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The effects of a virtual reality treatment program for online gaming addiction

Sung Yong Park[a], *Sun Mi Kim*[a,*], *Sungwon Roh*[b], *Min-Ah Soh*[c], *Sang Hoon Lee*[d], *Hyungjin Kim*[e], *Young Sik Lee*[a], *Doug Hyun Han*[a]

[a] *Department of Psychiatry, Chung-Ang University Medical Center, 102 Heukseok-ro, Dongjak-gu, Seoul 156-755, Republic of Korea*

[b] *Department of Psychiatry, Hanyang University College of Medicine, 222 Wangsimni-ro, Seongdong-gu, Seoul 133-791, Republic of Korea*

[c] *Department of Mental Health Research, Seoul National Hospital, Junggok 3-dong, Gwangjin-gu, Seoul 143-711, Republic of Korea*

[d] *Eun Hye Hospital, Simgok-dong, Seo-gu, Incheon 404-793, Republic of Korea*

[e] *Department of Psychology, Rice University, 6100 Main Street, Houston, TX 77005, USA*

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ABSTRACT

Background and objective: Neuroimaging studies have demonstrated dysfunction in the brain reward circuit in individuals with online gaming addiction (OGA). We hypothesized that virtual reality therapy (VRT) for OGA would improve the functional connectivity (FC) of the cortico-striatal-limbic circuit by stimulating the limbic system.

Methods: Twenty-four adults with OGA were randomly assigned to a cognitive behavior therapy (CBT) group or VRT group. Before and after the four-week treatment period, the severity of OGA was evaluated with Young's Internet Addiction Scale (YIAS). Using functional magnetic resonance imaging, the amplitude of low-frequency fluctuation (ALFF) and FC from the posterior cingulate cortex (PCC) seed to other brain areas were evaluated. Twelve casual game users were also recruited and underwent only baseline assessment.

Results: After treatment, both CBT and VRT groups showed reductions in YIAS scores. At baseline, the OGA group showed a smaller ALFF within the right middle frontal gyrus and reduced FC in the cortico-striatal-limbic circuit. In the VRT group, connectivity from the PCC seed to the left middle frontal and bilateral temporal lobe increased after VRT.

Conclusion: VRT seemed to reduce the severity of OGA, showing effects similar to CBT, and enhanced the balance of the cortico-striatal-limbic circuit.

1. Introduction

Online gaming addiction (OGA) has considerable importance in public health, education, and related fields. Typically, OGA is defined as a pattern of excessive and prolonged online gaming that results in a cluster of cognitive and behavioral symptoms, including progressive loss of control over gaming, tolerance, and withdrawal symptoms. Recently, Internet

* *Corresponding author*. Tel.: +82 2 6299 1519; fax: +82 2 6298 1508.
E-mail addresses: architers@hanmail.net (S.Y. Park), sunmikim706@gmail.com (S.M. Kim), swroh@hanyang.ac.kr (S. Roh), soho27@gmail.com (M.-A. Soh), lnh409@naver.com (S.H. Lee), hk19@rice.edu (H. Kim), hawkeyelys@hanmail.net (Y.S. Lee), hduk@yahoo.com (D.H. Han).

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gaming disorder, which shares common concepts with online gaming addiction as explained above, was introduced in Section III of the Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [1] as a condition needing further investigation. Similar to other addictive disorders, Internet gaming disorder requires further investigation of the prevalence, clinical course, and possible biological etiological factors based on neurobiological studies in order to determine its merit as an independent disorder [2].

Neuroimaging studies of functional brain changes in response to video game playing have suggested that gaming cues activate brain reward systems in both healthy individuals (i.e., casual game users) and individuals with OGA. Gaming cues have been shown to stimulate the brain dopaminergic circuit in healthy individuals according to functional magnetic resonance imaging (fMRI) studies [3–5] and in a positron emission tomography study [6]. The involvement of the brain reward circuit in response to gaming has also been shown in individuals with OGA. Functional changes in the cortico-limbic circuit have been consistently reported in fMRI studies using gaming cues in participants with OGA [7–9]. Long-term continuous Internet game playing may also lead to structural brain changes [10,11]. Although the findings of functional neuroimaging studies indicate that similar brain regions related to the brain reward system are activated in response to gaming cues in both healthy volunteers and individuals with OGA, structural neuroimaging studies have demonstrated differences between these two groups. Weng et al. [10] reported that adolescents with OGA have reduced cortical thickness within the orbitofrontal cortex (OFC) and show gray matter atrophy in the right OFC, bilateral insula, and right supplementary motor area compared to healthy participants. Yuan et al. [11] indicated that impaired gray and white matter integrity of the right OFC and bilateral insula is positively correlated with severity of OGA. These studies suggest dysfunction in the OFC and insula in people with OGA. This dysfunction of the OFC and insula is a neurobiological marker of addictive disorders and is related to impaired impulse control, cognitive flexibility, and reward-related decision making [12–14]. To summarize the literature on the neurobiology of Internet gaming, in response to Internet game playing, the cortico-striatal-limbic circuit seems to be activated in a balanced way in healthy individuals. However, long-term, continuous, and excessive Internet game playing in OGA may decrease activity in most areas of the brain except in the striatum, which indicates a neurobiological imbalance.

