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Changes in brain activity in response to problem solving during the abstinence from online game play

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Background and aims: Several studies have suggested that addictive disorders including substance abuse and pathologic gambling might be associated with dysfunction on working memory and prefrontal activity. We hypothesized that excessive online game playing is associated with deficits in prefrontal cortex function and that recovery from excessive online game playing might improve prefrontal cortical activation in response to working memory stimulation. *Methods:* Thirteen adolescents with excessive online game playing (AEOP) and ten healthy adolescents (HC) agreed to participate in this study. The severity of online game play and playing time were evaluated for a baseline measurement and again following four weeks of treatment. Brain activation in response to working memory tasks (simple and complex calculations) at baseline and subsequent measurements was assessed using BOLD functional magnetic resonance imaging (fMRI). *Results:* Compared to the HC subjects, the AEOP participants exhibited significantly greater activity in the right middle occipital gyrus, left cerebellum posterior lobe, left premotor cortex and left middle temporal gyrus in response to working memory tasks during baseline measurements. After four weeks of treatment, the AEOP subjects showed increased activity within the right dorsolateral prefrontal cortex and left occipital fusiform gyrus. After four weeks of treatment, changes in the severity of online game playing were negatively correlated with changes in the mean β value of the right dorsolateral prefrontal cortex in response to complex stimulation. *Conclusions:* We suggest that the effects of online game addiction on working memory may be similar to those observed in patients with substance dependence.

Keywords: working memory, online game addiction, functional magnetic resonance imaging, premotor cortex, dorsolateral prefrontal cortex

INTRODUCTION

Online game addiction and brain imaging findings

Disruptions in the maintenance of regular life, occupational, educational and social interaction due to online game play have been reported in adolescents with problematic online game play (Ha et al., 2006; Young, 1996). Internet addiction and problematic online gaming constitute an important public health concern in South Korea (Fitzpatrick, 2008). With an 80.6% high-speed internet market penetration and 99% of elementary and middle school students in South Korea using the internet (Korea Agency for Digital Opportunity & Promotion [KADO], 2009; Korean Statistical Information Service [KOSIS], 2009), one million Korean adolescents (9–19 years old) are regarded as at high risk for internet addiction (S. K. Park, Kim & Cho, 2008). In addition, the rates of school drop-outs, job loss and divorce in individuals with internet addiction are thought to be higher than those observed in healthy subjects (KADO, 2009; KOSIS, 2009).

Recent studies of internet addiction using cue-induced functional magnetic resonance imaging (fMRI) have shown that internet addiction, substance abuse and pathologic gambling shared similar brain activity in responses to internet (Han et al., 2011; Han, Hwang & Renshaw, 2010; Yuan, Qin, Liu & Tian, 2011), substance (Franken, 2003; Maas et al., 1998; Wilson, Sayette & Fiez, 2004) and gambling cues (Crockford, Goodyear, Edwards, Quickfall & el-Guebaly, 2005; Goudriaan, de Ruiter, van den Brink, Oosterlaan & Veltman, 2010). For example, fMRI studies of game cue-induced brain activity have noted that excessive online game players show increased activity in the dorsolateral prefrontal cortex (DLPFC), orbitofrontal cortex (OFC), anterior cingulate, nucleus accumbens, and caudate nucleus, relative to a healthy comparison group (Han et al., 2010; Ko et al., 2009). In fMRI studies, subjects with cocaine and alcohol dependence were noted to have altered cue-induced activation in the nucleus accumbens, amygdala, striatum, anterior cingulate cortex, OFC and DLPFC (Franken, 2003; Wilson et al., 2004). In fMRI studies, pathological gamblers have also shown inncreased activity in response to gambling cues in the prefrontal, parahippocampal region and OFC (Crockford et al., 2005; Goudriaan et al., 2010), and these findings are consistent with the results from fMRI studies of substance abusers in response to substance cues (van Holst, van den Brink, Veltman & Goudriaan, 2010). Although there are few published comparisons of online game addiction and pathological gambling, several lines of evidence suggest that the two disorders share common characteristics and pathophysiology. For example, both disorders have

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been characterized as non-chemical addictions with obsessive compulsive features (Walker, 1989) and individuals experience "high" or extreme excitement, during game play (Young, 1996). Moreover, the DSM-IV criteria for pathological gambling have been widely used in the definition of internet addiction in early studies by Young (1996, 1998) and subsequent studies by other investigators (Beard & Wolf, 2001).

