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Differential regional gray matter volumes in patients with on-line game addiction and professional gamers

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Abstract

Patients with on-line game addiction (POGA) and professional video game players play video games for extended periods of time, but experience very different consequences for their on-line game play. Brain regions consisting of anterior cingulate, thalamus and occipito-temporal areas may increase the likelihood of becoming a pro-gamer or POGA. Twenty POGA, seventeen pro-gamers, and eighteen healthy comparison subjects (HC) were recruited. All magnetic resonance imaging (MRI) was performed on a 1.5 Tesla Espree MRI scanner (SIEMENS, Erlangen, Germany). Voxel-wise comparisons of gray matter volume were performed between the groups using the two-sample *t*-test with statistical parametric mapping (SPM5). Compared to HC, the POGA group showed increased impulsiveness and perseverative errors, and volume in left thalamus gray matter, but decreased gray matter volume in both inferior temporal gyri, right middle occipital gyrus, and left inferior occipital gyrus, compared with HC. Pro-gamers showed increased gray matter volume in left cingulate gyrus, but decreased gray matter volume in left middle occipital gyrus and right inferior temporal gyrus compared with HC. Additionally, the pro-gamer group showed increased gray matter volume in left cingulate gyrus and decreased left thalamus gray matter volume compared with the POGA group. The current study suggests that increased gray matter volumes of the left cingulate gyrus in pro-gamers and of the left thalamus in POGA may contribute to the different clinical characteristics of pro-gamers and POGA.

Keywords

Cingulate gyrus; Functional magnetic resonance imaging; On-line game addiction; Pro-gamer; Thalamus

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Conflict of interest All other authors declare that they have no conflicts of interest.

1. Introduction

1.1. The comparison between patients with on-line game addiction, pro-gamers, and healthy comparison subjects

Recently, there have been several studies suggesting that Internet addiction may be harmful enough to be categorized as a “psychiatric disorder” (Grant et al., 2010; Shapira et al., 2000; Dell'Osso et al., 2008). Grant et al. (2010) have proposed that Internet addiction should be classified as one category of ‘behavioral addiction’ considering its natural course, clinical symptoms, tolerance, comorbidity, and neurobiological aspects. Other authors have referred to Internet addiction as a subtype of impulse control disorder (Shapira et al., 2000; Dell'Osso et al., 2008). Among Asian countries with a high incidence of Internet addiction (Fitzpatrick, 2008), South Korea is one of the most endemic areas.

In parallel with patients who suffer from on-line game addiction, there is another population in South Korea characterized by extensive on-line game playing, professional gamers (pro-gamers), who do not meet criteria for addiction. There are currently 259 StarCraft pro-gamers on twelve StarCraft teams in South Korea (KeSPA, 2010). As with other professional sports players, pro-gamers have contracts, an annual salary, and belong to teams in a gamer's village. To become a pro-gamer, candidates must complete a two step processing including a competition involving 3000 aspirants to select 1 pro-gamer. During team practice, pro-gamers practice StarCraft 7–10 h/day (9:00AM–5:00PM, 7:00PM–10:00PM). Each team has one general manager and two or three strategy coaches. As noted above, there are definite differences between patients with on-line addiction and pro-gamers in terms of regular life patterns, meeting criteria for addiction, and game playing ability (as evidenced by the difficult process of becoming a pro-gamer).

Given the above findings, we thought that differences in the regional brain volumes might play a critical role in determining whether an individual game player developed into a pro-gamer or a POGA. In the 12 month follow up study with 75 patients alcohol dependence and 43 healthy controls, patients with relapse showed smaller volumes than controls in superior frontal gyrus, amygdala, and hippocampus (Durazzo et al., 2011). In functional brain imaging studies of alcohol use, different patterns of brain activation have also demonstrated differences between individuals with alcohol dependence/abuse and sommeliers. After a sip of alcohol, in response to alcohol cues, patients with alcohol dependence had increased activation in the left dorsolateral prefrontal cortex and anterior thalamus, compared to social drinkers (George et al., 2001). However, in sommeliers, brain activation was found bilaterally in the insular and dorsolateral prefrontal cortex (Castriota-Scanderbeg et al., 2005), which is implicated in high-level cognitive processes such as working memory and selection of behavioral strategies (Huettel et al., 2004). The different patterns of brain volumes between POGA and pro-gamers provide insights into the vulnerability and resistance to gaming addiction in POGA and healthy controls.

