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Original article

# Internet addiction disorder and comorbidities in children and adolescents

## Trastorno de adicción a Internet y comorbilidades en niños y adolescentes

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**ABSTRACT**

**Introduction:** Internet addiction disorder (IAD) is characterized by an individual's inability to control his/her Internet use, which may result in marked distress and functional impairment. Systematic reviews show that excessive screen-time is negatively associated with well-being and positively associated with reduced quality of life in young people. There is growing evidence that IAD is related to comorbidities such as depression but relatively little is known about fatigue in adolescents with IAD. **Material and methods:** We studied 94 participants with IAD and 88 controls, all aged 12-17 years. Depression was assessed by the Beck depression inventory scale (BDI-II, Georgian version), and fatigue by the pediatric quality of life initiative (PEDS QL, Georgian version) multidimensional fatigue scale. **Results:** Adolescents with severe IAD are 5.63 times more likely to show symptoms of moderate or severe depression than children with mild or moderate Internet addiction. Those with severe IAD showed 6.62 times more cognitive fatigue, 7.81 times higher sleep/rest fatigue and 11.11 times higher general fatigue than children with mild and moderate Internet addiction. **Conclusions:** IAD can lead to depression and fatigue, which can affect adolescents' psychological and social well-being. Mechanisms for prevention and ongoing support are needed for adolescents and their families. Further research is needed to clarify the relationship between IAD and depression, that is, does Internet addiction lead to depression or is depression itself a risk factor for IAD? A further limitation is that IAD was treated as one entity rather than two distinct types (generalized and specific IAD).

**Keywords:** Internet addiction disorder, fatigue, depression, prefrontal cortex, adolescents.

***RESUMEN***

***Introducción:*** *El trastorno de adicción a Internet (TAI) se caracteriza por la incapacidad de un individuo para controlar su uso de Internet, lo que puede dar lugar a un marcado malestar y a un deterioro funcional. Las revisiones sistemáticas muestran que el exceso de tiempo frente a la pantalla se asocia negativamente con el bienestar y positivamente con la reducción de la calidad de vida en los jóvenes. Cada vez hay más pruebas de que el TAI está relacionado con comorbilidades como la depresión, pero se sabe relativamente poco sobre la fatiga en los adolescentes con TAI.* ***Material y métodos:*** *Se estudiaron 94 participantes con TAI y 88 controles, todos ellos de 12 a 17 años de edad. La depresión se evaluó con la escala del inventario de depresión de Beck (BDI-II, versión georgiana), y la fatiga con la escala de fatiga multidimensional de la iniciativa de calidad de vida pediátrica (PEDS QL, versión georgiana).* ***Resultados:*** *Los adolescentes con TAI grave tienen 5.63 veces más probabilidades de mostrar síntomas de depresión moderada o grave que los niños con adicción a Internet leve o moderada. Los niños con adicción grave a Internet mostraron 6.62 veces más fatiga cognitiva, 7.81 veces más fatiga de sueño/descanso y 11.11 veces más fatiga general que los niños con adicción leve y moderada a Internet.* ***Conclusiones:*** *El TAI puede provocar depresión y fatiga, lo que puede afectar al bienestar psicológico y social de los adolescentes. Se necesitan mecanismos de prevención y apoyo continuo para los adolescentes y sus familias. Se necesitan más investigaciones para aclarar la relación entre el TAI y la depresión, es decir, ¿la adicción a Internet conduce a la depresión o la depresión en sí misma es un factor de riesgo para el TAI? Otra limitación es que el TAI se trató como una sola entidad en lugar de dos tipos distintos (TAI generalizado y específico).*

***Palabras clave:*** *Trastorno de adicción a Internet, fatiga, depresión, corteza prefrontal, adolescentes.*

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## INTRODUCTION

Internet addiction disorder (IAD), also called problematic or pathological Internet use, is characterized by an individual's inability to control his or her use of the Internet, which may eventually result in marked distress and functional impairment of general life, such as academic performance, social interaction, occupational interest and behavioral problems.[1] Some researchers and mental health practitioners see excessive Internet use as a symptom of another disorder, such as anxiety or depression, rather than a separate entity.[2] IAD could be considered an impulse control disorder (not otherwise specified). However, there is a growing consensus that this constellation of symptoms is an addiction.[3] The American Society of Addiction Medicine (ASAM) recently released a new definition of addiction and classified it as a chronic brain disorder, officially proposing for the first time that addiction is not limited to substance use.[4] All addictions, whether chemical or behavioral, share certain characteristics, including salience, compulsive use (loss of control), mood modification and the alleviation of distress, tolerance and withdrawal, and continuation despite negative consequences.

According to the DSM-V, IAD is a compulsive-impulsive spectrum disorder that involves online and/or offline computer usage[5,6] and consists of at least three subtypes: excessive gaming, sexual preoccupations and e-mail/text messaging.[7] All of the variants share the following four components: 1) excessive use, often associated with a loss of sense of time or a neglect of basic drives; 2) withdrawal, including feelings of anger, tension, and/or depression when the computer is inaccessible; 3) tolerance, including the need for better computer equipment, more software or more hours of use; and 4) negative repercussions, including arguments, lying, poor achievement, social isolation and fatigue.[8]

The cause of IAD is unknown, although a known risk factor for IAD is a family history of Internet gambling.[9] Furthermore, a strong association was found between parental depression and IAD in their children, which means that IAD is not an individual matter of young people but a family problem.[10] Familial risk for Internet gambling is due to both shared environmental and genetic transmission. Genetic factors in aggregate appear to account for 50% of the risk. The specific genes that account for the aggregate genetic risk have not yet been identified, but it seems likely that many genes are implicated in the pathogenesis of IAD, including the dopamine D2 receptor gene. In addition, the so-called serotonin transporter polymorphism 5-HTTLPR could also play a role.[11]

