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*MINIREVIEWS*

# Neurobiological risk factors for problematic social media use as a specific form of Internet addiction: A narrative review

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## Abstract

Problematic social media use (PSMU) is a behavioral addiction, a specific form of problematic Internet use associated with the uncontrolled use of social networks. It is typical mostly for modern adolescents and young adults, which are the first generations fully grown up in the era of total digitalization of society. The modern biopsychosocial model of the formation of behavioral addictions, postulating the impact of a large number of biological, psychological, and social factors on addictive behavior formation, may be quite applicable to PSMU. In this narrative review, we discussed neurobiological risk factors for Internet addiction with a focus on current evidence on the association between PSMU and structural/functional characteristics of the brain and autonomic nervous system, neurochemical correlations, and genetic features. A review of the literature shows that the vast majority of the mentioned neurobiological studies were focused on computer games addiction and generalized Internet addiction (without taking into account the consumed content). Even though a certain number of neuroimaging studies have been conducted for PSMU, there is practically no research on neuropeptide and genetic associations for PSMU to date. This fact points to the extremely high relevance of such studies.

**Key Words:** Internet addiction; Problematic social media use; Addictive behavior physiopathology; Neurobiology; Genetics

**Core Tip:** The analysis of sources showed that the vast majority of neurobiological research was focused on the study of computer games addiction and generalized Internet addiction (without taking into account the content consumed). There is practically no research on neuropeptide and genetic associations for problematic social media use to date. This fact points to the extremely high relevance of such studies.

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## INTRODUCTION

The last few decades have been characterised by the complete digitalization of society and the ubiquitous penetration of Internet technologies into our daily lives[1,2]. The advantages associated with the widespread introduction of Internet technologies into people's daily lives are undeniable (for example, quick access to a large amount of information and various services, rapid dissemination of news on a global scale, the introduction of Internet technologies related to health, *etc*.). However, a certain number of Internet users, mainly adolescents and young adults, experience the phenomenon of Internet addiction or "problematic/compulsive use of the Internet" which is associated with several psychosocial problems[2,3]. The global concern about the impact of problematic Internet use (PIU) from the public and social health points of view became especially acute during the coronavirus disease (COVID) pandemic when each person had to use the Internet more often, and initially, predisposed individuals were losing control, showed more and more signs of pathological addictive behavior when diving into the network[4]. In particular, this trend has affected the most technologically advanced segments of society – the first generations who grew up surrounded by the Internet and gadgets – adolescents and young adults[5]. The situation can be significantly aggravated by the neurophysiological consequences of the pandemic, predisposing to the development of depression and anxiety, which are important risk factors of problematic social media use (PSMU)[6].

The modern "component bio-psychosocial model" of behavioral addiction formation postulates an individual combination of genetic/biological, psychological, social, and cultural factors leading, in the case of PSMU, to overuse of social media and negative consequences (Figure 1).

In this narrative review, we shall discuss neurobiological risk factors for Internet addiction with a focus on current evidence on the association between PSMU and structural/functional characteristics of the brain and autonomic nervous system, neurochemical correlations, and genetic features.

To find relevant publications, a search was conducted in PubMed, Scopus, Web of Science, and Reference Citation Analysis (https://www.referencecitationanalysis.com) for English-language sources using the following keywords and MeSH terms: "Internet addiction", "problematic social media use", "pathological social network use", "social media", "social networking", "specific Internet addiction", "video game addiction", "gaming disorder", "neurobiology", "behavior, addictive/physiopathology", "brain/physiopathology", "sympathetic nervous system", "parasympathetic nervous system", "neural pathways/physiopathology", "neurotransmitters", "biochemical correlates", "twin study", "genetics", "gene frequency", "genetic predisposition to disease", "polymorphism, single nucleotide".

## TERMINOLOGY

The phenomenon of Internet addiction[7,8] was first described in the mid-1990s. There is currently no accepted formal definition of addictive online behaviour. Specialized literature offers such interchangeable terms as "problematic interactive media use"[9], "problematic Internet use", "pathological Internet use", "compulsive Internet use", and, finally, "Internet addiction". The European Network for Problematic Usage of the Internet (European research group) recommended in a recent review (2022) to use the term "problematic Internet use", as the most appropriate at this moment[4].

