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ATTENTION-DEFICIT DISORDER (R BUSSING, SECTION EDITOR)

Emerging Association Between Addictive Gaming and Attention-Deficit/Hyperactivity Disorder

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Abstract Children's and adolescent's use of computer games and videogames is becoming highly popular and has increased dramatically over the last decade. There is growing evidence of high prevalence of addiction to computer games and videogames among children, which is causing concern because of its harmful consequences. There is also emerging evidence of an association between computer game and videogame addiction and attention deficit/hyperactivity disorder (ADHD). This is indicated by the occurrence of gaming addiction as a co-morbid disorder of ADHD, common physiological and pharmacological mechanisms, and potential genetic association between the two disorders. A proper understanding of the psychological and neurotransmitter mechanisms underlying both disorders is important for appropriate diagnostic classification of both disorders. Furthermore, it is important for development of potential pharmacological treatment of both disorders. Relatively few studies have investigated the common mechanisms for both disorders. This paper reviews new findings, trends, and developments in the field. The paper is based on a literature search, in Medline and PUBMED, using the keywords *addictive gaming* and *ADHD*, of articles published between 2000 and 2012.

Keywords Addictive gaming · Attention-deficit/hyperactivity disorder · ADHD · Computer games and video games · Reward · Internet addiction · Problematic internet use

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Introduction

Children's and adolescent's use of computer games and videogames is becoming highly popular and has increased dramatically over the last decade. The amount of time children spend in the use of the internet, videogames, and media over the past decade has increased dramatically to an average of approximately three hours per day in the general population [1••]. There is growing evidence of high prevalence of computer game and videogame addiction among children, which is causing concern because of its harmful consequences [2••, 3••]. There is also emerging evidence of an association between computer game and videogame addiction and attention deficit/hyperactivity disorder (ADHD). Currently, it is not clear whether computer game and videogame playing meets criteria for a syndrome, e.g., DSM-IV or ICD-10 definition of a clinically significant pattern (consistent co-occurrence and time course) of behavioral and psychological signs and symptoms that cause distress or impairment. In 2007, the American Psychiatric Association reviewed whether or not video game addiction should be added to the DSM-V to be released in 2012. The conclusion was that there was insufficient evidence to include computer game addiction as a psychiatric disorder. (Note: internet use disorder is currently being recommended for further study (see http://www.dsm5.org/proposedrevision/Pages/proposedrevision.aspx?rid=573)).

The purpose of this review is to evaluate the literature on the relationship between addictive gaming and ADHD. Studies indicate ADHD is a risk factor for the duration of time children and adolescents play computer games and videogames. What are less understood are the physiological and neuropharmacological mechanisms that underlie both disorders which may shed light on diagnosis and treatment issues. The review will summarize what is already known on this topic. It will also describe new findings, trends, and developments in the field.

Diagnosis and Prevalence of Internet or Computer Game Dependency

Diagnostic assessment of internet or computer game dependency remains problematic. Different studies in different countries have used different scales to assess the prevalence of computer game addiction. A national Harris Poll survey of 1,178 US youths aged 8–18 years found that 8.5 % of computer gamers were pathological players according to standards established for pathological gambling [4]. Among 323 German children ranging in age from 11 to 14 years, 9.3 % (N=30) met criteria for dependency and pathological gaming using DSM-IV and ICD-10 criteria [5]. A second study of 7,069 computer-game players reported that 11.9 % met three of the diagnostic criteria for addiction [6]. Third, among 221 computer game players, 6.3 % have met the ICD-10 criterion of addiction [7]. A German national survey of 7,000 gamers found that 12 % met three of the criteria for internet addiction [6]. Results of a German nationwide survey of 44,610 male and female ninth-graders in 2007 and 2008 showed that 3 % of male and 0.3 % of female students were diagnosed as dependent on video games. Video game dependency (VGD) was accompanied by increased levels of psychological and social distress in the form of lower school achievement, increased truancy, reduced sleep time, limited leisure activity, and increased thoughts of committing suicide. In addition, it becomes evident that personal risk factors were crucial for VGD [8].

Among 2,327 Norwegian youth, 2.7 % (4.2 % of the boys, 1.1 % of the girls) fulfilled the criteria for pathological playing following a "Diagnostic Questionnaire for Internet Addiction of Young"; 9.8 % (14.5 % of the boys, 5 % of the girls) were considered to be engaging in "at risk playing" [9]. In the UK, a survey of 387 adolescents (12–16 years of age) found that 20 % were computer-dependent on a scale adapted from the DSM-III-R criteria for pathological gambling [10]. Finally, a survey of 3,975 Turkish undergraduate students found that the most preferred type of game was violent games; whereas preference for strategy and fantasy role-play games increased with age, preference for other games decreased [11].