Liu et al.[12] found differences in functional magnetic resonance images (fMRI) between people with and without addictions in brain regions such as the prefrontal cortex (PFC), orbitofrontal gyrus (OFG), striatum, cerebellum, brainstem, right cingulate gyrus, bilateral parahippocampus, right frontal lobe, left superior frontal gyrus, left precuneus, right postcentral gyrus, right middle occipital gyrus, right inferior temporal gyrus, left superior temporal gyrus and middle temporal gyrus – all of which are involved in the development of IAD.[12] Zhou et al.[13] found that adolescents with IAD had lower gray matter density (GMD) in the left anterior cingulate cortex, left posterior cingulate cortex, left insula and left lingual gyrus. Thus, participants with IAD had multiple structural changes in the brain, and such changes correlated significantly with the duration of their Internet addiction.[14]

There is growing literature that computer and Internet usage could have a positive effect on children's self-esteem, socialization and improvement in reaction time.[15] It is important to understand the negative impact of IAD on children's psychological well-being. Systematic reviews have concluded that excessive screen-time is negatively associated with well-being and positively associated with ill-being in young people.[16-18] There is growing evidence that IAD is related to elevated levels of comorbidities affecting relational, academic, familial and occupational activities, and depression could be considered one of the most common comorbidities among them.[19-22] Depression is ranked as one of the world's most burdensome diseases according to the World Health Organization.[23] It is indisputable that depression is related to IAD, but there is a lack of evidence regarding whether there is a strong correlation between the severity of IAD and the rate of depression.[24] There is no doubt that IAD affects many domains of psychological well-being, but no study has assessed the relationship between IAD and fatigue, which seems to be one of the main persisting comorbidities of children and adolescents with IAD.

Emerging evidence suggests that fatigue is a central component of the cognitive and clinical characteristics of stress-related exhaustion disorder considering IAD among them. Fatigue is a multidimensional phenomenon with physical, emotional, behavioral and cognitive components.[25] Although there is growing evidence regarding the mechanism and prevalence of fatigue in different neurological conditions, less is known about it in participants with various disorders related to exhaustion, including IAD. Thus, fatigue, including general fatigue, sleep/rest and cognitive fatigue, may be of special importance in children with excessive Internet use.[26] According to Krabbe et al.,[27] patients with exhaustion complain about mental tiredness during and after cognitive testing together with impaired performance in tasks involving executive functioning and complex attention. Another concern is the condition of clinical burnout, where patients reveal not only cognitive deficits but also impaired performance

on cognitive tests, as the process seems to be effortful and fatiguing for them.[28] Patients with burnout demonstrate excessive fatigue and effort while performing attentional tasks leading to impaired task performance.[29] Thus, it is known that exhaustion can lead to fatigue, including general fatigue, sleep/rest and cognitive fatigue, but there is no evidence regarding the occurrence of fatigue during IAD and the underlying mechanisms. We aimed to describe depression and fatigue in adolescents diagnosed with IAD.

## MATERIAL AND METHODS

**Participants.** In total, 182 children aged 12 to 17 years old were included: 105 boys and 76 girls.

**Procedures.** IAD was diagnosed by the Georgian version of the Young test,[30] a reliable and valid measure consisting of 20 items. Participants with scores less than 20 were considered as nonfrequent Internet users and were identified as controls. Those with scores from 20-49 were considered to have mild IAD; those with scores from 50-79 points were considered to have moderate IAS, and those with scores from 80–100 points were considered to have severe IAD.

Signs reported as main complaints of participants were depression and fatigue. Depression was assessed by the Georgian version of the Beck depression inventory scale (BDI-II) designed for individuals aged 13 and over. Each answer was scored on a scale of 0 to 3. Scores of 0-13 represent minimal depression, 14-19 indicate mild depression, 20-28 represent moderate depression, and 29-63 represent severe depression. Complaints presented as depression signs were divided into two components: affective components and physical or somatic components. Affective components contain 14 items: 1) sadness, 2) past failure, 3) loss of pleasure, 4) guilt, 5) punishment feeling, 6) self-dislike, 7) self-criticism, 8) suicidal thoughts, 9) crying, 10) agitation, 11) loss of interest, 12) indecisiveness, 13) worthlessness, and 14) irritability. The somatic part contains five items: 1) energy, 2) sleep, 3) appetite, 4) concentration, and 5) tiredness/fatigue. Fatigue was assessed by the Georgian version of the pediatric quality of life initiative (PEDS QL) multidimensional fatigue scale.[31] The scale comprises 18 items and three subscales: 1) general fatigue (GF) (6 items), 2) sleep/rest fatigue (SRF) (6 items); 3) cognitive fatigue (CF) (6 items). The questionnaire comprises parallel child self-reports for all ages, including 13-18 years of age. The participants rated how often a particular problem occurred in the past month using a 5-point Likert scale (0 = never a problem; 1 = almost never a problem; 2 = sometimes a problem; 3 = often a problem; 4 = almost always a problem). Each item was reverse scored and rescaled to a 0-100 scale so that higher scores indicated fewer symptoms of fatigue (0 = 100; 1 = 75; 2 = 50; 3 = 25, 4 = 00). Cross-sectional analysis was performed to assess the associations between IAD and the risk of depression, general fatigue, cognitive fatigue and sleep/rest fatigue.

### Measures

IAD was considered an exposure variable, and depression, general fatigue, cognitive fatigue and sleep/rest fatigue were considered outcomes. Gender was considered a possible confounder/moderator. Outcome variables were grouped as follows:

1. Depression: no depression (coded as "0") vs any manifestation of depression (coded as "1").
2. General fatigue, cognitive fatigue and sleep/rest fatigue: never a problem/almost never a problem (coded as "0") vs having problems (sometimes, often or almost always) (coded as "1").