In this context, pharmacological studies of OGA have been conducted targeting mood and impulsivity by regulating the synaptic availability of dopamine or serotonin in the cortico-striatal-limbic circuitry using methylphenidate [15], bupropion [16–18], and escitalopram [19]. As a non-pharmacological treatment for OGA, cognitive behavior therapy (CBT) has been examined [17]. CBT is a simple, problem-oriented psychological treatment applied to many psychiatric problems, including addictive disorders [20]. Kim et al. [17] have reported that CBT in combination with bupropion is effective in reducing the severity of OGA in adolescents with major depression, especially in improving anxiety symptoms and life satisfaction as well as reducing time spent on Internet gaming. Du et al. [21] have reported that CBT for OGA in middle and high school students decreases Internet use and yields improvement in conductivity, mood problems, and other psychiatric symptoms. Young [18] has reported that CBT for adults with OGA is effective for controlling problematic Internet use, and its effects persist for six months.

Virtual reality therapy (VRT) is a psychotherapy method that uses virtual reality technology. It has been shown to be effective for anxiety disorders, including specific phobias and posttraumatic stress disorder [22]. Additionally, VRT has been shown to be beneficial for managing some forms of addictive disorder, including nicotine and alcohol dependence [23–25]. In previous studies of VRT for alcohol dependence, VRT decreased craving for alcohol by regulating neurobiological imbalance in the limbic system [26]. VRT stimulated the limbic system (the nucleus accumbens and the amygdala) and reduced the craving response to alcohol stimuli [26]. A VRT program for alcohol dependence uses the technique of repeatedly pairing craving-inducing, alcohol-related stimuli with scenes of the aversive consequences of alcohol [26,27]. With this technique, a VRT program is expected to stimulate both the nucleus accumbens (associated with craving) and the amygdala (associated with aversion), facilitating limbic-regulated responses to rewarding stimuli [27]. A VRT program for alcohol has been shown to be more effective for reducing the craving for alcohol than is general cognitive behavioral therapy [25].

Based on a review of the literature, we focused on a VRT program for addictive disorders that can help balance activation within the brain reward circuit by stimulating the limbic system. Accordingly, we developed a VRT program for the treatment of OGA that can stimulate the limbic system using mechanisms similar to VRT for alcohol dependence. We sought to investigate the therapeutic efficacy of VRT for OGA by balancing the limbic circuit via fMRI assessment before and after treatment. In addition, we sought to compare the treatment effects of VRT for OGA to CBT for OGA, because CBT is one of the most effective non-pharmacological treatment methods for OGA [28]. We hypothesized that VRT for OGA would decrease the severity of OGA with an effectiveness similar to that of CBT. We also hypothesized that VRT for OGA would improve the functional connectivity (FC) of the cortico-limbic circuit through repetitive stimulation of the limbic region.

2. Methods

2.1. *Participants*

Through advertisements posted at Chung-Ang University Medical Center, 24 adults with OGA and 12 casual game users were recruited from January to December 2012. Participants with OGA ($N = 24$) were randomly assigned to the CBT group ($N = 12$) or the VRT group ($N = 12$). All participants were screened by a trained psychiatrist based on the Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Patient Edition (SCID-I/P) [29]. All participants were evaluated through an interview regarding excessive game playing patterns and completed the 20-item Young's Internet Addiction Scale (YIAS) [18]. Because this study was conducted before the publication of the DSM-5 [1], the inclusion and exclusion criteria was adopted

from previous studies on OGA [7,30]. Inclusion criteria for the OGA group were: (1) adult males at least 18 years of age; (2) >30 h per week Internet game playing time; (3) disruption of regular life due to excessive Internet gaming; (4) maladaptive behaviors or distress in school or work due to excessive Internet gaming; and (5) a YIAS score >50. All participants with OGA had spent the most of their time online (more than 90% of the time online) playing online games. Inclusion criteria for the casual gaming group were: (1) adult males at least 18 years of age; (2) Internet game playing time <3 days/week and <1 h per day; and (3) a YIAS score <50. Exclusion criteria for both groups were: (1) a history of or current episode of another axis I psychiatric disease; (2) severe alcohol or other substance abuse; and (3) a history of head trauma or other neurologic disease.

The Chung-Ang University Hospital Institutional Review Board approved the research protocol for this study. Written informed consent was obtained from every participant.

2.2. Study procedure

The current study was designed as a four-week, prospective trial, including pre-treatment evaluation, active treatment (CBT or VRT, eight sessions, twice a week), and post-treatment evaluation. The severity of OGA was evaluated with the YIAS before and after the treatment period. At baseline, Beck's Depression Inventory (BDI) [31] for assessing depressive symptoms, Beck's Anxiety Inventory (BAI) [32] for assessing anxiety levels, and the Korean version of the WHO adult attention deficit/hyperactivity disorder (ADHD) self-report scale (ASRS-K) [33,34] for evaluating comorbid ADHD symptoms were also administered. All participants with OGA underwent fMRI scanning before and after the treatment period. Casual game users underwent only baseline assessment including clinical scales and fMRI scanning without being assigned to a treatment group.