1.2. The neural circuitry mediating on-line game playing

In a comparison of brain circuitry between patients with on-line game addiction, pro-gamers, and healthy comparison subjects we might expect to see changes within brain cortex

related to (1) addiction to on-line game play, (2) the visuospatial system (visual system and attentive ability), and (3) comorbid disorders including major depression, attention deficit hyperactivity disorder, and impulse control disorder (Table 1).

1.2.1. Cingulate gyrus: executive function, salience, and visuospatial attention

—The anterior cingulate has frequently been mentioned in studies of substance addiction because of its role in conflict resolution (executive function) and attention maintenance (salience) (Goldstein and Volkow, 2002), as well as in pathologic gambling (Camchong et al., 2007). The executive function of the anterior cingulate appears to be involved in dealing with conflict, response inhibition, performance monitoring, completion of behavior, arousal/drive state, and error monitoring (Paus, 2001; Bush et al., 2002). Impairment of these functions could potentially damage an individual's ability to check inappropriate behavior (Goldstein et al., 2007). Within a pathway from the thalamus to the hippocampus, the cingulate gyrus is known to be responsible for focusing attention (attention maintenance) on emotionally significant events and regulating addictive behaviors (Mayberg, 1997). Previous studies of Internet addiction have reported decreased volume within the cingulate gyrus and hyperactivity of the anterior cingulate in response to on-line game stimulation (Ko et al., 2009; Zhou et al., 2011).

Cortical maturation in the anterior cingulate, lateral prefrontal, and right inferior frontal gyrus is thought to regulate visuospatial attention in fronto-striatal-thalamo attention circuits (Westlye et al., 2010). Interestingly, visuospatial attention is reported to be closely linked with on-line game play (Green and Bavelier, 2003; Dye et al., 2009). Ten days of video game playing has been reported to enhance visuospatial capacity in healthy subjects (Green and Bavelier, 2003). Expert video game players demonstrated superior cognitive control abilities in a performance switching task, compared to non-video game players (Karle et al., 2010).

Deficits of anterior cingulate function are well known to be associated with major depressive disorder, ADHD, and impulse control disorders (Mayberg et al., 2000; Ha et al., 2006). Several studies of Internet addiction have noted the significant comorbidity of major depressive disorder, attention deficit hyperactivity disorder, and impulse control disorder (Ha et al., 2006; Dell'Osso et al., 2008).

1.2.2. Thalamus: reinforcement and alerting—In substance addiction, the thalamus is thought to be associated with conditioned responses (expectation) (Volkow et al., 2003). Interactions between drug effects and conditioned responses (expectation) are likely to produce the reinforcing effects of drug abuse (Robinson and Berridge, 1993). The thalamus also demonstrates increased activity in response to higher dopamine availability in the striatum (caudate and putamen) due to monetary reward (Asensio et al., 2010). Interestingly, on-line video game playing has been reported to be associated with dopamine release in striatum and activation of thalamus (Koepp et al., 1998; Han et al., 2008).

Tomasi et al. (2007) have suggested a deficit of three components of attention, including alertness, orienting, and executive function, in cocaine abusers. The thalamus, an essential brain area for visual, auditory, and somatosensory information processing, is an important

structure in the alerting component of attention (Fan et al., 2005), including spatial attention (Christian et al., 2006). The lateral geniculate body of the thalamus, a primary processor of visuospatial information in the central nervous system, is located within the major pathway from the retina to the visual cortex (Horvath, 1998).

In an analysis of conventional volumes and surface morphology of the thalamus, Ivanov et al. (2010) suggested that hyperactivity scores would be associated with smaller regional volumes on the lateral thalamic surface and inattention scores would be associated with larger regional volumes on the medial thalamic surface in patients with ADHD.

1.2.3. Occipital cortex and inferior temporal cortex: damage of visual cortex—

The temporal-occipital junction has also been reported to be associated with substance and behavioral addiction (Park et al., 2010; Wang et al., 2010; Hermann et al., 2007; Fehr et al., 2008). In a comparison of patients with alcohol dependence and healthy comparison subjects, patients with alcohol dependence showed a lower blood oxygen level dependent (BOLD) signal bilaterally in the occipital area (Hermann et al., 2007). Acute administration of nicotine decreased brain glucose oxidation, glutamate-glutamine neurotransmitter cycling, and GABA synthesis in the occipital cortex in smokers (Wang et al., 2010). In an 18F-fluorodeoxyglucose positron emission tomography study, patients with internet addiction showed decreased metabolism bilaterally in the occipital cortex compared to healthy volunteers (Park et al., 2010).