Griffiths [12] has operationally defined addictive behavior as any behavior that features what he believes are the six core components of addiction (i.e., salience, mood modification, tolerance, withdrawal symptoms, conflict, and relapse). He further argued that videogame addiction fulfills the criterion of addiction by virtue of meeting these criteria. In his view, since many videogame users are excessive users and not addicts, videogame addiction may be a medium for satisfaction of arousal and reward (see the section on mechanisms of reward). In addition to the neuro-chemical basis of addiction there are accompanying behavioral markers of dependence in adolescents, for example stealing, truancy, not doing homework, irritability if unable to play, etc. Finally, single case studies have shown that videogame addiction was used to compensate for deficiencies in one's life in areas such as inter-personal relationships, physical appearance, disability, coping, etc. Griffith [13] argued that although there are some educational, social, and therapeutic benefits to videogames, taken in excess playing 24 hours a day 7 days a week could lead to addiction and, in some cases, to a gambling problem. Finally, Griffiths [14] concluded that adverse effects of videogame addiction are relatively minor and temporary. The effects can be resolved spontaneously with reduced frequency of play and they may affect only a small group of players.

Attention Deficit/Hyperactivity Disorder (ADHD)

ADHD is a complex disorder which has many causes, including genetic and environmental causes. ADHD is usually diagnosed in childhood, usually during play and school, and it is characterized by difficulties in concentration, short attention span, and psycho-motor restlessness [15, 16].

Blum et al. [17••] have reviewed the literature on ADHD and have suggested that some cortical regions associated with attention, impulse control, and stimulus integration abilities are not fully active in this disorder. People with ADHD suffer from stimuli overload; that is, they have heightened awareness of incoming stimuli, particularly sight, sound, and touch [18]. They are so bombarded by the normal stimuli in their environment that they cannot filter out the background noise, and have trouble focusing or concentrating on a problem or a task. Because of their inability to focus, those with ADHD have trouble completing what they start. They have difficulties with making plans and even more difficulty in carrying out plans in an orderly fashion.

ADHD as a Predictor of Internet and Videogame Addiction

Very little is known about factors associated with the outcome of internet and videogame addiction. A single prospective study followed over 2,000 adolescents for two years and investigated whether psychiatric symptoms could predict the development of internet addiction. ADHD was the most significant predictor for the development of internet addiction. Controlling for sex, hostility was the major predictor for internet addiction in males whereas ADHD was the major predictor for internet addiction in females [19•]. These findings are consistent with the results of previous cross-sectional studies looking at the association between internet addiction and ADHD [20–24].

Treatment of co-Morbid Internet and Videogame Addiction in ADHD

There is further evidence of an association between internet videogame addiction and ADHD stemming from a single treatment study. In this study methylphenidate (MPH) was administered to 62 Korean children diagnosed with ADHD and internet video game addiction [25•]. After eight weeks of treatment, measures of internet use scores and internet usage times were significantly reduced and these measures were positively correlated with the degree of improvement in attention. The authors suggest that internet video game playing might be a means of self-medication for ADHD children. In addition, they cautiously suggest that MPH might be evaluated as a potential treatment of internet addiction.

It is plausible that ADHD and internet or gaming addiction may share a bidirectional relationship whereby the symptoms of ADHD make playing computer games and videogames more attractive while gaming may exacerbate the symptoms of ADHD by reinforcing them, for example inattention, disinhibition, impulsive response, and craving for immediate reward (1). On the other hand playing videogames online with friends may improve attention, visual spatial skills, and working memory [26, 27] but this improvement does not necessarily apply to recreational video gamers with ADHD.

In summary, there is a growing body of evidence of an association between computer game and videogame addiction and ADHD. Although other psychiatric conditions, for example anxiety and depression may also be associated with gaming addiction it is ADHD which is the strongest predictor of this addiction. The following sections will describe possible psycho-biological mechanisms that may underlie both conditions.

Psychobiological Mechanisms Underlying Computer Game and Videogame Addiction and ADHD

Psychobiological Mechanisms Underlying Computer Game and Videogame Addiction

Three different mechanisms have been suggested as driving excessive computer gaming, although there have been very few psycho-physiological investigations of these putative underlying mechanisms. First, it has been suggested that computer games are inadequate means of coping with frustration, stress, and fears (25). Second, and consistent with the stress-coping mechanism, it has been suggested that in-game reinforcement and skill significantly affect a number of affective measures, most notably excitement, arousal and frustration [28]. Third, excessive computer game playing may be maintained by stimulatory effects on reward and sensitization [29], similar to the long-term changes in the brain reward circuitry believed to maintain substance dependence.

There is evidence supporting the hypothesis that computer game and videogame playing activates the dopamine reward circuitry in the brain. When participants with online game addiction were presented with gaming pictures and mosaic control pictures while undergoing functional magnetic resonance imaging (fMRI), activation of the brain's craving areas including the right orbito-frontal cortex, right nucleus accumbens, bilateral anterior cingulate and medial frontal cortex, right dorso-lateral prefrontal cortex, and right caudate nucleus were observed [30•]. Thus, the results suggest that the gaming urge/craving in online gaming addiction and craving in substance dependence might share a common neurobiological mechanism.