All of the above are umbrella terms, *i.e.*, reflect generalized (without reference to specific content and technology) PIU. Among the specific types of Internet activity, the following can be considered potentially addictive: Problematic video game use, PSMU, problematic Internet pornography use, Internet gambling, and web surfing addiction[10,11].

Only one of these five addictive behavior types, namely the problematic use of video games, is currently officially considered a mental disorder (Internet gaming disorder, diagnostic and statistical manual of mental disorders, fifth edition, American Psychiatric Association, 2013; gaming disorder, international classification of diseases-11, 2019). Recently, other specific forms of PIU have also been singled out: Online gambling disorder (it also includes intensive betting on online exchanges), online

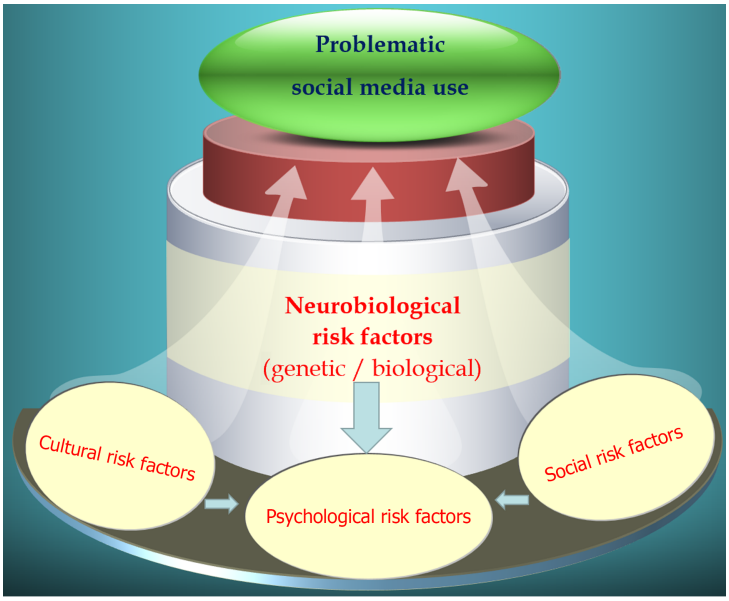


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**Figure 1 Component bio-psychosocial model of problematic social media use.**

buying-shopping disorder, Internet streaming disorder, cyberchondria, cyberbullying, and digital hoarding[4].

PSMU is a behavioral addiction, a specific form of PIU associated with the uncontrolled use of social networks. It is typical mostly for modern adolescents and young adults, which are the first generations fully grown up in the era of total digitalization of society. There are currently no universally recognized and official criteria for the diagnosis of PSMU. The European Network for Problematic Usage of the Internet (European research group) suggests the following definition[4]: PSMU is a persistent state of control loss when using social networks, manifested by: Violation of control over interaction with social websites (for example, in terms of time, frequency, and duration of use); predominance of time spent on social networks over other life interests and activities; negative consequences, *i.e.*, the use of social networks leads to significant distress or deterioration in personal, family, social, educational, professional activities, or other important areas of functioning; continued or increased use of social networks, despite the negative consequences (for example, poor school performance, negative impact on health, social isolation, interpersonal conflicts, neglect of duties); duration, *i.e.*, the use of social networks can be continuous or episodic and repetitive but manifests itself over a long period (at least 12 mo).

Although the criteria for the diagnosis of PSMU are not formally established, the existing validation methods using questionnaires are based on the interpolation of classical symptoms for chemical and non-chemical types of addictive behavior[12]. Currently, there is a consensus on diagnostic criteria that clearly distinguish the pathological component of addiction from the normal daily use of the Internet by adolescents: The clinical diagnosis of PSMU, as well as generalized Internet addiction, should include six obvious signs[11,13,14]: Salience and mood modification, such as behavioral, cognitive, and emotional preoccupation: The growing importance of a social network for an adolescent in his or her system of interests and values; the use of a social network leads to a positive change in the emotional state; Compulsivity and loss of control: An obsessive desire to use the social network, impulsivity, loss of time control, excessive use of the social network (especially while reducing the allocated time for other activities); Tolerance: The need to spend more and more time communicating on a social network, including to alleviate episodes of dysphoria; Withdrawal/abstinence symptoms: Mood changes in the absence of access to a social network (depression, anxiety, aggressiveness); Conflict, impaired role performance: Loss of previous interests and entertainment, loss of educational, cultural, sports, and other opportunities as a result of excessive use of social networks; disputes and lies regarding the use of the social network; continued use of social networks, despite the negative consequences. Relapse: Rapid return to the use of the network after abstinence, unsuccessful independent attempts to control the use of the social network.

