

INFLUENCE OF DOPAMINERGIC SYSTEM ON INTERNET ADDICTION

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Internet addiction is a clinical anomaly with strong negative consequences on social, work-related, family, financial, and economic function of a person. It is regarded as a serious public health issue. The basic idea of this paper is to, based on the currently available body of research work on this topic, point out to neurobiological pathos of Internet addiction, and its connection to the dopaminergic system. Dopamine contains all physiological functions of neurotransmitters and it is a part of catecholamine family. Five dopaminergic receptors (D1 - D5) belong to the super family of receptors related to G-protein. Through these receptors, dopamine achieves its roles: regulation of voluntary movement, regulation of center of pleasure, hormonal regulation, and regulation of hypertension. In order to recognize an Internet user as an addict, he or she needs to comply with the criteria suggested by the American Psychiatric Association (APA). Phenomenological, neurobiological, and pharmacological data indicates similarities in pathopsychology of substance addiction and pathological gambling, which are indirectly related to the similarity with the Internet addiction. Responding to stimuli from the game, addicts have shown more brain activity in the nape region, left dorsolateral, prefrontal cortex, and left parahippocampal gyrus than in the control group. After the six-week bupropion therapy, desire to play Internet and video games, the total duration of playing, and induced brain activity in dorsolateral prefrontal cortex are lowered with the addicts. *Acta Medica Medianae* 2011;50(1):60-66.

Key words: Internet, addiction, dopaminergic system

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Introduction

Internet addiction is a contemporary problem which spreads more and more in the young population, but also in the work-able citizenry. Most people are not unaware of the seriousness and pathology of this type of addiction.

This is a clinical anomaly with strong negative consequences on social, work-related, family, financial, and economic function of a person (1).

It is regarded as a serious public health issue (2).

Internet addiction is the consequence of the attempt to escape reality, which is full of stress and problems that an individual faces on a daily basis.

Basic idea of this paper is to, based on the currently available body of research work on this topic, point out to neurobiological pathos of Internet addiction, and its connection to the dopaminergic system. This was partially observed through the analogy between Internet addiction

and pathological gambling. Furthermore, this is explored through the results of the research effort that focused on the bupropion influence on the patients diagnosed with Internet addiction.

From all available research work, guided with existing analogies and knowledge, it is possible to provide certain suggestions for further investigation of this complex and current psychopathological anomaly.

Epidemiology

It is not possible to talk exactly on the topic of this new psychopathological anomaly. This is since the Internet addiction is usually measured with the non-standardized, and, more often than not, arbitrary measuring devices, and sometimes on insufficient sample as well. This is a customary drawback of existing research on this topic.

If the focus is placed on the addiction of adolescents, who are particularly sensitive group for this type of disease, the results are found for most European countries. In Poland (3), on the 120-student sample, it was shown that every fourth individual suffers from Internet addiction. In Rome, Italy (4), on the 2,853-sample of high school students, where different addiction shapes were investigated, the prevalence of Internet addiction was 7%. Additional research in Italy (5) has shown on a 275-student sample that 5.4% of them have symptoms of addiction.

In Greece (6), the 2,200-student sample has shown the prevalence of Internet addiction in 8.2%. The most observed type of addiction is net gaming, which was established with 50.9% of addicts. 46.8% of addicts had symptoms of information saturation.

Three research efforts are especially significant in investigating the prevalence of Internet addiction among adolescent population. First one is from Germany (7), which indicates the prevalence of adolescent addiction of Internet usage and playing Internet games in 1.5-3.5% of the whole population.

The next research results were obtained in Vienna (8), and they indicate addiction among 12.3% of adolescents. This study has shown that the examinees with addiction symptoms have shown other psychosocial and psychopathological anomalies, such as social conflicts, maladaptive forms of behavior, focus anomalies, and school phobias.

Especially significant is the research effort by Lemon et al. in the Netherlands (9), which observed the development and validation scale for addiction estimates for playing Internet games among adolescents. This scale can be now treated as a validated testing instrument. This research was performed on two independent samples; one was on 644 youths aged 12 - 18 years; the other sample was of 573 youths of the same age group. Results indicate the prevalence of Internet gaming addiction of 9.3%.

