Altered Functional Disconnectivity in Internet Addicts with Resting-State Functional Magnetic Resonance Imaging

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Objective: In this study, we used resting-state fMRI data to map differences in functional connectivity between a comprehensive set of 8 distinct cortical and subcortical brain regions in healthy controls and Internet addicts. We also investigated the relationship between resting state connectivity strength and the level of psychopathology (ex. score of internet addiction scale and score of Barratt impulsiveness scale).

Background: There is a lot of evidence of relationship between Internet addiction and impaired inhibitory control. Clinical evidence suggests that Internet addicts have a high level of impulsivity as measured by behavioral task of response inhibition and a self report questionnaire.

Method: 15 Internet addicts and 15 demographically similar non-addicts participated in the current resting-state fMRI experiment. For the connectivity analysis, regions of interests (ROIs) were defined based on the previous studies of addictions. Functional connectivity assessment for each subject was obtained by correlating time-series across the ROIs, resulting in 8x8 matrixs 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 between group differences.

Results: Between group, the 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 was significantly stronger in control group than in the Internet addicts, while the connectivity in between the orbito frontal cortex and insula showed stronger negative correlation in the Internet addicts relative to control group ($p < 0.001$, uncorrected). No significant relationship between functional connectivity strength and current degree of Internet addiction and degree of impulsitivy was seen.

Conclusion: This study found that Internet addicts had declined connectivity strength in the orbitofrontal 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.

Application: The results might help to develop theoretical modeling of Internet addiction for Internet addiction discrimination.

Keywords: Internet addiction, Inhibitory control, Resting-state fMRI, Functional connectivity, Orbitofrontal cortex

1. Introduction

Internet addiction means that one uses or is absorbed in the Internet excessively, and cannot adjust or control the use of the Internet, and thus, some psychological, social and job-related problems occur (Young, 1998). Due to recent development of the Internet and smartphone, the number of Internet addicts rapidly increases globally. As the damages, according to Internet addiction, get serious, because of social, emotional and psychological problems, arising from the Internet use, the interest in Internet addition increases gradually (Kim et al., 2010; Shaw and Black, 2008; Dong et al., 2011).

Despite such seriousness of Internet addiction, studies or information on Internet addiction is still insufficient, and a dispute arises on whether to diagnose Internet addition as mental disorder, owing to the lack of empirical evidence. In DSM-V (APA, 2013), Internet addiction is named Internet game use disorder; however, no agreement on nosology or diagnosis standard is made. The reason is that Internet addiction has the common characteristics found in impulsiveness control, behavior addiction and obsessive disorder (Aboujaoude et al., 2006). Although, there is a dispute on whether Internet addiction should be classified as behavior addition or impulsiveness control disorder, it seems obvious that Internet addition is related with high impulsiveness and the deficient inhibitory control ability.

Cao et al. (2007) found that Internet addicts had high impulsiveness and deficient inhibitory control ability by using the Go-No task and a self-report questionnaire (BIS-2 scale). In the study measuring the executive function of Internet addicts using the event-related potential (ERP) and Go-No task, the Internet addicts did not efficiently process information and did not control impulsiveness, compared to the control group (Dong et al., 2010). In the research using the functional magnetic resonance imaging (fMRI) and color-word stroop task, it was revealed that Internet addicts were lacking in response inhibition processing ability, compared to non-addicts (Dong et al., 2012). Likewise, several studies show empirical and physiological evidence on the Internet addicts' impulsiveness and deficient response inhibition. However, all these studies show task-based results, namely, brain's functional impairment, when a specific stimulus was presented. If brain's functional activity has impairment, the functional abnormality should be reported, when no stimulus was presented, that is, in the resting-state brain as well.

Recently, some studies are carried out in order to understand brain function in the resting-state without external stimulus or without performing of a specific task. Human's brain weighs only 2% of total human body weight, but, the brain is known to consume 20% of total energy (Shulman, 2004). Also, of the energy used by the brain, 60-80% of energy is known to be used in the resting-state. Given that metabolic load, of which consumption increases in the recognition process, accounts for 0.5% - less than 1% of the energy used in the resting-state, the understanding of the brain in the resting-state is important (Raichle and Mintun, 2006).