However, PSMU must be distinguished from intensive adaptive use of social networks. Adaptive intensive use of social networks itself does not have obvious negative consequences, has little effect on the parameters of well-being, and in many individual cases can play a positive role in the development of an adolescent by increasing a "social capital"[15-17].

## PREVALENCE

The latest summarized data show that the average prevalence of PSMU among adolescents in 29 European countries is 7.4%[18]. The recent systematic review by Cheng *et al*[19] showed a high ethnic and geographic heterogeneity of PSMU prevalence within 5%–26%. The highest levels of PSMU prevalence are registered in collectivist societies in Asia and Africa[19]. Recent cross-national analysis of the psychometric characteristics from the social media disorder scale (SMDS) questionnaire among adolescents from 44 countries has shown high levels of validity and reliability (comparative fit index and Tucker–Lewis index = 0.963 and 0.951, root mean square error of approximation = 0.057)[20]. SMDS is recommended by the research group European Network for Problematic Usage of the Internet as preferred, since it evaluates primarily the psychopathological aspects of addiction, while the recently criticized Bergen social media addiction scale questionnaire does not clearly distinguish between simple excessive or prolonged use of social networks from pathological one, with signs of addiction[4]. The prevalence figures obtained by the authors of the SMDS were 7.3%-11.6% for the Dutch adolescent cohort[21]. Other studies using the SMDS have found similar results: 9.9%-10.0% in a Dutch sample in a longitudinal study[22], 9.4% in a representative sample of 3408 Finnish adolescents[23], and 8.0% in a large sample of Russian adolescents ($n$ = 4514)[24].

## PSYCHIATRIC AND SOMATIC COMORBIDITY

A large number of foreign studies have convincingly shown the pronounced comorbidity of Internet addiction with a wide range of psychopathological conditions. Depressive disorder and attention deficit hyperactivity disorder have the strongest association with Internet addiction, while anxiety disorder, obsessive-compulsive disorder; social phobia, and suicidal behavior also have a smaller but significant association[25-28]. A recent meta-analysis by Shannon *et al*[12] has shown that PSMU, as a specific form of Internet addiction, also reveals a moderate, but statistically significant, association with depression, anxiety, and stress[12]. Another recent meta-analysis demonstrated a significant but weak negative association of PSMU with life satisfaction and self-esteem (as parameters of well-being) and a moderate positive association with depression and loneliness (as indicators of distress)[29].

At present, not much is known about the association of Internet addiction with psychosomatic diseases, although such a connection is highly likely, given the presence of common pathogenesis factors (anxiety-depressive and obsessive-compulsive disorders). The study by Wei *et al*[30] based on an Internet survey demonstrated the association of Internet addiction with chronic pain syndromes, which the authors link with psychosomatic diseases and muscle overstrain. The study conducted by Cerutti *et al*[31] did not reveal a statistically significant association between Internet addiction and tension headache/migraine, although, in general, somatic symptoms were more often reported in the Internet addiction group[31]. In addition, it was discovered that PIU among adolescents was associated with chronic conditions, back pain, overweight, musculoskeletal pain, and also with sleep disorders[32,33]. According to a recent systematic review, a wide range of somatic health problems are associated with smartphone addiction among adults[34]. A general decrease in immune functions was observed in Internet-addictive individuals, which the authors link with a common risk factor, *i.e.*, stress, which can affect the activity of the sympathoadrenal axis and increase cortisol production[35]. It is characteristic that the high activity in the sympathetic part of the autonomic nervous system was detected when analyzing the heart rate of adolescents with Internet addiction[36,37]. A decrease in the quality of life, including the parameters of somatic health, was demonstrated in a systematic review by Masaeli and Billieux[38]. A pronounced connection between Internet addiction with the general level of somatization was revealed among young adults[39].

## PATHOGENESIS OF INTERNET ADDICTION FROM A NEUROBIOLOGY POINT OF VIEW

To date, several etiopathogenetic models of the formation of Internet-dependent behavior among adolescents and young adults have been proposed[40]. Some researchers suggest the presence of mainly neurobiological risk factors linked with the lack of maturity in certain parts of the adolescent brain, which is manifested by insufficient effectiveness of volitional control, high impulsivity, and an overly activated brain reward circuitry[41,42]. However, the most recognized by researchers at present is the "component biopsychosocial model", which assumes a combination of psychosocial problems and neurobiological risk factors[40,43-45].