Dopamine – Biosynthesis, Receptors, Dopaminergic Paths

Dopamine contains all physiological functions of neurotransmitters and it is a part of catecholamine family. It is synthesized from the tyrosine's amino acid. Tyrosine enters the neural ending via an active transport process, and, further on, it is exchanged to dihydroxyphenylalanin (DOPA) in the cytosol by the way of tyrosine hydroxylase. Further on, dopamine enters synaptic vesiculi by the way of active transport, where under the influence of dopamine-beta-decarboxylase it is transformed in noradrenaline.

After its influence on receptors, dopamine, as any other catecholamine noradrenaline, takes the surrounding cells to the neural endings where it is dissolved under the influence of monoaminooxidase (MOA) and catechol-O-methyltransferase (COMT) (10).

Medicament therapy with the goal of influencing the dopaminergic neurotransmission is used to deal with numerous psychiatric and neurological anomalies, including Parkinson's disease, schizophrenia, bipolar disorder, Huntington's disease, attention-deficit disorder and hyperactivity, and Tourette syndrome.

Five dopaminergic receptors (D1 - D5) belong to super family of receptors related to G-protein. Through these receptors, dopamine achieves its roles: regulation of voluntary movement, regulation of center of pleasure, hormonal regulation, and regulation of hypertension (11).

Two subtypes of D receptors (D1 and D5) activate adenylate cyclase. The other three types (D2 thru D4) inhibit adenylate cyclase and activate K⁺ channels (12).

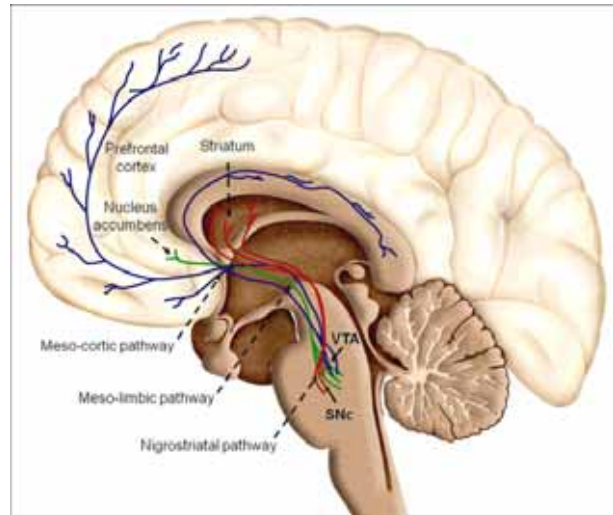


Figure 1. Dopaminergic pathways

Dopaminergic neurons are localized in the middle brain structures – substantia nigra (SNc) and ventral tegmental area (VTA). Their axons lead to striatum (nucleus caudatus, putamen and striatum ventralis with nucleus accumbens), of the dorsal and ventral prefrontal cortex. Additional brain structures that are the part of the center of the reward are the motoric field of the frontal lobe, and they are also parts of the temporal slice, globus pallidus and subthalamic nucleus of the basal ganglia and several others (13).

How to Classify Internet Addiction?

Experts are divided about this subtitle's question. This behavior would certainly not attract as much scientific interest and examination if, in and of itself, it does not carry the properties of dysfunctional behavior as well as the anomalies that include the deficiencies in impulse control. However, although it was not included in the official mental anomalies list of the European and American medical societies, this by no means indicates that the interest in Internet addiction have subsided. These efforts are undertaken to properly understand the anomaly and to improve the measures in how to subside its debilitating influence for the addict's psyche and social behavior (14). All this research helped to define a clear set of diagnostic criteria for the Internet addiction.

In order to recognize an Internet user as an addict, he or she needs to comply with the criteria suggested by the American Psychiatric Association (APA) (15). Conforming to this official recommendation, Internet addiction is defined as "maladaptive form of Internet usage which leads to clinically significant damages and which assumes the presence of at least three or more

criteria defined below, in the period of 12 months" (16).