Human visual cortex could be sensitive to and possibly damaged by large amounts of visual stimuli during on-line game playing (Lyskov et al., 1998; Herrmann, 2001; Pereverzeva and Murray, 2008). A number of functional imaging studies have evaluated the posterior inferior temporal cortex, posterior fusiform gyrus, and posterior superior temporal cortex, which are involved in the processing of human motion (Grossman and Blake, 2002; Peuskens et al., 2005).

1.3. Hypothesis

In line with the published addiction literature, we thought that brain regions consisting of anterior cingulate, thalamus and occipito-temporal areas would increase the likelihood of becoming a pro-gamer or POGA (Fig. 1). In these circuits, decreased volumes of anterior cingulate and increased volumes of thalamus (reciprocal with hyperfunctional striatum) would reinforce impulsive behavior (addictive behavior) in patients with on-line game addiction (POGA). In contrast to POGA, increased volumes of anterior cingulate (healthy anterior cingulate) in pro-gamers would regulate thalamus by modulating visual and auditory stimulation and reduce the development of addiction.

2. Methods

2.1. Subjects

Twenty patients with on-line game addiction, seventeen pro-gamers and eighteen healthy comparison subjects were recruited at Chung Ang University Medical Center. All subjects were screened with the Structured Clinical Interview for DSM-IV and the Beck Depression Inventory (BDI) (Beck et al., 1961). The research protocol was approved by the Chung Ang

University Hospital Institutional Review Board. Written informed consent was provided by all participants. There were no significant differences in age ($F(2,52) = 0.04, p = 0.96$), education years ($F(2,52) = 0.05, p = 0.95$), economic state ($\chi^2 = 2.24, p = 0.69$), BDI scores ($F(2, 52) = 1.19, p = 0.31$) or alcohol drinking ($\chi^2 = 0.13, p = 0.94$)/smoking habit ($\chi^2 = 0.83, p = 0.66$) between patients with on-line game addiction, pro-gamers, and healthy comparisons. However, there were significant differences in terms of on-line game playing time ($F(2, 52) = 65.4, p < 0.01$), total internet use time ($F(2, 52) = 108.9, p < 0.01$), and Young's internet addiction scale (YIAS) ($F(2, 52) = 64.4, p < 0.01$) between the three groups (Table 2).

2.2. Patients with on-line game addiction (POGA) group

The criteria for on-line game addiction in the current study are similar to those used in a previous study (Han et al., 2010). These criteria are also consistent with DSM-IV criteria for substance abuse: 1) extensive game play time (more than 4 h per day/30 h per week) (Ko et al., 2009); 2) a score of more than 50 on the YIAS (Young, 1996; Ha et al., 2010); and 3) impaired behaviors or distress due to a maladaptive pattern of internet video game play. Exclusion criteria were: 1) BDI scores >19 ; 2) other axis I psychiatric disorders including substance abuse; and 3) head injury or trauma history. The mean age of the POGA group was 20.9 ± 2.0 years old and mean education level was 12.0 ± 1.7 years. Duration of illness (problematic on-line game play) was 4.9 ± 0.9 years. These subjects played on-line games 9.0 ± 3.7 h/day and used the Internet 13.1 ± 2.9 /day. YIAS scores for the POGA group were 81.2 ± 9.8 . During the most recent 12-month period, on-line game play in all subjects had gradually increased. In addition, all patients in the POGA group reported a persistent desire for on-line gaming everyday as well as unsuccessful efforts to cut down or control on-line game play. School grades and work performance had decreased. All POGAs also showed disruption of their daily routine (sleeping during the day and gaming at night, irregular meals, and poor hygiene) and were irritable, aggressive, and violent when family members asked them to stop playing on-line games. Seven POGAs were absent from school for more than 6 months due to on-line game playing in Internet cafés and six POGAs were expelled from school for frequent absences and for stealing money in order to participate in on-line game play. Three POGAs only participated in on-line game playing after finishing school and did not obtain a job or participate in a significant social role. Two POGAs borrowed \$30,000 over three months from an usurer for on-line game playing. Two POGAs lost his job due to frequent absences from work without notice.

2.3. Pro-gamer group

Pro-gamers on the 000 StarCraft pro-game team who are the members of the Korea eSports Association (KeSPA) were recruited. Exclusion criteria were: 1–3 same with POGA group; and 4) impaired behaviors or distress due to maladaptive pattern of on-line game play. The age of the pro-gamers was 20.8 ± 1.5 years and education level was 12.0 ± 1.1 years. The average career length of the pro-gamers was 4.9 ± 1.7 years. Thirteen of the pro-gamers graduated from high school or university. Two pro-gamers were student gamers, which is similar to being a student athlete. Two pro-gamers quit high school to become a pro-gamer with the consent of teachers and parents. Pro-gamers played StarCraft an average of $9.4 \pm$

1.6 h/day and used the Internet an average of 11.6 ± 2.1 h/day. The mean YIAS score of pro-gamers was 40.8 ± 15.4 .