Middle and late stages of adolescence in brain development are characterized by different time frames of the formation of the limbic system and prefrontal cortex lobes[46]. The prolonged development of the prefrontal cortex in comparison with the limbic system during adolescence leads to weakened inhibition from cortex lobes concerning underlying subcortical structures and increased impulsivity, which contributes to a high risk of addictive behavior[47].

To date, a large number of studies have been devoted to the pathogenesis of Internet addiction using various neuroimaging techniques, including magnetic resonance imaging, positron and single photon emission computed emission tomography. These techniques have revealed a number of structural brain changes associated with Internet addiction[48-50]: Dcreased grey matter density in several areas, including prefrontal and orbitofrontal cortical layers and an additional motor area[51]; abnormal functional activity of brain regions associated with reward dependence[41]; activation of sensorimotor synchrony with a concomitant decrease in audiovisual synchrony[52]; activation of brain regions associated with compulsive craving and impulsivity; increased glucose metabolism in brain regions associated with impulsivity, reward dependence and the urge to repeat sensations[53]; increased dopamine secretion with a concomitant decrease in dopamine receptor availability in the striatum[54]. Meta-analysis of 40 neurophysiological studies of PIU has shown that, regardless of the content, Internet-dependent behavior is characterized by a significant violation of inhibitory control, stop-signal task, decision-making, and working memory[55]. The meta-analysis by Zhang *et al*[56] has revealed the presence of a common pattern in a brain structural change related to chemical and behavioral addictions: Changes in prefrontal and insula areas associated with increased impulsivity[56]. Several meta-analyses and reviews have been published recently: Structural and functional brain alterations for a specific form of PIU – computer games addiction[57-59]. The features of electroencephalography in Internet addiction were analyzed in a recent review by Sharifat and Suppiah[60]. Distinctive characteristics of functional electroencephalography were revealed among patients with computer game addiction[61].

It should be noted that most of the above-mentioned studies have been conducted for cases of computer games addiction or generalized (undifferentiated by the content consumed) Internet addiction. The recently proposed for various types of behavioral addictions updated interaction of person-affect-cognition-execution (I-PACE) model theoretically substantiates the neurobiological mechanism of addictive behavior, which consists in an imbalance between structures of frontostriatal circuits (limbic/reward-oriented brain circuits and prefrontal control)[62]. The model has been intensively studied for gambling and gaming disorders, but not for PSMU. Despite this, a line of structural and functional neuroimaging findings concerning the I-PACE model for PSMU was published to date[63-68]. Neuroimaging studies for PSMU were analyzed by Wegmann *et al*[69]; a conclusion was made about the significant association of PSMU with reward processing and reinforcement learning. A recent study by Sadeghi *et al*[70] has revealed that email addiction positively correlates with depression and gray matter volume of the left rostrolateral prefrontal cortex closely involved in cognitive processes[70].

There is some evidence of autonomic nervous system dysfunction involvement in the pathogenesis of Internet addiction, in particular, by the imbalance of the sympathetic and parasympathetic divisions[71, 72]. A general decrease in immune functions was revealed among Internet-addictive individuals. The authors link this fact with a common risk factor, *i.e.* stress, which can affect the activity of the sympathoadrenal axis and increase cortisol production[35]. The role of chronic stress in the formation of PSMU has been shown by several studies[12,73,74]. It is characteristic that the high activity of the autonomic nervous system's sympathetic part was observed when analyzing the heart rate of adolescents with Internet addiction[36,37]. Data on the level of cortisol for Internet addiction are contradictory[75-77]; additional research is required, in particular, concerning the long-term cortisol content, which can be a good marker of chronic stress and mental problems[78].

Several neurotransmitters and neurotrophic factors may be involved in the neurobiological mechanisms of Internet addiction formation[79-81]. Neurochemical pathways include metabolic disorders of dopamine, serotonin, opioids, and some other neurotransmitters that affect reward processing, executive functioning, salience attribution, and habit formation, as well as in the case of substance-use disorders[82]. The participation of these neurotransmitters is partially confirmed by the effectiveness of some pharmacological agents controlling the corresponding neurochemical pathways [83,84]. Exercise-based interventions also may be efficient for Internet addiction (including PSMU)[85], by regulating the autonomic nervous system, the morphology of some parts in the central nervous system, and the exchange of neurotrophic factors and neurotransmitters, in particular dopamine[72].