1. Tolerance is defined two-fold:

- Need for more significant and continuous increase of time spent on the Internet, in order to achieve satisfaction, and
- Increasingly lowered effect of pleasure with continuous usage of the same amount of time spent on Internet.

2. Withdrawal, manifested in one of the two

ways:

- Properties of withdrawal syndrome: Attempt to cease and reduce Internet usage is complicated and prolonged, where two or more following symptoms are developed after several days of this property: psychomotoric agitation, anxiety, obsessive thoughts about Internet, fantasies and day dreaming about Internet, voluntary and involuntary finger movements, as is the case while typing. Symptoms of 1b cause stress and difficulties in social, professional, or some other significant sphere of every day life.
- Internet usage is related to the avoidance of withdrawal symptoms.

3. Internet is accessed more often and it is used longer than planned.

4. There is a constant desire or unsuccessful attempt to cease or lower the amount of time spent on Internet.

5. Large amount of time when the individual is not on Internet is spent by performing activities related to Internet.

6. Important social, professional, and recreational activities are neglected and reduced to the maximum due to Internet usage.

7. Internet is used despite the awareness of continual physical, social, professional or psychological problems, which are caused with excessive Internet usage (insomnia, marital issues, late arrivals to work, neglecting professional obligations, feeling of abandonment by others, etc).

8. Fatigue or nervousness due to the attempts to lower or cease Internet usage.

9. Internet is used as a type of escape from every day problems and feelings such as helplessness, guilt, anxiety, and depression.

10. Internet user hides the truth about the amount of usage from their family members.

11. The user continuously returns to Internet despite the exorbitant costs of the excessive Internet usage (online shopping etc.).

Internet usage is a psychophysical anomaly which includes the occurrence of tolerance, which is the phenomenon that the same amount of Internet usage over time becomes incapable to satisfy the user, who, in order to obtain the same amount of satisfaction as before, has to increase the Internet usage. This anomaly also entails the occurrence of the withdrawal symptoms (tremor, anxiety, moodiness etc. when this person is not using the Internet), affective disturbances (depression and irritability), and skewed social relations, such as the loss and devastation of any quantity and quality in communication with the

environment. If this definition of Internet addiction is now compared to the more well-known definitions of drug and alcohol addictions, it is clear that there are almost no differences in these two terms, other than impossibility of the intake of a detrimental substance in an addict's organism in the case of the Internet addiction. The fact that no detrimental substance can be taken by an addict lead many scientists to doubt the mere notion of Internet abuse as addiction in the formal sense (14).

It is more and more understood that the basis of the addictive behavior is represented in an anomaly of the center of gratification. This center is regarded as a controller of all motivationally driven activity, such as food intake, education of the youth, sex. Detrimental to the normal functioning of a human being, basic instincts can pale if challenged in front of the addiction, whether this is about the behavioral or substance addiction (17).

Subtypes of Internet Addiction (18)

Generalized Internet addiction is not as common and it includes a multidimensional, excessive usage of Internet service and content, commonly without a specific goal of this usage. This form is mostly related to the social interaction such as chatting, instant messaging, forums and discussion groups, and general addiction for the computer and Internet, such as online surfing, search engine usages based on hobbies etc. However, it is more common that people grow addicted to the specific online content and activities rather than general Internet usage.

There is no consensus with regards to the exact number of assumptions of the subtypes of Internet abuse. However, four or five types are most commonly defined, and, in his work, Hinić accentuates concept 6+1 subtypes:

1. Cyber-Relational Addiction
2. Cybersexual Addiction
3. Information Overload
4. Net Gaming
5. Compulsive Online Shopping
6. Computer and IT Addiction
7. Mixed type of addiction

Etiology of Internet Addiction

There are different explanations with regards to the factors that represent potential culprits of the pathological Internet usage.

Behavioral approach (18) is based on the instrumentalist school of thought and the law of affect and it maintains that the behavioral pattern that brings awards is strengthened in the characteristic behavior of every being. "Awards" offered by Internet are many. This false security offered by Internet makes socially anxious and phobic persons prime target to become Internet addicts.