2.2.1. Cognitive behavior therapy (CBT)

A total of 12 participants were in the eight-session CBT group. CBT groups were led by a group of experts including a psychiatrist, nurse, psychologist, and social worker. An expert led each session associated with their area of knowledge. Each session lasted for about 2 h. The CBT protocol was adopted from Kim et al. [17] and consisted of eight sessions (S): S1-Introduction and review of problematic outcomes of excessive Internet gaming in terms of regular life, school, and business; S2-Motive for excessive Internet gaming; S3-Stress management; S4-Identity and responsibility; S5-Five steps of change; S6-Solving problems and decision making; S7-Recovery of family relationships; and S8-Future plans.

2.2.2. Virtual reality therapy (VRT)

The other 12 participants were in the eight-session VRT group. The VRT design of the current study is similar to previously published studies on VRT for alcohol dependence [25,26]. Participants individually completed one pre-interview and eight sessions of VRT, which consisted of three steps: (1) relaxation (5 min), (2) simulation of a high-risk situation (10 min), and (3) sound-assisted cognitive reconstruction (10 min). These three stages were performed in the same order during every session. The VR system consisted of a wide screen for stereoscopic images, VR goggles through which participants viewed the images, a separate monitor for the therapist, a keyboard input, and a computer platform. The VR room consisted of two divided spaces: the operating room and the control room. In the operating room, there was a 55-in. three-dimensional video display monitor (1920 × 1080 resolution) for displaying relaxing videos, gaming cues, and aversion-inducing stimuli. A participant wearing VR goggles was seated in a comfortable chair 2 m from the monitor in the operating room (Fig. 1). In the control room, there was another monitor and a computer for the therapist controlling the VRT session. A trained psychiatrist carried out all treatment procedures by instructing the participant and managing the VR system using a keyboard and microphone in the control room.

2.2.2.1. Pre-interview. The pre-interview was conducted by a psychiatrist about 30 min prior to the first of eight sessions of VRT. First, pictures of each participant were taken, and their voices were recorded. Next, participants answered "What are the most precious things in your life?" and "What is the most difficult problem caused by your excessive game play?" Then, narration and scenes were selected to provide emotional stimulation to the participants. Finally, participant demographics, photos, and voice files were input into the VR program. These files were used for the last step of the VRT session, the sound-assisted cognitive reconstruction step.

2.2.2.2. Relaxation. During relaxation, participants were exposed to a relaxing video with relaxing sounds for about 5 min. A participant could choose one of eight different videos that he found the most comfortable. Participants were instructed to watch the video on the monitor and remain as relaxed as possible. The purpose of this step was to relieve tension at the beginning of each session. The therapist was able to control the run-time depending on the state of the participant.

2.2.2.3. High-risk situation. During the high-risk situation, participants were exposed to gaming cues from the game that he or she usually played for 10 min (for example, scenes of betting or receiving cards, scenes of shooting, scenes of leveling-up, and scenes of the last exciting stages of games). This VRT program allowed the participants to select which over-gaming situations to view during the high-risk situation. This purpose was to induce the craving for game play.

2.2.2.4. Sound-assisted cognitive reconstruction. In the middle of the most exciting scenes of the games, an aversion-inducing noise (an annoying beep or siren) was played to pair the exposure of high-risk situation stimuli and aversion-inducing stimuli. In other words, aversion-inducing noise caused the participant to feel annoyed and anxious, so that he could develop an aversive response during the most exciting scenes of the games. Almost simultaneous with aversion-inducing noise, participants were exposed to stimuli illustrating the aversive consequences of long-term pathological gaming. We used the voice recordings and photos from participants recorded during the pre-interview. The participant's photos were integrated into the scenes of aversive consequences of long-term pathological gaming, such as conflicts with family members, low school achievement, losing his or her job,