2.4. Healthy comparison group

Age and education matched male subjects who used the Internet and played on-line games less than 3 h/day and less than 3 day/week were recruited as healthy comparison subjects (HC). The age of HCs was 20.9 ± 2.1 years and education level was 12.1 ± 1.1 years. Three HCs were high school students, eight were university students, and seven were office workers. HC subjects played on-line games an average of 1.0 ± 0.7 h/day and used the Internet an average of 2.8 ± 1.1 h/day. The mean YIAS score of healthy comparison subjects was 41.6 ± 10.6 .

2.5. Impulsiveness scale and executive function assessment

The Barratt Impulsiveness Scale-Korean version (BIS-K) was used for the assessment of impulsiveness in patients and subjects (Barratt, 1965; Patton et al., 1995; Lee, 1992). This scale is a 23-item self-report questionnaire consisting of three subscales: cognitive, motor, and non-planning. Internal consistency of this scale has been reported to have a Cronbach alpha coefficient = 0.82. For assessing executive function involving strategic planning, organized searching, and the ability to use environmental feedback (Marazziti et al., 2008), a computerized version of the Wisconsin Card Sorting Test (CNT4.0, Maxmedica Inc) was used (Kim et al., 2006).

2.6. MR imaging processing and data analysis

All MR imaging was performed on a 1.5 Tesla Espree MRI scanner (SIEMENS, Erlangen, Germany). 3D T1-weighted magnetization-prepared rapid gradient echo (MPRAGE) data were collected with the following parameters: TR = 1500 ms; TE = 3.00 ms; Inversion time = 1100 ms; FOV = 256×256 mm; Flip angle = 15° ; 128 slices; $1.0 \times 1.0 \times 1.33$ mm voxel size.

Image processing was conducted using the voxel-based morphometry toolbox (VBM5.1) (<http://dbm.neuro.uni-jena.de/vbm/>) implemented in SPM5 running on Matlab 7.5. VBM in SPM5 consists of tissue segmentation, bias correction, and spatial normalization in a unified model (Ashburner and Friston, 2005). The segmented images were smoothed with a 12 mm full-width half-maximum Gaussian kernel for the subsequent statistical analysis.

Voxel-wise comparisons of gray matter volume were performed between the groups using the two-sample *t*-test with SPM5. The significance of group differences was estimated by the theory of random Gaussian fields, and significance levels were set at uncorrected *P* 0.001, while the cluster size was set at >100 voxels.

3. Results

3.1. Impulsivity and executive function

Eighteen of 20 POGA, fifteen of 17 pro-gamers, and seventeen of 18 HC completed the BIS-K and the Wisconsin Card Sorting Test. The POGA group showed higher mean scores

on the BIS-K-total ($F(2, 48) = 13.6, p < 0.01$), cognitive ($F(2, 48) = 8.7, p < 0.01$), motor ($F(2, 48) = 12.6, p < 0.01$) and non-planning ($F(2, 48) = 15.1, p < 0.01$) scales, compared to pro-gamers and HC. There was no significant difference between pro-gamers and HC. In the Wisconsin Card Sorting Test, the pro-gamer group required fewer trials to complete six categories ($F(2, 48) = 12.5, p < 0.01$) and total errors ($F(2, 48) = 8.2, p < 0.01$), compared to the POGA and HC. POGA showed increased perseverative errors, compared to pro-gamers and HC ($F(2, 48) = 8.7, p < 0.01$).

YIAS scores of the POGA subjects were positively correlated with scores on the BIS-K-total ($r = 0.56, p = 0.02$), motor ($r = 0.58, p = 0.01$), and non-planning ($r = 0.54, p = 0.02$) scales. There was no significant correlation between the scores of Wisconsin Card Sorting Test measures and YIAS scores.