Bio-medicinal approach assumes the existence of the so-called addictive types of personalities in which the changes in functioning of specific hereditary and congenital factors lead to specific imbalance of chemical compounds and neurotransmitters (19). It is thought that this may be one of the reasons why some people exhibit extremely high feelings during the process of drug abuse. This is applicable to Internet since there are many similar, entertaining activities on it, which are, in turn, similar to the activities listed above (18).

Psychodynamic approach (18) generally considers that the source of most anomalies or psychological problems lies in early childhood and traumatic experiences from early periods of life.

Cognitive-behavioral model assumes that specific dysfunctional assurances are sufficient to produce the symptom set associated with this dysfunction (20). One of often cited examples are cognitive dysfunctional assurances about oneself that entail the lack of self-confidence, self-criticism etc. Verbal formulations of these assurances, applied on Internet, would be in the following form: "I am a nobody offline, but somebody online? (21)"

Personalized approach (18) observes an individual on the Internet through idiosyncratic personality model, and the attention is drawn to the individual characteristics and experience.

Socio-culturological approach (18) takes into account that Internet is addictive since it is a social phenomenon with amplified sociological properties.

Psycho-pathological approach (18) indicates the psychopathological background of this phenomenon. An individual with specific problems in social interactions, or with pre-existing psychological problems and anomalies, tries to compensate the symptoms of abandonment, unhappiness or some other concrete, dysfunctional model of behavior with their virtual relations and elevated consumption of online content.

Neurobiological research with the goal of invention of neurological basis or pathways can be used to establish the causal connections. Researches into various aspects of internet addiction, along with the fields of genetics and neurobiology, also assisted in obtaining more information on this topic.

- Recently, genetic polymorphism of the transporter gene of serotonin (5HTTLPR) has been found in people that abuse the Internet (22). However, since this polymorphism is gathered with multitude of other different psychiatric conditions such as moodiness, anxiety disorders, alcoholism, nicotine addiction, this finding needs corroboration in well-controlled population.

- Voxel-based morphometry (VBM) Zoy et al. (23) came up with interesting results. Specifically, brain gray matter density was compared between the control group comprised of 18 healthy adolescents and clinical group of 18 adolescents with the Internet addiction diagnosis. It was shown that the GMD was significantly lower in the clinical group specifically in the region of the frontal left

cingular cortex, back left cingular cortex, the left insula, and the left gyrus lingual. GMD-deficient regions in addicts were conceptually connected with the regions responsible for emotional behavior modulation. Even though the histological change that yields this diagnosis is not completely understood, some studies suggest the histopathological correlation between the size of this deficiency that involves the loss of synaptical contacts, enlarged neuron density, and decrease in glial cells and glial markers (24). As it is shown in other studies, Internet-addicted adolescents more often than not have more emotional problems in behavior or they suffer from emotional problems (25-29). More recently, the insula was pointed out as the region with a key role in addiction. Many studies have shown that the inter-insular activity is in correlation with the impulse control level of an individual under examination (30-33). The fact that the cingular gyrus is a key part of the limbic system means that it participates in the control of emotions, behavior, motivation, and other emotional states (34).

From all the above said, it is clear that none of the theories is sufficient to describe the Internet addiction completely, but that some combination of the above is needed to explain the anomaly in a specific individual (35).

Analogy between pathological gambling and Internet addiction

Considering the nature of pathological gambling – insufficient impulse control that excludes the need of toxic substances – the researchers who work on the analysis of this phenomenon established that the phenomenon of the pathological gambling is the closest and the most similar form of that of the addiction. This means that criteria that refer to this form of addiction are applicable when one is analyzing Internet addiction as well.