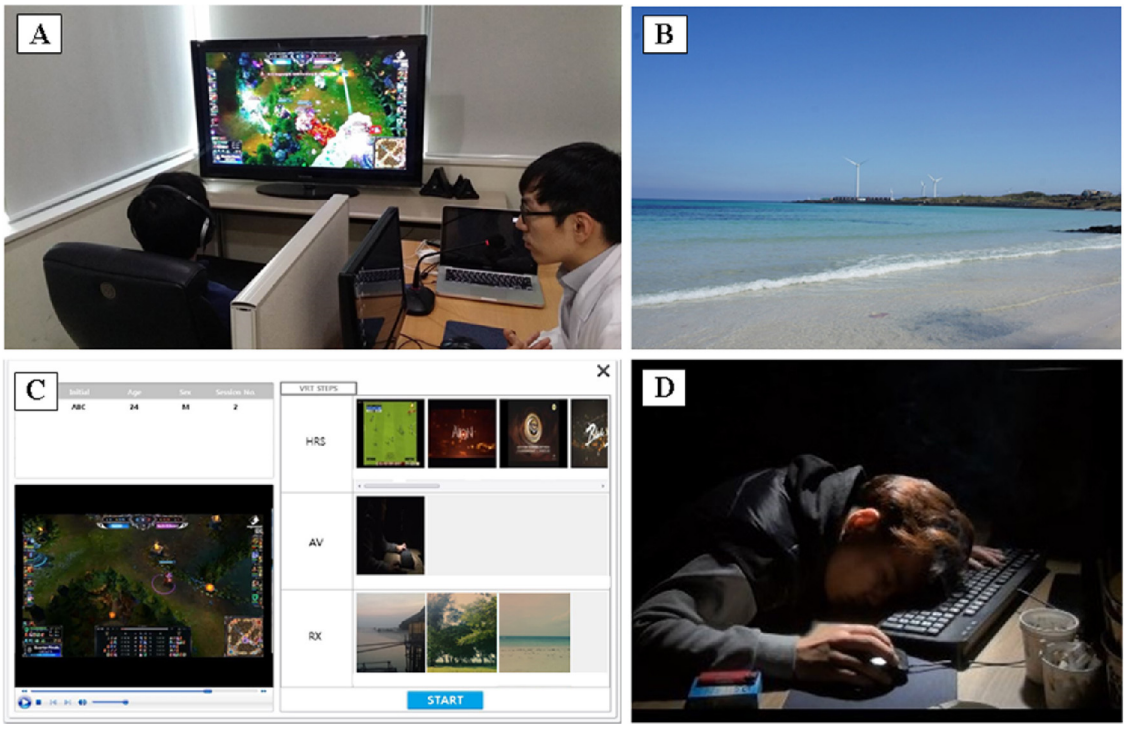

Fig. 1 – The virtual reality (VR) system used in this study. (A) The VRT room: a participant is being exposed to gaming cues during a high-risk situation, (B) one of the movie thumbnails of relaxing videos, (C) the control screen of the VR system, and (D) one of the visual stimuli of the aversive consequences of long-term pathological gaming.

and health problems. Finally, the voice files that contained the participant's answers to the questions about the most precious things in their lives were played. In this final step, we helped the participant by reinforcing and suggesting positive themes.

2.2.3. *Resting-state fMRI assessment*

2.2.3.1. *Preprocessing of resting-state fMRI data*. We used a 3.0 T Philips Achieva scanner to acquire all MRI data. Resting-state fMRI images were acquired axially with an echo-planar imaging sequence using the following parameters: TR/TE = 3000/40 ms, 40 slices, 64 × 64 matrix, 90° flip angle, 230-mm FOV, and 3-mm section thickness without a gap. The scan time was 720 s, and 230 volumes were obtained for each scan.

We used the Data Processing Assistant for Resting-State fMRI (DPARSFA, http://www.restfmri.net), a software tool that works with Statistical Parametric Mapping (SPM8, http://www.fil.ion.ucl.ac.uk/spm/software/spm8/), to analyze acquired fMRI data. All images were corrected for slice acquisition time differences, realigned, normalized, spatially smoothed with a 4-mm FWHM kernel, de-trended, and temporally band-pass filtered (0.01–0.08 Hz). We used an independent component-based noise correction method in order to regress out physiological and other sources of noise, including head motion-related covariates and white matter and cerebrospinal fluid signals. After preprocessing, the amplitude of low-frequency fluctuation (ALFF) and FC were calculated using the Resting-State fMRI Data Analysis toolkit (REST, http://resting-fmri.sourceforge.net).

2.2.3.2. *Amplitude of low-frequency fluctuation (ALFF) calculation*. An ALFF calculation was conducted to assess the intensity of regional spontaneous brain activity [35]. Time series were transformed to the frequency domain using a fast Fourier transform, and the power spectrum was acquired. To calculate the ALFF, the square root of the power spectrum was calculated and then averaged across 0.01–0.08 Hz at each voxel [36]. For standardization, the ALFF of each voxel was divided by the global mean ALFF value.

2.2.3.3. *Functional connectivity (FC) analysis*. FC analysis was used to evaluate functional brain connectivity or functional integration. The protocol consisted of extracting the average blood-oxygen-level-dependent (BOLD) time courses from a seed region and computing Pearson's correlation coefficients between the average time course and the BOLD time course of every other voxel. The correlation coefficients were converted to normally distributed z-scores using Fisher's z-transform. In first-level analysis, within-group FC maps with the posterior cingulate cortex (PCC) as the seed region were assessed using one-sample t-test analysis in SPM8. In second-level analysis of the changes after eight weeks of treatment, group FC maps with the PCC were analyzed using a paired t-test. The resulting maps were set to a threshold of $p < 0.05$ with family-wise error correction for multiple comparisons with more than 40 contiguous voxels and were subjected to cluster analysis (derived from an uncorrected $p < 0.001$ and 40 extended voxels).

2.2.3.4. *The posterior cingulate cortex (PCC) as the seed region of interest*. We selected the PCC as the seed region of interest

because it is closely related to the cortico-limbic circuit and the limbic system, and it also plays a role in cognitive control, including visual-spatial and sensorimotor processes. Dysfunction of the PCC is related to deficient executive function, impulsivity, and prominent behavioral or emotional problems [37,38]. In a resting state fMRI study of OGA, connectivity with the PCC was positively correlated with the severity of OGA in the right precuneus, thalamus, caudate, nucleus accumbens, supplementary motor area, and lingual gyrus [39].

2.3. Statistical analysis

We compared the ALFF maps of the OGA and casual gaming groups using a voxel-based two-sample *t*-test with a whole brain mask with age, years of education, and six head motion parameters as covariates at baseline. The resulting maps were set to threshold using a $p < 0.05$ false discovery rate correction for multiple comparisons with more than 40 contiguous voxels and were subjected to cluster analysis (derived from an uncorrected $p < 0.001$ and 40 extended voxels).

