects at least an 8% increase in extracellular endogenous DA levels (Breier et al., 1997). The relationship between IGD and the levels of dopaminergic receptor availability in the striatum were further researched in one human study. Results showed IGD patients had decreased levels of DA D2 receptor access in the striatum, right putamen, and bilateral dorsal caudate (S. H. Kim et al., 2011). Thus, these areas should be utilized for localized treatment methods. To summarize this section, both nicotine addiction and IGD caused a release of DA in the striatum, but DA receptors were decreased in both.

## Structural abnormalities within frontostriatal circuits in nicotine addiction and IGD

Previous studies demonstrated that nicotine addiction was related to structural alterations in certain brain regions, including gray matter, cortical thickness, and subcortical volume, which may be incompletely responsible for different neural dysfunctions (Li et al., 2015; Yuan et al., 2017; Yuan, Yu, et al., 2018; Yuan, Zhao, et al., 2018; Zhang et al., 2011). This is similar in IGD.

***Gray-matter volume and density abnormalities in nicotine addicts and gamers.*** There is frequent literature reporting gray matter or density abnormalities in nicotine dependence. There was a decrease in gray matter in the PFC, bilateral OFC, anterior cingulate cortex (ACC), and right DLPFC, which was documented in nicotine addicts in most literature (Almeida et al., 2008; X. Zhang, Salmeron et al., 2011). Neuroimaging studies showed the OFC, ACC, and DLPFC regulate the limbic reward regions and executive functions (Goldstein & Volkow, 2011; Pistillo, Clementi, Zoli, & Gotti, 2015); decreased PFC volume/density is related to addiction and predisposes individuals to nicotine addiction. Voxel-based morphometry (VBM) is a time-saving technique compared to the traditional manual brain volume morphometric measurement approaches. VBM is an automated option to the methods used to detect the differences in gray matter (GM) between groups (Ashburner & Friston, 2000). One study analyzed gray matter density (GMD) alterations in teens with IGD via VBM analysis, which revealed a lower GMD in the left insula (INS), left ACC, left lingual gyrus, and left posterior cingulate cortex (PCC) (Zhou et al., 2011). GM volume changes in IGD were also detected by VBM. Compared with controls, IGD showed significantly decreased GM volume in the cerebellum, bilateral DLPFC, OFC, supplementary motor area (SMA), and left rostral ACC areas (Yuan et al., 2011). Another VBM

study showed increased left striatal GM volume contrasting recurrent versus non-recurrent players against 154 healthy 14-year-old adolescents (Kühn et al., 2011). In other youths with IGD, cortical thickness was increased in INS and right inferior temporal gyrus (ITG) and decreased in the superior temporal sulcus, right inferior parietal cortex (IPC), right precuneus, right posterior cingulate gyrus (PCG), and left middle temporal gyrus (MTG). A positive correlation was found between left INS cortical thickness and severity of symptoms (S. Wang et al., 2018). Such findings reinforce the similarities between nicotine addiction and IGD abnormalities in the brain, suggesting IGD has detrimental outcomes as an addiction.

***Cortical thickness and subcortical volume abnormalities in nicotine addiction and IGD.*** There are plenty of studies on the differences between cortical thickness and subcortical striatal volume in nicotine addicts versus controls (Das et al., 2012; Janes et al., 2015; Kühn et al., 2010; Li et al., 2015). Li et al. discovered that adult nicotine addicts exhibited notable thinning of the cortex, including the left ACC and right lateral OFC (Li et al., 2015). Considering that the PFC is associated with control of craving and inhibition, decreased cortical thickness may decrease factors that protect against nicotine intake, which makes it difficult for nicotine addicts to give up nicotine. It was also discovered that young adult nicotine addicts had a larger volume in the right caudate compared to non-addicts. The caudate encompasses nigrostriatal DA pathways, which are necessary for processing reward and craving in addiction. Therefore, increase in the volume of the caudate relates to reward and craving pathways, hence raising the amount of nicotine addiction risk factors (Das et al., 2012; Janes et al., 2015; Kühn et al., 2010; Li et al., 2015). Taken together, the striatal and frontal deficits in nicotine addicts reveal that the imbalance between cognitive control and reward drive behaviors is related to nicotine addiction and relapse. FreeSurfer was used to assess cortical thickness from MRI images. Local cortical thickness was calculated based on the differences between gray-white matter and pial vertices. A previous study revealed that increased cortical thickness was mainly located in the precuneus, left PCC, middle frontal cortex, middle temporal and inferior temporal cortices and diminished cortical thickness was in the INS, left lateral OFC, lingual gyrus, entorhinal cortex, IPC, and right postcentral gyrus in IGD (Yuan, Cheng et al., 2013). Subcortical volumetric segmentation can also be performed by FreeSurfer 5.0. Yuan, Wei et al. (2016) detected that the volume of the NAc and right caudate in IGD were significantly increased compared with controls. Meanwhile, NAc volumes had a positive correlation with test scores in IGD (Yuan, Yu, Cai et al., 2017). Furthermore, a study by Yuan, Wei et al. (2016) demonstrated increased volume in the NAc and right caudate including decreased resting-state functional connectivity (RSFC) strength of the OFC–NAc and DLPFC–caudate in IGD subjects. NAc volumes had a positive correlation with test scores in IGD. The DLPFC–caudate RSFC and caudate volume had a correlation with abnormal cognitive control (Stroop task) in IGD due to reduced frontostriatal RSFC strength (Yuan, Yu, Cai et al., 2017). In a recent study by Wang et al. (2019), there was a group × sex interaction in the MFG, left SFG, left SMG, right PCC, and right superior parietal lobe (SPL). For instance, IGD males had lower cortical thickness, while IGD females had higher cortical thickness in the right PCC. There was a negative correlation in the cortical thickness of women, craving, and IGD-related test scores, which showed how much IGD influenced the female brain in particular. Gender differences were predominantly associated with cognitive and reward functions (Z. Wang, Y. Hu et al., 2019). Hence, it is important to see if such gender differences are found in female nicotine addicts.

***Diffusion tensor imaging (DTI).*** DTI measures white matter (WM) microstructure by assessing how much water diffusion deviates from isotropic diffusion in WM with wider deviations from isotropic diffusion showing more consistent directionality of water diffusion along the axon, meaning higher WM integrity. A fractional anisotropy (FA) value is measured from a normalized standard deviation of the radial eigenvalue (λR) and axial eigenvalue (λ1). DTI allows WM region comparisons at the entire brain level. FA value increases or decreases reflect the quality of WM integrity (Yuan, Yu, Bi et al., 2017).

WM diffusion characteristics of the ventral and dorsal frontostriatal circuits relevant to nicotine addiction behavior is still unknown, particularly in young adults, thus probabilistic tractography and DTI were used to study them (Yuan, Yu et al., 2018). They showed nicotine addicts had lower FA and increased radial diffusivity in the left medial OFC and NAc tracts, but decreased FA in the right DLPFC and caudate tracts. FA values in the right dorsal fibers were negatively correlated with cognitive test results (Stroop task) in nicotine addicts whereas the left ventral fiber mean diffusivity values were positively correlated with craving in nicotine addicts (Yuan, Yu et al., 2018).

In another DTI study, nicotine addicts showed weaker tract strength in the left striatal-medial-orbitofrontal cortex (mOFC), striatal-ventral-lateral prefrontal cortex (vlPFC), PCC, and striatal-inferior-frontal gyrus (IFG). In abstained nicotine addicts, they had increased craving associated with left striatal-mOFC and striatal-vlPFC tract strength. The strength of the tract of the left DLPFC expected a relapse in nicotine addicts with a 68.3% accuracy. Hence, decreased strength of the frontostriatal tracts in nicotine-addicted males could act as potential markers for craving and relapse (Yuan, Zhao et al., 2018).

One study discovered that IGD patients had increased FA, meaning increased WM integrity, in the left PCC and thalamus (Dong, DeVito, Huang, & Du, 2012). In another study, the WM changes by tract-based spatial statistics (TBSS) revealed that IGD had decreased FA in brain regions such as the corpus callosum, orbito-frontal WM, cingulum, corona radiata, internal/external capsules, and inferior fronto-occipital fasciculus, which are involved in decision-making, emotions and their processing, cognitive control, and executive attention (Fuchun Lin et al., 2012). They also

researched the fiber integrity and cognitive control in adolescents with IGD by using DTI tractography methods. The study mainly looked at the salience network (SN) roles in regulating communication of neurocognitive networks. The results showed that the right SN tract had decreased FA in IGD adolescents. Right SN tract FA values had a negative correlation with errors from the incongruent condition in IGD teenagers (Xing et al., 2014). Another study examined the relationship between functional magnetic resonance imaging (fMRI) and the behavioral Internet Addiction Test (IAT) in IGD subjects. NAc and mOFC had decreased RSFC with the ventral tegmental area (VTA) in IGD. VTA-left mOFC and VTA-right NAc RSFC strength had a negative correlation with IAT in IGD individuals. IGD had decreased structural connectivity in VTA-NAc, but this connectivity was not correlated with IAT. This led the research team to believe that the VTA-mOFC and VTA-NAc pathways were important in the mechanism of IGD involving DA modulation as seen in other addictions (R. Wang, Li et al., 2019).