First, we used descriptive statistics (frequency calculations). We used the Mantel-Haenszel test to assess whether the risk of depression, general fatigue, cognitive fatigue and sleep/rest fatigue is correlated with the increase in IAD severity. In addition, subanalysis among groups of children with IAD was performed. We compared the children with severe IAD by Young's test (80-100 scores) to those with moderate (50-79 scores) and mild (20-49 scores) for IAD. We used the Mantel-Haenszel test to compare the odds of having depression, general fatigue, sleep/rest fatigue and cognitive fatigue among children with mild/moderate IAD and severe IAD. For this subanalysis, we used slightly different grouping (only four children showed no signs of depression and two showed no signs of cognitive fatigue) for outcome variables:

1. Depression: no depression/mild depression (code as "0") vs moderate and severe depression (coded as "1").
2. Cognitive fatigue: never a problem/almost never a problem/sometimes a problem (coded as "0") vs almost always or often a problem.
3. General fatigue and sleeping fatigue: never a problem/almost never a problem (coded as "0") vs. having problems (sometimes, often or almost always) (coded as "1").



The exposure variable (IAD) was grouped into two categories: mild/moderate and severe IAD.

## RESULTS

Ninety-four participants of 182 were considered to have IAD (58 boys and 36 girls) and 88 (48%) participants were considered as nondependent and then served as controls.

'Nondependent' means that the Internet is mainly used to manage email, look for information or download software. Of the ninety-four children with IAD, 8 (8.51%) had mild IAD, 29 (30.85%) had moderate IAD, and 57 (60.64%) had severe IAD *(Table 1)*.

High scores on the Young test are related to the occurrence of cognitive, sleep/rest or general fatigue, while lower scores on the test correlate with an absence of the abovementioned comorbidities *(Figures 1 to 3)*. Seventy-four percent of children with IAD with severe depression showed high scores on the Young test, i.e. ranging from 80 to 100 *(Figure 4)*.

The odds of having cognitive fatigue, sleep/rest fatigue, general fatigue and depression increased by 2.43, 2.03, 2.4 and 3.67 times, respectively, per increase in IAD severity (No addiction, Mild addiction, Moderate addiction and Severe addiction) *(Table 2)*.

**Table 1:** Cohort characteristics (N = 182).

| | n (%) |
|---|---|
| Sex | |
| Boys | 105 (58.24) |
| Girls | 76 (41.76) |
| Age (years) | |
| 12 | 1 (0.55) |
| 13 | 23 (12.64) |
| 14 | 49 (26.92) |
| 15 | 39 (21.43) |
| 16 | 53 (29.12) |
| 17 | 17 (9.34) |
| Internet addiction (scores) | |
| No addiction (1-20) | 88 (48.35) |
| Mild addiction (21-49) | 8 (4.40) |
| Moderate addiction (50-79) | 29 (15.93) |
| Severe addiction (80+) | 57 (31.32) |
| Cognitive fatigue | |
| No problem | 19 (10.44) |
| Almost never a problem | 42 (23.08) |
| Sometimes a problem | 60 (32.97) |
| Often a problem | 39 (21.43) |
| Almost always a problem | 22 (12.09) |
| Sleeping fatigue | |
| No problem | 36 (19.78) |
| Almost never a problem | 68 (37.36) |
| Sometimes a problem | 59 (32.42) |
| Often a problem | 13 (7.14) |
| Almost always a problem | 6 (3.30) |
| General fatigue | |
| No problem | 37 (20.33) |
| Almost never a problem | 73 (40.11) |
| Sometimes a problem | 56 (30.77) |
| Often a problem | 11 (6.04) |
| Almost always a problem | 5 (2.75) |
| Depression | |
| No/minimal depression | 86 (47.25) |
| Mild depression | 20 (10.99) |
| Moderate depression | 15 (8.24) |
| Severe depression | 61 (33.52) |

There was no significant change in the test for trend after adjusting for gender, which indicates that gender does not play a role in the association between IAD and depression, general fatigue, sleep/rest fatigue and cognitive fatigue *(Table 3)*.

Adolescents with severe IAD are 6.62 times more likely to always/often have cognitive fatigue problems compared with children with mild or moderate IAD *(Table 4)*.

This observed association was statistically significant among boys (OR = 11.65 [95% CI 2.44-55.54], $p < 0.001$) but not among girls (OR = 2.33 [95% CI 0.56-9.63], $p = 0.2278$).

Children with severe IAD are 7.81 times more likely to at least sometimes experience sleep/rest fatigue compared to children with mild or moderate IAD *(Table 4)*. This association is equally significant among boys and girls (OR = 6.93 [95% CI 1.70-28.1], $p = 0.0016$ for boys and OR= 6.60 [95% CI 1.27-34.39 for girls]). The adjusted odds ratio was OR = 6.79 [95% CI 2.33-19.78], $p = 0.0096$).

Children with severe IAD are 11.11 times more likely to at least sometimes experience general fatigue compared to children with mild or moderate IAD *(Table 4)*. This association differed across genders: the observed association was stronger among boys (OR = 13.21 [95% CI 2.48-70.28], $p < 0.001$) than among girls (OR = 6.67 [95% CI 1.24-35.71], $p = 0.0104$).

Children with severe IAD are 5.63 times more likely to show symptoms of moderate or severe depression compared to children with mild or moderate IAD *(Table 4)*. This observed association was statistically significant only among boys (OR = 10.63 [95% CI 1.57-71.86], $p = 0.0024$) and not among girls (OR = 2.33 [95% CI 0.47-11.60], $p = 0.286$).

