Altered Resting-State Functional Connectivity in Internet Addicts

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Abstract—**The purpose of this study was to examine functional disconnectivity in Internet addicts using resting-state functional Magnetic Resonance Imaging (rs fMRI). Internet addicts and demographically similar non-addicts were scanned using rs fMRI. For the connectivity analysis, Regions Of Interests (ROIs) were defined based on previous studies of addictions. The functional connectivity assessment for each subject was obtained by correlating time-series across the ROIs, resulting in 8x8 matrix for each subject. Within-group functional connectivity patterns were observed by entering the z maps of the ROIs of each subject into second-level one sample *t* test. Two sample *t* test was also performed to examine differences between two groups. A significant increase was observed in positive functional connectivity between the Orbito Frontal Cortex (OFC) and several brain regions in the non-addicted group. However, no significant correlations in these structural connectivities were found in the Internet addiction group. The Internet addiction group presented significant negative connectivity between the OFC and insula. Our findings provide the evidence that Internet addicts have aberrant functional connectivity in the corticostriatal circuit at resting state. Particularly, we suggest that the OFC, which is associated with processing negative affect and behavioral inhibition, may play a crucial role in the pathophysiology of the Internet addiction.**

Keywords-Resting-state fMRI; Internet addicts; Functional connectivity; Orbitofrontal cortex

I. INTRODUCTION

Internet addiction disorder is marked by an inability to control one's Internet use, which eventually leads to psychological, social or work difficulties [1]. Internet addiction is defined as an Internet gaming disorder in DSM-V [2], but the nosology and optimal diagnostic criteria for an Internet gaming disorder remain controversial. The reason is that Internet addiction shares features in common with impulse control, behavioral addiction, and obsessive-compulsive disorders [3].

Regardless of whether Internet addiction is best conceptualized as a behavioral addiction or an impulse control disorder, Internet addiction has been speculated to be related to impaired inhibitory control. While impulsivity has always been recognized as central to Internet addiction, it is increasingly acknowledged to impact upon risk for and maintenance of addictive disorders.

Clinical evidence suggests that Internet addicts have a high level of impulsivity as measured by behavioral task of response inhibition (Go-No go task) and a self report questionnaire (BIS-2 scale) [4]. An Event-Related Potential (ERP) study of executive control ability (Go-No go task) found Internet addicts represented less efficient information processing and lower impulse control than controls [5]. In a functional Magnetic Resonance Imaging (fMRI) study using color-word stroop paradigm, Internet addicts also showed diminished efficiency of response inhibition processes relative to controls [6]. While numerous studies have focused on task-based ERP and fMRI related to Internet addiction and impulsivity, few studies have explored resting-state brain activity in relation to Internet addiction and impulsivity.

The purpose of this study was to examine functional disconnectivity in Internet addicts using resting-state fMRI.

II. METHODS

A. Participants

Fifteen individuals from the Internet addicts (15 men; mean = 22.20, SD = 3.07) and 15 from the normal group (15 males; mean = 22.47, SD = 2.53), both university students, participated in the current fMRI experiment. To sample the final participants of the experiment, the Korean translated/modified version of the Internet Addiction Scale (IAS) [1] and the K-scale [7] were used. The original IAS is a self-reported scale of the pathological use of the Internet (i.e., preoccupation, compulsive use, behavioral problems, emotional changes, impact on life related to Internet usage), consisting of 20 questions. Each question is based on a 5-point scale (1: Never to 5: Very). Individuals scoring 70 points or higher compose the Internet addiction group, for whom the Internet use can cause a serious problem in daily

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life; people by 40–69 points are categorized as a mild Internet addiction group, and those with 39 points and less are considered normal users. The Korean version of the IAS showed desirable internal consistency (Cronbach's α=. 9) [8].