As neural WM connectivity depends on the incorporation of the neural WM network, Zhai et al. (2016) used neural network topology to evaluate the WM network integrity in IGD using 16 adolescents with IGD and 16 controls (Zhai et al., 2016). The parameters of the WM network were computed and correlated with scores from the IAT in IGD. IGD subjects had diminished local efficiency, global efficiency, and enhanced shortest path length. Results showed decreased nodal efficiency in the pallidum, frontal cortex, and ACC in IGD. In addition, WM network global efficiency had correlations with IAT scores in IGD. The aberrant WM network topological organization in IGD and its association with IGD severity provided a novel outlook into the brain mechanisms of IGD from a WM network level, which may be similar to nicotine addiction. More research needs to be done in this area. To summarize this section, there were obvious structural abnormalities within frontostriatal circuits in nicotine addiction and IGD including gray-matter volume and density abnormalities, cortical thickness and subcortical volume abnormalities, and WM microstructure alterations.

## Resting state functional abnormalities within frontostriatal circuits in nicotine addiction and IGD

Resting state functional imaging researching regional fluctuations has been applied in some disease studies (Song et al., 2020; R. Wang, Li et al., 2019; Yuan, Qin, Liu et al., 2010; Yuan, Yu, Cai et al., 2017). Various neural responses in chronic nicotine addicts were reported in most resting-state fMRI studies (Bi et al., 2016; Bu et al., 2016; Li et al., 2016; Yu et al., 2018; Yuan, Yu et al., 2016). IGD individuals showed greater impulsiveness than normal users (Park et al., 2010). Individuals showed higher metabolism of glucose in the left caudate nucleus, right mOFC, and right INS responsible for controlling impulses, former somatic experiences, and reward processing. Ge et al. (2017) investigated changes in the RSFC of the DLPFC observed in both nicotine addiction and IGD. Both groups had decreased RSFC with the DLPFC in the right INS and left IFG with the DLPFC. IGD individuals showed increased RSFC in the left ITG and right inferior orbital frontal gyrus and decreased RSFC in the right MOG, supramarginal gyrus, and cuneus with the DLPFC. Researchers concluded that both groups have parallel neural pathways related to craving and impulsive behavior. Differences in RSFC with the DLPFC between these groups are possibly caused by visual and auditory stimulation generated by long-term IGD (Ge et al., 2017).

***Regional homogeneity abnormalities in nicotine addiction and IGD.*** Regional homogeneity (ReHo) assesses organization of intra-regional low-frequency (<0.08 Hz) blood oxygen level-dependent (BOLD) signal fluctuations via the Kendall's coefficient of concordance (KCC), which was used to assess spontaneous brain activity during resting state (Zang, Jiang, Lu, He, & Tian, 2004). Compared with healthy controls, nicotine addicts showed decreased ReHo in the right medial-frontal cortex, right inferior-frontal cortex (Tang et al., 2012; Zang et al., 2004), bilateral SFG, and right IFG (Wu, Yang, Zhu, & Lin, 2015), which has been reported in recent studies. These findings indicate that nicotine addiction correlates with abnormal homogeneity of spontaneous neural activity in the regional brain. The ReHo method shows regional low frequency fluctuation (LFF) temporal homogeneity despite intensities based on spatially-neighboring voxels having the same temporal patterns (Zang et al., 2004); amplitude of LFF (ALFF) is linked with localized neuronal activation (Yuan, Jin et al., 2013).

IGD group had higher ReHo brain regions, including the brainstem, cerebellum, bilateral para-hippocampal gyrus (PHG), right cingulate gyrus, right frontal lobe, left SFG, right postcentral gyrus, left precuneus, right ITG, right MOG, MTG, and left superior temporal gyrus (STG). Decreased ReHo brain areas were not located in the IGD group. Based on those findings, associations between increased synchronization among the brainstem, cerebellum, limbic lobe, apical lobe, and frontal lobe are related to reward pathways (Liu et al., 2010). Dong, Huang, and Du (2012) also investigated the regional homogeneity changes between 15 IGDs and 14 controls (Dong, Huang et al., 2012). Compared to controls, IGDs showed increased ReHo in the inferior parietal lobule, brainstem, left MFG, and left posterior cerebellum. These areas are believed to be correlated with sensory-motor control. However, IGDs showed diminished ReHo in parietal, temporal, and occipital brain areas, which coordinate hearing and visual actions. These results suggested that chronic online gaming increased neural synchronization in sensory-motor brain areas and lowered excitability in auditory and visual-related brain areas (Dong, Huang et al., 2012). Such regions should be targeted for future treatment.

***Amplitude of low frequency fluctuation abnormalities in nicotine addiction and IGD.*** LFF in resting state can reflect the spontaneous neural functioning of the brain, and ALFF offers detection of changes in oxygen levels during regional spontaneous activity. Therefore, changes in neural functional activation in resting state in nicotine addicts

revealed by ALFF had been reported in a previous study (Feng et al., 2015). Feng et al. (2015) discovered that adult nicotine addicts had higher fractional ALFF values in the right caudal region compared with controls. In addition, there was a positive correlation discovered among fractional ALFF values in the right caudate and craving score in young adult nicotine addicts, suggesting the caudate has an important role in craving in this particular group.

Another study employed ALFF to detect local characteristics of neural activation in teens with IGD and controls in resting-state (Yuan, Jin et al., 2013). Teenagers with IGD had increased ALFF values in the left precuneus, left mOFC, right PHG, bilateral midcingulate cortex (MCC), and left SMA. These abnormal areas were also shown in other addiction literature (Goldstein & Volkow, 2011; C. H. Ko et al., 2013; Liu et al., 2010; N. Ma et al., 2010; Yuan, Cheng et al., 2013; Yuan, Qin, Dong et al., 2010; Yuan, Qin, Wang et al., 2011). The findings depicted that abnormal brain activation in these areas may be due to the pathophysiology of IGD compared with nicotine addicts.

***Resting state functional connectivity abnormalities in nicotine addiction and IGD.*** RSFC measures the edge of associated activity among brain areas (Yuan, Yu et al., 2016). Mounting evidence revealed the differences of functional connectivity between nicotine addicts and controls (Janes, Nickerson, & Kaufman, 2012; Weiland, Sabbineni, Calhoun, Welsh, & Hutchison, 2015; Yuan, Yu et al., 2016). Young nicotine addicts exhibited reduced RSFC between the right caudate and several regions (i.e. bilateral OFC, right DLPFC, ACC) reported in a Yuan et al. study (Yuan et al., 2016). The results illustrated that information communication between the striatum and PFC in young nicotine addicts was different from controls (Yuan, Yu et al., 2016). In another study comparing non-addicts to nicotine addicts, those that smoked had increased GMV in the left putamen and decreased GMV in the left ACC, which was also negatively associated with years of nicotine addiction. Nicotine addicts had higher RSFC between the right amygdala and left ACC and right INS and left putamen, indicating deficits in frontostriatal areas (Bu et al., 2016).

Compared to the studies in nicotine addicts, Ding et al. (2013) utilized fMRI to detect altered Default Mode Network (DMN) functional connectivity (FC) in teens with IGD (Ding et al., 2013). Individuals with IGD had higher FC in the MTG and bilateral cerebellum posterior lobe. The right ITG and bilateral inferior parietal lobule had diminished connectivity. PCC connectivity had a positive correlation with Chen Internet Addiction Scale (CIAS) scores in the PCG, right precuneus, thalamus, caudate, NAc, lingual gyrus, and SMA, and a negative correlation with the left SPL and right cerebellum anterior lobe. These changes reflect those in drug addiction subjects (Janes et al., 2012; Tanabe et al., 2011; Y. Zhang, Tian et al., 2011).

Another study evaluated altered brain FC among subjects with IGD (C.-H. Ko et al., 2015). IGD individuals had decreased FC with the right amygdala over the left DLPFC and orbital frontal lobe (OFL) and the left amygdala over the DLPFC. There was increased FC with the bilateral amygdalae over the opposite INS than controls. The FC between the DLPFC and left amygdala, the left DLPFC and OFL and right amygdala had a negative correlation with impulsivity. The findings stated the amygdala is highly involved in the neuromechanism of IGD (C.-H. Ko et al., 2015) including nicotine addiction.