3.2. The regions in the comparison of gray matter volume between patients with on-line game addiction (POGA), pro-gamer, and healthy comparisons

3.2.1. Patients with on-line game addiction (POGA) vs. healthy comparison (HC)—Compared to HCs, the POGA group showed increased gray matter volume in the left thalamus ($-20, -31, 3$) ($\kappa_E = 595 (>200)$, $t = 3.45$, uncorrected $p = 0.001$) and decreased gray matter volume in the right inferior temporal gyrus ($60, -37, -19$, BA 20) ($\kappa_E = 1534$, $t = 4.95$, uncorrected $p < 0.001$), right posterior cingulate gyrus ($1, -50, 9$, BA 29) ($\kappa_E = 415$, $t = 4.37$, uncorrected $p < 0.001$), right middle occipital gyrus ($49, -72, -4$, BA 19) ($\kappa_E = 463$, $t = 4.20$, uncorrected $p < 0.001$), left inferior occipital gyrus ($-45, -77, -3$, BA 19) ($\kappa_E = 689$, $t = 4.15$, uncorrected $p < 0.001$), left inferior occipital gyrus ($-45, -92, -8$, BA 18) ($\kappa_E = 246$, $t = 4.06$, uncorrected $p < 0.001$), Right middle occipital gyrus ($49, -72, -4$, BA19) ($\kappa_E = 2514$, $t = 4.20$, uncorrected $p < 0.001$), and left inferior temporal gyrus ($-56, -27, -21$, BA 20) ($\kappa_E = 371$, $t = 3.94$, uncorrected $p < 0.001$) (Fig. 2) (Table 3).

3.2.2. Pro-gamer vs. healthy comparison (HC)—Relative to healthy comparison subjects, the pro-gamer group showed increased gray matter volume in left cingulate gyrus ($-18, 11, 35$, BA 32) ($\kappa_E = 213$, $t = 5.97$, uncorrected $p < 0.001$) and decreased gray matter volume in left middle occipital gyrus ($-46, -81, 0$, BA 19) ($\kappa_E = 1280$, $t = 7.00$, corrected $p = 0.009$, FDR<0.05) and right inferior temporal gyrus ($50, -74, -1$, BA19) ($\kappa_E = 262$, $t = 6.75$, corrected $p = 0.009$, FDR<0.05) (Fig. 2) (Table 3).

3.2.3. Pro-gamer vs. patients with on-line game addiction (POGA)—Compared to the POGA group, the pro-gamer group showed increased gray matter volume in left cingulate gyrus ($-2, 5, 30$, BA24) ($\kappa_E = 3310$, $t = 5.60$, uncorrected $p < 0.001$) and decreased gray matter volume in left thalamus ($-19, -26, 11$) ($\kappa_E = 684$, $t = 3.37$, uncorrected $p = 0.001$) (Fig. 2) (Table 3).

3.3. Correlation between clinical variables and brain regions

The gray matter volume of left cingulate gyrus in POGA and progmaers was negatively correlated with the scores of YIAS ($r = -0.61, p < 0.01$) and BIS total ($r = -0.49, p < 0.01$). The gray matter volume of thalamus in POGA and pro-gamers was positively correlated

with the score of YIAS ($r = 0.39, p = 0.02$). However, there was the trace of the correlation between thalamus and the score of BIS in POGA and pro-gamers ($r = 0.31, p = 0.07$).

4. Discussion

The results of this study suggest that clinically, increased impulsivity and perseverative errors may contribute to on-line game addiction. In addition, increased gray matter volumes of the left cingulate gyrus in pro-gamers and increased gray matter volumes of the left thalamus in POGA may also contribute to the differences that exist between pro-gamers and individuals with POGA. Moreover, the differences in terms of brain volumes between the Pro-gamer and POGA groups were lateralized to the left hemisphere. The left-hemisphere is thought to be associated with verbal working memory (Petrides et al., 1993) while the right hemisphere is linked with spatial working memory. Given these facts, we can speculate that right prefrontal cortex would be relatively preserved due to enhanced spatial working memory in both POGA and pro-gamer groups. Green and Bavelier (Green and Bavelier, 2003) found that 10 days video game playing enhanced visuospatial working memory in healthy adults. However, there are differences in playing styles between POGA and pro-gamers. Pro-gamers may regard playing games in competition as a narrative, which is derived from as an effect of practice to learn different strategies in their training sessions. In sports psychology, elite sports players usually use narrative mental intervention such as imagery and mental rehearsal, targeting, and self-feedback (Whelan et al., 1991). In addition, the use of oral narrative tasks is thought to be associated with creativity in performance (Alberts & Kormos, 2004). However, relative to healthy comparison subjects, both POGA and pro-gamer groups had decreased gray matter volumes in the occipital cortex and inferior temporal cortex.