Age, years of education, YIAS score, BDI score, BAI score, ASRS-K score, and FC were compared between OGA and healthy control groups (casual game users) using the Mann–Whitney-*U* test. Brain functional activity was compared between the 12 participants of the CBT group and the 12 participants of the VRT group using an independent *t*-test. For the determination of each treatment effect, a repeated measures of analysis of covariance (ANCOVA) and paired *t*-tests were used to assess changes in YIAS score and brain FC between baseline and week 8 in the CBT and VRT groups. All analyses were performed using Statistica 6.0 (2001, StatSoft, Tulsa, OK).

3. Results

3.1. Demographic and clinical characteristics

There were no significant differences between OGA and healthy controls in terms of age, years of education, or scaled scores of the BDI, BAI, and ASRS-K (Table 1). The OGA group scored significantly higher on the YIAS than the healthy control group ($F = 45.4$, $p < 0.01$). There were no significant differences between the CBT and VRT groups in age, years of education, or BDI, BAI, ASRS-K, and YIAS scores.

3.2. Changes in severity of OGA after treatment

After treatment, both CBT and VRT groups showed significantly reduced YIAS score. In the CBT group, YIAS score significantly decreased from 64.0 ± 11.4 to 48.2 ± 8.0 during the treatment period ($Z = 3.12$, $p = 0.05$; Table 2). In the VRT group, YIAS score significantly decreased from 60.8 ± 11.8 to 47.6 ± 7.6 after treatment ($Z = 3.06$, $p < 0.01$). There was no significant difference in YIAS score change between CBT and VRT groups ($F = 0.43$, $p = 0.52$).

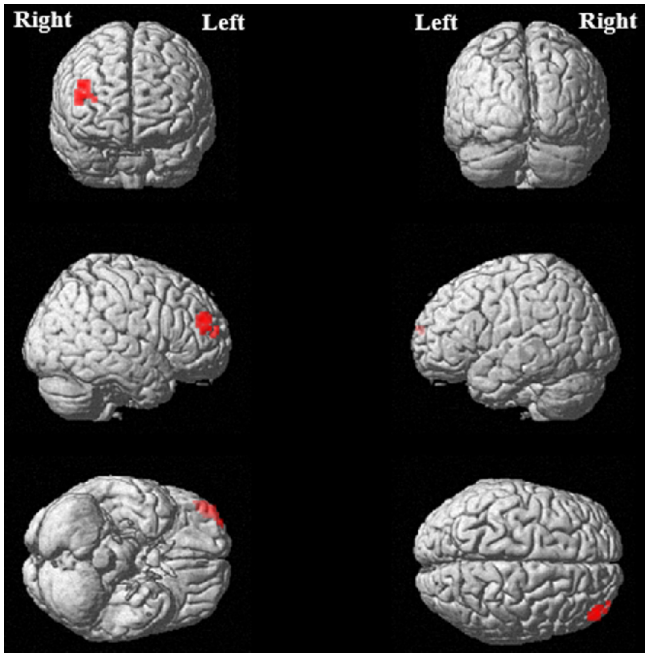

Fig. 2 – Brain regions that showed smaller amplitude of low-frequency fluctuation (ALFF) in the online game addiction (OGA) group in comparison with the healthy control group at baseline.

3.3. Changes in brain FC after treatment

3.3.1. ALFF of the OGA group and healthy control group at baseline

Individuals with OGA showed decreased activity within the right middle frontal gyrus (Talairach coordinates, 45, 48, 27, $P_{uncorrected} < 0.001$, $T = 4.63$ ($Z = 3.87$), $Ke = 41$; Fig. 2). There was no significant difference in brain activity between VRT and CBT groups.

The OGA group showed decreased activity within the right middle frontal gyrus (Talairach coordinates, 45, 48, 27, $P_{uncorrected} < 0.001$, $T = 4.63$ ($Z = 3.87$), $Ke = 41$) compared to the healthy control group.

3.3.2. Brain FC from the PCC seed to other areas of the brain at baseline

At baseline (before treatment), the healthy control group showed positive connectivity from the right PCC seed to the bilateral superior frontal gyrus, right medial frontal gyrus, and bilateral parietal cortices (Fig. 3; Table 3). At baseline, the OGA group showed positive FC from the PCC seed to the bilateral parietal cortices.

3.3.3. Changes in FC from the PCC seed to other brain areas in the OGA group after treatment

After treatment, the VRT group showed increased FC from the PCC seed to the right parietal, right brain stem, right superior temporal gyrus, left middle frontal gyrus, and left temporal fusiform gyrus (Fig. 4; Table 4). After treatment, the CBT group showed increased FC from the PCC seed to the right cerebellum, bilateral thalamus, and left occipital lingual gyrus.

Table 1 – Demographic and clinical characteristics of the participants at baseline.