Functional connectivity during resting-state means temporal connectivity of brain activity measured as neurophysiologic index in various brain areas. In functional magnetic resonance imaging (fMRI), temporal connectivity is analyzed between each brain area by setting BOLD signal in the low frequency (<0.1 Hz) band that is shown voluntarily during the resting-sate as the neurophysiologic index. Such a low frequency BOLD signal is known to reflect neural activity generated within the brain, and synaptic activity is reported to be concerned with dendritic potential.

Despite the importance of understanding on resting-state brain, almost no study on the functional deficiency of Internet addicts during the resting-state has been conducted thus far. In this regard, this study aims to examine Internet addict's brain connectivity deficiency during the resting-state using fMRI. In other words, this study investigates whether Internet addicts show functional brain impairment as exhibited in the preceding studies, based on stimulus presentation, or whether the area showing functional brain deficiency is the brain area related with control and inhibition.

2. Method

2.1 Participants

15 Internet addition risk group (average age of males and females: 22.20, standard deviation: 3.07) and 15 collegians of non-addict group (average age of males and females: 22.47, standard deviation: 2.53) participated in the fMRI experiment. This study recruited those who considered themselves as Internet addicts through online message board and offline PC rooms and school counseling office board. And then, first phase participants were selected through interview by a clinical expert. To sample final experiment participants for the fMRI experiment, the first phase 25 participants were measured using Internet Addiction Scale (IAS) (Young, 1998; Kim, 2000) translated and revised in Korean, and K Scale (Korean-version Internet Addition Self-Diagnosis Scale: Korea Agency for Digital Opportunity and Promotion, 2002). In the study of Lee et al. (2001), Cronbach's α coefficient (internal correspondence) of Korean-version IAS was 0.9. IAS consists of 20 questions as self-reporting scale on the pathological use of Internet addiction (compulsive use, behavioral problem, emotional change, and impacts of the Internet use on everyday life). Each question uses five-point scale (one point: Not at all ~ five points: Very so). If a participant receives 70 or higher points, he/she is classified as serious addiction group, where the Internet use causes serious problems in everyday life, 40-69 points is classified as light Internet addiction group, and 39 or lower points is classified as normal (or non-addict) online user. This study classified those who received 60 or higher points as Internet addiction group (M = 70.80, SD = 10.31), and those who received 39 or lower points as normal adult group (M = 28.60, SD = 7.35) ($p < 0.001$).

K Scale is the standardized Internet addition self-diagnosis scale, developed on the basis of the questionnaire survey of some 2,000 Internet users. K Scale consists of 20 questions, and includes four sub-scales: reality discernment disorder, positive expectation on the Internet, tolerance & withdrawal and self recognition on the Internet. Each question uses four-point scale (one point: Not at all) - four points (Very so). Those who receive 54 or higher points are classified as Internet addition group, and those who receive 53 or lower points as general use group. The IAS mean score of the Internet addiction group that participated in the fMRI experiment was 70.80 (SD = 9.31), and the mean score of K Scale was 60.00 (SD = 4.47). The IAS mean score of the normal group was 28.68 (SD = 7.35), and K Scale mean score was 32.60 (SD = 7.70) ($p < 0.001$). All the experiment participants signed an agreement, after they were informed of the experiment details. To find out if the Internet Addition group was higher in impulsiveness than the normal group, this study used Barrett Impulsiveness Scale-ver. 2 (BIS-II), which was translated in Korean and revised by Lee (2002). Barrett Impulsiveness Scale consists of 35 questions, and the participants were supposed to answer with Yes or No. The score scope is from 0 to 35. As the score is higher, it means impulsiveness is high. This scale's internal correspondence was 0.85.
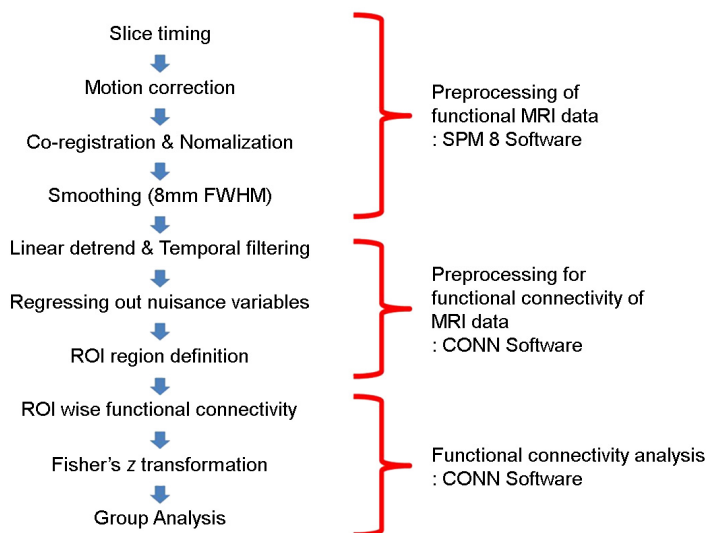
2.2 Functional MRI image acquisition