In addition, individuals with IGD demonstrated impaired executive control networks (ECNs), including ventromedial prefrontal cortex (vmPFC), DLPFC, and parietal cortex (Dong, Lin, & Potenza, 2015). Meanwhile, our group detected that the right DLPFC connectivity with the right PPC and the left DLPFC connectivity with the left PPC were stronger in controls compared with IGD subjects (Yuan, Wei et al., 2016). Atypical striatal and PFC function and structure were also found in IGD. In contrast, not much is known about changes in functional corticostriatal pathways in IGD. Lin and colleagues investigated functional corticostriatal circuit integrity related to neuropsychological measurements in IGD via resting-state FC (F. Lin et al., 2015). The study found that IGD individuals had decreased connectivity between the bilateral caudate head and inferior ventral striatum, ACC, and PCC, and between the superior ventral striatum and ventral anterior thalamus, right IFG, bilateral-dorsal/rostral ACC, and putamen/pallidum/INS/IFG, and between the dorsal caudate and thalamus, IFG, and dorsal/rostral ACC, and between the right IFG and left ventral rostral putamen. IGD patients had higher connectivity between the bilateral caudal cingulate motor area and left dorsal caudal putamen. Changed cotricostriatal functional pathways had a correlation with neuropsychological tests. This shows that IGD and nicotine addiction have associations with changes in corticostriatal functional circuits involving motivation and emotion processing as well as cognitive function (Lin et al., 2015).

The INS is involved in craving, processing of salience, and interoception, which are necessary for clinical demonstration of addiction. Zhang et al. (2015) examined resting-state FC of the INS and how it was associated with Internet gaming features in 74 IGD patients and 41 control subjects (Zhang et al., 2015). In comparison with controls, IGDs exhibited enhanced resting-state FC with the anterior INS and the putamen, ACC, precuneus, and angular gyrus involving craving, salience, attention, and self-monitoring. Those with IGD had higher resting-state FC between the posterior INS and precentral gyrus, postcentral gyrus, STG, and SMA, which control auditory processing, interoception, and movement respectively. These results implicate the INS in IGD symptoms (Zhang et al., 2015). Another research study investigated the FC of the insular sub-regions in subjects with action video game playing experience (AVG). Compared with controls, AVG experts showed increased functional integration of the INS between the posterior and anterior sub-regions, predominately in the left INS. Since these sub-regions dictate sensorimotor and attentional functions (Cauda et al., 2011), this agrees with results that attention is needed for sensorimotor actions (Gong et al., 2015).

Dong, Lin, and Potenza (2015) revealed there was an imbalanced FC between the ECN and reward pathways to elucidate IGD behaviors. NAc was used to determine the relationships between these networks (Dong, Lin, Hu, Xie, & Du, 2015). IGD individuals showed lower FC in the ECN and higher FC in the reward network (Dong, Lin, Hu et al., 2015). The link between the NAc-ECN had a negative correlation with the one in the NAc-reward network. Alterations in IGD neural synchrony in reward/control pathways found there was ineffectiveness/over-processing in the brain circuitry beneath such processes. The results suggested that executive control impairment led to ineffective inhibition of increased cravings for gaming (Dong, Lin, Hu et al., 2015), which may help us understand IGD.

To further elucidate the mechanisms of IGD, Wang et al. (2019) showed decreased medial PFC to PCC and left IPL to medial PFC connectivity. This suggests biomarker areas for IGD. Hence, it is necessary to study IPL-medial PFC-PCC pathway dysregulation (M. Wang, Zheng, Du, & Dong, 2019). Another study showed that there was decreased resting-state FC in the OFC as well as the frontostriatal, temporal, and occipital areas in IGD (J. Y. Kim et al., 2019). According to Chen et al. (2016), there was decreased FC in the left INS and left DLPFC but higher FC in the precuneus. The decreased frontostriatal circuitry may be associated with the urge to play online games through the NAc, which is controlled by the frontal lobe in IGD subjects. As a result, further research should focus on the dysregulation between the INS, NAc, and frontal lobe and impulsivity of IGD patients (Chen et al., 2016). Seok and Sohn (2018) found that the severity of IGD had a positive correlation with left caudate GM volume and a negative correlation with FC between the left caudate and right MFG, which are involved in reward and cognition (Seok & Sohn, 2018). In addition, Hong et al. (2013) investigated the changes of the functional network in IGD by doing a cross-sectional study and the results showed that adolescents with IGD had reduced FC spanning in a distributed network (Hong et al., 2013). Most inhibited connections are associated with cortico-subcortical pathways (24% = prefrontal and 27% = parietal cortices). The most highly implicated subcortical neural area was the bilateral putamen. No differences between groups were seen in network topological measurements, such as the small worldness ratio, clustering coefficient, and characteristic path length (Hong et al., 2013). A recent work by Wang et al. (2019) indicated that IGD subjects preferred risky choices and had decreased time in making those choices. ICA showed that IGD patients had increased FC in reward and executive control networks and decreased FC in the anterior salience network. This explains why IGD patients have difficulty ceasing gaming activity despite the consequences (Z. Wang, X. Liu et al., 2019), which might also justify why nicotine addicts can't get rid of their nicotine addiction.

There were also gender × group interactions associated with the right PCC, left MOG, right MTG, and right PCG. IGD males had decreased ReHo in the right PCC, which had a negative correlation with IAT scores. There was increased ReHo in IGD males in the left MOG and right MTG unlike females, which meant there were gender differences in executive, visual, and auditory functions that were affected by IGD (M. Wang, Hu, Wang, Du, & Dong, 2019). In another study, ALFF was lower in IGD males in the left SFG, which also had a negative correlation with Barratt Impulsiveness Scale-11 scores. These individuals had decreased FC between the PCC and the orbital section of the left SFG, right DLPFC, and right angular gyrus. This could be a possible biomarker for IGD inhibitive behavior function (Y. Sun et al., 2019). To summarize this section, there were significant differences in regional homogeneity abnormalities, amplitude of low frequency fluctuation abnormalities, resting state functional connectivity abnormalities, and gender interactions in nicotine addiction and IGD.

## Cue-reactivity task and functional connectivity in nicotine addiction and IGD

In a study by Elton, Chanon, and Boettiger (2019), they used a multivariate pattern analysis (MVPA) to detect neural responses to nicotine addiction and neutral pictures. They found that the rostral ACC and IFG showed differences related to nicotine addiction in attentional bias neural correlates. Correlates related to brain behavior were the same in both groups, but the effects of nicotine addiction could be detected in the bilateral MTG and right orbitofrontal gyrus. This meant numerous cognitive, emotional, and visual pathways were involved in attentional bias towards nicotine addiction cues, perpetuating this addiction (Elton et al., 2019). Faulkner et al. (2019) determined that nicotine addiction was responsible for decreasing cravings, bad mood, and NAc-OFC connectivity despite nicotine dose with a positive correlation with behavior and connectivity. A very high nicotine dose, however, decreased the right anterior INS-ACC connectivity and had a positive correlation with behavior (Faulkner et al., 2019). In a recent fMRI report, brain regions controlling attention had decreased activation when there was nicotine deprivation (Liberman et al., 2018). In other research involving teenagers, decreased nicotine addiction during an abstinence period was correlated with "recovery of function" in frontostriatal responses to non-nicotine addiction cue reward anticipation (Garrison et al., 2017).

Gender differences also existed in brain connectivity of nicotine addicts. Female nicotine addicts had lower interhemispheric ECN and DLPFC-dorsal striatum coupling than men. Non-nicotine addicted women had weaker ECN coupling after receiving nicotine. This meant that female nicotine addicts had lower connectivity in brain circuitry involving cognitive control as well as lower abstinence rates (McCarthy et al., 2019).

One research study was able to find IGD neural substrates via cue-induced gaming. The brain regions involved included the right OFC, right NAc, ACC, MFC, right DLPFC, and right caudate nucleus. Their activation had a positive correlation with urges to play video games and gaming cues (Dong, Liu, Zheng, Du, & Potenza, 2019).

Ko et al. (2013) found that the IGD group indicated the precuneus, bilateral DLPFC, left PHG, right ACC, and PCG

had activations to gaming cues compared to controls. Furthermore, IGD had stronger activation than the remission group in the right DLPFC and left PHG, which acted as neural activation markers for online gaming addiction. Those findings showed that the brain substrates of craving in IGD were like those of craving in drug addiction (Wilson, Sayette, & Fiez, 2004).