Although Griffith (1) has argued that computer game and videogame addiction fulfills the major criteria of addiction, namely salience, mood modification, tolerance, withdrawal symptoms, conflict, and relapse, his argument is based on single case studies. Currently, there are no psycho-physiological studies showing that computer game and videogame addiction result in sensitization, tolerance, and withdrawal, which are the highlight of addiction. Furthermore, although computer game and videogame play is highly addictive to some players there is little evidence suggesting that it results from a dysfunctional brain reward system. Third, there is no evidence for impulsivity or faulty decision making as indicated by performance in the gambling task or BART task [31].

Finally, there is little evidence for the role of genetic factors in video or computer game addiction. There is evidence linking internet addiction, high reward dependency, and polymorphism of the dopamine receptor D_2 Taq1A1 and catechol-*O*-methyltransferase (COMT) alleles. In particular, the DRD_2 Taq1A1 allele seems to be associated with reward dependence in excessive internet videogame-play adolescents [32•].

A subsequent Korean study [33] compared adolescents diagnosed with excessive internet use with healthy control subjects for genetic polymorphisms of the serotonin transporter gene and with respect to novelty seeking and harm avoidance on Cloninger's personality questionnaire (TPQ). They found that the excessive internet users had higher frequencies of the long-arm allele (SS-5HTTLPR), greater harm avoidance, and higher Beck depression inventory scores. SS-5HTTLPR frequency was closely related to harm avoidance in these excessive internet users. This study suggested that subjects with excessive internet use may have genetic and personality traits similar to those of depressed patients. It is plausible that there are two different types of internet-addicted individual, those who are addicted to videogames, who have high reward dependence and genetic predisposition for dopamine deficiency, and the general

population of internet-addicted individuals who are more prone to depression, harm avoidance, and deficient genetic serotonergic activity. The evidence for the use of computer game and videogame play for the purpose of stress relief and the resulting social isolation and depression merit genetic studies of serotonin in the particular group of computer game and videogame-addicted individuals.

Psychobiological Mechanisms Underlying ADHD

ADHD is also conceptualized as a condition that is associated with the brain's systems of reward and sensitization. There has been increased interest in ADHD as a heritable neuropsychiatric condition linked to pathogenesis of brain dopamine activity [34–36]. Blum et al. [17••] have suggested that ADHD is a subtype of a disorder known as reward deficiency syndrome (RDS). According to his theory, RDS refers to the breakdown of several neurotransmitters in the brain in which one reaction triggers another termed as the "reward cascade" [37] and resulting aberrant conduct [38]. The theory that is yet to be substantiated argues that reward deficiency may predispose individuals to addictive, impulsive, and compulsive behavior.

The brain's reward system involves interaction among brain neurotransmitters and associates craving behavior with the dopamine system, particularly the DRD_2 dopamine receptor gene [39]. Dopamine is a prevailing brain neurotransmitter that controls feelings of satisfaction and well-being [37, 38, 40]. Dopamine interacts with other neurotransmitters, for example serotonin and the opioids, which are related to the control of mood. Individuals with dopamine receptor D_2 gene abnormality have a reduced number of D_2 receptors in the brain. This results in lower dopaminergic activity in the brain's reward centers. These individuals tend to be involved in risky behavior, for example drug and alcohol abuse, extremely low-calorie diets, and high levels of stress [41]. These activities in turn increase dopamine activity in the brain. It is also shown that lower levels of dopamine activity result in aggressive behavior which stimulates the brain's dopamine activity [42, 43].

ADHD has been characterized as a disorder involving genes affecting dopamine, norepinephrine, serotonin, GABA, and other neurotransmitters [44]. Genetic variants of dopaminergic, noradrenergic and serotonergic genes are important to this disorder.

Brain Imaging Studies of Reward in Computer Game Playing

Chronic use of psycho-stimulants, for example cocaine and methamphetamine, results in long-term effects to the dopamine reward system. For example, compared with healthy subjects, detoxified cocaine-dependent subjects have reduced striatal D_2 receptor availability [45–47] and reduced drug-induced dopamine release [47, 48]. Playing a computer tank riding game was shown to release dopamine in vivo in the human brain comparable with the dopamine released as a response to pharmacological challenge with amphetamines [49]. Other behavioral models, for example monetary reward tasks [50] and non-hedonic food motivation [51] also released dopamine in brain meso-limbic reward centers.