Working memory in substance and behavioral addiction

Deficits in working memory are common cognitive dysfunctions in subjects with substance dependence (Brown, Tapert, Granholm & Delis, 2000; Moss, Kirisci, Gordon & Tarter, 1994; Tapert, Granholm, Leedy & Brown, 2002). Among several working memory functions, deficits in terms of problem solving have been reported in adolescents with alcohol abuse (Brown et al., 2000). Problem solving requires various cognitive processes, such as: active goal representation, maintenance and integration of relevant information, attentional selection, learning from error and self-regulatory capacities related to reward-seeking behavior (Goel & Grafman, 1995; Morris, Miotto, Feigenbaum, Bullock & Polkey, 1997). Difficulties in problem solving in subjects with marijuana abuse are associated with deficits in attention, learning and memory (Schwartz, Gruenewald, Klitzner & Fedio, 1989; Schweinsburg et al., 2008; Tapert et al., 2002). In the neurocognitive study performed by Goudriaan, Oosterlaan, de Beurs and van den Brink (2006), both pathological gamblers and individuals with alcohol dependence showed similar deficits on subtasks for measuring various executive functions: "inhibition, time estimation, cognitive flexibility and planning". Dysfunction of self-regulation for adaptive goals can cause perseverative behavior (repeated maladapted behaviors) in problem gamblers (Leiserson & Pihl, 2007). Pathological gamblers also showed decreased ventromedial prefrontal activation during performance of the Stroop task, a finding that is consistent with deficits of impulse control and working memory (Potenza et al., 2003).

Brain activation during problem solving in addiction

Previous studies have suggested that the DLPFC is essential for adaptive decision making by providing the capacity to maintain relevant goal in working memory (Goel & Dolan, 2000; Goldberg, Podell, Harner, Riggio & Lovell, 1994; Han, Daniels, Bolo, Arenella & Lyoo, 2008). The DLPFC is thought to play a critical role in monitoring and manipulating specific required information (Watanabe et al., 2001). Maladaptive problem solving and decision-making in pathological gamblers might be associated with posterior DLPFC dysfunction (Leiserson & Pihl, 2007). In two studies, dysfunctional activity in the DLPFC during working memory tasks and improvement in activity performance due to short term abstinence have been reported in subjects with marijuana addiction (Pope, Gruber, Hudson, Huestis & Yurgelun-Todd, 2001; Yurgelun-Todd et al., 1998). In addition to the involvement of the prefrontal cortex, there is also evidence that highlights the relationship between activation of the DLPFC and the premotor cortex during working memory tasks (Abe et al., 2007; Wallis & Miller, 2003). A reciprocal link between the DLPFC and premotor areas was activated when subjects performed "delayed-encoding recognition task" (Abe et al., 2007). Using tasks that require prompt switching between two arbitrary rules, Wallis and Miller (2003) suggested the neural connection for interpreting rules and linking them with motor responses.

Hypothesis

In this study, we hypothesized that activity of the prefrontal cortex in response to working memory tasks would be decreased in patients with online game addiction, compared to healthy controls. In addition, we hypothesized that recovery from excessive online game play would improve the activity of the prefrontal cortex in response to these tasks, mirroring the levels of healthy controls. We also hypothesized that the severity of online game play would be reduced and working memory function would be improved in the parallel with the increased brain activity.

METHODS

Subjects

Among the adolescents and parents who visited the Department of Psychiatry of Chung Ang University Medical Center for assessment and treatment of online game addiction, 13 families agreed to participate in this research study. In addition, ten healthy comparison adolescents (HC) who used the internet less than one hour per day were recruited. Youths with online game addiction aged ranging from 13 to 18 years old, and whose game play time of at least four hours per day and 30 hours per week (Han et al., 2010; Ko et al., 2009) was recruited. Participants scored in excess of 50 on the Young Internet Addiction Scale (YIAS) (Ha et al., 2006; Young, 1996), and had faced a difficulty with daily life resulting from excessive game play. These criteria were modified from the *Diagnostic and Statistical Manual of Mental Disorders-IV* (DSM-IV) criteria for pathological gambling and substance abuse, which had already been applied in our previous research (Han et al., 2010). Both patients and comparison subjects were screened using the Structured Clinical Interview from the DSM-IV and the Beck Depression Inventory (BDI) (Beck, Ward, Mendelson, Mock & Erbaugh, 1961). The exclusion criteria were subjects were excluded for diagnosed psychiatric disease, histories of substance abuse or dependence including alcohol and tobacco, and significant medical or neurological histories. Adolescents with contraindications to MRI scanning, such as claustrophobia or metal implants, were also excluded. The research protocol was approved by the Chung Ang University Hospital Institutional Review Board. Written informed consent was provided by the subjects and parents prior to beginning any of the study procedures.

