Brain Neuroadaptative Changes in Adolescents with Internet Addiction: An FDG-PET Study with Statistical Parametric Mapping Analysis

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Objectives: Internet addiction or pathologic internet use is one of the major mental health problems in children and adolescents in Korea. Internet addiction is defined as uncontrolled, markedly time-consuming internet use, which lasts for a period of at least six months. Internet addiction results in poor academic performance and negative parent-child relationships. By using [18]F-fluorodeoxyglucose-positron emission tomography (FDG-PET), we investigated the effects of internet addiction on functional changes occurring in the adolescent brain.

Methods: Adolescent patients with an internet addiction (4 boys and 2 girls: 15.6 ± 1.2 years) participated in this study. Eight healthy young adults (5 males and 3 females: 18–30 years old) with no previous history of psychiatric illness also participated as normal controls. Brain FDG-PET data was obtained with the participants in the resting condition and with no addictive stimuli.

Results: Statistic parametric mapping analysis of the brain FDG-PET data revealed hypometabolic changes in the visual information processing circuits and hypermetabolic changes in the prefrontal areas in the adolescents with internet addiction, as compared with normal controls (p<.001).

Conclusion: These results suggest a neuronal adaptation to excessive visual stimulation and synaptic plasticity due to internet addiction.

KEY WORDS: Internet addiction · Adolescents · Brain glucose metabolism · FDG-PET.

Introduction

Internet addiction or pathologic internet use is one of the major mental health problems among children and adolescents in Korea. ADHD, depression, school refusal and aggravated parent-child relationship are common comorbid conditions associated with internet addiction during childhood and adolescence. Internet addiction, first proposed by Goldberg in 1996, has also been described as "pathologic internet use" or "problematic internet use." In the present study, Internet addiction was defined as a) uncontrolled, b) markedly time-consuming internet use, c) resulting in academic, relational, or financial difficulties, d) not solely present during hypomanic or manic symptoms.

Behavioral scientists regard all kinds of addiction as a behavioral disorder that is a powerful contributing factor to the narrowing of behavioral repertoire. One of the most important perspectives in addiction research may prove to be the neurobiology of learning and memory that characterizes addiction as a habit, a particularly strong habit, marked by compulsivity and chronicity. It has been suggested that some neural circuits and molecular mechanisms would be involved in the persistent and compulsive behavioral features associated with addictions. Brain responses to addiction have implicated neuronal adaptations to excessive stimulation and...
A Korean version of the standardized self-rating scale for internet addiction, a modified and extended form of Young's internet Addiction Test, was also used for the assessment. The scale consists of 40 items rated on a 4-point scale and has 7 subscale domains: disturbance of adaptive functions, addictive automatic thoughts, tolerance, withdrawal, disturbance of reality testing, virtual interpersonal relationship, and deviations. In the study, the cut-off points for the subjects were as follows: total scores >108, or disturbance of adaptive functions subscale scores >26.

2. Normal controls

Healthy young adults (5 males and 3 females: 18–30 years old) were selected as a normal control group from individuals who visited the center for a periodic medical check-up. All of the control subjects were found to be free of any psychiatric or neurological illness by physical examinations, laboratory tests, the Minnesota Multiphasic Personality Inventory and the internet addiction scale.

3. Image acquisition

PET imaging was performed using a PET/CT scanner (Biograph, Siemens, USA). Approximately 222–370 MBq of FDG was injected intravenously according to the body weight of the patient. Twenty minutes after the injection, a transmission scan for attenuation correction was performed using a CT scanner. An emission scan was then acquired for 10 minutes. The subjects were situated in a dark and quiet room without addictive stimuli, comfortably lying in a resting position with eyes closed and ears unplugged from 10 minutes prior to the FDG injection until the end of the PET scan. Brain FDG-PET images were reconstructed from the acquired data using OSEM method.

4. Image analysis by statistical parametric mapping

Statistical parametric mapping analysis was performed using SPM2 (Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab 5.3 (Mathworks Inc., USA). Spatial normalization and global count normalization were performed under the default setting, and the normalized images were smoothed by convolution with a Gaussian kernel of 16 mm full-width-at-half-maximum (FWHM).

For any difference in regional glucose metabolism, the brain FDG-PET images of the patient group and the normal control group were compared using voxel-by-voxel analysis. The regions with uncorrected p-values less than 0.001 and a cluster of more than 100 contiguous voxels were considered to show a significant metabolic change. The results were displayed on the surface-rendered brain image.
To determine the functional anatomical location of a detected region, the Talairach brain coordinates were estimated by a nonlinear transformation from the Montreal Neurological Institute (MNI, McGill University, Montreal, Canada) space to the Talairach (Talairach Daemon Client. Ver.1.1, Research Imaging Center, University of Texas Health Science Center, San Antonio, USA) space. 