Another research group investigated the relationship between the PFC, particularly the OFC and ACC, and self-reported craving for IGD. Research findings showed that neural activity in the OFC and ACC in IGD enhanced the response to video-game cues unlike the control group (Han, Kim, Lee, Min, & Renshaw, 2010). The present findings suggest that stimuli activate the DLPFC, thalamus, OFC, and PHG (Han et al., 2011; Han et al., 2010; C. H. Ko et al., 2013). Craving-related brain regions induced by game figure cues in IGD were once again detected by Sun and colleagues (Yueji Sun et al., 2012). Compared with controls, IGD showed increased signal activity in brain areas mainly in the bilateral DLPFC, ACC, right insular/angular gyri, cerebellum, inferior parietal lobe, and ITG. Enhanced imaging signal densities had a positive correlation with the scale scores for craving in the bilateral PFC, ACC, and right IPL, which overlap with emotion-related and cognitive processing brain regions (Yueji Sun et al., 2012). Similar findings were found by Zheng et al. (2019) and Ma et al. (2019) (S. S. Ma et al., 2019; Zheng et al. 2019).

During monetary reward tasks, there was decreased FC between the vmPFC and the left caudate, but vmPFC connectivity was increased for the right NAc. IGD subjects that had stronger vmPFC-NAc connectivity had decreased learning for money reward. There was also decreased connectivity in the ventral striatum with the right vlPFC, dorsal ACC, and left pallidum. These findings imply that IGD causes higher reward salience and impairs goal-directed behavior (J. Kim & Kang, 2018).

Finally, there were significant (gender × group) interactions based on cue-related responses in the DLPFC. IGD women had decreased DLPFC engagement. This indicates that IGD impaired executive control and increased gaming cravings, making it harder to stop playing video games (Dong, Wang, Du, & Potenza, 2018). In another study, it was shown that game-related cues caused increased craving in IGD males. Post-gaming, men had increased activation in the MFG and MTG. Males also had greater activation in the thalamus compared to females. Thus, it was concluded men were more susceptible to developing IGD than women (Dong et al., 2018) as is the case with nicotine addiction. To summarize this section, there were significant differences in cue-reactivity task and functional connectivity as well as gender differences in nicotine addiction and IGD.

## DISCUSSION AND CONCLUSION

Similarities were detected in the implication of frontostriatal circuits in IGD and nicotine addiction, such as GM volume/density, WM properties, and resting state abnormalities, possibly qualifying IGD as a true addiction especially in light of the current social situations. Both have a top-down approach of the cortical regions to the striatum with overlapping reward and cognitive control pathways that play a crucial role in modulating addictive behavior. Such neural pathways are the key to treating both addictions using repetitive transcranial magnetic stimulation (rTMS) (Yuan et al., 2020) and transcranial direct current stimulation (tDCS) (Wu et al., 2020, 2021) as has been done in drug (Song, Zilverstand, Gui, Li, & Zhou, 2019) and alcohol addiction (Herremans & Baeken, 2012). However, there are many distinct differences between these two disorders. For example, there is increased volume in the right caudate in nicotine addiction and volume differences in the NAc in IGD, which were not detected in teenagers. Another limitation is the gender differences that exist in nicotine addiction and IGD, which is the future direction in our research and treatment plan. There are also confounding factors or methodological issues that need to be addressed regarding possible false associations between IGD and nicotine addiction since some gamers might be nicotine addicts or were former nicotine addicts. A meta-analysis should be done comparing both addictions as well as a summary of the treatment progress in nicotine addiction and IGD. Future studies should focus on the contribution of WM tracts of frontostriatal circuits to addiction behaviors. Assuming that greater WM coherence promotes information transmission of distributed regions, increased coherence may modulate neural activation in specific target areas, which might then influence behavior. More and more attention should be paid to the crucial roles of WM tracts in addiction. Even more, rTMS and tDCS interventions provide us with opportunities to test the more accurate roles of the frontal cortex and frontostriatal circuits in addiction. For instance, by enhancing and inhibiting the function of the DLPFC during addiction-related cues, researchers could assess the craving changes and their neural mechanisms. With the development of PET-MRI technology, we can integrate BOLD information and neurotransmitter receptor information to improve the understanding of the interactions between the PFC and subcortical striatal regions in addiction. We hope that all of these neuroimaging findings can lead to effective intervention and treatment of addiction.

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## REFERENCES


Almeida, O. P., Garrido, G. J., Lautenschlager, N. T., Hulse, G. K., Jamrozik, K., & Flicker, L. (2008). Smoking is associated with reduced cortical regional gray matter density in brain regions associated with incipient Alzheimer disease. *The American Journal of Geriatric Psychiatry*, *16*(1), 92–98. https://doi.org/10.1097/JGP.0b013e318157cad2.

American Psychiatric Association, A. (2013). *Diagnostic and statistical manual of mental disorders* (Vol. *5*). Washington, DC: American Psychiatric Association.

Ashburner, J., & Friston, K. J. (2000). Voxel-based morphometry–the methods. *Neuroimage*, *11*(6 Pt 1), 805–821. https://doi.org/10.1006/nimg.2000.0582.

Bi, Y., Yuan, K., Guan, Y., Cheng, J., Zhang, Y., Li, Y., … Tian, J. (2016). Altered resting state functional connectivity of anterior insula in young smokers. *Brain Imaging and Behavior*, 1–11. https://doi.org/10.1007/s11682-016-9511-z.

Breier, A., Su, T.-P., Saunders, R., Carson, R., Kolachana, B., De Bartolomeis, A., … Pickar, D. (1997). Schizophrenia is associated with elevated amphetamine-induced synaptic dopamine concentrations: Evidence from a novel positron emission tomography method. *Proceedings of the National Academy of Sciences*, *94*(6), 2569–2574. https://doi.org/10.1073/pnas.94.6.2569.

Brody, A. L., Mandelkern, M. A., London, E. D., Olmstead, R. E., Farahi, J., Scheibal, D., … Koren, A. O. (2006). Cigarette smoking saturates brain alpha 4 beta 2 nicotinic acetylcholine receptors. *Archives of General Psychiatry*, *63*(8), 907–915. https://doi.org/10.1001/archpsyc.63.8.907.

Brody, A. L., Mandelkern, M. A., Olmstead, R. E., Scheibal, D., Hahn, E., Shiraga, S., … McCracken, J. T. (2006). Gene variants of brain dopamine pathways and smoking-induced dopamine release in the ventral caudate/nucleus accumbens. *Archives of General Psychiatry*, *63*(7), 808–816. https://doi.org/10.1001/archpsyc.63.7.808.

Brody, A. L., Olmstead, R. E., London, E. D., Farahi, J., Meyer, J. H., Grossman, P., … Mandelkern, M. A. (2004). Smoking-induced ventral striatum dopamine release. *American Journal of Psychiatry*, *161*(7), 1211–1218. https://doi.org/10.1176/appi.ajp.161.7.1211.

Bu, L., Yu, D., Su, S., Ma, Y., von Deneen, K. M., Luo, L., … Li, Y. (2016). Functional connectivity abnormalities of brain regions with structural deficits in young adult male smokers. *Frontiers in Human Neuroscience*, *10*, 494. https://doi.org/10.3389/fnhum.2016.00494.

Cauda, F., D'Agata, F., Sacco, K., Duca, S., Geminiani, G., & Vercelli, A. (2011). Functional connectivity of the insula in the resting brain. *Neuroimage*, *55*(1), 8–23. https://doi.org/10.1016/j.neuroimage.2010.11.049.

Chen, C. Y., Yen, J. Y., Wang, P. W., Liu, G. C., Yen, C. F., & Ko, C. H. (2016). Altered functional connectivity of the insula and nucleus Accumbens in internet gaming disorder: A resting state fMRI study. *European Addiction Research*, *22*(4), 192–200. https://doi.org/10.1159/000440716.

Das, D., Cherbuin, N., Anstey, K. J., Sachdev, P. S., & Easteal, S. (2012). Lifetime cigarette smoking is associated with striatal volume measures. *Addiction Biology*, *17*(4), 817–825. https://doi.org/10.1111/j.1369-1600.2010.00301.x.

Di Chiara, G., & Imperato, A. (1988). Drugs abused by humans preferentially increase synaptic dopamine concentrations in the mesolimbic system of freely moving rats. *Proceedings of the National Academy of Sciences*, *85*(14), 5274–5278. https://doi.org/10.1073/pnas.85.14.5274.

Dong, G., DeVito, E., Huang, J., & Du, X. (2012). Diffusion tensor imaging reveals thalamus and posterior cingulate cortex abnormalities in internet gaming addicts. *Journal of Psychiatric Research*, *46*(9), 1212–1216. https://doi.org/10.1016/j.jpsychires.2012.05.015.

Dong, G., Huang, J., & Du, X. (2012). Alterations in regional homogeneity of resting-state brain activity in internet gaming addicts. *Behavioral and Brain Functions*, *8*(1), 1. https://doi.org/10.1186/1744-9081-8-41.

Ding, W.-n., Sun, J.-h., Sun, Y.-w., Zhou, Y., Li, L., Xu, J.-r., … Du, Y. S. (2013). Altered default network resting-state functional connectivity in adolescents with Internet gaming addiction. *Plos One*, *8*(3), e59902. https://doi.org/10.1371/journal.pone.0059902.