	CBT group ($N = 12$)	VRT group ($N = 12$)	Casual game users ($N = 12$)	Statistics
Age (years)	24.2 ± 3.2	23.6 ± 2.7	23.3 ± 2.9	$F = 0.26$, $p = 0.77$
Years of education	16.7 ± 2.3	16.8 ± 2.8	16.3 ± 2.9	$F = 0.06$, $p = 0.95$
YIAS	64.0 ± 11.4	60.8 ± 11.8	28.7 ± 4.9	$F = 45.4$, $p < 0.01$*
BDI	8.3 ± 4.2	8.5 ± 5.5	9.4 ± 3.6	$F = 0.27$, $p = 0.76$
BAI	4.5 ± 4.3	5.8 ± 5.5	8.3 ± 5.6	$F = 1.63$, $p = 0.21$
ASRS-K	9.8 ± 6.4	9.2 ± 5.1	8.6 ± 3.5	$F = 0.15$, $p = 0.86$

Note: CBT, cognitive behavior therapy; VRT, virtual reality therapy; YIAS, Young's Internet Addiction Scale; BDI, Beck's Depression Inventory; BAI, Beck's Anxiety Inventory; ASRS-K, Korean version of the WHO adult ADHD self-report scale.
* $p < 0.01$: statistically significant.

Table 2 – Changes in Young's Internet Addiction Scale (YIAS) scores after treatment.

	Pre-treatment	Post-treatment	Statistics
CBT group	64.0 ± 11.4	48.2 ± 8.0	$Z = 3.12$, $p = 0.05$
VRT group	60.8 ± 11.8	47.6 ± 7.6	$Z = 3.06$, $p < 0.01$*

Note: CBT, cognitive behavior therapy; VRT, virtual reality therapy.
* $p < 0.01$: statistically significant.

4. Discussion

4.1. *Changes in severity of OGA after treatment*

During the treatment period, both CBT and VRT groups showed significant reductions in severity of OGA as measured by YIAS. In addition, the 8-session VRT program for OGA improved the severity of OGA with an effectiveness similar to that of eight sessions of CBT. The VRT program used in the present study was newly developed, and we were able to show the effectiveness of the program, which consisted of three steps of relaxation, simulation of a high-risk situation, and sound-assisted cognitive reconstruction. One possible advantage of treatment using the VRT program is that it can be used in individuals with OGA who have comorbid psychiatric conditions. OGA frequently co-occurs with major depressive disorder, social anxiety disorder, or ADHD [40]. The virtual reality world of VRT may immerse patients with ADHD in the therapeutic process despite the challenge of maintaining their attention with conventional therapeutic techniques (including psychotherapy, education, and CBT). In addition, VRT may be a good treatment option for individuals with OGA and major depressive disorder or social anxiety disorder, who feel discomfort or fear related to group CBT. Another advantage of the VRT program is the shorter duration of sessions (30 min including preparation and wrap-up) in comparison with CBT sessions (about 2 h per session).

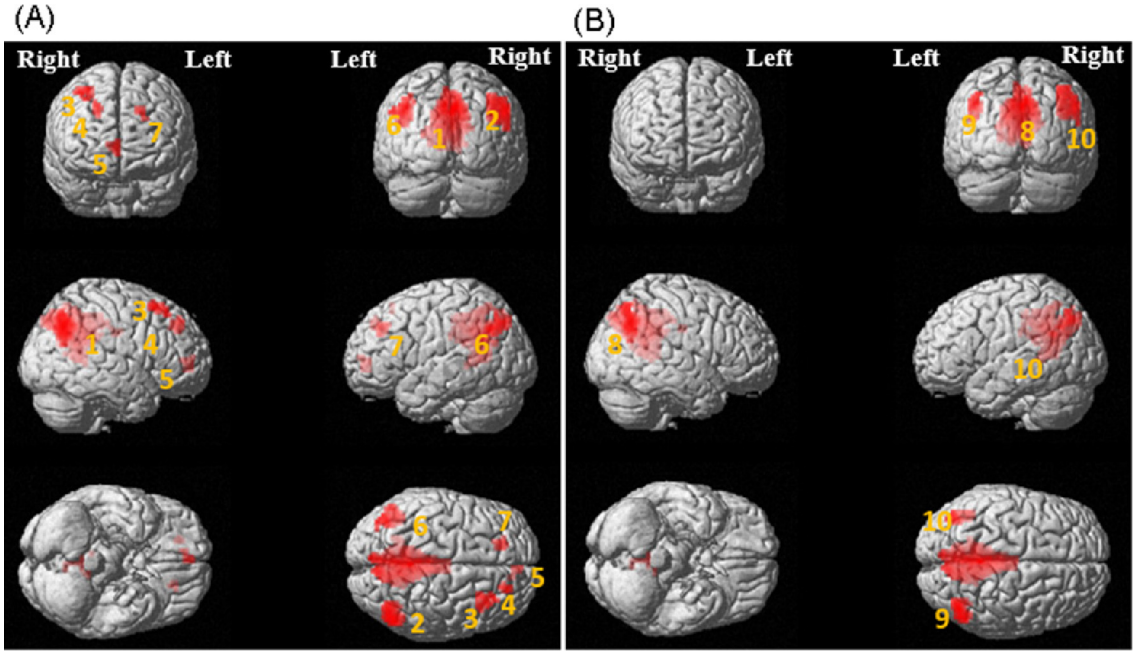

Fig. 3 – Brain functional connectivity (FC) from the posterior cingulate cortex (PCC) seed to other brain areas. (A) Healthy control group and (B) online gaming addiction (OGA) group.

Table 3 – Brain functional connectivity (FC) from the posterior cingulate cortex (PCC) seed to other brain areas.