Weinstein (2) described a brain-imaging study measuring dopamine release in the striatum by use of [^{I23}I] IBZM in single-photon computerized tomography (SPECT) during computer game playing by control subjects and former "ecstasy" users. Control subjects had a significant 10.5 % reduction in binding potential measure in the caudate after performance compared with their baseline measure, consistent with the results (13 %) reported by a previous study [49]. This is comparable to amounts of dopamine released by amphetamine [52] or methylphenidate [53, 54]. This finding implies that video game playing is capable of significant dopamine release that is comparable with the effects of psycho-stimulant drugs on the brain. It is plausible that individuals who are addicted to video-game playing derive much pleasure from playing these games because of extensive dopamine release during play. Weinstein (2) has also shown that, in contrast with healthy control subjects, former "ecstasy" users showed little change in D_2 binding potential in the caudate/putamen in response to videogame performance. This finding implies low brain dopamine response to natural reward, presumably because of previous sensitization to stimulant drugs that release a large amount of dopamine in their brain over time. It is speculated that individuals who are addicted to computer games and videogames would show tolerance to these games which would be indicated by lower dopamine release similar to ex-drug users. To our knowledge no studies have evaluated sensitization or tolerance to computer game or videogame-induced dopamine release in gaming addicts with or without ADHD.

Brain Imaging of Reward in ADHD

Neuroimaging studies, by SPECT, measuring the brain dopamine transporter (DAT) in ADHD patients revealed elevated striatal dopamine transporter [55, 56]. There is further evidence that striatal DAT availability was associated with response of ADHD patients to methylphenidate (MPH). Krause et al [57] found that ADHD individuals with low DAT availability failed to respond to MPH therapy. Another study by Volkow and colleagues [58] using [^{11}C]raclopride (D_2/D_3 receptor radioligand sensitive to competition with endogenous dopamine) in positron-emission tomography (PET) found reduced dopamine activity in specific brain

regions of adults with ADHD compared with control subjects. Deficiencies were seen at the level of both D_2 receptors and DA release in the caudate [58] and in the ventral striatum, the brain region involved with reward and motivation [59]. Consistent with this evidence, the depressed DA phenotype was associated with higher scores on self-report of methylphenidate liking [58]. Volkow and her colleagues [60] studied treatment-naive adults with ADHD after 12 months of clinical treatment with methylphenidate. Using [^{11}C] raclopride in PET and have found that dopamine enhancement in ventral striatum was associated with therapeutic response to methylphenidate, further corroborating the relevance of the dopamine reward/motivation circuitry in ADHD. Interestingly, if left untreated, individuals with ADHD are at high risk of substance abuse disorders [61]. The studies so far imply dopamine deficiency in the caudate and ventral striatum in ADHD which constitutes vulnerability for substance abuse disorders. It can be speculated that this dopamine deficiency might be also be high risk for computer games and videogames by virtue of their being highly stimulating and dopamine releasing in the brain.

A comparison of symptoms, behavioral response, genes, and treatment in ADHD and computer game and videogame addiction are listed in Table 1.

Limitations of the Literature on Internet and Videogame Playing

Despite the progress made in computer game and videogame addiction, there are currently no diagnostic instruments for internet and videogame addiction with adequate reliability and validity across cultures. A recent systematic analysis of different diagnostic instruments found that previous studies utilized inconsistent criteria to define internet addicts, applied recruiting methods that may cause serious sampling bias, and examined data using primarily exploratory rather than confirmatory data analysis techniques to investigate the degree of association rather than causal relationships among variables [62]. Thus, prevalence data on pathological internet use are limited by methodological difficulties concerning the diagnosis and the heterogeneity of diagnostic instruments. This makes it difficult to compare prevalence across countries. Second, treatment for internet addiction is based on intervention and strategies used in the treatment of substance use disorders. Psychosocial approaches are the mainstay of treatment, with very little study of pharmacological treatment. Because of the lack of methodologically adequate research, it is currently impossible to recommend any evidence-based treatment of internet addiction (3).

Table 1 ADHD and computer game and videogame addiction: comparison of symptoms, behavioral response, genes, and treatment

	ADHD	Computer game and videogame addiction
Symptoms	1) Inattention	1) Excessive play
	2) Hyperactivity	2) Social isolation [12]
	3) Impulsivity [15, 16]	
Behavioral response	To psycho-stimulants:	To videogames:
	Sensitization [63]	1) Sensitization?
	Tolerance?	2) Tolerance [12]
	Withdrawal?	3) Withdrawal [12]
		4) Craving/urges (30•)
		5) Reward dependence [42]
Genes	Dopamine: Dopamine Receptor $D_{1,2,4,5}$ Dopamine Transporter (DAT)	Dopamine: Dopamine Receptor D_2, catechol-*O*-methyltransferase (COMT) [42]
	Norepinephrine Alpha-2-adrenergic receptors 2A and 2C:(ADRA2A, ADRA2C)	Serotonin SERT: SS-5HTTLPR [43]
	Serotonin: 5-hydroxytryptamine (serotonin) receptor 1A (HTR1A) hydroxytryptamine (serotonin) receptor 1D alpha (HTR1DA), Serotonin Transporter (SERT)	
	GABA: gamma-aminobutyric acid (GABA) A receptor, beta 2GABRB2 (17••)	
Brain imaging	Elevated DAT density indicating striatal dopamine hypo-activity [55–59]	Activation of the craving circuit in the brain of computer-addicted individuals (30•)
Treatment	Norepinephrine and Dopamine stimulants	Norepinephrine and dopamine stimulants
	Methylphenidate [64]	Methylphenidate (25•)
	Amphetamine [65, 66]	
	Norepinephrine agents: α2-adrenergic agonists (clonidine, guanfacine) or atomoxetine [67–69]	