Dong, F., Li, X., Zhang, Y., Jia, S., Zhang, S., Xue, T., & Yu, D. (2021). Abnormal resting-state EEG power and impaired inhibition control in young smokers. *Neuroscience Letters*, *761*, 136120. https://doi.org/10.1016/j.neulet.2021.136120.

Dong, G., Lin, X., Hu, Y., Xie, C., & Du, X. (2015). Imbalanced functional link between executive control network and reward network explain the online-game seeking behaviors in Internet gaming disorder. *Scientific Reports*, *5*(5 Suppl 2), 1238–1242. https://doi.org/10.1038/srep09197.

Dong, G., Lin, X., & Potenza, M. N. (2015). Decreased functional connectivity in an executive control network is related to impaired executive function in Internet gaming disorder. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *57*, 76–85. https://doi.org/10.1016/j.pnpbp.2014.10.012.

Dong, G., Liu, X., Zheng, H., Du, X., & Potenza, M. N. (2019). Brain response features during forced break could predict subsequent recovery in internet gaming disorder: A longitudinal study. *Journal of Psychiatric Research*, *113*, 17–26. https://doi.org/10.1016/j.jpsychires.2019.03.003.

Dong, G., Wang, L., Du, X., & Potenza, M. N. (2018). Gender-related differences in neural responses to gaming cues before and after gaming: Implications for gender-specific vulnerabilities to internet gaming disorder. *Social Cognitive and Affective Neuroscience*, *13*(11), 1203–1214. https://doi.org/10.1093/scan/nsy084.

Elton, A., Chanon, V. W., & Boettiger, C. A. (2019). Multivariate pattern analysis of the neural correlates of smoking cue attentional bias. *Pharmacology, Biochemistry, and Behavior*, *180*, 1–10. https://doi.org/10.1016/j.pbb.2019.03.001.

Faulkner, P., Ghahremani, D. G., Tyndale, R. F., Paterson, N. E., Cox, C., Ginder, N., ... London, E. D. (2019). Neural basis of smoking-induced relief of craving and negative affect: Contribution of nicotine. *Addiction Biology*, *24*(5), 1087–1095. https://doi.org/10.1111/adb.12679.

Fehr, C., Yakushev, I., Hohmann, N., Buchholz, H.-G., Landvogt, C., Deckers, H., ... Dielentheis, T. (2008). Association of low striatal dopamine D 2 receptor availability with nicotine dependence similar to that seen with other drugs of abuse. *American Journal of Psychiatry*, *165*(4), 507–514. https://doi.org/10.1176/appi.ajp.2007.07020352.

Feng, D., Yuan, K., Li, Y., Cai, C., Yin, J., Bi, Y., ... Jin, C. (2015). Intra-regional and inter-regional abnormalities and cognitive control deficits in young adult smokers. *Brain Imaging and Behavior*, 1–11. https://doi.org/10.1007/s11682-015-9427-z.

Garrison, K. A., Yip, S. W., Balodis, I. M., Carroll, K. M., Potenza, M. N., & Krishnan-Sarin, S. (2017). Reward-related frontostriatal activity and smoking behavior among adolescents in treatment for smoking cessation. *Drug and Alcohol Dependence*, *177*, 268–276. https://doi.org/10.1016/j.drugalcdep.2017.03.035.

Ge, X., Sun, Y., Han, X., Wang, Y., Ding, W., Cao, M., & Zhou, Y. (2017). Difference in the functional connectivity of the dorsolateral prefrontal cortex between smokers with nicotine dependence and individuals with internet gaming disorder. *Bmc Neuroscience*, *18*(1), 1–10. https://doi.org/10.1186/s12868-017-0375-y.

Gentzke A. S., Wang T. W., Jamal A., Park-Lee E., Ren, C., Cullen, K.A., & Neff, L. (2020). Tobacco product use among middle and high school students, United States, 2020. *Morbidity and Mortality Weekly Report*, *69*(50);1881–1888 [accessed 2020 December 17]. http://dx.doi.org/10.15585/mmwr.mm6950a1.

Goldstein, R. Z., & Volkow, N. D. (2011). Dysfunction of the prefrontal cortex in addiction: Neuroimaging findings and clinical implications. *Nature Reviews Neuroscience*, *12*(11), 652–669. https://doi.org/10.1038/nrn3119.

Gong, D., He, H., Liu, D., Ma, W., Dong, L., Luo, C., ... Yao, D. (2015). Enhanced functional connectivity and increased gray matter volume of insula related to action video game playing. *Scientific Reports*, *5*(3), 33–33. https://doi.org/10.1038/srep09763.

Han, D. H., Bolo, N., Daniels, M. A., Arenella, L., Lyoo, I. K., & Renshaw, P. F. (2011). Brain activity and desire for Internet video game play. *Comprehensive Psychiatry*, *52*(1), 88–95. https://doi.org/10.1016/j.comppsych.2010.04.004.

Han, D. H., Kim, Y. S., Lee, Y. S., Min, K. J., & Renshaw, P. F. (2010). Changes in cue-induced, prefrontal cortex activity with video-game play. *Cyberpsychology, Behavior, and Social Networking*, *13*(6), 655–661. https://doi.org/10.1089/cyber.2009.0327.

Herremans, S. C., & Baeken, C. (2012). The current perspective of neuromodulation techniques in the treatment of alcohol addiction: A systematic review. *Psychiatria Danubina*, *24*(Suppl 1), S14–S20. https://doi.org/10.1111/j.1533-2500.2012.00562.x.

Hong, S.-B., Zalesky, A., Cocchi, L., Fornito, A., Choi, E.-J., Kim, H.-H., et al. (2013). Decreased functional brain connectivity in adolescents with internet addiction. *PloS One*, *8*(2), e57831. https://doi.org/10.1371/journal.pone.0057831.

Hou, H., Jia, S., Hu, S., Fan, R., Sun, W., Sun, T., ... Zhang, H. (2012). Reduced striatal dopamine transporters in people with internet addiction disorder. *BioMed Research International*. https://doi.org/10.1155/2012/854524.

Janes, A. C., Nickerson, L. D., & Kaufman, M. J. (2012). Prefrontal and limbic resting state brain network functional connectivity differs between nicotine-dependent smokers and non-smoking controls. *Drug and Alcohol Dependence*, *125*(3), 252–259. https://doi.org/10.1016/j.drugalcdep.2012.02.020.

Janes, A. C., Park, M. T. M., Farmer, S., & Chakravarty, M. M. (2015). Striatal morphology is associated with tobacco cigarette craving. *Neuropsychopharmacology*, *40*(2), 406–411. https://doi.org/10.1038/npp.2014.185.

Kim, J. Y., Chun, J. W., Park, C. H., Cho, H., Choi, J., Yang, S., ... Kim, D. J. (2019). The correlation between the frontostriatal network and impulsivity in internet gaming disorder. *Scientific Reports*, *9*(1), 1191. https://doi.org/10.1038/s41598-018-37702-4.

Kim, S. H., Baik, S.-H., Park, C. S., Kim, S. J., Choi, S. W., & Kim, S. E. (2011). Reduced striatal dopamine D2 receptors in people with Internet addiction. *Neuroreport*, *22*(8), 407–411. https://doi.org/10.1097/WNR.0b013e328346e16e.

Kim, J., & Kang, E. (2018). Internet game overuse is associated with an alteration of fronto-striatal functional connectivity during reward feedback processing. *Front Psychiatry*, *9*, 371. https://doi.org/10.3389/fpsyt.2018.00371.

Ko, C.-H., Hsieh, T.-J., Wang, P.-W., Lin, W.-C., Yen, C.-F., Chen, C.-S., ... Yen, Y. J. (2015). Altered gray matter density and disrupted functional connectivity of the amygdala in adults with Internet gaming disorder. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *57*, 185–192. https://doi.org/10.1016/j.pnpbp.2014.11.003.

Ko, C. H., Liu, G. C., Yen, J. Y., Chen, C. Y., Yen, C. F., & Chen, C. S. (2013). Brain correlates of craving for online gaming under cue exposure in subjects with Internet gaming addiction and in remitted subjects. *Addiction Biology*, *18*(3), 559–569. https://doi.org/10.1111/j.1369-1600.2011.00405.x.

Koepp, M. J., Gunn, R. N., Lawrence, A. D., Cunningham, V. J., Dagher, A., Jones, T., ... Grasby, P. M. (1998). Evidence for striatal dopamine release during a video game. *Nature*, *393*(6682), 266–268. https://doi.org/10.1038/30498.

Koob, G. F., & Le Moal, M. (2005). *Neurobiology of addiction*. Academic Press. https://doi.org/10.1111/nyas.13989.