## DISCUSSION

Our study shows IAD is strongly correlated with different negative habits leading to poor well-being in adolescents. A previous study proved that children with severe IAD are 5.63 times more likely to show symptoms of moderate or severe depression than children with mild or moderate IAD. Thus, the present study confirms previous results that depression is related to IAD. Depression in children with IAD could be explained by the fact that the prefrontal cortex (PFC) is the main area in the brain responsible for many aspects of mental and physical health, including those participating in the mechanism of addiction and withdrawal symptoms in participants with IAD. In addition to planning, prioritizing and organizing, the PFC plays an important role in the regulation of emotional processes.[32] The PFC is

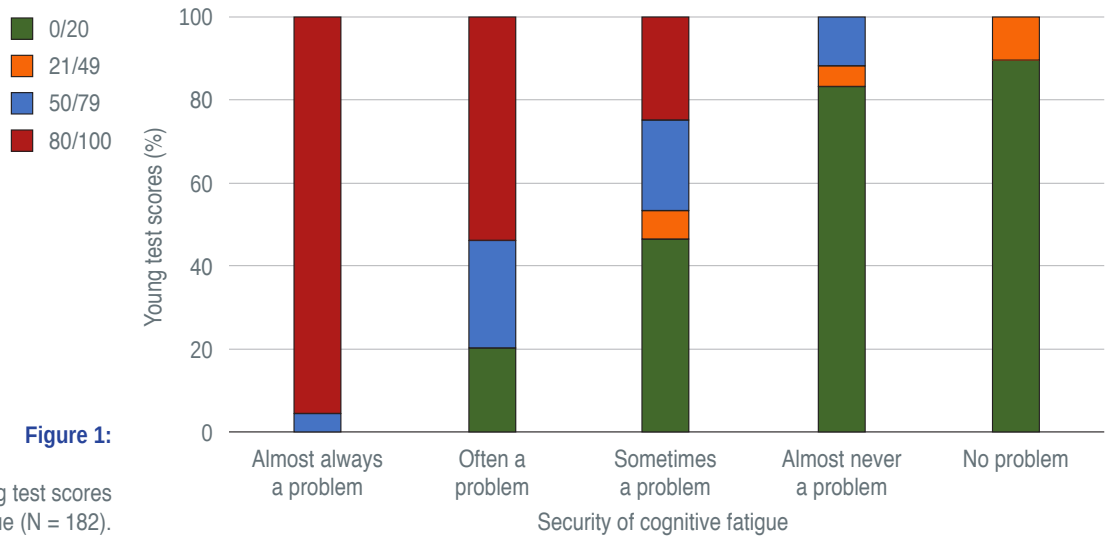


**Figure 1:**

Distribution of young test scores and cognitive fatigue (N = 182).

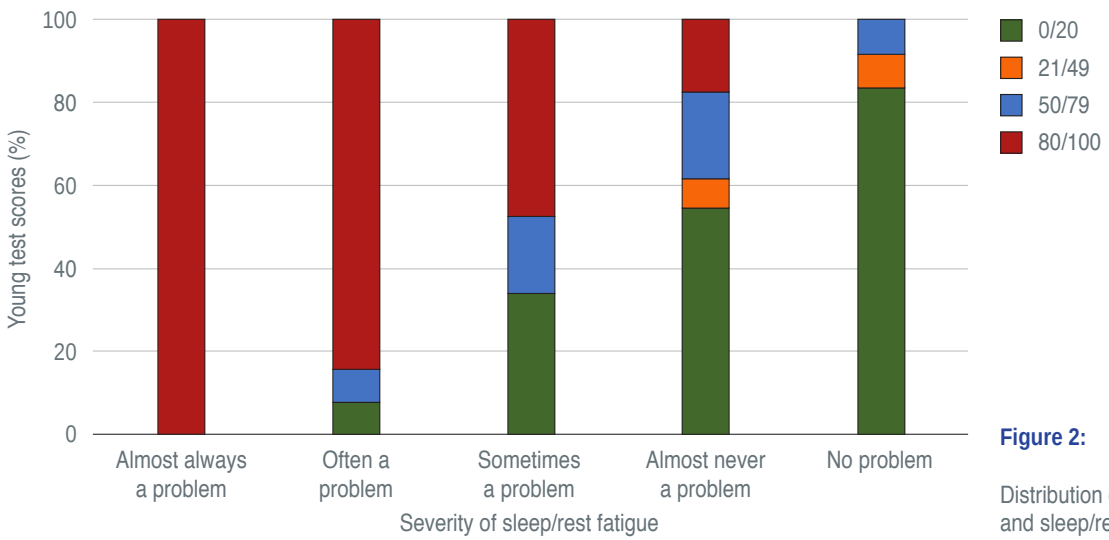


**Figure 2:**

Distribution of young test scores and sleep/rest fatigue (N = 182).

the key region of interest (ROI) in the pathophysiology of IAD. Voxel-based morphometry proved that in participants with IAD, atrophy of the bilateral dorsolateral prefrontal cortex (DLPFC) is the most prominent.[11] In addition, there is no doubt that the volume of the PFC is reduced in depressed patients, and this decrease is correlated with the duration of illness.[33] Thus, depression and IAD share identical anatomical substrates in their pathophysiological mechanism, atrophy of the PFC, which could easily explain the coexistence of depression and IAD. It is controversial whether one of the most common causes of depression could be dysregulation of the PFC, due to impaired regulation of glutamatergic and GABAergic transmission within the PFC. This process, in turn, could cause a negative impact on cognitive function and emotion through altered local processing of afferent information and generation of efferent activity for communication with distal structures of the brain, including the insula.[23] The insula is another shared ROI for both depression and IAD.[11] The insula, which plays an important role in social affect such as empathy, fear and happiness, is found to have reduced gray matter density in participants with IAD. The abnormal connection of atrophic PFC with atrophic insula is essential in generating the abnormal emotional reaction leading to depression. Thus, anatomical and functional impairment of the PFC could easily explain the coexistence of these two discrete conditions, IAD and depression.