Pathological gambling has a tendency to be combined with the broad spectrum of other anomalies, and it is ostensibly related to the higher rate of suicidal behavior as well. For most gamblers, this is a form of entertainment, but, for many persons, this activity brings with itself a wide variety of consequences on their family and their profession. Personal and social financial consequences are very serious, and many persons with this anomaly end up in courts of law due to this addiction. Understanding of the neurobiology of pathological gambling is slowly surfacing. Serotonin is related to the behavioral initiative and the inhibition loss, which are important at the start of the gambling cycle and with difficulties in stopping such a behavioral pattern. Norepinephrin is related to excitement and risk taking in the individuals that have the pathological gambling disease. Dopamine is related to positive and negative awards, depending on the component of this anomaly (36).

Phenomenological, neurobiological and pharmacological data indicates similarities in patho-

psychology of substance addiction and pathological gambling, which are indirectly related to the similarity with the Internet addiction (37).

Neuropharmacological mechanisms which were used to try to explain the addiction mechanisms indicate that all medical drugs as instruments of addiction, such as opioids, nicotine, amphetamine, cocaine, alcohol and others, increase the emission of dopamine in mesolimbic pathways.

Following this analogy, it is interesting to note the data obtain by many American researchers. Specifically, they came to conclusion that pathological gambling looks like the addiction of psychostimulus in many different ways. They contribute evidence that these similarities go well beyond the generic overlap of pathological gambling and substance addiction, as an anomaly class. More specifically, the whole range of evidence is submitted to corroborate that there exists a parallel and dominant role of dopamine in pathophysiology and the symptom profile between the two pathologies. Not wanting to stray away to far from the basic idea of this paper, I would mention only one result from these studies. Cocaine, amphetamine, and nicotine increase dopamine exertion in the brain, which is the neurotransmitter that affects behavior, our reactions and sensibilities towards satisfaction and pain. The more dopamine in the brain, the more happier we are.

Chaloperiodol was used in this research effort. It is an antagonist of the D2 receptor. The difference in its effect was followed between pathological gamblers and the control group. An oral dose of 3mg was chosen based on previous evidence that is well-received in a human organism and that it can be expected that it takes approximately 65-70% of the D2 receptor in physically healthy subjects.

Findings in pathological gamblers in this study were clear and convergent. Chaloperiodol treatment consistently increased the subjective feeling of satisfaction with the slot machine effects, such as pleasure and excitement. This treatment also enlarged a posteriori playing desire for gambling and the observation of gambling lingo while reading a specific passage, as well as the gambling-induced elevated systolic blood pressure. Contrary to this exhibited behavior, the control group that was comprised of non-gamblers was not specifically affected by chaloperiodol treatment, except the post playing elevated blood pressure.

It is conceivable that the dissociation between the physiological activation and the increased influence of the games in the two groups observed represents the difference in the desired level of physiological excitement in pathological gamblers in comparison to the control subjects that are not gamblers (38).

This phenomenon was proven in the experiments with animals. That is, the chaloperiodol treatment has shown the increased basal excretion of dopamine in the cortex and striatum of rats (39).

Bupropion Therapy of Internet Addicts

Bupropion is used to cure nicotine addiction today, i.e. as the assistance to smokers during their weaning from cigarettes. It is almost equally as efficient as nicotine substitution therapy, even with non-depressive patients, since it has far less unwanted effects than other therapies. In Serbia, it is registered as Ziban.

The mechanism by which bupropion helps patients to quit smoking is unknown. However, it is assumed that this favorable action is mediated by noradrenergic and dopaminergic mechanisms. Since the mediation most likely consists of both mechanisms, caution is needed when the therapy is prescribed to a specific patient (40).

In the research (41), the bupropion effect on Internet addicts was investigated. Bupropion was used in the therapy due to its low dopamine inhibition and reabsorption of noradrenalin, and since it has minimal effect on overtaking of indolamine (serotonin) and no effect on MOA. It was assumed that continuous bupropion therapy of six weeks in length would influence the decrease of the desire to play Internet games. Eleven subjects that meet the criteria of Internet addiction and play Starcraft more than 30 hours a week were juxtaposed with eight healthy control examinees that had experience in playing Starcraft less than three days a week for less than one hour per day. At the beginning and the end of the six-week long bupropion therapy, brain activity as a reaction to Starcraft presentation was estimated using functional magnetic resonance of the amplitude of 1.5T. On top of that, depression symptoms, desire to play, and the severity of the Internet addiction was estimated using the Beck Scale for depression and Young's scale for Internet addiction. Responding to stimuli from the game, addicts have shown more brain activity in the nape region, left dorsolateral, prefrontal cortex, and left parachipocampal gyrus than in the control group. After the six-week bupropion therapy and desires to play Internet and video games, the total duration of playing and induced brain activity in dorsolateral prefrontal cortex are lowered with the addicts.