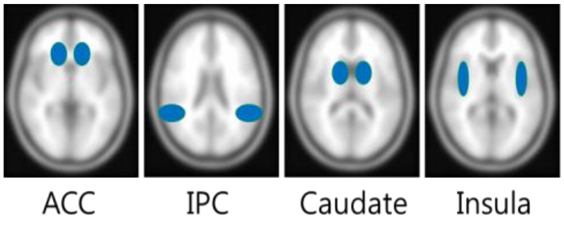
The K-scale is a Korean adults' Internet addiction self-diagnosis scale developed based on a survey of 146 university students. The scale consists of 20 questions and includes 4 subscales: disability to distinguish daily life and reality; the positive expectation of the Internet; tolerance and withdrawal; and self-awareness of the Internet. Each question is asked on a Likert-type 4-point scale (1: Never to 4: Very), with 53 points or below indicating that the individual should be classified as part of the general user group, whereas individuals with a score of 54 points or above are included in the Internet addiction group.

To obtain more accurate behavioral and neuroimaging data on Internet addicts, all subjects included in the Internet addiction group and the normal controls did not simultaneously experience other addictive diseases such as alcoholism or gambling addiction. The average IAS score of participants selected as the final Internet addicts was 70.80 (SD = 10.31), and the average K-scale score was 60.00 (SD = 4.47); the average IAS score of the control group was 28.60 (SD = 7.35), and their average K-scale score was 32.60 (SD = 7.70) ($p < 0.001$). All participants of the experiment provided their signed consent to voluntarily participate in the experiment after being thoroughly informed of the details of the experiment.

To determine whether Internet addicts were more impulsive than controls, Barrett's Impulsiveness Scale II (BIS-II), as adapted by Lee [9], was used. BIS-II consists of 35 questions with dichotomized "yes" (1) or "no" (0) answers. The total score ranges between 0 and 35, with higher scores indicating greater levels of impulsiveness. The scale was reported to be reliable (Cronbach's α=. 85) [10].

B. Regions of Interest for Network Analysis

On the basis of previous studies on the functional neuroimaging of addiction [11], the following regions, including the reward network, were considered a priori to be of particular interest: the Inferior Parietal Cortex (IPC), Anterior Cingulate Cortex (ACC), caudate nucleus, Putamen, Orbital Frontal Cortex (OFC), Dorso Lateral PreFrontal Cortex (DLPFC), amygdala, and insua. Thus, 8 seed regions were defined.



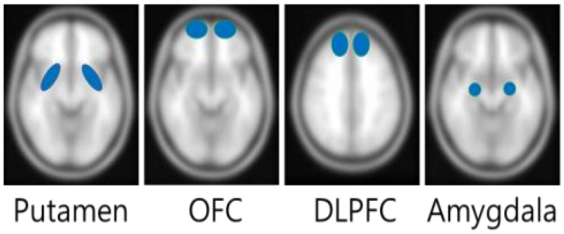


Figure 1. Selected ROIs for connectivity (ACC, Anterior Cingulate Cortex; IPC, Inferior Parietal Cortex; OFC, Orbito Frontal Cortex; DLPFC, DorsoLateral PreFrontal Cortex)

Figure 1 shows selected Regions Of Interest (ROIs) for connectivity analysis. These ROIs masks were built by using the WFU pick atlas 2.4 toolbox [12].

C. Functional MRI Image Acquisition

Imaging was conducted using a 3.0 T whole-body ISOL Technology FORTE scanner (ISOL Technology, Korea) equipped with whole-body gradients and a quadrature head coil. Single-shot echo-planar fMRI scans were acquired in 35 continuous slices, parallel to the anterior commissure–posterior commissure line. The parameters for fMRI included the following: the Repetition Time/Echo Time (TR/TE) were 3000/40 ms, respectively, flip angle was 80, field of view was 240 mm, matrix was 64 × 64, slice thickness was 4 mm, and the in-plane resolution was 3.75 mm. Three dummy scans from the beginning of the run were excluded to decrease the effect of non-steady state longitudinal magnetization. T1-weighted anatomic images were obtained using a 3-D FLAIR sequence (TR/TE = 280/14 ms, flip angle = 60, FOV = 240 mm, matrix = 256 × 256, slice thickness = 4 mm).