Another important result of our study was that children with severe IAD showed 6.62 times more cognitive fatigue, 7.81 times higher sleep/rest fatigue and 11.11 times higher general fatigue than those with mild and moderate IAD. Fatigue is multifactorial, including both cognitive and

physical components, and could be caused by structural lesions affecting the activation of pathways interconnecting the basal ganglia, thalamus, limbic system and different cortical centers.[34] In addition to structural lesions of the brain, fatigue could be caused by biological factors such as stress, which is the most common reason for fatigue.[35] Stress induces the production of cortisol, which could predispose patients to different types of fatigue. Moreover, cortisol plays a large role in the physical adaptation to increased energy demands during stress.[36] Participants suffering from alcohol dependency showed increased levels of cortisol during the withdrawal period. If we suppose that IAD shares a similar mechanism and signs with substance and alcohol addiction,[15,37] it is clear that participants with IAD experience the same process during withdrawal. Cortisol causes coordinated stress in different structures of the brain, especially in the frontal system, including both the PFC and orbitofrontal (OFC) cortices. As mentioned above, the PFC is the main ROI for IAD, but the OFC has the same critical role in the pathophysiology of IAD as the PFC. Voxel-based morphometry suggests that participants with IAD have atrophy of equal severity of both structures: bilateral dorsolateral prefrontal cortex (DLPFC) and OFC.[38] Moreover, the volume of the OFC is correlated with the scores in the Internet addiction test, measuring symptom severity.[39] Reduced OFC thickness, abnormal white matter fractional anisotropy and decreased functional connectivity with other parts of the brain, including the basal ganglia, are characteristic of IAD. Chun et al.[40] found that decreased activity of the frontal system, including the OFC, is related to increased cortisol levels as a response to stress. Cortisol causes a coordinated stress response not only in the OFC

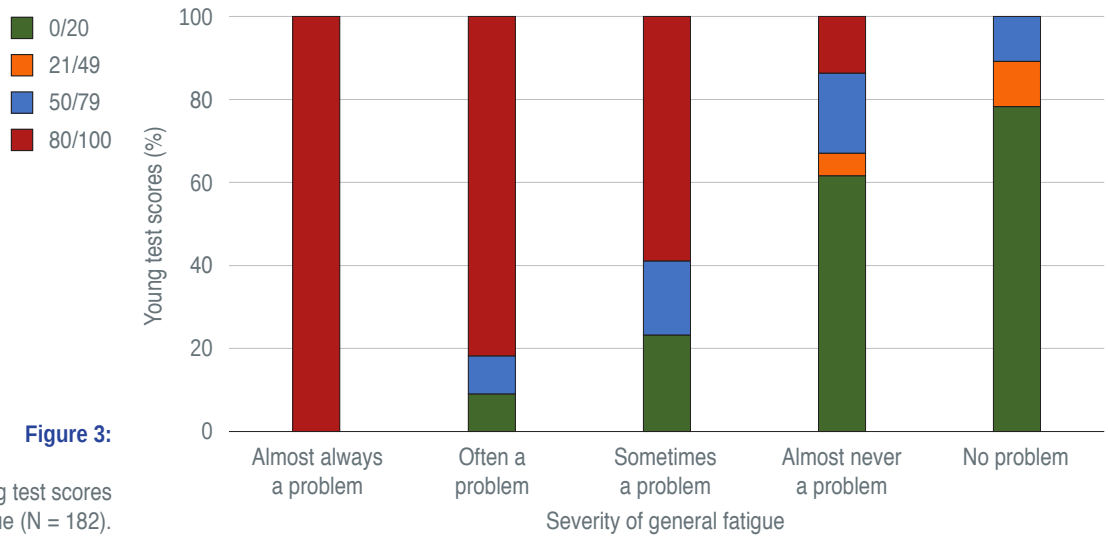


**Figure 3:**

Distribution of young test scores and general fatigue (N = 182).

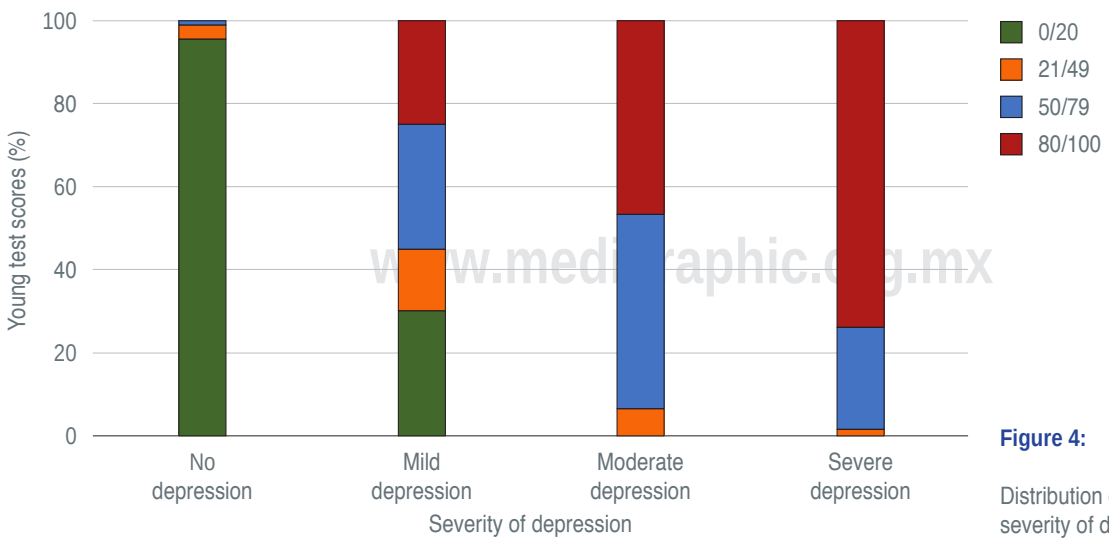




**Figure 4:**

Distribution of young test scores and severity of depression (N = 182).