For the fMRI experiment, MRI scanner (ISOL Forte 3.0T) placed in KAIST was used. For fMRI data, the T2*-weighted gradient echo-planar imaging (EPI) sequence was used. The parameter conditions were TR/TE 3000/40ms, flip angle 80°, FOV (field of view) 240m×24cm, matrix size 64×64 mm, slice thickness 4mm without gap and 35 slices. The test was carried out for 369 seconds including the dummy, and 120 volumes of images were obtained, except for 9 sec of dummy. To take the images of brain during resting-state, the participants were instructed not to think seriously, and not to sleep or doze off, while comfortably closing eyes during the brain image examination.

2.3 Analysis - Psychological data

To find out the differences of impulsiveness between groups, an independent group t-test was conducted using the SPSS 18.0 (Statistical Package for the Social Science, release 15.0, SPSS, Inc., Chicago IL).

2.4 Analysis - Functional connectivity of MRI data

The sequence diagram of the analysis on the functional connectivity during cerebral resting-state is demonstrated in Figure 1.
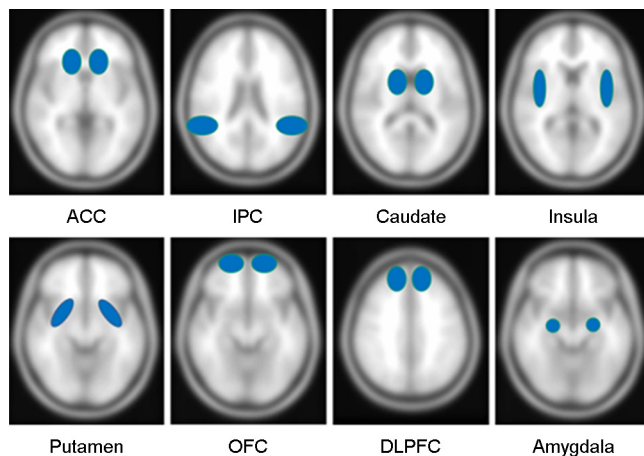
Slice timing
↓
Motion correction
↓
Co-registration & Nomalization
↓
Smoothing (8mm FWHM)

Preprocessing of
functional MRI data
: SPM 8 Software

Linear detrend & Temporal filtering
↓
Regressing out nuisance variables
↓
ROI region definition

Preprocessing for
functional connectivity of
MRI data
: CONN Software

ROI wise functional connectivity
↓
Fisher's *z* transformation
↓
Group Analysis

Functional connectivity analysis
: CONN Software

Figure 1. The flow chart of resting-state functional connectivity analysis

The fMRI data was analyzed using the SPM8 (http://www.fil.ion.ucl.ac.uk/spm/software/spm8) and CONN (http://www.nitrc.org/projects/conn). After realing the participant's head movement using 3-D rigid body registration, the translation and rotation of axes (x, y, z axes), generated in the realignment process, were calculated. After correcting the time gap between slices generated upon obtaining images by performing the slice timing process, each participant's functional MRI data was conformed to standardized coordinate system by location normalization to the standardized brain space using the template image (Montreal Neurologic Institute: MNI) provided by SPM. And then, final images were obtained by smoothing through the use of 8mm (FWHM) Isotropic Gaussian Kernel. After standardization of functional images in terms of space, temporal normalization was carried out to guarantee all participants' same location voxel by voxel correspondence.