4.1. Cingulate gyrus

There was a significant difference in gray matter volume in the left anterior cingulate gyrus between POGA and pro-gamers in the current results. In addition, the gray matter volume of the left cingulate gyrus was negatively correlated with measures of impulsivity and perseverative errors. Other studies of Internet addiction that reported different patterns of brain activation and gray matter volume in the prefrontal cortex (PFC), including the anterior cingulate and dorsolateral PFC, between patients with internet addiction and healthy comparison subjects (Ko et al., 2009; Zhou et al., 2011). An important difference between POGA and pro-gamers may lie in the ability of left anterior cingulate to control executive functioning and attention maintenance (salience) (MacDonald et al., 2000). Disrupted function of conflict resolution (executive function) in anterior cingulate of POGA could impair an individual's ability to monitor and inhibit inappropriate behavior (Goldstein et al., 2007). Alternatively, the larger left cingulate in the pro-gamers may be a predisposing factor for successful on-line game play (Karle et al., 2010; Westlye et al., 2010). In contrast to POGA, increased left anterior cingulate activity in pro-gamers may defuse reinforced behaviors induced by an overactive thalamus in response to dopamine discharge in the striatum. In addition, methylphenidate treatment, which acts on the cingulate (Udo de Haes et al., 2007), has been shown to improve attention symptoms and reduce on-line game playing time and the severity of internet addiction (Han et al., 2009).

In the comparison of Young's Internet Addiction Scale scores, POGA showed higher scores than pro-gamers and healthy comparison subjects. This may be correlated with incentive salience (craving) for internet use or on-line game playing. A study of alcohol cue-induced activation of the brain showed that brain areas such as the anterior cingulate, medial prefrontal cortex and striatum might be associated with incentive salience to alcohol-related stimuli (Grusser et al., 2004). Franken (2003) further emphasized the role of salience in addiction, which may lead to increases in craving and episodes of drug use, resulting in repeated drug use and drug seeking. The regulated lifestyle of the pro-gamer, with restricted behavioral disturbances, the endurance of a tight training schedule, and the pressure to win might be related to increased anterior cingulate activity (even better than healthy controls), compared to POGA.

4.2. Thalamus

In the current study, POGA also had differences in terms of regional volumes (increased GMV of thalamus and decreased GMV of middle frontal gyrus compared with healthy controls). In addition, the gray matter volume of the thalamus in POGA and pro-gamers was positively correlated with YIAS scores. The thalamus is a key target for dopamine and plays a major role in conditioned reinforcement and reward expectation (Sanchez-Gonzalez et al., 2005). In addition, striatal dopamine receptor availability has been associated with thalamic activity (Asensio et al., 2010). We presumed that the thalamus in POGAs would be tolerant to tremendous visual and auditory stimulation, which are increased during on-line game play. Furthermore, higher dopamine availability in the striatum during on-line game play makes the thalamus more active, which reinforces the effects of on-line game play in POGA. An imbalance of mesolimbic circuits (orbitofrontal gyri, anterior cingulate, and ventral striatum, amygdala and hippocampus) is thought to be associated with a distorted reward system (Luman et al., 2008). Taken together, we hypothesize that an unbalanced reward system (increased thalamus and decreased cingulate function) would influence someone who played extended periods of time to become either pro-gamers or POGA.

4.3. Occipital cortex and inferior temporal cortex

The gray matter volumes of occipital and inferior temporal cortex were reduced both in POGA and pro-gamers, compared to healthy volunteers. In addition, this area can be damaged by harmful visual stimuli (Lyskov et al., 1998; Herrmann, 2001; Pereverzeva and Murray, 2008; Harding and Fylan, 1999). Early adolescence has consistently been reported to be a critical period for the maturation of visual cortex (Prusky and Douglas, 2003; Crews et al., 2004). Early adolescence is also the critical period for synaptic pruning and myelination of the visual cortex in rodents (Gordon and Stryker, 1996). Pereverzeva and Murray (2008) suggested that neural activity in the human primary visual cortex might be correlated with the retinal information or perception. The human visual system is very sensitive to subtle details in movements, even in response to weakened stimuli such as point light walkers (Blake and Shiffrar, 2007). In response to match/mismatch conditions, greater brain activity in the right inferior occipital-temporal cortex was observed in non-problem gamblers compared with problem gamblers (Goodie, 2005). An increased prevalence of internet addiction or excessive on-line game play has mainly been reported in early adolescents (Yang et al., 2005; Ha et al., 2006). The decreased volume of the occipital

cortex (primary visual cortex) may be associated with the excessive exposure to visual stimulation (computer monitor) during on-line game play in both POGA and pro-gamers.