Talairach coordinates			Ke	T	$P_{FDR-corr}$	Regions
x	y	z				
(A) Healthy control group						
3	−42	24	1212	48.51	<0.001	1: right posterior cingulate gyrus
39	−69	48	206	14.08	<0.001	2: right superior parietal lobule, BA 7
30	30	51	48	5.37	<0.001	3: right superior frontal gyrus, BA 8
21	39	39	41	4.75	0.001	4: right superior frontal gyrus, BA 8
3	51	6	45	5.01	0.001	5: right medial frontal gyrus, BA 10
−42	−57	27	103	15.88	<0.001	6: left parietal precuneus, BA 19
−15	36	39	43	5.52	<0.001	7: left superior frontal gyrus, BA 9
(B) Online gaming addiction (OGA) group						
3	−42	24	1235	62.06	<0.001	8: right posterior cingulate gyrus
51	−63	33	151	5.59	0.001	9: right parietal, angular gyrus, BA 39
−42	−72	39	53	5.81	0.001	10: left parietal precuneus, BA 19

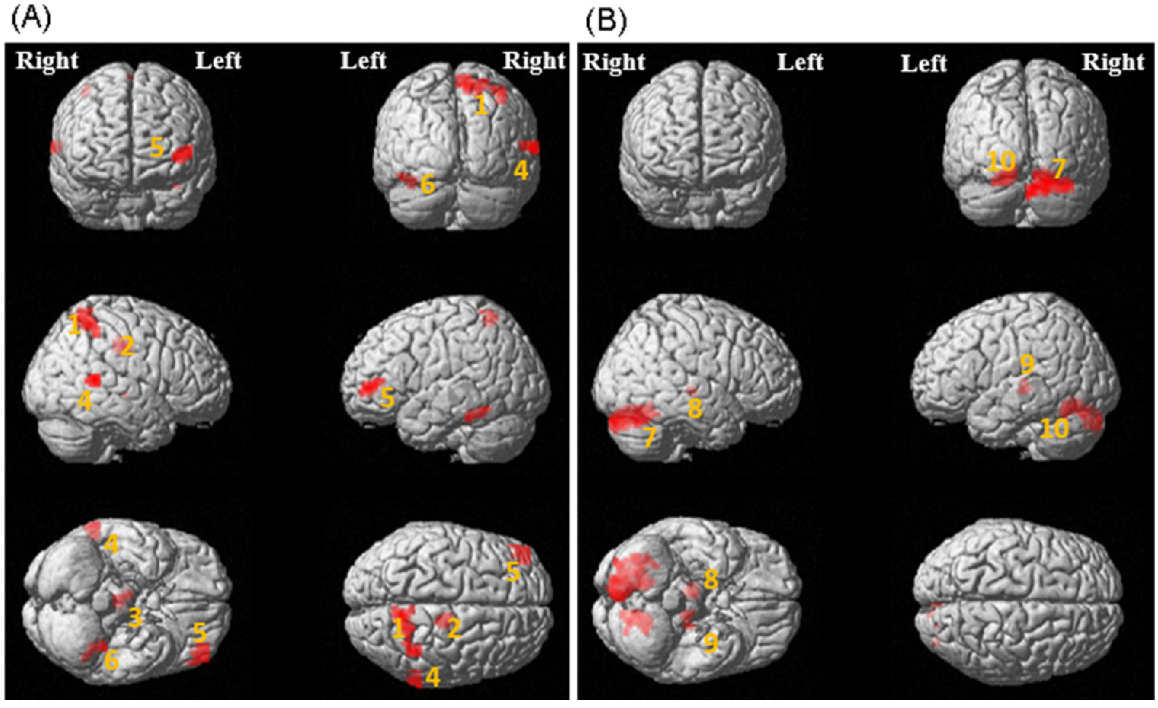

Fig. 4 – Changes in functional connectivity (FC) from the posterior cingulate cortex (PCC) seed to other brain areas after treatment. (A) Virtual reality therapy (VRT) group and (B) cognitive behavioral therapy (CBT) group

Table 4 – Changes in functional connectivity (FC) from the posterior cingulate cortex (PCC) seed to other brain areas after treatment.

Talairach code			Ke	T	$P_{uncorrected}$	Regions
x	y	z				
(A) Virtual reality therapy (VRT) group						
9	−60	63	93	8.11	<0.001	1: right parietal precuneus, BA 7
15	−21	36	54	6.87	<0.001	2: right cingulate gyrus, BA 31
6	−18	−6	41	6.59	<0.001	3: right brain stem red nucleus
66	−45	9	48	5.53	<0.001	4: right superior temporal gyrus, BA 22
−42	51	3	47	6.15	<0.001	5: left middle frontal gyrus, BA 10
−36	−39	−21	46	5.66	<0.001	6: left temporal fusiform gyrus, BA 20
(B) Cognitive behavioral therapy (CBT) group						
18	−66	−18	236	4.64	<0.001	7: right cerebellum, posterior lobe, declive
6	−21	−3	41	4.36	0.001	8: right thalamus
−12	−24	0	43	4.30	0.001	9: left thalamus
−12	−66	−15	69	4.29	0.001	10: left occipital lingual gyrus