Kühn, S., Romanowski, A., Schilling, C., Lorenz, R., Mörsen, C., Seiferth, N., ... Conrod, P. J. (2011). The neural basis of video gaming. *Translational Psychiatry*, *1*(11), e53. https://doi.org/10.1038/tp.2011.53.

Kühn, S., Schubert, F., & Gallinat, J. (2010). Reduced thickness of medial orbitofrontal cortex in smokers. *Biological Psychiatry*, *68*(11), 1061–1065. https://doi.org/10.1016/j.biopsych.2010.08.004.

Kuss, D. J., Kanjo, E., Crook-Rumsey, M., Kibowski, F., Wang, G. Y., & Sumich, A. (2018). Problematic mobile phone use and addiction across generations: The roles of psychopathological symptoms and smartphone use. *Journal of Technology in Behavioral Science*, *3*(3), 141–149. https://doi.org/10.1007/s41347-017-0041-3.

Lepido, D., & Rolander, N. (2020). Housebound Italian kids strain network with Fortnite marathon. Retrieved from: https://www.bloomberg.com/news/articles/2020-03-12/housebound-italian-kids-strain-network-with-fortnite-marathon.

Leroy, C., Karila, L., Martinot, J. L., Lukasiewicz, M., Duchesnay, E., Comtat, C., ... Reynaud, M. (2012). Striatal and extrastriatal dopamine transporter in cannabis and tobacco addiction: A high-resolution PET study. *Addiction Biology*, *17*(6), 981–990. https://doi.org/10.1111/j.1369-1600.2011.00356.x.

Li, Y., Yuan, K., Bi, Y., Guan, Y., Cheng, J., Zhang, Y., ... Tian, J. (2016). Neural correlates of 12-h abstinence-induced craving in young adult smokers: A resting-state study. *Brain Imaging and Behavior*, 1–8. https://doi.org/10.1007/s11682-016-9544-3.

Li, Y., Yuan, K., Cai, C., Feng, D., Yin, J., Bi, Y., ... Qin, W. (2015). Reduced frontal cortical thickness and increased caudate volume within fronto-striatal circuits in young adult smokers. *Drug and Alcohol Dependence*, *151*, 211–219. https://doi.org/10.1016/j.drugalcdep.2015.03.023.

Liberman, K., Van Schuerbeek, P., Herremans, S., Meysman, M., De Mey, J., & Buls, N. (2018). The effect of nicotine patches on craving in the brain: A functional MRI study on heavy smokers. *Medicine (Baltimore)*, *97*(39), e12415. https://doi.org/10.1097/md.0000000000012415.

Lin, F., Zhou, Y., Du, Y., Qin, L., Zhao, Z., Xu, J., ... Lei, H. (2012). Abnormal white matter integrity in adolescents with internet addiction disorder: A tract-based spatial statistics study. *PloS One*, *7*(1), e30253. https://doi.org/10.1371/journal.pone.0030253.

Lin, F., Zhou, Y., Du, Y., Zhao, Z., Qin, L., Xu, J., ... Lei, H. (2015). Aberrant corticostriatal functional circuits in adolescents with Internet addiction disorder. *Frontiers in Human Neuroscience*, *9*, 356. https://doi.org/10.3389/fnhum.2015.00356.

Liu, J., Gao, X., Osunde, I., Li, X., Zhou, S., Zheng, H., ... Li, L. J. (2010). Increased regional homogeneity in internet addiction disorder a resting state functional magnetic resonance imaging study (2009). *Chinese Medical Journal (England)*, *123*, 1904–1908. https://doi.org/10.3760/cma.j.issn.0366-6999.2010.14.014.

Liu, S., Wang, S., Zhang, M., Xu, Y., Shao, Z., Chen, L., & Yuan, K. (2021). Brain responses to drug cues predict craving changes in abstinent heroin users: A preliminary study. *NeuroImage*, *237*, 118169. https://doi.org/10.1016/j.neuroimage.2021.118169.

Livingstone, P. D., & Wonnacott, S. (2009). Nicotinic acetylcholine receptors and the ascending dopamine pathways. *Biochemical Pharmacology*, *78*(7), 744–755. https://doi.org/10.1016/j.bcp.2009.06.004.

Ma, N., Liu, Y., Li, N., Wang, C.-X., Zhang, H., Jiang, X.-F., ... Zhang, D. R. (2010). Addiction related alteration in resting-state brain connectivity. *Neuroimage*, *49*(1), 738–744. https://doi.org/10.1016/j.neuroimage.2009.08.037.

Ma, S. S., Worhunsky, P. D., Xu, J. S., Yip, S. W., Zhou, N., Zhang, J. T., ... Fang, X. Y. (2019). Alterations in functional networks during cue-reactivity in Internet gaming disorder. *Journal of Behavioral Addictions*, *8*(2), 277–287. https://doi.org/10.1556/2006.8.2019.25.

Marshall, D. L., Redfern, P. H., & Wonnacott, S. (1997). Presynaptic nicotinic modulation of dopamine release in the three ascending pathways studied by in vivo microdialysis: Comparison of naive and chronic nicotine-treated rats. *Journal of Neurochemistry*, *68*(4), 1511–1519. https://doi.org/10.1046/j.1471-4159.1997.68041511.x.

McCarthy, J. M., Dumais, K. M., Zegel, M., Pizzagalli, D. A., Olson, D. P., Moran, L. V., ... Janes, A. C. (2019). Sex differences in tobacco smokers: Executive control network and frontostriatal connectivity. *Drug and Alcohol Dependence*, *195*, 59–65. https://doi.org/10.1016/j.drugalcdep.2018.11.023.

Meng, Y., Deng, W., Wang, H., Guo, W., & Li, T. (2015). The prefrontal dysfunction in individuals with Internet gaming disorder: A meta-analysis of functional magnetic resonance imaging studies. *Addiction Biology*, *20*(4), 799–808. https://doi.org/10.1111/adb.12154.

Mulvihill, K. G. (2019). Presynaptic regulation of dopamine release: Role of the DAT and VMAT2 transporters. *Neurochemistry International*, *122*, 94–105. https://doi.org/10.1016/j.neuint.2018.11.004.

Pantling, A. (2020). Gaming usage up 75 percent amid coronavirus outbreak, Verizon reports. Retrieved from https://www.hollywoodreporter.com/news/gaming-usage-up-75-percent-coronavirus-outbreak-verizon-reports-1285140.

Park, H. S., Kim, S. H., Bang, S. A., un Yoon, E., Cho, S. S., & Kim, S. E. (2010). Altered regional cerebral glucose metabolism in internet game overusers: A 18 F-fluorodeoxyglucose positron emission tomography study. *CNS Spectrums: The International Journal of Neuropsychiatric Medicine*, *15*(3). https://doi.org/10.1017/S1092852900027437.

Petry, N. M., & O'Brien, C. P. (2013). Internet gaming disorder and the DSM-5. *Addiction*, *108*(7), 1186–1187. https://doi.org/10.1111/add.12162.

Pistillo, F., Clementi, F., Zoli, M., & Gotti, C. (2015). Nicotinic, glutamatergic and dopaminergic synaptic transmission and plasticity in the mesocorticolimbic system: Focus on nicotine effects. *Progress in Neurobiology*, *124*, 1–27. https://doi.org/10.1016/j.pneurobio.2014.10.002.

Salokangas, R. K., Vilkman, H., Ilonen, T., Taiminen, T., Haaparanta, M., Solin, O., ... Hietala, J. (2000). High levels of dopamine activity in the basal ganglia of cigarette smokers. *American Journal of Psychiatry*, *157*(4), 632–634. https://doi.org/10.1176/appi.ajp.157.4.632.

Seok, J. W., & Sohn, J. H. (2018). Altered gray matter volume and resting-state connectivity in individuals with internet gaming disorder: A voxel-based morphometry and resting-state functional magnetic resonance imaging study. *Front Psychiatry*, *9*, 77. https://doi.org/10.3389/fpsyt.2018.00077.

Singer, S., Rossi, S., Verzosa, S., Hashim, A., Lonow, R., Cooper, T., ... Lajtha, A. (2004). Nicotine-induced changes in neurotransmitter levels in brain areas associated with cognitive function. *Neurochemical Research*, *29*(9), 1779–1792. https://doi.org/10.1023/B:NERE.0000035814.45494.15.

Song, K., Li, J., Zhu, Y., Ren, F., Cao, L., Shao, Y., ... Huang, Z. G. (2020). Altered small-world functional network topology in patients with optic neuritis: A resting- state fMRI study. *bioRxiv*, *2020*.2006.2009.141432. https://doi.org/10.1101/2020.06.09.141432.

Song, S., Zilverstand, A., Gui, W., Li, H. J., & Zhou, X. (2019). Effects of single-session versus multi-session non-invasive brain stimulation on craving and consumption in individuals with drug addiction, eating disorders or obesity: A meta-analysis.