5. Limitation

There are several limitations to the current study. First, the number of subjects may not be enough to fully document the differences between groups. Replication of the present results will be important in order to demonstrate their generalizability. Second, we did not assess clinical evaluation including impulse controlling, conflict resolution, executive function which may represent the characters of POGA, pro-gamers, and healthy controls. Future studies should be interested in these differences between them. Finally, because the current study was a cross sectional study, it is difficult to say whether the results represent the cause or result of on-line game play. A larger sample would be important in future studies.

6. Conclusion

The current study reports morphometric abnormalities in the gray matter volumes of the left anterior cingulate, both inferior temporal cortices, and both occipital cortices in patients with online game addiction and pro-gamers. These findings provide new insights into the pathogenesis of on-line game addiction.

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Fig. 2.

Comparison of gray matter volume between patients with on-line game addiction (POGA), pro-gamer, and healthy comparisons. POGA: Patients with on-line game addiction.

Table 1

The neural circuitry mediating on-line game playing.

<i>Cingulate</i>		
Ko et al., 2009; Miedl et al., 2010	fMRI: activity	↑ AC and PC in POGA
Grusser et al., 2004; Goldstein et al., 2007		↑ AC in AD/Drug
Chua et al., 2009		↑ PC in smokers
Zhou et al., 2011	VBM: volume	↓ AC and PC in POGA
Konarski et al., 2008		↓ AC in MDD
Westlye et al., 2010	Cortical Thickness	Thick of AC ∝ VSFx
Mayberg et al., 2000	PET	↓Glc in AC of MDD
Green and Bavelier, 2003	Cog test	↑ VSFx in healthy on-line game player
Sun et al., 2008		↓ POGA may be related to VSFx
Fineberg et al., 2010	Review	↓ AC in PG
<i>Thalamus</i>		
George et al., 2001	fMRI: activity	↑ Thalamus in AD
Potenza et al., 2003		↑ Thalamus in PG
Wang et al., 2007		VSFx circuitry ∝ cravings for smoking
Due et al., 2002		↑ VSFx circuitry and attention in smokers
Tomasi et al., 2007		↓ VSFx in cocaine abuser
Raine et al., 1998		↑activity of thalamus in impulsive behavior
Dibbets et al., 2010		↑ conflict detection in thalamus in ADHD
Ivanov et al., 2010	VBM: volume	↑ lat. thalamus in ADHD
Asensio et al., 2010	PET	↓D2R availability in cocaine abuser
<i>Occipito-temporal cortex</i>		
Herrman et al., 2007	fMRI: activity	↓ OC in AD
Pereverzeva and Murray, 2008		VSFx ∝ visual cortex
Sasayama et al., 2010	VBM: volume	↓ temporal and occipital cortex in ADHD
Park et al., 2010	PET	↓ Glc metabolism of OC in POGA
Wang et al., 2010	MRS	↓Glc oxidation of OC in smokers
Harding and Jeavons, 1994	EEG	Photosensitivity seizure in temporal-occipital cortex

AC: anterior cingulate, PC: posterior cingulate, OC: occipital cortex, Cort Thick: cortical thickness, VSFx: visuospatial function, Cog test: cognitive test, MDD: major depressive disorder, POGA: patients with on-line game addiction, AD: alcohol dependence, ADHD: attention deficit hyperactivity disorder, PG: pathologic gambler, Glc: glucose, VBM: voxel-based morphometry, fMRI: functional magnetic resonance imaging, EEG: electroencephalogram.

Table 2

Demographic characteristics.