Conclusions

There is emerging evidence of an association between computer game and videogame addiction and ADHD. This is indicated by the occurrence of psychiatric co-morbidity between ADHD and gaming addiction. Both disorders seem to share a common mechanism of reward and sensitization which is mainly mediated by dopamine. Preliminary evidence seems to suggest that videogames activate the brain's dopamine reward system, resulting in significant dopamine release during exposure to videogame playing. This system is mainly controlled by brain dopamine neurotransmission but other neurotransmitters, for example serotonin, GABA, and glutamate, may play an important role in its regulation. There is further genetic evidence linking genes associated with dopamine release and turnover with internet and videogame addiction. Third, there is evidence suggesting that methylphenidate, a common stimulant treatment for ADHD, may be beneficial also for excessive internet and videogame players with ADHD. A proper understanding of the common psychological and neurotransmitter mechanisms underlying ADHD and computer game and videogame addiction is therefore important for appropriate diagnosis and pharmacological treatment of individuals with both conditions. Future studies should illuminate the psychobiological mechanisms for both conditions and explore new trends and developments in the diagnosis and treatment of both conditions.

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References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. •• Weiss MD, Baer S, Allan BA, Saran K, Schibuk H. The screens culture: impact on ADHD. ADHD Atten Def Hyp Disord. 2011;3:327–34. *This is an updated review regarding gaming addiction and ADHD.*
2. •• Weinstein A. Computer and video game addiction. Am J Drug Alc Abuse. 2010;36(5):268–76. *This is a comprehensive review on gaming addiction.*
3. •• Weinstein A, Lejoyeux M. Internet addiction or excessive internet use. Am J Drug Alc Abuse. 2010;36(5):277–83. *This is a comprehensive review on internet addiction.*
4. Harris Interactive Videogame Addiction 2007. http://www.harrisinteractive.com/news/allnewsbydate.asp?newsid=1196
5. Grusser SM, Thalemann R, Albrecht U, Thalemann CN. Excessive computer usage in adolescents–results of a psychometric evaluation. Wien Klin Wochenschr. 2005;117(5-6):188–95 [Article in German].
6. Grusser SM, Thalemann R, Griffiths MD. Excessive computer game playing: evidence for addiction and aggression? Cyberpsycho Behav. 2007;10(2):290–2.
7. Woelfling K, Thalemann R, Grusser SM. Computer game addiction: a psychopathological symptom complex in adolescence. Psychiat Prax. 2008;35(5):226–32 [Article in German].
8. Rehbein F, Kleimann M, Mößle T. Prevalence and risk factors of video game dependency in adolescence: results of a German nationwide survey. Cyberpsychol Behav Soc Netw. 2010;13(3):269–77.
9. Johansson A, Götestam KG. Problems with computer games without monetary reward: similarity to pathological gambling. Psychol Rep. 2005;95(2):641–50.
10. Griffiths MD, Hunt N. Dependence on computer games by adolescents. Psychol Rep. 1998;82(2):475–80.
11. Tahiroglu AY, Celik GG, Uzel M, Ozcan N, Avci A. Internet use among Turkish adolescents. Cyberpsychol Behav. 2008;11(5):537–43.
12. Griffiths MD. A "components" model of addiction within a biopsychosocial framework. J Sub Use. 2005;10:191–7.
13. Griffiths MD. Videogame addiction: further thoughts and observations. Int J Ment Health Addiction. 2008;6:182–5.
14. Griffiths MD. Videogame addiction: fact or fiction? In: Willoughby T, Wood E, editors. Children's Learning in a digital world. Oxford: Blackwell Publishing; 2007. p. 85–103.
15. APA. Diagnostic and statistical manual of mental disorders (DSM-IV). Washington, D.C: American Psychiatric Association; 1994.
16. APA. Diagnostic and statistical manual of the American Psychiatric Association. Washington, DC: American Psychiatric Association; 2000.
17. •• Blum K, Chen AL-C, Braverman EB, Comings DE, Chen TJH, Arcuri V, Blum SH, Downs BW, Waite RL, Notaro A, Lubar J, Williams L, Prihoda TJ, Palomo T, Berman MO. Attention-deficit-hyperactivity disorder and reward deficiency syndrome. Neuropsychiatr Dis Treat. 2008;4(5):893–918. *This is a highly relevant review on ADHD and reward.*
18. Miller D, Blum K. Overload: Attention deficit disorder and the addictive brain. Salt Lake City, Utah: Woodland Publishing Company; 2008.
19. • Ko CH, Yen JY, Chen CS, Yeh YC, Yen CF. Predictive values of psychiatric symptoms for internet addiction in adolescents: a 2 year prospective study. Arch Pediatr Adolesc Med. 2009;163(10):937–43. *This is the only prospective study on internet addiction.*
20. Chan PA, Rabinowitz T. A cross-sectional analysis of video games and attention deficit hyperactivity disorder symptoms in adolescents. Ann Gen Psychiatry. 2006;5:16.
21. Ha JH, Yoo HJ, Cho IH, Chin B, Shin D, Kim JH. Psychiatric comorbidity assessed in Korean children and adolescents who screen positive for internet addiction. J Clin Psychiatry. 2006;67(5):821–6.
22. Yen JY, Ko CH, Yen CF, Wu HY, Yang MJ. The comorbid psychiatric symptoms of internet addiction: attention deficit and hyperactivity disorder (ADHD), depression, social phobia, and hostility. J Adolesc Health. 2007;41(1):93–8.
23. Yen JY, Yen CF, Chen CS, Tang TC, Ko CH. The association between adult ADHD symptoms and internet addiction among college students: the gender difference. Cyberpsychol Behav. 2009;12(2):187–91.
24. Yoo HJ, Cho SC, Ha J, Yune SK, Kim SJ, Hwang J, Chung A, Sung YH, Lyoo IK. Attention deficit hyperactivity symptoms and internet addiction. Psychiatry Clin Neurosci. 2004;58(5):487–94.
25. • Han D, Lee Y, Na C, Ahn J, Chung U, Daniels M, Haws C, Renshaw P. The effect of methylphenidate on Internet video game play in children with attention-deficit/hyperactivity disorder. Compr Psychiatry. 2009;50(3):251–6. *This is the only pharmacologic study of internet and gaming addiction with ADHD.*