**Table 2:** Unadjusted tests for trend: increasing risk of cognitive fatigue, sleep/rest fatigue, general fatigue and depression with increased risk for IAD severity.

| | Odds ratio | 95% confidence interval | p-value for trend |
|---|---|---|---|
| Cognitive fatigue | 2.43 | 1.93-3.06 | < 0.001 |
| Sleep/rest fatigue | 2.03 | 1.63-2.53 | < 0.001 |
| General fatigue | 2.40 | 1.93-2.99 | < 0.001 |
| Depression | 3.67 | 2.96-4.55 | < 0.001 |

**Table 3:** Adjusted for gender tests for trend: increasing risk of cognitive fatigue, sleep/rest fatigue, general fatigue and depression with increased risk for IAD severity.

| | Odds ratio | 95% confidence interval | p-value for trend |
|---|---|---|---|
| Cognitive fatigue | 2.52 | 1.98-3.21 | < 0.001 |
| Sleep/rest fatigue | 2.01 | 1.59-2.54 | < 0.001 |
| General fatigue | 2.39 | 1.88-3.06 | < 0.001 |
| Depression | 3.80 | 3.02-4.79 | < 0.001 |

**Table 4:** Unadjusted MH odds ratios.

| | Odds Ratio | 95% Confidence interval | p-value |
|---|---|---|---|
| Cognitive fatigue | 6.62 | 2.37-18.44 | < 0.001 |
| Sleep/rest fatigue | 7.81 | 2.69-22.66 | < 0.001 |
| General fatigue | 11.11 | 3.47-35.55 | < 0.001 |
| Depression | 5.63 | 1.68-18.93 | 0.0016 |

but also in the PFC.[41] Considering the importance of both the PFC and OFC in the cortisol production withdrawal process, participants with IAD will experience excessive cortisol production, which itself could affect frontostriatal connectivity.[42] This pathological neural network is extremely important, as frontostriatal connectivity means activation of the nucleus accumbens, which affects reward processing in addiction disorders, including IAD. Thus, the occurrence of both general and sleep/rest fatigue could be explained by this pathophysiological circuit leading to excessive cortisol production by the OFC and PFC atrophy, which can be seen in participants with IAD.

It is known that cognitive fatigue means failure to sustain attention to optimize task performance during acute but sustained mental effort. Thus, it could be described as a decline in attention network performance.[43] Evidence suggests that cognitive fatigue is a central component of the cognitive and clinical characteristics of stress-related exhaustion disorders, including IAD. The leading process causing cognitive fatigue in children and adolescents with IAD is impaired response inhibition. Response inhibition, a core component of executive function, means the ability to inhibit inappropriate or irrelevant responses. Cognitive fatigue is one of the main processes related to impaired response inhibition.[44] A possible explanation for cognitive fatigue in children with IAD is abnormal neuronal circuits, which are responsible for both response inhibition leading to cognitive fatigue and IAD. These neuronal networks contain complex anatomical and neurochemical processes. There are two main regions of the brain that are critical for both IAD and impaired response inhibition, the PFC and inferior frontal gyrus (IFG).[45]

The first and most important domain in the mechanism of response inhibition leading to cognitive fatigue is activation of the frontal area, including the PFC, and connectivity with the basal ganglia, especially with the striatum, which was proven with functional imaging studies.[34] It is clear that a higher volume in the left ventral striatum is associated with frequent video game playing and even excessive gambling, which itself can be related to the striatal release of dopamine.[46] Individuals with higher striatal volume might experience video gaming as more rewarding in the first place. This in turn could facilitate skill acquisition and lead to further reward resulting from playing. Volumetric differences in the striatum have previously been associated with addiction to drugs and alcohol. Moreover, activation of the striatum has been associated with anticipation and feedback in reward associated with IAD.[47] Thus, in addition, the normal regulation of striatal dopamine activity by signals passing from the PFC is disrupted.[11] This process initiates

the cascade of neuroanatomical changes, as abnormal striatal dopamine activity can lead to disrupted prefrontal regulation of the midbrain structures, which could then cause impairment of response inhibition.[48] Another part of the frontal system that could be considered an ROI in terms of response inhibition is the IFG. It is clear that the IFG is activated in participants with IAD. This activation due to strong interconnection will lead to activation of the right striatum, which will strengthen the effect of the abnormal interconnection of the striatum with the PFC and can be considered another reason for response inhibition in participants with IAD. Thus, this circuit between the frontal system (PFC and OFC) and the basal ganglia, including the striatum-midbrain, and abnormal release of dopamine in participants with IAD, can be considered the main anatomical mechanism of IAD with respect to response inhibition.

Another important piece of evidence for cognitive fatigue is that disruption of cortical-subcortical loops, including the ventral striatum, anterior cingulate cortex and thalamus, can be considered a key chain in its pathogenesis.[25,34] This finding could easily explain the link between IAD and cognitive fatigue, as volumetric changes in the striatum, anterior cingulate cortex and thalamus are responsible for both impaired response inhibition leading to cognitive fatigue and IAD. According to Gavelin et al.,[26] participants with a high level of cognitive fatigue have a smaller caudate nucleus and putamen than participants with low-moderate cognitive fatigue. Furthermore, the authors noted that an indirect negative effect of caudate nucleus volume on working memory performance was found to be the reason for abnormal response inhibition and cognitive fatigue as a result. The caudate nucleus can be considered an ROI in participants with IAD. By studying the resting state brain of participants with IAD by means of 18-FDG-PET to measure glucose metabolism, it was demonstrated that glucose metabolism was increased in the right orbitofrontal cortex and in parts of the basal ganglia, including the caudate nucleus and insula.[49] Although the insula is another ROI for IAD, it can also be discussed as a brain structure implicated in response inhibition leading to cognitive fatigue.[50]

## Key points

**What's known**

1. Excessive screen-time reduces quality of life in young people and may be associated with depression.
2. Relatively little is known about fatigue in adolescents with Internet addiction disorder (IAD).