After the pre-processing of fMRI data using SPM8 is finished, this study undertook pre-processing for the analysis of MRI connectivity during the resting-state. Through band-pass filtering, the specific frequency area's signal related to nerve cell activity signal was extracted (0.01Hz<f<0.08Hz). To remove noise not related with nerve cell activity signal, the residual signal was calculated. Residual signal was removed through regression analysis using entire areas of brain, cerebrospinal fluid and six brain movement calibration parameters as nuisance covariates.

Concerning the executive function of Internet addicts, based on the preceding studies, brain areas (inferior parietal cortex (IPC), anterior cingulate gyrus, caudate nucleus, putamen, orbito frontal cortex (OFC) and dorsolateral prefrontal cortex (DLPFC)) were designated as ROIs (Figure 2) (Dong et al., 2012; Cabeza and Nyberg, 2000). The mask image of each region of interests was defined using WFU PickAtlas Tool 2.4. In all voxels of the brain areas designated as ROIs, signals were extracted, and the correlation of each region of interests was calculated through Pearson's Correlation Coefficient by setting the mean value of the signals as the representative signal. And, the functional brain connectivity map of ROIs was calculated by imaging the correlation coefficient values to the brain. For statistical analysis within the group, each participant's functional brain connectivity map was analyzed

through one sample t-test. For multiple comparison analysis on the analyzed statistical map, the false discovery rate method was used, and the statistical map was made at the significance level of $p < 0.05$. To analyze differences between the two groups, this study carried out a permutation test, and the test was conducted at the significance level of $p < 0.05$. Also, Pearson's Correlation Coefficient was calculated in order to calculate the correlation between the mean values of Fisher's Z value in the ROIs areas and the scores of Internet addiction seriousness and impulsiveness.

Figure 2. Selected ROIs for connectivity (ACC, Anterior Cingulate Cortex; IPC, Inferior Parietal Cortex; OFC, Orbito Frontal Cortex; DLPFC, DorsoLateral PreFrontal Cortex)

3. Results

3.1 Result of psychological data

The Internet addiction group (M = 18.27, SD = 5.29) showed significantly higher impulsiveness, compared to the normal adult group (M = 7.87, SD = 5.35) (t28 = -5.34, $p < 0.001$).

3.2 Within group analysis

The normal adult group showed a positive correlation in the functional connectivity of caudate nucleus - anterior cingulate cortex, putamen - insula, putamen - caudate nucleus, dorso lateral prefrontal cortex - inferior parietal cortex, dorso lateral prefrontal cortex - orbito frontal cotrex, and amygdala - putamen during the resting-state. The normal adult group showed a negative correlation in the functional connectivity of dorso lateral prefrontal cortex - insula ($p < 0.05$, FDR) (Table 1).

The Internet addiction group demonstrated a positive correlation in functional connectivity between the areas of caudate nucleus - anterior cingulate cortex, putamen - anterior cingulate cortex, putamen - insula, caudate nucleus - putamen, dorso lateral prefrontal cortex - inferior parietal cortex, dorso lateral prefrontal cortex - orbito frontal cotrex, and amygdala - putamen. The Internet addiction group demonstrated a negative correlation in functional connectivity between the areas of orbito frontal cortex - insula, and dorso lateral prefrontal cortex - insula ($p < 0.05$, FDR) (Table 2). Unlike the normal adult group, the functional connectivity of orbito frontal cortex - anterior cingulate cortex, orbito frontal cortex - inferior parietal cortex, orbito frontal cortex - putamen, and amygdala - insula was not significantly shown.