*Brain Stimulation*, *12*(3), 606–618. https://doi.org/10.1016/j.brs.2018.12.975.

Stephen, B. (2020). This is Twitch's moment [internet]. Retrieved from https://www.theverge.com/2020/3/18/21185114/twitch-youtube-livestreaming-streamelements-coronavirus-quarantine-viewership-numbers.

Sun, Y., Wang, Y., Han, X., Jiang, W., Ding, W., Cao, M., . . . Zhou, Y. (2019). Sex differences in resting-state cerebral activity alterations in internet gaming disorder. *Brain Imaging and Behavior*, *13*(5), 1406–1417. https://doi.org/10.1007/s11682-018-9955-4.

Sun, Y., Ying, H., Seetohul, R. M., Xuemei, W., Ya, Z., Qian, L., . . . Ye, S. (2012). Brain fMRI study of crave induced by cue pictures in online game addicts (male adolescents). *Behavioural Brain Research*, *233*(2), 563–576. https://doi.org/10.1016/j.bbr.2012.05.005.

Tanabe, J., Nyberg, E., Martin, L. F., Martin, J., Cordes, D., Kronberg, E., . . . Tregellas, J. R. (2011). Nicotine effects on default mode network during resting state. *Psychopharmacology (Berl)*, *216*(2), 287–295. https://doi.org/10.1007/s00213-011-2221-8.

Tang, J., Liao, Y., Deng, Q., Liu, T., Chen, X., Wang, X., . . . Hao, W. (2012). Altered spontaneous activity in young chronic cigarette smokers revealed by regional homogeneity. *Behavioral and Brain Functions*, *8*(1), 1. https://doi.org/10.1186/1744-9081-8-44.

Tomasi, D., & Volkow, N. D. (2013). Striatocortical pathway dysfunction in addiction and obesity: Differences and similarities. *Critical Reviews in Biochemistry and Molecular Biology*, *48*(1), 1–19. https://doi.org/10.3109/10409238.2012.735642.

Volkow, N. D., Koob, G. F., & McLellan, A. T. (2016). Neurobiologic advances from the brain disease model of addiction. *New England Journal of Medicine*, *374*(4), 363–371. https://doi.org/10.1056/NEJMra1511480.

Volkow, N. D., Wang, G.-J., Fowler, J. S., Tomasi, D., & Telang, F. (2011). Addiction: Beyond dopamine reward circuitry. *Proceedings of the National Academy of Sciences*, *108*(37), 15037–15042. https://doi.org/10.1073/pnas.1010654108.

Volkow, N. D., Wang, G.-J., Tomasi, D., & Baler, R. D. (2013). Unbalanced neuronal circuits in addiction. *Current Opinion in Neurobiology*, *23*(4), 639–648. https://doi.org/10.1016/j.conb.2013.01.002.

Wang, M., Hu, Y., Wang, Z., Du, X., & Dong, G. (2019). Sex difference in the effect of Internet gaming disorder on the brain functions: Evidence from resting-state fMRI. *Neuroscience Letters*, *698*, 44–50. https://doi.org/10.1016/j.neulet.2018.12.038.

Wang, S., Liu, J., Tian, L., Chen, L., Wang, J., Tang, Q., . . . Zhou, Z. (2018). Increased insular cortical thickness associated with symptom severity in male youths with internet gaming disorder: A surface-based morphometric study. *Front Psychiatry*, *9*, 99. https://doi.org/10.3389/fpsyt.2018.00099.

Wang, Z., Hu, Y., Zheng, H., Yuan, K., Du, X., & Dong, G. (2019). Females are more vulnerable to Internet gaming disorder than males: Evidence from cortical thickness abnormalities. *Psychiatry Research Neuroimaging*, *283*, 145–153. https://doi.org/10.1016/j.pscychresns.2018.11.001.

Wang, Z., Liu, X., Hu, Y., Zheng, H., Du, X., & Dong, G. (2019). Altered brain functional networks in Internet gaming disorder: Independent component and graph theoretical analysis under a probability discounting task. *CNS Spectrums*, *24*(5), 544–556. https://doi.org/10.1017/s1092852918001505.

Wang, R., Li, M., Zhao, M., Yu, D., Hu, Y., Wiers, C. E., . . . Yuan, K. (2019). Internet gaming disorder: Deficits in functional and structural connectivity in the ventral tegmental area-Accumbens pathway. *Brain Imaging and Behavior*, *13*(4), 1172–1181. https://doi.org/10.1007/s11682-018-9929-6.

Wang, M., Zheng, H., Du, X., & Dong, G. (2019). Mapping Internet gaming disorder using effective connectivity: A spectral dynamic causal modeling study. *Addictive Behaviors*, *90*, 62–70. https://doi.org/10.1016/j.addbeh.2018.10.019.

Weiland, B. J., Sabbineni, A., Calhoun, V. D., Welsh, R. C., & Hutchison, K. E. (2015). Reduced executive and default network functional connectivity in cigarette smokers. *Human Brain Mapping*, *36*(3), 872–882. https://doi.org/10.1002/hbm.22672.

Weinstein, A., & Lejoyeux, M. (2015). New developments on the neurobiological and pharmaco-genetic mechanisms underlying internet and videogame addiction. *The American Journal on Addictions*, *24*(2), 117–125. https://doi.org/10.1007/s11682-015-9358-8.

Weinstein, A., & Lejoyeux, M. (2020). Neurobiological mechanisms underlying internet gaming disorder. *Dialogues in Clinical Neuroscience*, *22*(2), 113. https://doi.org/10.31887/DCNS.2020.22.2/aweinstein.

Weinstein, A., Livny, A., & Weizman, A. (2017). New developments in brain research of internet and gaming disorder. *Neuroscience and Biobehavioral Reviews*, *75*, 314–330. https://doi.org/10.1007/s11682-018-9929-6.

Wilson, S. J., Sayette, M. A., & Fiez, J. A. (2004). Prefrontal responses to drug cues: A neurocognitive analysis. *Nature Neuroscience*, *7*(3), 211–214. https://doi.org/10.1038/nn1200.

Wonnacott, S., Sidhpura, N., & Balfour, D. J. (2005). Nicotine: From molecular mechanisms to behaviour. *Current Opinion in Pharmacology*, *5*(1), 53–59. https://doi.org/10.1016/j.coph.2004.12.002.

Wu, L. L., Potenza, M. N., Zhou, N., Kober, H., Shi, X. H., Yip, S. W., & Zhang, J. T. (2020). A role for the right dorsolateral prefrontal cortex in enhancing regulation of both craving and negative emotions in internet gaming disorder: A randomized trial. *European Neuropsychopharmacology*, *36*, 29–37. https://doi.org/10.1016/j.euroneuro.2020.04.003.

Wu, L. L., Potenza, M. N., Zhou, N., Kober, H., Shi, X. H., Yip, S. W., & Zhang, J. T. (2021). Efficacy of single-session transcranial direct current stimulation on addiction-related inhibitory control and craving: A randomized trial in males with Internet gaming disorder. *Journal of Psychiatry & Neuroscience: JPN*, *46*(1), E111. https://doi.org/10.1503/jpn.190137.

Wu, G., Yang, S., Zhu, L., & Lin, F. (2015). Altered spontaneous brain activity in heavy smokers revealed by regional homogeneity. *Psychopharmacology*, *232*(14), 2481–2489. https://doi.org/10.1007/s00213-015-3881-6.

Xing, L., Yuan, K., Bi, Y., Yin, J., Cai, C., Feng, D., et al. (2014). Reduced fiber integrity and cognitive control in adolescents with internet gaming disorder. *Brain Research*, *1586*, 109–117. https://doi.org/10.1016/j.brainres.2014.08.044.

Young, K. S. (1998). Internet addiction: The emergence of a new clinical disorder. *CyberPsychology & Behavior*, *1*(3), 237–244. https://doi.org/10.1089/cpb.1998.1.237.

Young, K. (2010). Internet addiction over the decade: A personal look back. *World Psychiatry*, *9*(2), 91–91. https://doi.org/10.1002%2Fj.2051-5545.2010.tb00279.x.

Yu, D., Yuan, K., Bi, Y., Luo, L., Zhai, J., Liu, B., . . . Lu, X. (2018). Altered interhemispheric resting-state functional connectivity in young male smokers. *Addiction Biology*, *23*(2), 772–780. https://doi.org/10.1111/adb.12515.

Yuan, K., Cheng, P., Dong, T., Bi, Y., Xing, L., Yu, D., . . . Tian, J. (2013). Cortical thickness abnormalities in late adolescence with online gaming addiction. *PloS One*, *8*(1), e53055. https://doi.org/10.1371/journal.pone.0053055.