26. Green CS, Bavelier D. Action video game modifies visual selective attention. Nature. 2003;423:534–7.
27. Klingberg T, Fernell E, Olesen PJ, Johnson M, Gustafsson P, Dahlstrom K, Gillberg CG, Forssberg H, Westerberg H. Computerized training of working memory in children with ADHD a randomized, controlled trial. J Am Acad Child Adolesc Psychiatry. 2005;44(2):177–86.
28. Chumbley J, Griffiths M. Affect and the computer game player: the effect of gender, personality, and game reinforcement structure on affective responses to computer game-play. Cyberpsychol Behav. 2006;9(3):308–16.
29. Thalemann R, Wolfling K, Grusser SM. Specific cue reactivity on computer game-related cues in excessive gamers. Behav Neurosci. 2007;121(3):614–8.
30. • Ko CH, Liu GC, Hsiao S, Yen JY, Yang MJ, Lin WC, Yen CF, Chen CS. Brain activities associated with gaming urge of online gaming addiction. J Psychiatr Res. 2009;43(7):739–47. *This is a brain imaging study on gaming addiction.*
31. Ko CH, Hsiao S,, Liu GC, Yen JU, Yang MJ, Yen CF. The characteristics of decision making, potential to take risks, and personality of college students with Internet addiction. Psychiatry Res; 2010:121-125.
32. • Han DH, Young SL, Yang KC, Kim EY, Lyoo IK, Renshaw PF. Dopamine genes and reward dependence in adolescents with excessive internet video game play. J Addict Med. 2007;1(3):133–8. *This is a genetic study on internet and gaming addiction.*
33. • Lee Y, Han D, Yang K, Daniels M, Na C, Kee B, Renshaw P. Depression like characteristics of 5HTTLPR polymorphism and temperament in excessive internet users. J Affect Disord. 2009;109(1):165–9. *This is a genetic study on internet and gaming addiction.*
34. Shaw P, Gornick M, Lerch J, Addington A, Seal J, Greenstein D, Sharp W, Evans A, Giedd JN, Castellanos FX, Rapoport JL. Polymorphisms of the dopamine D4 receptor, clinical outcome, and cortical structure in attention-deficit/ hyperactivity disorder. Arch Gen Psychiatry. 2007;64:921–31.
35. Swanson JM, Kinsbourne M, Nigg J, Lanphear B, Stefanatos GA, Volkow N, Taylor E, Casey BJ, Castellanos FX, Wadhwa P. Etiologic subtypes of attention-deficit/hyperactivity disorder: brain imaging, molecular genetic and environmental factors and the dopamine hypothesis. Neuropsychol Rev. 2007;17:39–59.
36. Volkow ND, Wang GJ, Newcorn J, Telang F, Solanto MV, Fowler JS, Logan J, Ma Y, Schultz K, Pradhan K, Wong C, Swanson JM. Depressed dopamine activity in caudate and preliminary evidence of limbic involvement in adults with attention-deficit/hyperactivity disorder. Arch Gen Psychiatry. 2007;64:932–40.
37. Blum K, Kozlowski GP. Ethanol and Neuromodulator influences. A cascade model of reward. In: Ollat H, Parvez S, Parvez H, editors. Alcohol and behaviour: basic and clinical aspects progress in alcohol research. Utrecht, Netherlands: VSP; 1990.
38. Blum K, Cull JG, Braverman ER, Comings DE. Reward deficiency syndrome. Am Sci. 1996;84:132.
39. Blum K, Kozlowski GP. Ethanol and neuromodulator influences a cascade model of reward. In: Ollat H, Parvez S, Parvez H, editors. Alcohol and behaviour: basic and clinical aspects. Progress in alcohol research. Utrecht, Netherlands: VSP; 1990.
40. Blum K, Payne JE. Alcohol and the addictive brain: new hope for alcoholics from biogenetic research, vol. xiv. New York: Free Press; 1991. p. 320.
41. Faraone SV. Report from the 4th international meeting of the attention deficit hyperactivity disorder molecular genetics network. Am J Med Genet B Neuropsychiatr Genet. 2003;121:55–9.
42. Blum K, Sheridan PJ, Wood RC, Braverman ER, Chen TJ, Cull JG, Comings DE. The D2 dopamine receptor gene as a determinant of reward deficiency syndrome. J R Soc Med. 1996;89: 396–400.