D. Analysis- Functional MRI Preprocessing

The first 4 time points of the resting-state were discarded to avoid the instability of the initial MRI signal. After that, preprocessing steps, carried out with the SPM 8 toolbox, consist of slice-timing correction for interleaved acquisition, motion correction, and spatial normalization into a standard template provided by the Montreal Neurological Institute (MNI). The normalized images were smoothed with 8-mm Gaussian kernel. For the resting-state data, linear detrending and band-pass filtering (0.01-0.08 Hz) were performed by using conn toolbox. In addition, the head motion parameters, averaged signals from white matter, cerebrospinal fluid, and global brain signal were regressed out to remove the possible spurious variances derived from cardiac and respiratory fluctuations [13][14].

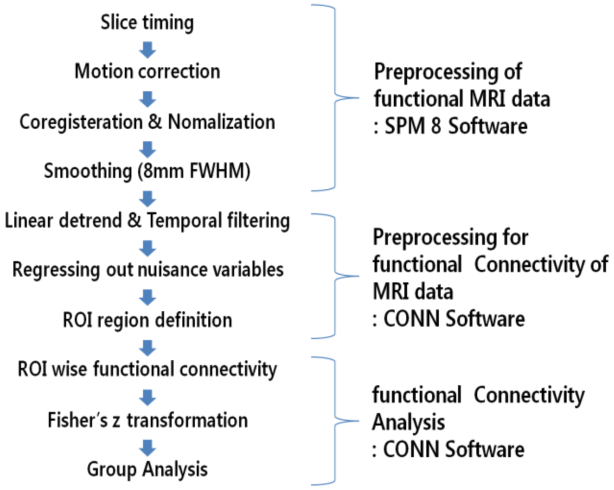


Figure 2. The flow chart of resting-state functional connectivity analysis

E. *Analysis- Functional Connectivity: ROI-Wise Manners*

After extracting the 8 ROIs for each subjects, we computed the functional connectivity between each pair of the 8 ROIs.

Functional connectivity analysis were conducted in ROI-wise manners. For ROI-wise functional connectivity computing the correlations between ROIs, network functional connectivity was conducted at one to one basis.

The ROI-to-ROI functional connectivity analysis was performed by averaging the time series in the two seed regions, respectively, and then, computing the Pearson's R correlation coefficient between the two averaged time series. Therefore, we obtained an 8*8 matrix for each subject in resting-state, with each element representing the strength of the functional connectivity between the corresponding two brain regions within the reward network. Specifically, the diagonal element was self-correlated to the corresponding region. Finally, the resulting correlation coefficients then were normalized to z-scores with Fisher's r-to-z transformation.

F. *Analysis - Statistical Analysis*

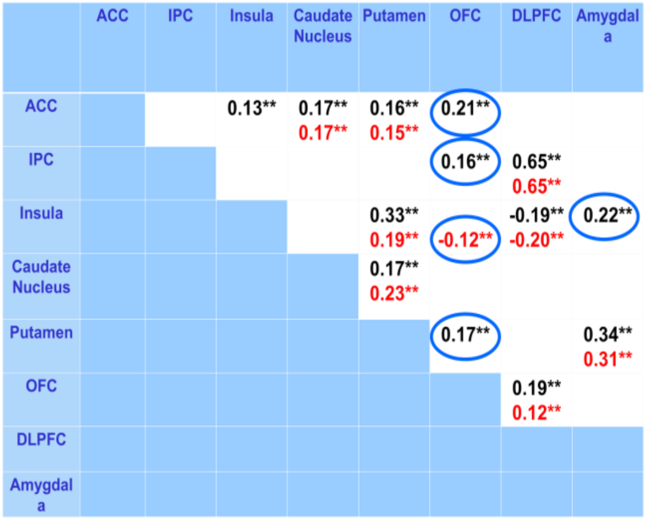
To determine whether the correlations between regions were significantly nonzero across subjects, we performed one-sample t test for each group. To examine the differences in the strength of connectivity between the two groups in resting-state, we performed two sampled t tests on the elements with significant nonzero connections of either control or Internet addicts. The significance threshold between group differences was set at $p < 0.05$, and the False Discovery Rate (FDR) [15] procedure was used to find a threshold that would restrict the expected proportion of type I errors to $q = 0.05$.