Study procedures

At the baseline measurement, the severity of online game addiction, working memory function, and brain activity in response to complex calculations were assessed in both the AEOP and HC participants. The severity of online game play was evaluated using YIAS scores and by assessing weekly online game play time each week, as measured by subject self-report and by parental reporting. When different reports of online game play time between the child and their parents were suggested, the record of the parent was adopted. Working memory function was assessed using the arithmetic and digit-span sub-scale scores of the K-WISC-III (KADO, 2009). At the end of the four-week treatment period, working memory function, brain activity during complex calculations, and severity of online game addiction were assessed again for the AEOP participants. Brain activation in response to working memory tasks (simple and complex calculations) at baseline and subsequent measurements following four weeks of treatment were assessed using BOLD fMRI.

During the four-week treatment period, the AEOP participants were provided with education concerning how to reduce online game play. Two adolescents in the online game addiction group dropped out during the treatment period due to resistance against attempts to reduce their online game playing. One adolescent refused the final assessment and fMRI scanning without giving a specific reason. Finally, baseline demographic, behavioral, cognitive and neuroimaging data from total 23 subjects (13 AEOP + 10 HC) were analyzed. Follow-up data for 20 subjects (10 AEOP + 10 HC) were also analyzed.

Education for online game playing

All of the adolescents and parents were asked to visit the outpatient department twice per week for four weeks to receive education concerning reducing online game play, to determine the actual time spent playing and to engage in a four-week treatment protocol. The same four-week intervention protocol is used for all patients who are referred to our university-based internet addiction clinic and has previously been described in detail. The educational program consists of eight sessions using materials that were designed to promote healthy internet use (Han et al., 2007; KOSIS, 2009; Lee et al., 2008).

Assessment of brain activity and calculation task presentation

All of the MR imaging was performed using 3T blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI, Achieva 3.0, Philips, Eindhoven, The Netherlands). The video used was 450 seconds long and consisted of five continuous 90-second segments. Each 90-second segment consisted of three 30-second sub-segments: a white cross on a black background (B), a simple calculation (S, a simple addition and subtraction of numbers) and a complex calculation (C, selecting color and size, calculating numbers and memorizing the answers). The five segments were ordered as follows: B-S-C, B-C-S, C-B-S, S-B-C and C-S-B (Figure 1). This stimulation was presented through an IFIS-SA^{TM} system (MRI Device Corporation, Waukesha, WI, USA) during a single fMRI scanning session. For the fMRI session, 180 echo planar images (EPI, 33 transverse slices, 4.0 mm thickness, voxel size of 1.8 × 1.8 × 4.0 mm, TE = 30 msec, TR = 3000 ms, Flip angle = 90°, in-plane resolution = 128 × 128 pixels, field of view (FOV) = 230 × 230 mm) were recorded at three-second intervals. For examination of anatomical structures, 3D T1-weighted magnetization-prepared rapid gradient echo (MPRAGE) data were collected (TR = 2000 ms, TE = 4.00 ms, FOV = 256 × 256 mm, 340 slices, 0.9 × 0.9 × 1.0 mm voxel size, flip angle = 30°).

Simple and complex calculations

We designed simple and complex calculation tasks. Specially, the complex calculation task was designed to measure executive function, goal maintaining, response inhibition and error monitoring, as excessive internet game users are known to exhibit dysfunctions in their regulatory control and selective attention (H. S. Park et al., 2010). The simple calculation task was designed to compare the subject's brain activity during the performance of two different tasks. One