This suggests that bupropion therapy can alter the desire and brain activity in the ways similar to the ones observed with substance addictions or the ones that have substance abuse issues.

At the end, it is important to mention that every computer user is faced to the electromagnetic field radiation effects. The number of research efforts that deals with this problem is not small, neither in Serbia (42) nor around the world (43) and the results show that the effects of this radiation should arouse concern.

Conclusion

Revision Council DSM-IV decided that Internet Addiction will not be defined in DSM-V

(whose completion is expected by 2012). This is due to the insufficient number of research efforts. However, this defect will be included in the addendum of the practitioner's book with the goal of stimulating additional studies. Certainly, one of the guidelines in this matter should be the need for more research which will better explain the issue at hand.

Future research should focus on establishing the co-morbidity, i.e. psychopathological defects that follow the Internet addiction.

Furthermore, it may be needed to repeat the research related to the efficiency of the bupropion therapy for curing the Internet addiction in the manner to include larger

population and establish whether the observed correlation can be repeated.

The role of the opioid system in formation of the neurobiological basis for Internet addiction should certainly be investigated further.

In the end, it would be necessary to perform one larger examination of how prevalent the Internet addiction is in the adolescent subjects.

The topic for further research can also be genetic examination of the addicts and the following of possible gene mutations that predominantly synthesize D receptors, but also other receptors which are connected with neurotransmitters, and to observe potential anomalies in these mutations as well.

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UTICAJ DOPAMINERGIČKOG SISTEMA NA ZAVISNOST OD INTERNETA

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Zavisnost od Interneta je klinički poremećaj sa snažnim negativnim posledicama na socijalno, radno, porodično, finansijsko i ekonomsko funkcionisanje ličnosti. Smatra se ozbiljnim javnim zdravstvenim problemom. Osnovna ideja ovog rada je da na osnovu do sada u svetu sprovedenih istraživanja ukaže na neurobiološku osnovu zavisnosti od interneta, pre svega njenu povezanost sa dopaminergičkim sistemom. Dopamin poseduje sve fiziološke funkcije neurotransmitera i pripada kateholaminima. Dopaminergički receptori, kojih ima pet (D1, D2, D3, D4, i D5), pripadaju superfamiliji receptora vezanih za G-protein. Preko ovih receptora dopamin ostvaruje svoje uloge: u regulaciji voljnog kretanja, regulaciji centra za zadovoljstvo, hormonalnoj regulaciji, regulaciji hipertenzije (11).

Da bi korisnik Interneta bio okarakterisan i prepoznat kao zavisnik, mora da zadovolji kriterijume predložene od strane Američkog udruženja psihijatarata (APA).

Fenomenološki, neurobiološki i farmakološki podaci ukazuju na sličnosti u patopsihologiji zavisnosti od supstanci i patološkog kockanja, a time indirektno i na sličnosti sa samom zavisnošću od Interneta.

U odgovoru na nadražaje od strane igre, zavisnici su pokazali veću moždanu aktivnost u potiljačnom režnju, levom dorzolateralnom prefrontalnom korteksu i levom parahipokampalnom girusu nego kod kontrolne grupe. Nakon 6 nedelja terapije bupropionom, žudnja za igranjem internet i video igara, ukupno vreme igranja i indukovana aktivnost mozga u dorzolateralnom prefrontalnom korteksu su smanjeni kod zavisnika. *Acta Medica Medianae* 2011;50(1):60-66.

Ključne reči: internet, zavisnost, dopaminergički sistem