43. Blum K, Braverman ER, Holder JM, Lubar JF, Monastra VJ, Miller D, Lubar JO, Chen TJ, Comings DE. Reward deficiency syndrome: a biogenetic model for the diagnosis and treatment of impulsive, addictive, and compulsive behaviors. J Psychoactive Drugs. 2000;32(Suppl i-iv):1–112.
44. Comings DE, Gade-Andavolu R, Gonzalez N, Wu S, Muhleman D, Blake H, Chiu F, Wang E, Farwell K, Darakjy S, Baker R, Dietz G, Saucier G, MacMurray JP. Multivariate analysis of associations of 42 genes in ADHD, ODD and conduct disorder. Clin Genet. 2000;58:31–40.
45. Volkow ND, Fowler JS, Wolf AP, Schlyer D, Shiue CY, Alpert R. Effects of chronic cocaine abuse on postsynaptic dopamine receptors. Am J Psychiatry. 1990;147:719–24.
46. Volkow ND, Fowler JS, Wang GJ, Hitzemann R, Logan J, Schyler DJ. Decreased dopamine D2 receptor availability is associated with reduced frontal metabolism in cocaine abusers. Synapse. 1993;14:169–77.
47. Volkow ND, Wang GJ, Fowler JS, Logan J, Gatley SJ, Hitzemann R. Decreased striatal dopaminergic responsiveness in detoxified cocaine-dependent subjects. Nature. 1997;386:830–3.
48. Martinez D, Broft A, Foltin RW, Slifstein M, Hwang D-R, Huang Y, Perez A, Frankel WG, Cooper T, Kleber HD, Fischman MW, Laruelle M. Cocaine dependence and D2 receptor availability in the functional subdivisions of the striatum: relationship with cocaine-seeking behavior. Neuropsychopharmacology. 2004;29:1190–202.
49. Koepp MJ, Gunn RN, Lawrence AD, Cunningham VJ, Dagher A, Jones T, Brooks DJ, Bench CJ, Grasby PM. Evidence for striatal dopamine release during a video game. Nature. 1998;393:266–8.
50. Zald DH, Boileau I, El-Dearedy W, Gunn R, McGlone F, Dichter GS, Dagher A. Dopamine transmission in the human striatum during monetary reward tasks. J Neuroscience. 2004;24 (17):4105–12.
51. Volkow ND, Wang G-J, Fowler JS, Logan J, Jayne M, Franchesi D, Wong C, Gatley SJ, Gifford AN, Ding Y-S, Pappas N. "Non-hedonic" Food Motivation in Humans Involves Dopamine in the Dorsal Striatum and Methylphenidate Amplifies This Effect. Synapse. 2002;44:175–80.
52. Farde L, Nordström AL, Wiesel FA, Pauli S, Halldin C, Sedvall G. Positron emission tomography analysis of central D1 and D2 dopamine receptor occupancy in patients treated with classical neuroleptics and clozapine. Arch Gen Psychiat. 1992;49:538–44.
53. Volkow ND, Wang GJ, Fowler JS, Logan J, Schlyer D, Hitzemann R, Lieberman J, Angrist B, Pappas N, MacGregor R, Burr G, Cooper T, Wolf AP. Imaging endogenous dopamine competition with [11 C] raclopride in the human brain. Synapse. 1994;16: 255–62.
54. Booij J, Korn P, Linszen DH, van Royen EA. Assessment of endogenous dopamine release by methylphenidate challenge using iodine-123 iodobenzamide single-photon emission tomography. Euro J Nuc Med. 1997;24(6):674–7.
55. Krause J, Dresel SH, Krause KH, la Fougere C, Ackenheil M. The dopamine transporter and neuroimaging in attention defi cit hyperactivity disorder. Neurosci Biobehav Rev. 2003;27:605–13.
56. Krause J, Krause KH, Dresel SH, la Fougere C, Ackenheil M. ADHD in adolescence and adulthood, with a special focus on the dopamine transporter and nicotine. Dialogues Clin Neurosci. 2006;8:29–36.
57. Krause J, la Fougere C, Krause KH, Ackenheil M, Dresel SH. Influence of striatal dopamine transporter availability on the response to methylphenidate in adult patients with ADHD. Europ Arch Psychiatry Clin Neurosci. 2005;255:428–31.
58. Volkow ND, Wang GJ, Newcorn J, Telang F, Solanto MV, Fowler JS, Logan J, Ma Y, Schulz K, Pradhan K, Wong C, Swanson JM. Depressed dopamine activity in caudate and preliminary evidence of limbic involvement in adults with attention-deficit/hyperactivity disorder. Arch Gen Psychiatry. 2007;64:932–40.