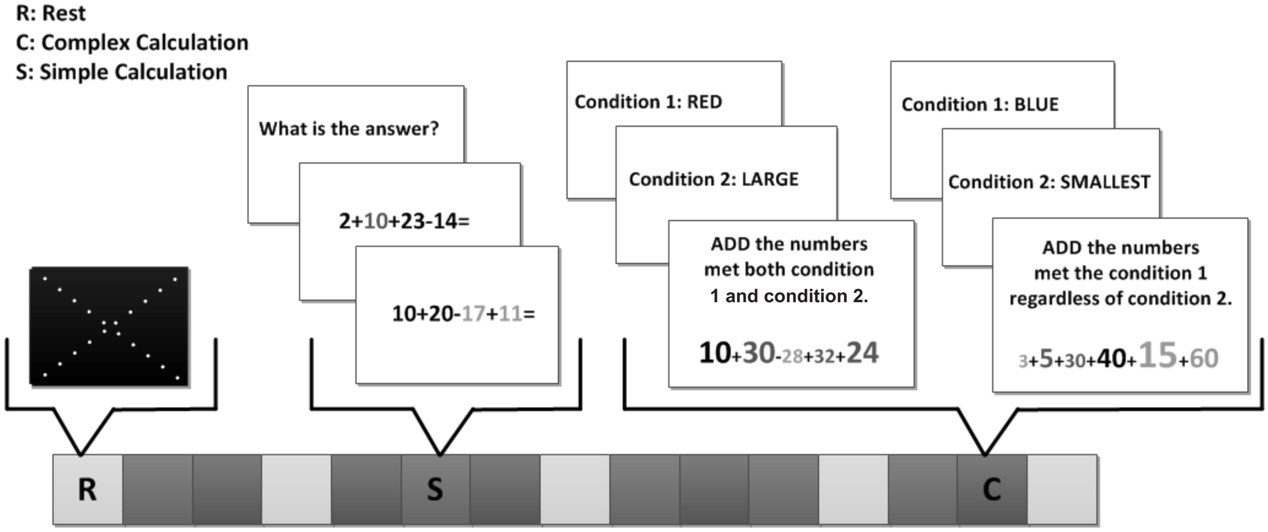

Figure 1. Design for working memory stimulation including color, size and recall

Simple calculation: calculating the sum of all numbers without considering the colors and font sizes of the numbers.
Complex calculation: calculating the sum of all numbers with considering the colors and font sizes of the numbers.

was a simple mental arithmetic exercise, while the other one was a complex calculation, which requires higher working memory capacity.

After the practice sessions, the subjects performed the calculation tasks while in the fMRI scanner. The subjects were asked to perform mental arithmetic (silent calculations without speaking and avoiding lip or tongue movements). During the 30-second calculation period, five arithmetic problems appeared on the screen. Each problem consisted of a problem description and the addition or subtraction of five or six digits, flashed with five-second latency between problem presentations.

Simple calculation: Subjects were asked to calculate the sum of all numbers presented on the screen. The subjects were not asked to consider the colors and font sizes of the numbers. In addition, the subjects did not need to memorize the answers.

Complex calculation: The subjects were asked to consider the color (e.g. black, blue, red, green or yellow) and font size (e.g. largest, large, medium, small or smallest) of numbers that they were to add. Each question was composed of three steps. In the first step, the subjects were informed of the color they should remember and consider when they calculate the sum. In the second step, the information about font size was provided. Then, in the last step, subjects were asked to calculate a sum by using the conditions defined in the first and second steps. Five different arithmetic problems in each epoch appeared on the screen in the same way. In addition, subjects were asked to memorize the answers and to verbally recite them during the last five seconds of each calculation period. The performance was measured by the number of total correct answers during complex calculation.

fMRI data analysis

The Brain Voyager software package (BVQX 1.9, Brain Innovation, Maastricht, The Netherlands) was used to analyze the fMRI data acquired at baseline and subsequent measurements. A multi-scale algorithm supplied by the BVQX was used to co-register the fMRI time sequence data from each participant to a 3D anatomical volume data set for the same participant. The structural data sets were normalized into standard Talairach stereotaxic space (Talairach & Tournoux, 1988). A nonlinear transformation was then applied to the T2*-weighted fMRI data. Subsequent pre-processing steps included slice scan time correction and 3D motion correction. The functional data were spatially smoothed using a Gaussian kernel with an FWHM of 6 mm and temporally smoothed using a Gaussian kernel of 4 s with algorithms supplied by BVQX.

Statistical analysis

A general linear model (GLM) and random effects analysis (RFX) were used in order to analyze the time-courses of fMRI signals on a voxel-by-voxel basis and to generate individual and group statistical maps of brain activation. For all analyses, the associations were regarded as significant when the false discovery rate (FDR)-corrected p values were less than or equal to 0.05 in 100 adjacent voxels. In an interaction between groups (AEOP vs. HC) and stimuli (simple vs. complex) with specific contrast (complex stimuli in AEOP > complex stimuli in HC), four clusters of significant activation were noted at baseline and following four week intervention measurements. The mean β values of the clusters between the baseline and subsequent measurements were analyzed using a paired t-test. Differences in YIAS scores and online game play times between the AEOP and HC groups were compared using non-parametric Mann–Whitney U tests. As a second-level analysis for the AEOP, the changes in the mean β values in the clusters during the four weeks of treatment and changes in the YIAS scores were analyzed using Pearson correlations.

RESULTS

Group characteristics

There were no differences in age (AEOP: 14.5 ± 1.1 years, HC: 14.2 ± 1.3 years, $z = 0.69$, $p = 0.49$), years of education (AEOP: 7.4 ± 0.9 years, HC: 7.2 ± 1.3 years, $z = 0.42$, $p = 0.68$) and BDI scores (AEOP: 9.4 ± 2.5 years, HC: 7.1 ± 4.9 years, $z = 1.1$, $p = 0.26$) between the AEOP and HC groups (Table 1).

