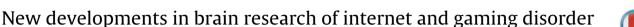
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#### A R T I C L E I N F O

#### ABSTRACT

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Keywords: Internet gaming disorder Brain imaging fMRI Dopamine Reward There is evidence that the neural mechanisms underlying Internet Gaming Disorder (IGD) resemble those of drug addiction. Functional Magnetic Resonance Imaging (fMRI) studies of the resting state and measures of gray matter volume have shown that Internet game playing was associated with changes to brain regions responsible for attention and control, impulse control, motor function, emotional regulation, sensory-motor coordination. Furthermore, Internet game playing was associated with lower white matter density in brain regions that are involved in decision-making, behavioral inhibition and emotional regulation. Videogame playing involved changes in reward inhibitory mechanisms and loss of control. Structural brain imaging studies showed alterations in the volume of the ventral striatum that is an important part of the brain's reward mechanisms. Finally, videogame playing was associated with dopamine release similar in magnitude to those of drugs of abuse and lower dopamine transporter and dopamine receptor D<sub>2</sub> occupancy indicating sub-sensitivity of dopamine reward mechanisms.

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#### 1. Introduction

Internet Gaming Disorder (IGD) involves excessive or poorly controlled preoccupations, urges or behaviors regarding computer and videogame play that lead to impairment or distress. There are three different models proposed for IGD: an impulse-control disor-

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http://dx.doi.org/10.1016/j.neubiorev.2017.01.040 0149-7634/© 2017 Elsevier Ltd. All rights reserved. der, an obsessive-compulsive disorder, and a behavioral addiction model (Grant et al., 2010). The behavioral addiction model argues that IGD shows the features of excessive use despite adverse consequences, withdrawal phenomena, and tolerance that characterize substance use disorders. In the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association, 2013), IGD is identified in Section III as a condition warranting more clinical research and experience before it might be considered for inclusion as a formal disorder (see (Weinstein et al., 2014; Weinstein and Aboujaoude, 2015) for review). The work group moved from a broad conceptualization (along the lines of problematic internet use) to a narrower one, focusing primarily on pathological online gaming and avoiding use of the term "addiction". Noteworthy, the DSM-5 does not offer sufficient guidance on how to approach individuals with suspected Internet-related psychopathology or how to design or interpret research studies into this topic. Instead, clinicians and researchers have to rely on proposed definitions, along with several screening and assessment instruments developed for problematic internet use and problematic video game use (Weinstein and Aboujaoude, 2015).

There is a debate whether IGD is the best clinical term for diagnosing Internet addiction. For example, Young (Young, 1998) considers online games a specific subtype of Internet activities, and she developed her Internet addiction criteria that were based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria for pathological gambling (American Psychiatric Association, 1994). Her theory states that online game addicts gradually lose control over their game play; that is, they are unable to decrease the amount of time spent playing while immersing themselves increasingly in this particular recreational activity and eventually develop problems in their real life (Young, 2009). Table 1 describes the proposed inclusion criteria for IGD

Surveys in the US and Europe have indicated prevalence rates of between 1.5% and 8.2%, of the country's population with varying diagnosis methods between countries (Durkee et al., 2012). Cross-sectional studies on samples of patients reported high comorbidity of IGD with psychiatric disorders, especially affective disorders, anxiety disorders and attention deficit hyperactivity disorder (ADHD) (Weinstein et al., 2014; Weinstein and Aboujaoude, 2015). Previous reviews have described brain-imaging studies in IGD until 2013 (Weinstein and Lejoyeux, 2015; Zhu et al., 2015; Kuss and Griffiths, 2012). In view of the rapid developments in brain research in IGD, this review will update these studies with new developments in brain imaging of IGD between 2013 and now. Secondly, it will analyze these findings in relation to the three models proposed for IGD namely behavioral addiction, impulse control disorder and obsessive-compulsive disorder in order to improve our clinical definition and diagnosis of this disorder. Finally, we will bring parallel evidence from brain imaging studies in pathological gambling which is now recognized as a behavioral addiction (American Psychiatric Association, 2013) and with compulsive sexual disorder.