**What's new**

1. Adolescents with severe IAD are more likely to show symptoms of moderate or severe depression than children with mild or moderate IAD.
2. Those with severe IAD showed more fatigue than children with mild and moderate Internet addiction.

**What's relevant**

1. The study showed that IAD can lead to depression and fatigue, which can affect adolescents' psychological and social well-being.
2. Mechanisms for prevention and ongoing support are needed for adolescents and their families.

## CONCLUSIONS

Thus, our study showed that the existence of depression as well as fatigue, including general, sleep/rest and cognitive fatigue, in adolescents with IAD can be explained by complex neuroanatomical and neurobiological processes, and the substrates for these processes are the structures that have critical roles and equal contributions to the etiology of IAD as well as to depression and fatigue.

Our study has several limitations. It would be interesting to know if there are differences in depression and fatigue rates between two distinct types of IAD – generalized and specific IAD. Future research should also examine whether depression and fatigue are along a continuum coexisting with IAD. The most important question here is to identify which one is primary and which is secondary – that is, does IAD lead to depression, as we have shown here, or is depression itself a risk factor for IAD? Furthermore, it is important to examine whether there are gender differences between the frequency of depression and fatigue associated with IAD, as the evidence is unclear.

## REFERENCES


1. Aboujaoude E. Problematic Internet use: an overview. World Psychiatry. 2010; 9 (2): 85-90.
2. Kratzer S, Hegerl U. Is "Internet Addiction" a disorder of its own?--a study on subjects with excessive internet use. Psychiatr Prax. 2008; 35 (2): 80-83.
3. Grant JE, Potenza MN, Weinstein A, Gorelick DA. Introduction to behavioral addictions. Am J Drug Alcohol Abuse. 2010; 36 (5): 233-241.
4. American Society of Addiction Medicine. Public policy statement: definition of addiction. 2011 [Accessed 21 August 2011].
5. Dell'Osso B, Altamura AC, Allen A, Marazziti D, Hollander E. Epidemiologic and clinical updates on impulse control disorders: a critical review. Eur Arch Psychiatry Clin Neurosci. 2006; 256 (8): 464-475.
6. Hollander E, Sten DJ. Clinical manual of impulse-control disorders. Arlington, VA: American Psychiatric Publishing; 2006.
7. Block JJ. Issues for DSM-V: internet addiction. Am J Psychiatry. 2008; 165 (3): 306-307.
8. Clarke D. Impulsiveness, locus of control, motivation and problem gambling. J Gambl Stud. 2004; 20 (4): 319-345.
9. Oei TP, Raylu N. Familial influence on offspring gambling: a cognitive mechanism for transmission of gambling behavior in families. Psychol Med. 2004; 34 (7): 1279-1288.
10. Lam LT. Parental mental health and Internet Addiction in adolescents. Addict Behav. 2015; 42: 20-23.