There were significant differences between the two groups in terms of the YIAS scores ($z = 3.91$, $p < 0.01$) and the total playing time/total internet use time at baseline ($z = 3.83$, $p < 0.01$). The mean game play times (34.4 ± 6.4 hours/week) in the 13 AEOP subjects were recorded by the patients themselves and confirmed by parental reports. The mean internet use in the ten HC subjects was 11.7 ± 9.5 hours/week. The mean YIAS scores of the AEOP and HC groups at baseline were 71.2 ± 9.4 and 27.1 ± 5.3, respectively. During the treatment period, the mean YIAS score (baseline (B): 71.2 ± 9.4, 4 weeks (4 w): 50.9 ± 16.2, $z = 3.32$, $p < 0.01$) and the mean time of game play (B: 34.4 ± 6.4 hours/week, 4 w: 22.9 ± 11.6, $z = 3.01$, $p < 0.01$) decreased.

In comparisons of the working memory test at the baseline measurement, the AEOP group (10.2 ± 3.0) showed lower digit-span scores than the HC group (13.6 ± 3.1) ($z =$

Table 1. The demographic data, score of Young Internet Addiction Scale, playing game time and BDI score among GP and AEOP

Characteristics	AEOP ($n = 13$)	HC ($n = 10$)	Statistics
Age, mean ± SD, y	14.5 ± 1.1	14.2 ± 1.3	$z = 0.69$, $p = 0.49$
Education, mean ± SD, y	7.4 ± 0.9	7.2 ± 1.3	$z = 0.42$, $p = 0.68$
B_YIAS	72.2 ± 8.4	41.4 ± 4.5	$z = 3.91$, $p < 0.01$
BP_game	34.3 ± 6.4	11.7 ± 9.5	$z = 3.83$, $p < 0.01$
F_YIAS	50.9 ± 16.2	–	$z = 1.37$, $p = 0.17$
FP_game	22.9 ± 9.3	–	$z = 2.67$, $p < 0.01$
BDI score	9.4 ± 2.5	7.1 ± 4.9	$z = 1.1$, $p = 0.26$
Game genre			
RPG	5	3	
FPS	4	4	
RTS	3	2	
Others	1	1	

Healthy Comparison Subjects (HC), subjects with excessive internet video game player (AEOP), B_YIAS: Young Internet Addiction Scale score at baseline, F_YIAS: Young Internet Addiction Scale score at 4 weeks, BP_game: playing online game time at baseline, FP_game: playing online game time at 4 weeks, RPG: role playing game, FPS: first person shooting game, RTS: real time simulation game

2.25, $p = 0.02$). However, there were no significant differences in arithmetic scores (AEOP: 10.8 ± 2.2, HC: 11.1 ± 2.0, $z = 0.34$, $p = 0.73$). During the treatment period, there were no significant changes in the mean arithmetic scores ($z = 1.5$, $p = 0.13$) or the mean time of the digit-span scores ($z = 1.22$, $p = 0.22$) for the AEOP subjects.

When performing the complex calculation, the AEOP group (20.8 ± 2.6) showed lower scores than the HC group (24.0 ± 3.2) ($z = 2.28$, $p = 0.02$). After four weeks of treatment, the scores for the complex calculations did not change for the AEOP subjects (B: 20.8 ± 2.6, 4 weeks: 21.9 ± 3.4) ($z = 1.51$, $p = 0.13$).

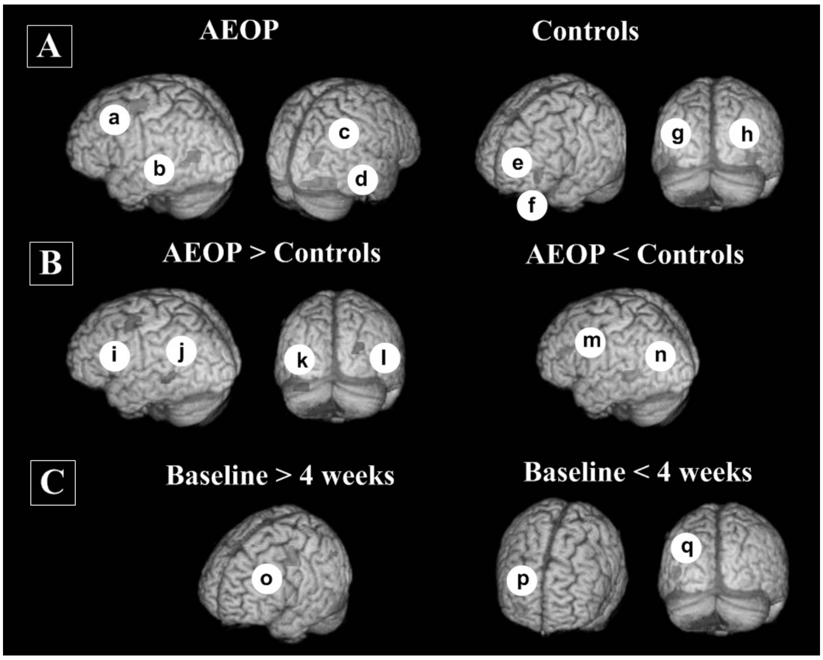

Figure 2. Clusters in response to complex > simple calculation at baseline and 4 weeks