To investigate the relationship between resting state connectivity strength and degree of Internet addiction and degree of impulsivity, the correlation between functional connectivity of ROIs and scores of Internet addiction were assessed.

III. RESULTS

Table 1 provides functional networks showing significant connectivity of each ROI between controls and Internet addicts.

TABLE 1. CORRELATION COEFFICIENT BETWEEN ROIs BLACK: NON-ADDICTION, RED: INTERNET ADDICTION



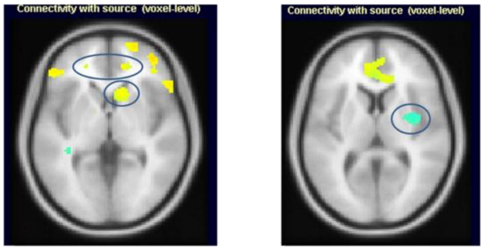
	ACC	IPC	Insula	Caudate Nucleus	Putamen	OFC	DLPFC	Amygdala
ACC			0.13**	0.17** 0.17**	0.16** 0.15**	0.21**		
IPC						0.16**	0.65** 0.65**	
Insula					0.33** 0.19**	-0.12**	-0.19** -0.20**	0.22**
Caudate Nucleus					0.17** 0.23**			
Putamen						0.17**		0.34** 0.31**
OFC							0.19** 0.12**	
DLPFC								
Amygdala								

(* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, FDR)

In resting state, controls showed increased connectivity in several pair regions, including connectivity between the caudate nucleus and the anterior cingulate cortex, between the putamen and the insula, between the putamen and the caudate nucleus, between the dorso lateral prefrontal cortex and the inferior parietal cortex, between the dorso lateral prefrontal cortex and the orbito frontal cotrex, and between the amygdala and the putamen, while showed decreased connectivity between the dorso lateral prefrontal cortex and the insula ($p < 0.05$, FDR).

In Internet addicts, a significant increase was observed in functional connectivity between the caudate nucleus and the anterior cingulate cortex, between the putamen and the anterior cingulate cortex, between the putamen and insula, between the caudate nucleus and the putamen, between the dorso lateral prefrontal cortex and the inferior parietal cortex, between the dorso lateral prefrontal cortex and the orbito frontal cotrex, between the amygdala and the putamen, and a significant decrease was observed in functional connectivity between the orbito frontal cortex and the insula, between the dorso lateral prefrontal cortex and the insula ($p < 0.05$, FDR).

Between group analysis revealed that the connectivity in between the orbito frontal cortex and inferior parietal cortex, between orbito frontal cortex and putamen, between the orbito frontal cortex and anterior cingulate cortex, between the insula and anterior cingulate cortex, and between amydgala and insula were significantly stronger in control group than in the Internet addicts (Figure 3a), while the connectivity in between the orbito frontal cortex and insula showed stronger negative correlation in the Internet addicts relative to control group (Figure 3b) ($p< 0.001$, uncorrected).



a) OFC-ACC correlation map in non-addiction group *b)* OFC-insula correlation map in internet addiction group

Figure 3. Significant differences in resting state functional network connectivity between groups. Yellow: positive correlation, Blue: negative correlation

No significant relationship between functional connectivity strength and current degree of Internet addiction and degree of impulsitivy was seen.

IV. CONCLUSIONS

This study found that Internet addicts had declined connectivity strength in the Orbito Frontal Cortex (OFC) and other regions (e.g., ACC, IPC, and insula) during resting-state. It may reflect deficits in the OFC function to process information from different area in the corticostriatal reward network. Evidence indicates that the OFC participates in the executive control of information processing and behavioral expression by inhibiting neural activity associated with irrelevant, unwanted, or uncomfortable information, or actions [16]. The role of the OFC in inhibition has gained increasing prominence in the literature due to the dramatic rise in research investigating the neural correlates of social and emotional processing [16][17] .

Our findings provide the evidence that Internet addicts have aberrant functional connectivity in the corticostriatal circuit at resting state. Particularly, we suggest that the OFC, which is associated with processing negative affect and behavioral inhibition, may play a crucial role in the pathophysiology of the Internet addiction.

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