Oxytocin, which is called the hormone of trust, social connection, and emotional attachment, is promising for the PSMU study. It plays an extremely important role in establishing emotional social contacts, including those using social networks[80,86]. Bonassi *et al*[87] showed that a low level of parental care was associated with low activity on Instagram for carriers of the A-allele in the polymorphic region rs2254298 for the oxytocin receptor gene[87]. The same group of researchers identified a greater number of followers among carriers of the A/A genotype in the region rs53576 for the oxytocin receptor gene in comparison with carriers of the G-allele[88].

A significant number of studies show a pathophysiological relationship between the functioning of the oxytocinergic system and the formation of various forms of addictive behavior[89]. The effectiveness of exogenous oxytocin in the treatment of various addiction types has been shown both in experimental animal studies[90] and in a whole series of clinical studies[89]. It is assumed that the relief of physical symptoms and an increase in emotional tone during withdrawal, reduction of anxiety, increased susceptibility to verbal interventions, facilitating the restoration of social contacts, and, finally, the physiological reduction of established tolerance are the main mechanisms of oxytocin therapeutic

impact for chemical addictions. The hypothesis of oxytocin's antistress effect as a possible protective factor seems convincing since psychological stress is an important etiological cause of the development of pathological addictions[91].

The following are promising neurotransmitters and neurotrophic factors in addition to oxytocin, whose role in the pathogenesis of addictive Internet behavior in adolescents is also highly probable, but still insufficiently studied:

Melanocortin (α-Melanocyte-stimulating hormone). An important role of melanocortin in the development of pathological addiction is suggested by recent studies by Orellana *et al*[92]. There was a tendency to increase melatonin levels in the presence of computer games addiction[93];

Neurotensin. It is actively involved in the modulation of dopamine signalling and the formation of pathological addictions, attempts have been made to treat some addictions with synthetic neurotensin [94];

Orexin. It is supposed to be involved in the formation of sleep disorders and addictive behavior[95]. Choi *et al*[93] demonstrated an increase of orexin in the plasma of adolescents with Internet gaming disorder a while ago[93];

Substance P (neurokinin A). Impairment in the production of substance P is thought to be associated with the development of various pathological addictions; active attempts are currently being made to treat addiction by modulating the activity of neurokinin receptors[96,97];

Brain-derived neurotrophic factor (BDNF). This is a neurotrophic factor that plays a role in the development of addiction[98,99]. Data on the association of BDNF expression with Internet-addictive behavior are contradictory. Some authors found elevated plasma levels among addicts, the others did not confirm such an association[72,81]. A recent study by Choi *et al*[93], which has been mentioned above, found no direct link between addiction and BDNF levels, although it revealed a negative correlation with the time spent playing a computer game[93].

Glial cell line-derived neurotrophic factor (GDNF). It is a neurotrophic factor that plays an important role in supporting the function of dopaminergic neurons. A decrease in the level of GDNF in plasma was detected among Internet gaming addicts; besides, the expression of BDNF was negatively correlated with the severity of computer games addiction[100].

It is important to note that the vast majority of studies on neuropeptides and neurotrophic factors have been conducted for computer game addiction, as in the case of neuroimaging and neurophysiological research methods.

## GENETICS OF INTERNET ADDICTION

Unlike other types of addictive behavior (for example, substance abuse or gambling), a very small number of studies have been devoted to the search for genetic predictors of Internet addiction. In the first twin study (2014) the authors managed to prove the presence of an innate component based on the results of a survey of 825 adolescents from the Chinese population. The component was estimated at 58%–66%[101]. Similar results were obtained a little later in the study of Turkish (19%–86%, 2014[102]) Dutch (48%, 2016[103]), Australian (41%, 2016[104]), and German (21%–44%, 2017[105]) twin cohorts. Positive genetic correlations (20%–40%, 2012) were also discovered in the study of various mobile phone use patterns by twins[106]. Although these data are limited by the volume of samples and various ethnic and geographic conditions, there is likely a tendency for a greater contribution of genetic factors in males.