## Results

### 1. Clinical features of the subjects with internet addiction

The demographic and clinical characteristics of the six adolescents with internet addiction are described in Table 1. The mean intelligence of the subjects was 101.66 ± 14.15 on the K-WISC-III full scale scores. Of the six adolescents with internet addiction, two had conduct disorder, two had depressive disorder, and two had ADHD, as comorbid psychiatric conditions.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Sex/Age (years)</th>
<th>K-WISC-III</th>
<th>Comorbid conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>F/16</td>
<td>80 (83/83)</td>
<td>Conduct disorder with school dropout</td>
</tr>
<tr>
<td>B</td>
<td>F/15</td>
<td>88 (86/96)</td>
<td>Conduct disorder with school dropout</td>
</tr>
<tr>
<td>C</td>
<td>M/16</td>
<td>106 (96/120)</td>
<td>Depressive disorder with school dropout</td>
</tr>
<tr>
<td>D</td>
<td>M/14</td>
<td>113 (120/98)</td>
<td>Depressive disorder</td>
</tr>
<tr>
<td>E</td>
<td>M/16</td>
<td>113 (114/109)</td>
<td>Attention-deficit hyperactivity disorder</td>
</tr>
<tr>
<td>F</td>
<td>M/14</td>
<td>110 (114/103)</td>
<td>Attention-deficit hyperactivity disorder</td>
</tr>
</tbody>
</table>

### 2. FDG-PET findings

SPM analysis showed a significant reduction of FDG uptake in the bilateral occipital fusiform gyri and parahippocampal regions in the adolescents with internet addiction in the resting condition with no addictive stimuli, as compared with the young adult controls by statistical voxel-based analysis (p<0.001, uncorrected) (Table 2, Fig. 1). The left parietal precuneus, inferior parietal lobe, middle temporal gyrus, and in the right posterior cingulate also showed significant hypometabolism in the adolescents with internet addiction (p<0.001, uncorrected) (Table 2, Fig. 1).

Hypermetabolic changes were detected in the prefrontal areas in the subjects with internet addiction, as compared with the control group by statistical voxel-based analysis (p<0.001, uncorrected) (Table 2, Fig. 2). The right inferior frontal gyrus, left superior frontal gyrus, and bilateral middle frontal gyri in the prefrontal areas showed significantly hypermetabolic changes (p<0.001, uncorrected) (Table 2, Fig. 2).

<table>
<thead>
<tr>
<th>Regions</th>
<th>Brodmann area</th>
<th>Talairach</th>
<th>T</th>
<th>Cluster size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Hypometabolism</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right parahippocampal gyrus</td>
<td>36</td>
<td>24</td>
<td>-38</td>
<td>-12</td>
</tr>
<tr>
<td>Right occipital fusiform gyrus</td>
<td>19</td>
<td>25</td>
<td>-55</td>
<td>-14</td>
</tr>
<tr>
<td>Left occipital fusiform gyrus</td>
<td>18</td>
<td>-30</td>
<td>-80</td>
<td>-18</td>
</tr>
<tr>
<td>Left parahippocampal gyrus</td>
<td>36</td>
<td>-24</td>
<td>-38</td>
<td>-10</td>
</tr>
<tr>
<td>Left parietal precuneus</td>
<td>31</td>
<td>-10</td>
<td>-58</td>
<td>30</td>
</tr>
<tr>
<td>Right posterior cingulate</td>
<td>29</td>
<td>14</td>
<td>-50</td>
<td>16</td>
</tr>
<tr>
<td>Left middle temporal gyrus</td>
<td>21</td>
<td>-66</td>
<td>-44</td>
<td>-8</td>
</tr>
<tr>
<td>Left middle temporal lobe</td>
<td>21</td>
<td>-62</td>
<td>-6</td>
<td>-12</td>
</tr>
<tr>
<td>Left inferior parietal lobule</td>
<td>39</td>
<td>-48</td>
<td>-68</td>
<td>42</td>
</tr>
<tr>
<td>2) Hypermetabolism</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right inferior frontal gyrus</td>
<td>47</td>
<td>58</td>
<td>28</td>
<td>-6</td>
</tr>
<tr>
<td>Right middle frontal gyrus</td>
<td>10</td>
<td>30</td>
<td>59</td>
<td>24</td>
</tr>
<tr>
<td>Left superior frontal gyrus</td>
<td>8</td>
<td>-28</td>
<td>48</td>
<td>40</td>
</tr>
<tr>
<td>Left middle frontal gyrus</td>
<td>10</td>
<td>-30</td>
<td>58</td>
<td>26</td>
</tr>
</tbody>
</table>

Voxel size = 2 x 2 x 2 mm, Cluster level in voxels > 100, Height threshold : T = 3.93 (p<0.001, uncorrected)
Discussion

Addiction is a chronic brain disease, modulated by genetic, developmental, experiential, and environmental factors. The understanding of the neurobiological basis of addiction is important not only for the treatment of the illness but also as a model for how experiences modify neural circuitry and thereby behavior.346

Most neurobiological studies of addiction have concentrated on substance addictions. Previous literature on internet addiction has been primarily focused on the clinical and psychosocial aspects of the condition, because internet addiction is a newly established disease in the field of psychiatry. Thus, the neurobiological changes that accompany internet addiction have yet to be determined. No previous studies have been reported on the metabolic changes in the brains of patients with internet addiction.