A PubMed search was conducted using the search terms 'Internet addiction' 'Internet Gaming Disorder' and 'Pathological Internet use,' each of which was combined with each of the terms 'brain imaging,' or 'fMRI' or 'PET' or 'resting state' using the conjunction 'AND.' Each term was required to be present in the 'Title/Abstract' of the paper. The search was further restricted by 'English' as the publication language and Publication Date from 2008 to May 2016. The only studies that were selected for the review were original research papers that were published in peer-reviewed journals. The search has yielded eligible 52 studies including 16 studies of the resting state, 13 studies of functional connectivity, 18 activation studies and 5 studies of pharmacology. As a general caution, throughout this review, in making group comparisons, there are

#### Table 1

Internet gaming disorder criteria in the Diagnostic and Statistical Manual of Mental Disorders. (*DSM-5*) Internet Gaming Disorder Proposed Criteria.

Persistent and recurrent use of the Internet to engage in games, often with other players, leading to clinically significant Impairment or distress as indicated by five (or more) of the following in a month period: Preoccupation with Internet games. (The individual thinks about previous gaming activity or anticipates playing the next game; Internet gaming becomes a dominant activity in daily life). Note: This disorder is distinct from Internet gambling, which is included under gambling disorder. 2. Withdrawal symptoms when Internet gaming is taken away. (These symptoms are typically described as irritability, anxiety, or Sadness, but there are no physical signs of pharmacological withdrawal). 3. Tolerance-the need to spend increasing amounts of time engaged in Internet games 4. Unsuccessful attempts to control the participation in Internet games. 5. Loss of interests in previous hobbies and entertainment as a result of, and with the exception of, Internet games, 6. Continued excessive use of Internet games despite knowledge of psychosocial problems. 7. Has deceived family members, therapists, or others regarding the amount of Internet gaming. 8. Use of Internet games to escape or relieve a negative mood (e.g., feelings of helplessness, guilt, anxiety). 9. Has ieopardized or lost a significant relationship, job, or educational or career opportunity because of participation in Internet games. Note: Only non-gambling Internet games are included in this disorder. Use of the Internet for required activities in a business or profession is not included; nor is the disorder intended to include other recreational or social Internet use. Similarly, sexual Internet sites are excluded. Specify current severity: Internet gaming disorder can be mild, moderate, or severe depending on the degree of disruption of normal activities. Individuals with less severe Internet gaming disorder may exhibit fewer symptoms and less disruption of their lives. Those with severe

Internet gaming disorder will have more hours spent on the computer and more severe loss of relationships or career or school opportunities.

In Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5). 2013, American Psychiatric Association. pp. 795–796.

reported differences between IGD group and control groups but these differences do not imply a causal role of IGD. Group differences may reflect predisposing factors rather than decreases due to IGD.

## 1.1. Background- the neural mechanisms underlying reward and the effects of drugs of abuse

There is a vast body of pre-clinical evidence that the dopaminergic system mediates reward in general and the rewarding effects of drugs (Koob, 1992; Di Chiara and North, 1992; Wise, 1996; Di Chiara and Bassareo, 2007). The mesolimbic dopamine (DA) pathway that includes DA cells in ventral tegmental area projecting into nucleus accumbens seems to be crucial for drug reward (Wise, 2009). Other DA pathways such as the meso-striatal pathway includes DA cells in substantia nigra projecting into dorsal striatum and meso-cortical pathway includes DA cells in the ventral tegmental area projecting into frontal cortex are now also recognized as contributing to drug reward and addiction (Wise, 2009). The mode of DA cell firing also differently modulates the rewarding and conditioning effects, of drugs (predominantly phasic DA cell firing) compared with the changes in executive function that occur in addiction (predominantly tonic DA cell firing) (Wanat et al., 2009).

Brain imaging studies using Positron Emission Tomography (PET) in humans showed that the stimulant drugs cocaine and methylphenidate released dopamine in the striatum (Volkow et al., 1996a) and there is further evidence that the dopaminergic striatal-thalamic-orbitofrontal circuit mediates the rewarding effects of cocaine (Volkow et al., 1997a; Volkow et al., 1997b). Similarly,

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