Thus, the presence of a genetic component in Internet addiction formation has been convincingly shown by twin studies by the example of different populations, but no specific genes involved in the mechanisms of such heritability have been identified. Small pilot studies, however, verified polymorphic regions of nine candidate genes, the following are among those:

r1800497 [dopamine D2 receptor gene (*DRD2*), Taq1 A1 allele] and rs4680 [methionine variant of dopamine degradation enzyme catecholamine-o-methyltransferase gene (*COMT*)] – the first of such studies (2006–2007) conducted among adolescents in South Korea and showed an association between minor alleles connected with low dopamine production (rs4680) and a low number of dopamine receptors in the prefrontal cortex (rs1800497) with the presence of pathological Internet gaming disorder [107]. At the same time, *DRD2* A2 allele (high-activity) homozygotes and A1 allele (low-activity) carriers demonstrated no significant differences concerning Internet addiction; neither differences were revealed when comparing *COMT* high-activity (H) variant homozygotes and low-activity (L) variant carriers [108]. Later, the association of the C allele carrier rs1800497 (*DRD2* gene) with computer games addiction was confirmed for young adults[109]. Another study did not prove such a fact[110]. It is known that the *DRD2* gene is in linkage disequilibrium with the *ANKK1* gene, which plays a significant role in the formation of chemical addictions[111]. Therefore, by now, it is not possible to accurately establish the association of Internet addiction with the reception of dopamine at the DRD2 level[45]. The association of the homozygous variant Val/Val (GG) rs4680 (Val158Met, *COMT* gene) with addiction to computer games was further confirmed by the study by Yen *et al*[112] in 2022; In addition, a recent study by Kim *et al*[113] showed that the presence of interpersonal stress for *DRD2* rs6277 T allele and

rs1800497 Taq1 A1 allele showed higher scale values of computer games addiction[113].

rs6277 (promoter of the *DRD2* gene, *141C Ins/Del* polymorphism) – although a direct association between rs6277 polymorphism and Internet addiction has not been established, the *-141C* polymorphism may play a role in the pathogenesis of addiction as a mediator of temperament characteristics[110]; the dopamine D4 receptor gene (*DRD4* gene, VNTR polymorphism in exon 3) – as it was shown, the carriers of *DRD4* 4R/4R variants are more predisposed to the formation of generalized Internet addiction[108]. More recent studies have not shown an association with Internet-addictive behavior[114,115];

rs25531 (serotonin transporter gene (*SS-5HTTLPR*), short allelic variants) – the research by Lee *et al*[116] demonstrated that short allelic variants of the serotonin transporter gene might be associated with Internet addiction. Similar data were later obtained by Sun *et al*[108] but for men only[108]. As a large number of studies have shown, these genetic variants are also linked to a predisposition to depression, which is the most frequently detected comorbid condition among Internet-addictive individuals. Recent studies revealed that a link between depression and autistic personality traits with generalized Internet addiction could be modulated by such polymorphism (*5-HTTLPR*/rs25531), as well as ethnic and geographic factors[115,117].

rs1044396 [nicotinic acetylcholine receptor subunit alpha 4 gene (*CHRNA4*)] – study by Montag *et al*[118] revealed an association between Internet addiction and the rs1044396 CC genotype, which can also be associated with nicotine addiction and attention disorders. Later, Jeong *et al*[119] conducted a pilot study of the target exome, involving 30 adults with addiction to computer games and 30 healthy individuals, which included a study of 72 candidate genes. This study showed a statistically convincing association with one site only – rs1044396. No such association was found in another study[114];

rs2229910 [neurotrophic tyrosine kinase receptor type 3 gene (*NTRK3*)]– Kim *et al*[120] have conducted in turn a pilot study of the target exome involving 30 adults with addiction to computer games and 30 healthy individuals, which included a study of 83 polymorphic sites. Their study also revealed a statistically convincing association with one site only – rs2229910, presumably also associated with anxiety-panic, depressive disorders, obsessive-compulsive disorder, and psychologically determined eating disorders;

rs28364027 [Corticotropin Releasing Hormone Receptor 1 gene (*CRHR1*)] – a study involving Korean adolescent boys revealed that carriers of the AA genotype and the A allele were more predisposed to online computer games addiction[114]. It was previously determined that corticotropin-releasing hormone was involved in the mechanisms of negative effects realization when weaning from the addiction factor[121] and was associated with the risk of alcohol dependence for adolescents, especially when combined with stressful effects[122-124];