11. Montag C, Reuter M. Internet addiction: neuroscientific approaches and therapeutical interventions. Switzerland: Springer International Publishing; 2015.
12. Liu J, Gao XP, Osunde I, Li X, Zhou SK, Zheng HR et al. Increased regional homogeneity in internet addiction disorder: a resting state functional magnetic resonance imaging study. Chin Med J (Engl). 2010; 123 (14): 1904-1908.
13. Zhou Y, Lin FC, Du YS, Qin LD, Zhao ZM, Xu JR et al. Gray matter abnormalities in Internet addiction: a voxel-based morphometry study. Eur J Radiol. 2011; 79 (1): 92-95.
14. Weng CB, Qian RB, Fu XM, Lin B, Han XP, Niu CS et al. Gray matter and white matter abnormalities in online game addiction. Eur J Radiol. 2013; 82 (8): 1308-1312.
15. Anderson CA, Funk JB, Griffiths MD. Contemporary issues in adolescent video game playing: brief overview and introduction to the special issue. J Adolesc. 2004; 27 (1): 1-3.
16. Costigan SA, Barnett L, Plotnikoff RC, Lubans DR. The health indicators associated with screen-based sedentary behavior among adolescent girls: a systematic review. J Adolesc Health. 2013; 52 (4): 382-392.
17. Babic MJ, Smith JJ, Morgan PJ, Eather N, Plotnikoff RC, Lubans DR. Longitudinal associations between changes in screen-time and mental health outcomes in adolescents. Ment Health Phys Act. 2017; 12: 124-131.
18. Twenge JM, Campbell WK. Associations between screen time and lower psychological well-being among children and adolescents: Evidence from a population-based study. Prev Med Rep. 2018; 12: 271-283.
19. King DL, Delfabbro PH, Zwaans T, Kaptsis D. Clinical features and axis I comorbidity of Australian adolescent pathological Internet and video game users. Aust N Z J Psychiatry. 2013; 47 (11): 1058-1067.
20. Brunborg GS, Mentzoni RA, Froyland LR. Is video gaming, or video game addiction, associated with depression, academic achievement, heavy episodic drinking, or conduct problems? J Behav Addict. 2014; 3 (1): 27-32.
21. Bargeron AH, Hormes JM. Psychosocial correlates of internet gaming disorder: psychopathology, life satisfaction, and impulsivity. Comput Hum Behav. 2017; 68: 388-394.
22. Lindenberg K, Kindt S, Szasz-Janocha C. Internet addiction in adolescents. Switzerland: Springer Nature; 2020.
23. Hare BD, Duman RS. Prefrontal cortex circuits in depression and anxiety: contribution of discrete neuronal populations and target regions. Mol Psychiatry. 2020; 25 (11): 2742-2758.
24. Sariyska R, Reuter M, Lachmann B, Montag C. Attention deficit/hyperactivity disorder is a better predictor for problematic internet use than depression: evidence from Germany. J Addict Res Ther. 2015; 6: 209.
25. Chaudhuri A, Behan PO. Fatigue in neurological disorders. Lancet. 2004; 363 (9413): 978-988.
26. Gavelin HM, Neely AS, Dunas T, Eskilsson T, Jarvholm LS, Boraxbekk CJ. Mental fatigue in stress-related exhaustion disorder: Structural brain correlates, clinical characteristics and relations with cognitive functioning. Neuroimage Clin. 2020; 27: 102337.
27. Krabbe D, Ellbin S, Nilsson M, Jonsdottir IH, Samuelsson H. Executive function and attention in patients with stress-related exhaustion: perceived fatigue and effect of distraction. Stress. 2017; 20 (4): 333-340.
28. Oosterholt BG, Maes JH, Van der Linden D, Verbraak MJ, Kompier MA. Cognitive performance in both clinical and non-clinical burnout. Stress. 2014; 17 (5): 400-409.
29. van Dam A, Keijsers GP, Eling PA, Becker ES. Testing whether reduced cognitive performance in burnout can be reversed by a motivational intervention. Work & Stress. 2011; 25 (3): 257-271.
30. Young KS. Internet addiction: the emergence of a new clinical disorder. CyberPsychology & Behavior. 1998; 1 (3): 237-244.
31. Varni JW, Seid M, Rode CA. The PedsQL: measurement model for the pediatric quality of life inventory. Med Care. 1999; 37 (2): 126-139.
32. Chan RC, Shum D, Toulopoulou T, Chen EY. Assessment of executive functions: review of instruments and identification of critical issues. Arch Clin Neuropsychol. 2008; 23 (2): 201-216.
33. Savitz J, Drevets WC. Bipolar and major depressive disorder: neuroimaging the developmental-degenerative divide. Neurosci Biobehav Rev. 2009; 33 (5): 699-771.
34. Chaudhuri A, Behan PO. Fatigue and basal ganglia. J Neurol Sci. 2000; 179 (S1-2): 34-42.
35. Smith C. Elements of molecular neurobiology. Chichester: John Wiley; 2002.
36. Dedovic K, Duchesne A, Andrews J, Engert V, Pruessner JC. The brain and the stress axis: the neural correlates of cortisol regulation in response to stress. Neuroimage. 2009; 47 (3): 864-8671.
37. Weinstein A, Lejoyeux M. New developments on the neurobiological and pharmaco-genetic mechanisms underlying internet and videogame addiction. Am J Addict. 2015; 24 (2): 117-125.
38. Yuan K, Qin W, Wang G, Zeng F, Zhao L, Yang X et al. Microstructure abnormalities in adolescents with internet addiction disorder. PLoS One. 2011; 6 (6): e20708.
39. Young K. Caught in the net: how to recognize the signs of Internet addiction – And a winning strategy for recovery. New York, NY: John Wiley & Sons, Inc; 1998.
40. Chun JW, Choi J, Cho H, Choi MR, Ahn KJ, Choi JS et al. Role of frontostriatal connectivity in adolescents with excessive smartphone use. Front Psychiatry. 2018; 9: 437.
41. Arnsten AF, Raskind MA, Taylor FB, Connor DF. The effects of stress exposure on prefrontal cortex: translating basic research into successful treatments for post-traumatic stress disorder. Neurobiol Stress. 2015; 1: 89-99.
42. Pruessner JC, Dedovic K, Khalili-Mahani N, Engert V, Pruessner M, Buss C et al. Deactivation of the limbic system during acute psychosocial stress: evidence from positron emission tomography and functional magnetic resonance imaging studies. Biol Psychiatry. 2008; 63 (2): 234-240.
43. Holtzer R, Shuman M, Mahoney JR, Lipton R, Verghese J. Cognitive fatigue defined in the context of attention networks. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn. 2011; 18 (1): 108-128.
44. Guo Z, Chen R, Liu X, Zhao G, Zheng Y, Gong M et al. The impairing effects of mental fatigue on response inhibition: An ERP study. PLoS One. 2018; 13 (6): e0198206.
45. Swick D, Ashley V, Turken AU. Left inferior frontal gyrus is critical for response inhibition. BMC Neurosci. 2008; 9: 102.
46. Kuhn S, Romanowski A, Schilling C, Lorenz R, Morsen C, Seiferth N et al. The neural basis of video gaming. Transl Psychiatry. 2011; 1 (11): e53.
47. Schlagenhauf F, Sterzer P, Schmack K, Ballmaier M, Rapp M, Wrase J et al. Reward feedback alterations in unmedicated schizophrenia patients: relevance for delusions. Biol Psychiatry. 2009; 65 (12): 1032-1039.
48. Thanos PK, Wang GJ, Volkow ND. Positron emission tomography as a tool for studying alcohol abuse. Alcohol Res Health. 2008; 31 (3): 233-237.
49. Park HS, Kim SH, Bang SA, Yoon EJ, Cho SS, Kim SE. Altered regional cerebral glucose metabolism in internet game overusers: a 18F-fluorodeoxyglucose positron emission tomography study. CNS Spectr. 2010; 15 (3): 159-166.
50. Cai W, Ryali S, Chen T, Li CS, Menon V. Dissociable roles of right inferior frontal cortex and anterior insula in inhibitory control: evidence from intrinsic and task-related functional parcellation, connectivity, and response profile analyses across multiple datasets. J Neurosci. 2014; 34 (44): 14652-14667.