		1. POGA (20)	2. Pro-gamer (17)	3. Healthy (18)	F/ χ^2 , p	Duncan
Age (years)		20.9 ± 2.0	20.8 ± 1.5	20.9 ± 2.1	0.04, 0.96	1 = 2 = 3
Education (years)		12.0 ± 1.7	12.1 ± 1.1	12.1 ± 1.1	0.05, 0.95	1 = 2 = 3
Career/duration of illness (years)		4.9 ± 0.9	4.9 ± 1.7	–	–	
Handedness (right/left)		19/1	16/1	17/1	0.01, 0.99	1 = 2 = 3
Smoking (smoker/non-smoker)		7/13	4/13	4/14	0.83, 0.66	1 = 2 = 3
Drinking (drinking/non-drinking)		9/11	8/8	9/9	0.13, 0.94	1 = 2 = 3
Economic state	High	2	1	1	2.24, 0.69	1 = 2 = 3
	Middle	14	10	14		
	low	4	6	3		
Internet use (hours/day)		13.1 ± 2.9	11.6 ± 2.1	2.8 ± 1.1	108.9, <0.01	1 = 2 > 3
Online game (hours/day)		9.0 ± 3.7	9.4 ± 1.6	1.0 ± 0.7	65.4, <0.01	1 = 2 > 3
YIAS score		81.2 ± 9.8	40.8 ± 15.4	41.6 ± 10.6	64.4, <0.01	1 > 2 = 3
BDI score		9.4 ± 5.2	7.2 ± 4.1	7.5 ± 6.6	1.19, 0.31	1 = 2 = 3
BIS						
Total		61.5 ± 6.4	51.8 ± 8.4	50.1 ± 6.9	13.6, <0.01	1 > 2 = 3
Cognitive		15.5 ± 1.8	13.4 ± 2.2	13.1 ± 1.8	8.7, <0.01	1 > 2 = 3
Motor		21.4 ± 2.3	18.1 ± 3.1	17.4 ± 2.3	12.6, <0.01	1 > 2 = 3
Non-planning		24.4 ± 2.7	20.3 ± 3.1	19.6 ± 2.9	15.1, <0.01	1 > 2 = 3
WCST						
Total trials to complete 6 categories		101.9 ± 17.9	76.5 ± 12.1	97.8 ± 17.6	12.5, <0.01	2 < 1 = 3
Total error		29.5 ± 18.7	11.3 ± 6.9	24.8 ± 12.5	8.2, <0.01	2 < 1 = 3
Perseverative error		16.3 ± 9.7	7.1 ± 2.9	11.3 ± 3.6	8.7, <0.01	1 > 2 = 3

POGA: patients with on-line game addiction, YIAS: Young Internet Addiction Scale, BDI: Beck Depression Inventory, Career: career of pro-gamer, Economic state (NTS, 2009) high: family income >\$30,000/year; middle \$12,000–\$30,000; low < \$12,000, BIS: Barratt Impulsiveness Scale, WCST: Wisconsin Card Sorting Test.

Table 3

Regional comparison of gray matter volume between patients with on-line game addiction (POGA), pro-gamer, and healthy comparison subjects.

<u>Talairach</u>			κ_E	t	p value	Regions
x	y	z				
<i>Patients with on-line game addiction vs Healthy comparison subjects</i>						
Patients with on-line game addiction > Healthy comparison subjects						
-20	-29	2	1527	4.25	$p_{\text{uncorrected}} < 0.0001$	left thalamus
-37	-60	35	602	4.60	$p_{\text{uncorrected}} < 0.0001$	left parietal angular gyrus BA39
Patients with on-line game addiction < Healthy comparison subjects						
59	-38	-19	2421	6.45	$P_{\text{FDR-corr}} = 0.001$	right inferior temporal gyrus, BA 20
48	-71	-5	1146	5.75	$P_{\text{FDR-corr}} = 0.001$	right middle occipital gyrus, BA 19
-44	-76	-4	2067	4.15	$P_{\text{FDR-corr}} = 0.002$	left inferior occipital gyrus, BA 19
-47	-55	-10	703	4.06	$P_{\text{FDR-corr}} = 0.002$	left temporal fusiform gyrus, BA 37
-57	-27	-21	1056	3.94	$P_{\text{FDR-corr}} = 0.002$	left inferior temporal gyrus, BA20
<i>Pro-gamers vs healthy comparison subjects</i>						
Pro-gamers > healthy comparison subjects						
-18	11	35	461	6.83	$P_{\text{FDR-corr}} = 0.02$	left cingulate gyrus, BA 32
-3	5	31	1247	4.57	$p_{\text{uncorrected}} < 0.0001$	left cingulate gyrus, BA 24
23	-8	43	743	4.21	$p_{\text{uncorrected}} < 0.0001$	right middle frontal gyrus, BA 6
Pro-gamers < healthy comparison subjects						
-46	-82	-1	4123	7.90	$P_{\text{FDR-corr}} < 0.001$	left middle occipital gyrus, BA 19
-62	-34	-10	2486	4.94	$P_{\text{FDR-corr}} = 0.003$	left middle temporal gyrus, BA21
50	-74	-1	3580	7.35	$P_{\text{FDR-corr}} < 0.001$	right inferior temporal gyrus, BA 19
<i>Pro-gamer vs Patients with on-line game addiction</i>						
Pro-gamer > Patients with on-line game addiction						
-3	6	31	3310	5.09	$P_{\text{FDR-corr}} = 0.02$	left cingulate gyrus, BA 24
Pro-gamer < Patients with on-line game addiction						
-18	-26	11	2550	4.67	$p_{\text{uncorrected}} < 0.0001$	left thalamus

$P_{\text{FDR-corr}}$: corrected FDR<0.05, $p_{\text{uncorrected}}$: uncorrected.