Table 1. Correlation coefficient between two ROIs in healthy controls ($p < 0.05$, FDR)

Control group	ACC	IPC	Insula	Caudate	Putamen	OFC	DLPFC	Amygdala
ACC			0.13**	0.17**	0.16**	0.21**		
IPC						0.16**	0.65**	
Insula					0.33**		-0.19**	0.22**
Caudate					0.17**			
Putamen						0.17**		0.34**
OFC							0.19**	
DLPFC								
Amygdala								

(*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, Abbreviations: ACC, Anterior Cingulate Cortex; IPC, Inferior Parietal Cortex; OFC, Orbito Frontal Cortex; DLPFC, Dorso Lateral Prefrontal Cortex, Black: Significant functional connectivity in both groups Red: Significant functional connectivity in healthy controls only)
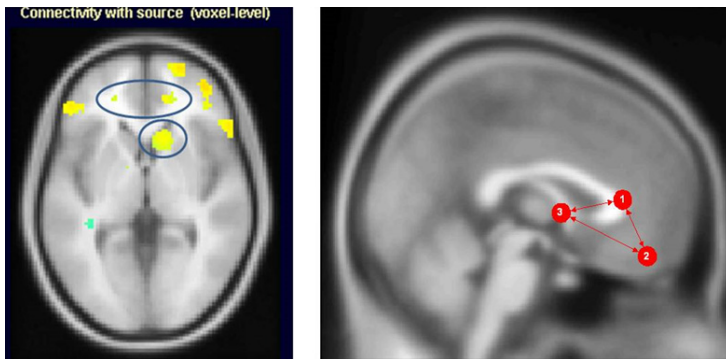
Table 2. Correlation coefficient between two ROIs in sexual addicts ($p < 0.05$, FDR)

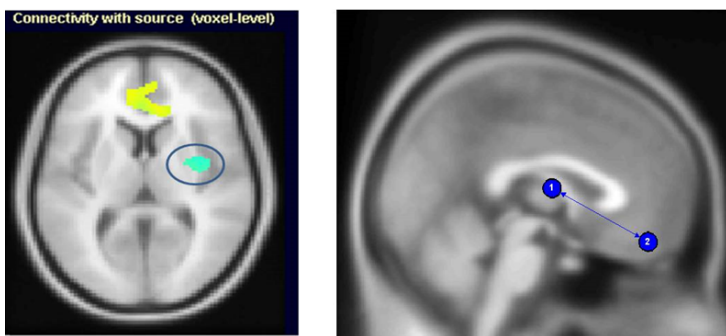| Control group	ACC	IPC	Insula	Caudate	Putamen	OFC	DLPFC	Amygdala
ACC				0.17**	0.15**			
IPC							0.65**	
Insula					0.19**	-0.12**	-0.20**	
Caudate					0.23**			
Putamen								0.31**
OFC							0.12**	
DLPFC								
Amygdala								

(*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, Abbreviations: ACC, Anterior Cingulate Cortex; IPC, Inferior Parietal Cortex; OFC, Orbito Frontal Cortex; DLPFC, Dorso Lateral Prefrontal Cortex, Black: Significant functional connectivity in both groups Red: Significant functional connectivity in sexual addicts only)

3.3 Between group analysis

To find out the differences of functional connectivity between the two groups, the functional connectivity of circuitry including orbito frontal cortex in the Internet addiction group was lower than the normal adult group, as a result of two sample t test with the significance level of $p < 0.001$ (uncorrected). Namely, the functional connectivity of orbito frontal cortex - putamen, and orbito frontal cortex - anterior cingulate cortex in the normal adult group significantly increased, compared to the Internet addiction group (Figure 3). The Internet addiction group's functional connectivity of orbito frontal cortex - insula was lower than the normal adult group (Figure 4).

Figure 3. Group differences of resting state functional connectivity- Healthy controls > Internet addicts (1- Anterior cingulate cortex; 2- Orbitofrontal cortex; 3- Putamen, p < 0.05 FDR correction)

Figure 4. Group differences of resting state functional connectivity- Healthy controls < Internet addicts (1- Orbitofrontal cortex; 2- Putamen, p < 0.001 uncorrected)

3.4 Relationship between resting state connectivity strength and degree of internet addiction

According to the observation of correlation between Internet addiction symptom score and functional connectivity strength, there was no area, in which the correlation between Internet addiction symptom score and functional connectivity strength was observed.