A: Clusters of AEOP (adolescents with excessive online game play) in response to complex > simple calculation at baseline, uncorrected $p < 0.001$, a: left precentral gyrus (–23, –12, 51, voxels = 20, BA6), b: left middle temporal gyrus (–48, –62, –1, voxels = 23, BA37), c: right middle occipital gyrus (42, –64, 3, voxels = 43, BA37) and d: right occipital fusiform gyrus (25, –79, –18, voxels = 100, BA19). Clusters of healthy comparison subjects in response to complex > simple calculation at baseline, uncorrected $p < 0.001$ value, e: left inferior frontal gyrus gyrus (–41, 42, 1, voxels = 22, BA10), f: left amygdala (–23, –3, –16, voxels = 20), g: left occipital fusiform gyrus (–38, –64, –11, voxels = 72, BA19), and h: right occipital fusiform gyrus (41, –68, –9, voxels = 65, BA19).

B: Clusters of significant interaction between stimuli (complex vs. simple) and subject factors (AEOP vs. HC) at baseline, FDR < 0.05, $p < 0.002$, AEOP > Control: Interaction between group and stimuli with specific contrast (complex-rest in AEOP > complex-rest stimuli in HC), i: left frontal precentral gyrus (–34, –11, 44, voxels = 21, BA6), j: left middle temporal gyrus (–44, –48, 2, voxels = 25), k: left cerebellum posterior lobe (21, –64, –22, voxels = 35), and l: right middle occipital gyrus (36, –66, 3, voxels = 42, BA19), AEOP < Controls: Interaction between group and stimuli with specific contrast (complex-rest in AEOP < complex-rest stimuli in HC), m: left inferior frontal gyrus (–57, 14, 13, voxels = 20, BA44), and n: left parahippocampal gyrus (–27, –50, –4, voxels = 24, BA19).

C: Change in brain activity during four-week treatment period in AEOP. Baseline > 4 weeks: Interaction between group (AEOP at baseline vs. AEOP at 4 weeks) and stimuli (complex vs. simple) with specific contrast (complex-rest in baseline AEOP > complex-rest after 4 weeks AEOP), uncorrected $p < 0.001$, left precentral gyrus (–29, –15, 56, voxels = 20, BA6), Baseline < 4 weeks: Interaction between group (AEOP at baseline vs. AEOP at 4 weeks) and stimuli (complex vs. simple) with specific contrast (complex-rest in baseline AEOP < complex-rest after 4 weeks AEOP), uncorrected $p < 0.001$, p: right superior frontal gyrus (22, 56, –2, voxels = 20, BA10), and q: left occipital lingual gyrus (–24, –73, –5, voxels = 30, BA19).

Clusters in response to complex calculations at the baseline measurements

In response to the complex > simple calculation stimuli at the baseline measurement, the AEOP subjects showed four significant clusters at the uncorrected $p < 0.001$ value: left precentral gyrus (–23, –12, 51, voxels = 20, BA6), left middle temporal gyrus (–48, –62, –1, voxels = 23, BA37), right middle occipital gyrus (42, –64, 3, voxels = 43, BA37) and right occipital fusiform gyrus (25, –79, –18, voxels = 100, BA19) (Figure 2). The AEOP subjects showed no significant clusters in response to complex < simple calculation stimuli at the baseline measurement.

In response to the complex > simple calculation stimuli at the baseline measurement, the healthy comparison subjects showed four significant clusters at the uncorrected $p < 0.001$ value: left inferior frontal gyrus (–41, 42, 1, voxels = 22, BA10), left occipital fusiform gyrus (–38, –64, –11, voxels = 72, BA19), left amygdala (–23, –3, –16, voxels = 20) and right occipital fusiform gyrus (41, –68, –9, voxels = 65, BA19) (Figure 2). The healthy comparison subjects showed no significant clusters in response to complex < simple calculation stimuli at the baseline measurements.

Clusters of significant interaction between stimuli and subject factors at the baseline measurements

In an interaction between groups (AEOP vs. HC) and stimuli (complex vs. simple) with specific contrast (complex-rest in AEOP > complex-rest in HC), four clusters of activity were identified at baseline (FDR < 0.05, $p < 0.002$): left frontal precentral gyrus (–34, –11, 44, voxels = 21, BA6), left middle temporal gyrus (–44, –48, 2, voxels = 25), left cerebellum posterior lobe (21, –64, –22, voxels = 35), and right middle occipital gyrus (36, –66, 3, voxels = 42, BA19) (Figure 2).