59. Volkow ND, Wang GJ, Newcorn J, Fowler JS, Telang F, Solanto MV, Logan J, Wong C, Ma Y, Swanson JM, Schulz K, Pradhan K. Brain dopamine transporter levels in treatment and drug naïve adults with ADHD. Neuroimage. 2007;34:1182–90.
60. Elkins IJ, McGue M, Lacono WG. Prospective effects of attention-deficit/hyperactivity disorder, conduct disorder, and sex on adolescent substance use and abuse. Arch Gen Psychiatry. 2007;64:1145–52.
61. Volkow ND, Wang J-J, Tomas D, Kollins SH, Newcorn JH, Teland FW, Fowler JS, Logan J, Wong CT, Swanson JM. Methylphenidate-elicited dopamine increases in ventral striatum are associated with long-term symptom improvement in adults with attention deficit hyperactivity disorder. J Neurosci. 2012;32(3):841–9.
62. Byun S, Ruffini C, Mills JE, Douglas AC, Niang M, Stepchenkova S, Lee SK, Loutfi J, Lee JK, Atallah M, Blanton M. Internet addiction: meta synthesis of 1996-2006 quantitative research. Cyberpsychol Behav. 2009;12(2):203–7.
63. Swanson J, Gupta S, Guinta D, Flynn D, Agler D, Lerner M, Williams L, Shoulson I, Wigal S. Acute tolerance to methylphenidate in the treatment of attention deficit hyperactivity disorder in children. Clin Pharmacol Ther. 1999;66:295–305.
64. Schachter HM, Pham B, King J, Langford S, Moher D. How efficacious and safe is short-acting methylphenidate for the treatment of attention-deficit disorder in children and adolescents? A meta-analysis. CMAJ. 2001;165(11):1475–88.
65. Gillberg C, Melander H, von Knorring A-L, Janols L-O, Thernlund G, Hägglöf B, Eidevall-Wallin L, Gustafsson P, Kopp S. Long-term stimulant treatment of children with attention-deficit hyperactivity disorder symptoms a randomized, double-blind, placebo-controlled trial. Arch Gen Psychiatry. 1997;54(9):857–64.
66. Biederman J, Boellner SW, Childress A, Lopez FA, Krishnan S, Zhang Y. LisdexamfetamineDimesylate and mixed amphetamine salts extended-release in childrenwith ADHD: a double-blind, placebo-controlled, crossover analog classroom study. Biol Psychiatry. 2007;62:970–6.
67. Perwien AR, Kratochvil CJ, Faries DE, Vaughan BS, Spencer T, Brown RT. Atomoxetine treatment in children and adolescents with attention-deficit hyperactivity disorder: what are the long-term health-related quality-of-life outcomes? J Child Adolesc Psychopharmacol. 2006;16:713–24.
68. Spencer T, Biederman J, Heiligenstein J, Wilens T, Faries D, Prince J, Faraone SV, Rea J, Witcher J, Zervas S. An open-label, dose ranging study of atomoxetine in children with attention deficit hyperactivity disorder. J Child Adolesc Psychopharmacol. 2001;11:251–65.
69. Spencer TJ, Faraone SV, Michelson D, Adler LA, Reimherr FW, Glatt SJ, Biedeman J. Atomoxetine and adult attention-deficit/hyperactivity disorder: the effects of comorbidity. J Clin Psychiatry. 2006;67:415–20.