4.2. ALFF of the OGA and healthy control groups at baseline

At baseline, the OGA group showed smaller ALFF within the right middle frontal gyrus and less FC in the cortico-striatal-limbic circuit in comparison with the healthy control group. This is in accordance with recent functional neuroimaging studies that found changes in ALFF in patients with addictive disorders. Changes in ALFF in the fronto-striatal circuit in addictive disorders may reflect a deficit of modulation in prefrontal areas [41,42]. Jiang et al. [41] reported that substance addicts have decreased ALFF in the bilateral medial orbit frontal cortices, left dorsal lateral prefrontal cortex, and bilateral dorsal anterior cingulate cortices as well as increased ALFF in the bilateral angular gyri, bilateral precuneus, bilateral supramarginal gyri, left posterior cingulate cortex, and left middle frontal gyrus. Most recently, Kühn and Gallinat [42] reported that excessive Internet use is significantly negatively associated with severity of clinical symptoms and with right frontal pole gray matter volume. Furthermore, the severity of clinical symptoms is positively correlated with ALFF in the striatum [42].

4.3. Brain FC from the PCC seed to other brain areas at baseline

At baseline, the healthy control group showed positive connectivity from the right PCC seed to the bilateral superior frontal gyrus, right medial frontal gyrus, and bilateral parietal cortices, while the OGA group showed positive FC from the PCC seed to the bilateral parietal cortices at baseline. These findings suggest that individuals with OGA display altered resting-state patterns of brain activity especially in regions within the default mode network (DMN). The DMN includes the PCC, precuneus, medial frontal cortex, ventral anterior cingulate cortex, and lateral and inferior parietal cortices [43]. Interestingly, because the DMN is activated at rest and not during task stimulation, it is related to self-referential processing [44]. Although different components of the DMN have been suggested, one of the most consistently included regions of the DMN is the PCC. The PCC is thought to be associated with monitoring of internal and external environments [43]. Neurobiological studies have suggested that the PCC contributes to attentional processes and is associated with reward receipt, magnification, and visual-spatial processing in addiction disorders [39]. Recently, Ding et al. [39] showed altered FC within regions of the DMN in adolescents with OGA using PCC as a seed region. This alteration was similar to that seen in patients with substance dependence, such as nicotine dependence [45]. Tanabe et al. [45] reported reduced activity in regions within the DMN in nicotine dependence and suggested that the cognitive influences of nicotine may lead to a network shift from monitoring and processing of internal information to external information.

4.4. Changes in FC from the PCC seed to other brain areas in the OGA group after treatment

In the CBT group, connectivity from the PCC seed to the bilateral thalami and right cerebellum increased across the 8-session treatment period. In other words, CBT was shown to enhance PCC-thalamus-cerebellum connectivity. It has recently become clear that the cerebellum is reciprocally connected to the thalamus and basal ganglia [46]. Neuroimaging studies have reported that cognitive deficits in addicted individuals are related to abnormal cerebellar activity [47]. It has also been suggested that the cerebellum, through its connections with the thalamus and basal ganglia, plays a role in the sensorimotor network that supports automatized behavioral reactions toward drug-related stimuli [48,49]. We cautiously surmise that increased thalamus-cerebellum connectivity at rest would prevent abnormal cue reactivity of those regions in response to stimuli that increase craving.

In the VRT group, connectivity from the PCC seed to the left middle frontal and bilateral temporal lobe also increased during the 8-session treatment period. For this study, we developed a VRT program to increase balanced activation within the brain reward circuit by stimulating the limbic system. With repeated pairing of craving-inducing, game-related stimuli and scenes of the aversive consequences of gaming, the VRT program was expected to stimulate both the striatum (responsible for craving) and the temporal lobe (responsible for aversion) and to facilitate limbic-regulated responses to rewarding stimuli. In this study, VRT was shown to reduce the severity of OGA with effectiveness similar to CBT. In addition, VRT enhanced the FC in the left middle frontal-PCC-bilateral temporal lobe and improved balance in the cortico-striatal-limbic circuit. It has been suggested that the prefrontal cortex plays a role in the memory network that supports emotional and cognitive links between the environment and drug craving [42]. It means that VRT program may able to prevent habitual emotionless game use by facilitating limbic-regulated responses to rewarding stimuli.

4.5. Limitations

There are several limitations to the current study. First, the small number of participants limits the generalizability of the results. The small sample size may have also limited our ability to control for multiple comparisons in fMRI analyses. Second, because our study focuses on neuroimaging assessments, other neuropsychological variables such as intelligence, working memory function, and the personality of participants were not thoroughly investigated. These neuropsychological characteristics may have affected the results. Third, the cues used in the VRT program were not previously validated, and we could not ensure that the gaming-related stimuli actually induced craving or that the aversive scenes were actually aversive to participants. Fourth, the absence of follow-up data for healthy control participants after VRT decreased the confidence of the current study. Future research is needed to estimate stimulation-elicited subjective responses. Lastly, there could be ethical concerns surrounding the use of aversive stimuli during VRT. The intensity of aversive stimuli should be always discussed and adjusted because aversive stimuli have the potential of provoking anxiety and defensive aggression.

5. Conclusion

Treatment of OGA using VRT seemed to reduce the severity of OGA and was as effective as CBT; it also enhanced balance in the cortico-striatal-limbic circuit. The VRT program may be able to prevent habitual, emotionless game use by facilitating limbic-regulated responses to rewarding stimuli.

Conflicts of interest

The authors have no conflicts of interest to declare.

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