In an interaction between groups (AEOP vs. HC) and stimuli (complex vs. simple) with specific contrast (complex-rest in AEOP < complex-rest stimuli in HC), two clusters of activity were identified at baseline (FDR < 0.05, $p < 0.002$): left parahippocampal gyrus (–27, –50, –4, BA19) and left inferior frontal gyrus (–57, 14, 13, BA44) (Figure 2). There were no specific clusters in response to simple calculation tasks between the AEOP and HC subjects.

Change in brain activity during the four-week treatment period in the AEOP subjects

In an interaction between group (AEOP at baseline vs. AEOP at 4 weeks) and stimuli (complex vs. simple) with specific contrast (complex-rest in baseline AEOP > complex-rest after 4 weeks AEOP), adolescents with excessive online game playing showed no significant clusters at FDR < 0.05. However, the left precentral gyrus (–29, –15, 56, voxels = 20, BA6) was identified at an uncorrected $p < 0.001$ (Figure 2).

In an interaction between the group (AEOP at baseline vs. AEOP at 4 weeks) and stimuli (complex vs. simple) with specific contrast (complex-rest in baseline AEOP < complex-rest after 4 weeks AEOP), adolescents with excessive online game playing showed no significant clusters at FDR < 0.05. However, two clusters of activity were identified in AEOP group at uncorrected $p < 0.001$: right superior frontal gyrus (22, 56, –2, voxels = 20, BA 10) and left occipital lingual gyrus (–24, –73, –5, voxels = 30, BA 19) (Figure 2).

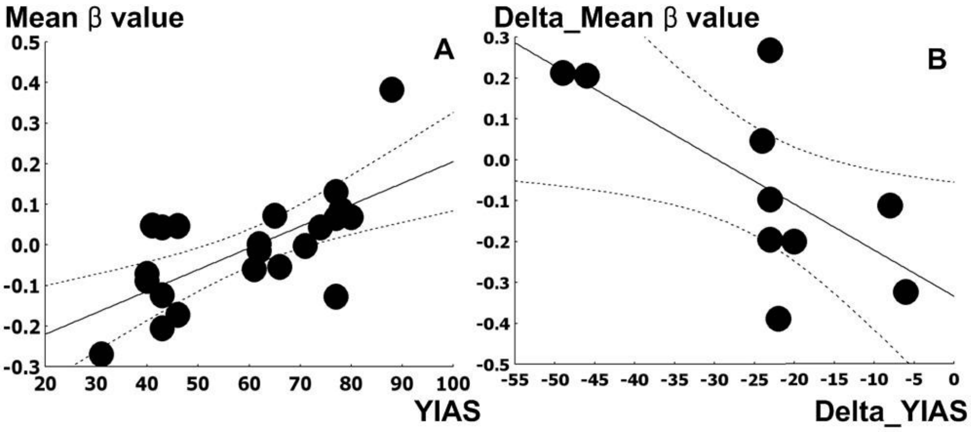

Figure 3. The correlation of YIAS scores and mean beta values of clusters (95% confidential interval)

A: The correlation between baseline Young Internet Addiction Scale (YIAS) scores and the mean β values of left precentral gyrus ($r = 0.66$, $p < 0.01$) in all subjects in response to complex stimulation.

B: The correlation between the change of YIAS scores (delta _YIAS) and the changes of the mean β values (delta_β values) of right superior frontal gyrus ($r = –0.64$, $p = 0.04$) in individuals with problematic online game play in response to complex stimulation during 4 weeks follow-up period.

After four weeks of treatment, the mean β values of left precentral gyrus ($t = 2.12$, $p = 0.04$) decreased and the mean β values of right superior frontal gyrus increased ($t = 2.69$, $p = 0.02$).

Correlations between scales of internet addiction, cravings, BDI, and brain activity

The baseline YIAS scores ($r = 0.66$, $p < 0.01$) and total game play times ($r = 0.49$, $p = 0.02$) for all subjects were correlated with the mean β values of the left precentral gyrus in response to complex stimulation. In addition, following four weeks of treatment, the changes in YIAS scores were negatively correlated with changes in the mean β values of right superior frontal gyrus ($r = –0.64$, $p = 0.04$) in response to complex stimulation (Figure 3). However, there was no correlation between YIAS scores, playing time and mean β value in other clusters at the four-week measurement.

DISCUSSION

During four weeks of treatment, there were no significant changes in working memory according to the complex calculation scores, arithmetic and digit-span sub-scale scores of K-WISC-III (KADO, 2009). However, brain activity in response to complex stimulation changed in the dorsolateral prefrontal cortex and premotor cortex of the AEOP group.