4. Conclusion

This study discovered that the Internet addicts' connectivity in other areas (i.e. ACC, IPC, insula) connected with orbito frontal cortex declined during the resting-state. This means that the orbito frontal cortex function, receiving and processing the information from the brain area of cortex-striate reward circuitry, was impaired.

Orbito frontal cortex is the part of prefrontal cortex as the approximant area to vetromedial prefrontal cortex. Orbito frontal cortex is known to play a role of receiving large amount of projection from the areas, including amygdala, dorsolateral prefrontal corte and anterior cingulate cortex, and sending the received information.

According to preceding studies, orbito frontal cortex plays a role of executive control upon information processing and behavior

expression by controlling improper, unnecessary and unpleasant stimulating information or behavior-related neural activity. According to nerve study on social and emotional processing, orbito frontal cortex is not only in charge of control function, but plays an important role in the case of reward and punishment-related learning through error prediction function.

Birbaumer et al. (2005) discovered that the activation of orbito frontal cortex of psychopaths was lower than normal people, and proved that the psychopaths showed reduced activation pattern of limbic system-prefrontal cortex circuitry.

In a study targeting Attention Deficit Hyperactivity Disorder patients, the difficulties in control of reward and impulsiveness of the Attention Deficit Hyperactivity Disorder patients were found to be related with functional impairment of cerebral reward circuitry including orbito frontal cortex (Fox et al., 2009).

Volkow (2001) asserted addiction is related to the anatomical and functional pathology of orbito frontal cortex, and the behavioral problems (loss of control, desire, high impulsiveness, commitment) are related with the impairment of striato-thalamo-orbito frontal circuitry. Pathologic gambling patients, known as behavioral addition similar to the Internet addiction, have neurologic impairment at orbito frontal cortex and ventromedial prefrontal cortex, and are reported to have deficiency in executive function, due to the impairment (Cavedini et al., 2002). Looking at the behaviors of pathological gamblers, they do not show any problems in terms of usual clinical psychological scale or intelligent ability; however, they pursue immediate satisfaction that can be obtained right away in the short-term, although they sufficiently recognize that the result of gambling is negative from the long-term perspective in the case of decision making. Such a decision making problem and impulsiveness are the characteristics exhibited in the Internet addiction group, which is another behavioral addiction, in addition to pathologic gambling (Ko et al., 2010). In other words, the abnormal activation pattern of orbito frontal cortex can be inferred that it is related with basic neurologic cause on the impulsive and irresponsible behaviors.

The results of this study demonstrate the functional connectivity related to orbito frontal cortex, which is in charge of decision making and impulsiveness control, decreased in the Internet addiction group, compared to the normal adult group. The Internet addiction group was demonstrated to have significantly higher impulsiveness than the normal adult group.

To gather up the results of the preceding studies through stimulus presentation and the results of this study using the resting-state, the Internet addicts showed the deficient functional activity and connectivity of orbito frontal cortex, irrelevant of the status of stimulus. This actually implies that the problematic behaviors (commitment, desire and high impulsiveness on the Internet use) of the Internet addicts are related to the functional deficiency of orbito frontal cortex, as found in the other addiction group.

However, the problems of this study are as follows: The impairment degree of cerebral function cannot be predicted, according to the seriousness of Internet addiction, since the participants do not precisely know the occurrence period of the Internet addiction, and do not see the correlation of orbito frontal cortex impairment degree, according to the Internet addiction period. Also, further study seems to be required targeting adolescents in that the age bracket the most easily exposed to the Internet use is adolescent period, and such a period is when the frontal lobe develops the most.

Despite such limitations, the study on the Internet addiction group can be important data to pathologically diagnose the Internet addiction under the situation that almost no study on brain function related to Internet addicts is found domestically and internationally. The results of the abnormality on the orbito frontal cortex circuitry in the Internet addiction symptom examined through this study are expected to be used as objective indicator on the diagnosis classification of addiction disorder, which is classified on the basis of clinical symptom.

Acknowledgements

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