rs1137070 [monoamine oxidase-A gene (*MAOA*), EcoRV polymorphism] – the association of this polymorphism with an addiction to computer games with a mediator effect of hostility was evaluated for young adults. Participants with the TT rs1137070 genotype had a higher odds ratio of 2.52 (1.37-4.64) for gambling addiction compared with carriers of the C allele[125];

rs2268498 [oxytocin receptor gene (*OXTR*)] – it has been shown that male carriers of the TT genotype (but not female) have lower levels of generalized Internet addiction compared to C allele carriers[126];

rs6265 (*BDNF* gene) – Russian researchers discovered in 2019–2020 that genetic polymorphism of *BDNF* rs6265 (Val66Met), as well as the abovementioned *DRD4* exon 3 VNTR and *NTRK3* rs2229910, are were with the risk of generalized Internet addiction for young adults[127].

The latest (2022) review by Werling and Grünblatt[128] and the data presented in this article demonstrate that all currently known studies of genetic associations have been conducted for computer games addiction or (less often) for generalized Internet addiction. As far as is known, not a single study of genetic associations concerning PSMU has been published.

## DISCUSSION

Neurobiology and genetics research on Internet-addictive behavior conducted over the last 10–15 years has allowed accumulating the necessary amount of knowledge to make certain intermediate conclusions, summarized recently in a significant number of meta-analyses and reviews. A large number of neuroimaging and neurophysiological studies have shown that Internet addiction is characterized by certain structural and functional features of the brain, accompanied by a significant violation of inhibitory control (increased impulsivity as a common factor in various forms of addictive behavior), stop-signal task, decision-making, and working memory. It has been discovered that, like other types of chemical and behavioral addictions, Internet addiction is characterized by an impairment of the metabolism of dopamine, serotonin, opioids, and some other neurotransmitters, which affects reward processing, executive functioning, salience attribution, and habit formation. A small number of pilot projects partially confirm the genetic basis of Internet addiction pathogenesis, previously demonstrated by twin studies.

An important aspect and trend in modern research on Internet-addictive behavior is an attempt to avoid the study of generalized, undifferentiated Internet addiction in favor of analyzing its specific

forms, such as computer games addiction and PSMU[24,129,130]. At the same time, the vast majority of the mentioned neurobiological studies were focused on computer games addiction (*e.g.* 85% of patients for functional magnetic resonance imaging[131]) and generalized Internet addiction (without taking into account the consumed content). Even though a certain number of neuroimaging studies have been conducted for PSMU[66,67,69], there is practically no research on neuropeptide and genetic associations for PSMU to date. Attempts to use neuroimaging to look for common neurobiological mechanisms between PSMU and other addictions have so far produced conflicting results, at least in relation to the prefrontal cortex[66,67,132-134].

Although studies of generalized Internet addiction – especially for women – can be partially extrapolated to PSMU (taking into account common gender and psychosocial characteristics for some populations[24]), it is extremely important to study the directly verified PSMU, which differs significantly from computer games addiction. Further research is needed to better identify commonalities and differences in the neurobiology of different types of addictive online behavior in the context of the content consumed, the devices and technologies used, and the stability of symptoms across age. The study of neuropeptides directly involved in social bonding: Oxytocin and vasopressin, as well as orexin, melatonin, and neurotrophic factors (BDNF and GDNF), looks promising for PSMU neuromolecular associations.

Genetic studies conducted on small samples, conflicting and still quite scarce, should also be expanded to specific forms of Internet addiction, such as PSMU and smartphone addiction. Replication studies with a large number of participants are urgently needed, as well as genome-wide association and polygenic risk score estimate projects.

## CONCLUSION

In this narrative review, we discussed neurobiological risk factors for Internet addiction with a focus on current evidence on the association between PSMU and structural/functional characteristics of the brain and autonomic nervous system, neurochemical correlations, and genetic features. A review of the literature shows that the vast majority of the mentioned neurobiological studies were focused on computer games addiction and generalized Internet addiction (without taking into account the consumed content). Even though a certain number of neuroimaging studies have been conducted for PSMU, there is practically no research on neuropeptide and genetic associations for PSMU to date. This fact points to the extremely high relevance of such studies.

## FOOTNOTES

**Author contributions:** Tereshchenko SY analyzed the data and wrote the manuscript.

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