Yuan, K., Jin, C., Cheng, P., Yang, X., Dong, T., Bi, Y., . . . Tian, J. (2013). Amplitude of low frequency fluctuation abnormalities in adolescents with online gaming addiction. *PloS One*, *8*(11), e78708. https://doi.org/10.1371/journal.pone.0078708.

Yuan, K., Qin, W., Dong, M., Liu, J., Sun, J., Liu, P., . . . Tian, J. (2010). Gray matter deficits and resting-state abnormalities in abstinent heroin-dependent individuals. *Neuroscience Letters*, *482*(2), 101–105. https://doi.org/10.1016/j.neulet.2010.07.005.

Yuan, K., Qin, W., Liu, J., Guo, Q., Dong, M., Sun, J., . . . Tian, J. (2010). Altered small-world brain functional networks and duration of heroin use in male abstinent heroin-dependent individuals. *Neuroscience Letters*, *477*(1), 37–42. https://doi.org/10.1016/j.neulet.2010.04.032.

Yuan, K., Qin, W., Liu, Y., & Tian, J. (2011). Internet addiction: Neuroimaging findings. *Communicative & Integrative Biology*, *4*(6), 637–639. https://doi.org/10.4161/cib.17871.

Yuan, K., Qin, W., Wang, G., Zeng, F., Zhao, L., Yang, X., . . . Tian, J. (2011). Microstructure abnormalities in adolescents with internet addiction disorder. *PloS One*, *6*(6), e20708. https://doi.org/10.1371/journal.pone.0020708.

Yuan, K., Wei, Q., Yu, D., Bi, Y., Xing, L., Jin, C., . . . Tian, J. (2016). Core brain networks interactions and cognitive control in internet gaming disorder individuals in late adolescence/early adulthood. *Brain Structure and Function*, *221*(3), 1–16. https://doi.org/10.1007/s00429-014-0982-7.

Yuan, K., Wen, X., Wang, S., Liu, S., Shao, Z., Zhang, M., & Yu, D. (2020). Potential neural mechanism of single session transcranial magnetic stimulation on smoking craving. *Science China Information Sciences*, *63*, 1–3. https://doi.org/10.1007/s11432-019-2816-x.

Yuan, K., Yu, D., Bi, Y., Li, Y., Guan, Y., Liu, J., . . . Tian, J. (2016). The implication of frontostriatal circuits in young smokers: A resting-state study. *Human Brain Mapping*, *37*(6), 2013–2026. https://doi.org/10.1002/hbm.23153.

Yuan, K., Yu, D., Bi, Y., Wang, R., Li, M., Zhang, Y., . . . Tian, J. (2017). The left dorsolateral prefrontal cortex and caudate pathway: New evidence for cue-induced craving of smokers. *Human Brain Mapping*, *38*(9), 4644–4656. https://doi.org/10.1002/hbm.23690.

Yuan, K., Yu, D., Cai, C., Feng, D., Li, Y., Bi, Y., . . . Tian, J. (2017). Frontostriatal circuits, resting state functional connectivity and cognitive control in internet gaming disorder. *Addiction Biology*, *22*(3), 813–822. https://doi.org/10.1111/adb.12348.

Yuan, K., Yu, D., Zhao, M., Li, M., Wang, R., Li, Y., . . . Tian, J. (2018). Abnormal frontostriatal tracts in young male tobacco smokers. *Neuroimage*, *183*, 346–355. https://doi.org/10.1016/j.neuroimage.2018.08.046.

Yuan, K., Zhao, M., Yu, D., Manza, P., Volkow, N. D., Wang, G. J., & Tian, J. (2018). Striato-cortical tracts predict 12-h abstinence-induced lapse in smokers. *Neuropsychopharmacology*, *43*(12), 2452–2458. https://doi.org/10.1038/s41386-018-0182-x.

Zang, Y., Jiang, T., Lu, Y., He, Y., & Tian, L. (2004). Regional homogeneity approach to fMRI data analysis. *Neuroimage*, *22*(1), 394–400. https://doi.org/10.1016/j.neuroimage.2003.12.030.

Zhai, J., Luo, L., Qiu, L., Kang, Y., Liu, B., Yu, D., . . . Yuan, K. (2016). The topological organization of white matter network in internet gaming disorder individuals. *Brain Imaging and Behavior*, 1–10. https://doi.org/10.1007/s11682-016-9652-0.

Zhang, J. T., Yao, Y. W., Li, C. S. R., Zang, Y. F., Shen, Z. J., Liu, L., . . . Fang, X. Y. (2015). Altered resting-state functional connectivity of the insula in young adults with Internet gaming disorder. *Addiction Biology*, *21*(3), 743–751. https://doi.org/10.1111/adb.12247.

Zhang, M., Liu, S., Wang, S., Xu, Y., Chen, L., Shao, Z., . . . Yuan, K. (2021). Reduced thalamic resting-state functional connectivity and impaired cognition in acute abstinent heroin users. *Human Brain Mapping*, *42*(7), 2077–2088. https://doi.org/10.1002/hbm.25346.

Zhang, X., Salmeron, B. J., Ross, T. J., Geng, X., Yang, Y., & Stein, E. A. (2011). Factors underlying prefrontal and insula structural alterations in smokers. *Neuroimage*, *54*(1), 42–48. https://doi.org/10.1016/j.neuroimage.2010.08.008.

Zhang, Y., Tian, J., Yuan, K., Liu, P., Zhuo, L., Qin, W., . . . Liu, Y. (2011). Distinct resting-state brain activities in heroin-dependent individuals. *Brain Research*, *1402*, 46–53. https://doi.org/10.1016/j.brainres.2011.05.054.

Zheng, H., Hu, Y., Wang, Z., Wang, M., Du, X., & Dong, G. (2019). Meta-analyses of the functional neural alterations in subjects with Internet gaming disorder: Similarities and differences across different paradigms. *Progress in Neuropsychopharmacology & Biological Psychiatry*, *94*, 109656. https://doi.org/10.1016/j.pnpbp.2019.109656.

Zhou, Y., Lin, F. C., Du, Y. S., Qin, L. D., Zhao, Z. M., Xu, J. R., . . . Lei, H. (2011). Gray matter abnormalities in Internet addiction: A voxel-based morphometry study. *European Journal of Radiology*, *79*(1), 92–95. https://doi.org/10.1016/j.ejrad.2009.10.025.

## ABBREVIATION LIST

| | |
|---|---|
| ACC | Anterior cingulate cortex |
| ALFF | Amplitude of LFF |
| AVG | Action video game |
| BOLD | Blood oxygen level-dependent |
| CIAS | Chen Internet Addiction Scale |
| DA | Dopamine |
| DAT | Dopamine transporter |
| DLPFC | Dorsolateral prefrontal cortex |
| DMN | Default mode network |
| DOPA | Dihydroxyphenylalanine |
| DTI | Diffusion tensor imaging |
| ECNs | Executive control networks |
| FA | Fractional anisotropy |
| FC | Functional connectivity |
| fMRI | Functional magnetic resonance imaging |
| GM | Gray matter |
| GMD | Gray matter density |
| GMV | Gray matter volume |
| IAT | Internet addiction test |
| IFG | Inferior frontal gyrus |
| IGD | Internet gaming disorder |
| INS | Insula |
| IPC | Inferior parietal cortex |
| ITG | Inferior temporal gyrus |
| KCC | Kendall's coefficient of concordance |
| LFF | Low frequency fluctuation |
| MCC | Midcingulate cortex |
| MFG | Middle frontal gyrus |
| mOFC | Medial orbitofrontal cortex |
| MOG | Middle occipital gyrus |
| MRI | Magnetic resonance imaging |
| MTG | Middle temporal gyrus |
| MVPA | Multi-variate pattern analysis |
| NAc | Nucleus accumbens |
| OFC | Orbitofrontal cortex |
| OFL | Orbital frontal lobe |
| PCC | Posterior cingulate cortex |
| PCG | Posterior cingulate gyrus |
| PET | Positron emission tomography |
| PFC | Prefrontal cortex |
| PHG | Para-hippocampal gyrus |
| PPC | Posterior parietal cortex |
| RAC | Raclopride |
| ReHo | Regional homogeneity |
| RSFC | Resting-state functional connectivity |
| rTMS | Repetitive transcranial magnetic stimulation |
| SFG | Superior frontal gyrus |
| SMA | Supplementary motor area |
| SN | Salience network |
| SPECT | Single photon emission computed tomography |
| SPL | Superior parietal lobe |
| STG | Superior temporal gyrus |
| SUD | Substance use disorder |
| TBSS | Tract-based spatial statistics |
| tDCS | Transcranial direct current stimulation |
| VBM | Voxel-based morphometry |
| vlPFC | Ventral lateral prefrontal cortex |
| vmPFC | Ventromedial prefrontal cortex |
| VTA | Ventral tegmental area |
| WM | White matter |