The goal of this study was to identify changes in regional glucose metabolism in the brains of adolescents with internet addiction. Regional glucose metabolism in the brain has been interpreted as an indicator of the activity of synapses and dendritic spines.36 Therefore, glucose metabolic changes observed in the present study may be suggestive of changes in neural connectivity and synaptic activity in the affected brain regions as a result of internet addiction.

The SPM analysis performed in this study showed significant decreases in the activity of the bilateral occipital and parahippocampal regions, the right posterior cingulate, left parietal precuneus, inferior parietal cortex, middle temporal gyrus in the adolescents with internet addiction. The hypometabolic brain regions in this study are reportedly attributed to visuo-spatial information processing and visuo-motor learning circuits.19,20 The occipital and parahippocampal regions showing hypometabolism in the present study play a critical role in object recognition and memory.20 The left parietal precuneus, inferior parietal lobule, and middle temporal gyrus seen hypoactive glucose metabolism in this study
have been involved in visual search, attentional filtering, and encoding, retention and retrieval of visual representations, along with occipital and parahippocampal cortices.\textsuperscript{19,20,21} It has also been reported that the posterior cingulate and left precentral play a role in visuo-motor sequence learning acquisition and retrieval.\textsuperscript{21,22,23} The role of the posterior cingulate has also been associated with monitoring sensory events and orientation.\textsuperscript{24}

These changes in the brain seem to occur as a result of neural adaptation to excessive visual stimuli from compulsive internet use and altered synaptic connectivity which leads to altered responses to environmental stimuli. The prolonged excessive saccade eye movement and visual attention with swift keyboard, mouse button tapping or joystick handling during internet game, chatting or web browsing may be associated with the brain changes observed in the adolescents with internet addiction.

Prior studies suggested that the patterns of glucose metabolism in addiction circuits, which are hyperactive in the absence of substance-related addictive stimuli and hyperactive during intoxication, are similar to the changes seen in epilepsy characterized by an increase in the activity of the abnormal foci during the ictal period and by decreased activity during the interictal period.\textsuperscript{5,6} In this study, the hypometabolic changes which observed in the absence of addictive stimuli seem to be consistent with the patterns reported in the literature.

It is well established that the striato-thalamo-orbitofrontal circuits are associated with substance addiction.\textsuperscript{5,6} The striato-thalamo-orbitofrontal circuits have been reported to become hypofunctional during withdrawal and without drug stimulation in substance addiction, resulting in a decreased drive for goal-motivated behaviors. In this study, hypermetabolic changes were observed in the dorsolateral and ventral prefrontal areas in the adolescents with internet addiction. The prefrontal areas are reportedly involved in executive functions such as motor response control, decision-making, working memory and attention.\textsuperscript{27} The hypermetabolic changes seen in the adolescents with internet addiction may be associated with striving for impulse control or behavioral inhibition under the study condition with no addictive stimuli. It is also possible that the prefrontal hypermetabolism in our results may be based on age-associated differences between the groups. That is why the subjects with internet addiction were younger than the normal controls and the prefrontal brain regions are dynamically changed during adolescence, correlating with synaptogenesis and pruning.\textsuperscript{7,9}

Common molecular findings in addiction circuits with those in learning and memory circuits have led to a much more integrative view of the brain regions involved that accounts for the cognitive and behavioral symptoms in addiction.\textsuperscript{5,7} It may be possible that the involvement of the visual attention and information processing pathways which play a crucial role in academic activities may contribute to poor academic performance in adolescents with internet addiction. In this study we found hypometabolic changes in the left parietal and middle temporal regions, which are involved in syntactic and semantic understanding in language communication with arithmetic measures.\textsuperscript{28,29} These findings may also be associated with poor school work in adolescents with internet addiction.

Limitations of the present study include the small sample size, which was a consequence of the limited PET availability. We did not study age- and sex-matched normal adolescents as controls for ethical reasons in the use of radioisotopes. And we could not exclude comorbid conditions. Considering the above limitations, It is likely that our results may not be specific to internet addiction even though we used p-value <0.01 in order to diminish type I errors. However, our findings are very suggestive that the neural circuits involved in addiction may rely on the characteristics of the addicted stimuli and that internet addiction during childhood and adolescence may exert negative influence on brain maturation process.

\textbf{Conclusion}

In conclusion, we examined the functional changes in the brains of adolescents with internet addiction using FDG-PET and SPM analysis. The hypometabolic and hypermetabolic changes in the visual information processing circuits and prefrontal areas may contribute to cognitive and behavioral symptoms in adolescents with internet addiction.

\textbf{References}