Dorsolateral prefrontal cortex

In the current study, after four weeks of treatment, activity in the right superior frontal gyrus (Brodmann area 10) in response to complex problem solving stimuli significantly increased for the AEOP group. In addition, following four weeks of treatment, reductions in the severity of online game play were negatively correlated with changes in the mean β value of the right DLPFC in response to complex stimulation.

The prefrontal cortex plays an essential role in working memory, in line with the ability to select and maintain different goals, to shift, and to prevent impulsive perseveration. DLPFC dysfunction may lead to disorganized, perseverative, and otherwise inappropriate behaviors (Goldberg et al., 1994; Kane & Engle, 2002; Leiserson & Pihl, 2007). Neurocognitive and neuroimaging studies using the “Tower of London task” developed by Shallice (1982) have shown that the right prefrontal region is involved in the construction of plans for problem solving (Burgess, Veitch, de Lacy Costello & Shallice, 2000; Feigenbaum, Polkey & Morris, 1996; Miotto, Bullock, Polkey & Morris, 1996; Morris et al., 1997). It has been suggested that although both the left and right DLPFC are involved in the problem-solving process, the two regions may have differentiable functional characteristics (Newman, Carpenter, Varma & Just, 2003). The right side of the prefrontal region seems to be more important for making plans, while the left side of the prefrontal region seems to be more engaged with the execution of plans (Newman et al., 2003). However, other fMRI studies using the “Tower of London task” have shown that while the DLPFC region is critical for problem-solving, neither of the two hemispheres have a dominant function (Lazeron et al., 2000; Van den Heuvel et al., 2003).

Two studies have noted increased DLPFC activity in response to working memory tasks within short abstinence periods (Pope et al., 2001; Yurgelun-Todd et al., 1998). In a study of the recovery time of cognition impaired by marijuana use, subjects showed cognitive errors on days 0, 1 and 7 after last use on word recall task (Pope et al., 2001). However, on the 28th day of abstinence, users demonstrated improvement in cognitive and neural functioning, and users and normal controls demonstrated no differences on any tests (Pope et al., 2001). Yurgelun-Todd et al. (1998) also conducted an fMRI study using a working memory task after 24 hours and 4 weeks of abstinence in participants with heavy marijuana dependence. Marijuana smokers showed attenuated activity in the DLPFC and increased activity in the anterior cingulate compared to controls after just 1 day of abstinence. After 28 days from the last use, prefrontal activity of marijuana smokers was recovered (Yurgelun-Todd et al., 1998).

Premotor cortex

Compared to healthy control participants, the AEOP participants showed significantly greater activity in the left frontal precentral gyrus (Brodmann area 9) in response to complex problem solving stimuli at study baseline. The severity of online game play in all subjects was correlated with the mean β values of the left premotor cortex in response to complex stimulation. During the treatment period, the activity of the premotor cortex activity decreased.

Increased premotor activation in the AEOP group might be associated with compensatory neural responses for prefrontal dysfunction (Jacobsen, Pugh, Constable, Westerveld & Mencl, 2007; Tapert et al., 2004). The DLPFC and premotor cortex were functionally linked in the performance of working memory tasks (Abe et al., 2007; di Pellegrino & Wise, 1993; Wallis & Miller, 2003). Previous studies using a double delay task have supported the concept of a transfer of information from the prefrontal to premotor cortexes and from cognitive function to motor control (di Pellegrino & Wise, 1993; Wallis & Miller, 2003). Abe et al. (2007) divided working memory manipulation into two subtypes of attentional selection and sequence generation. The selective concentration for particular information is thought to be associated with the DLPFC, and alteration of a certain item into a sequence for the dorsal premotor cortex is involved (Abe et al., 2007).

Limitations

There are several limitations to the current study. First, sample size and treatment duration of this study may have been insufficient to thoroughly reflect the effects of treatment. Second, there might be a practice effect, since the AEOP participants performed the same task twice. Third, formal neuropsychological testing was not applied to adolescents with problematic online game play in the current study. Several studies have reported that intelligence (IQ), impulsivity and temperament are associated with problematic online game play (Khazaal et al., 2011; M. H. Park et al., 2011). Inclusion of neuropsychological assessment will be necessary in future research.

CONCLUSIONS

Brain activation in response to working memory stimulation in the prefrontal cortex was defected in adolescents with excessive online game play. Over a four-week treatment period, the activity of prefrontal cortex in response to working memory stimulation increased. In addition, increased activity in prefrontal cortex was associated with decreased severity of online game addiction in adolescents with problematic online play. These findings are similar to those observed in patients with substance dependence after receiving treatment for substance abuse. We suggest that the dysfunction of working memory in individuals with problematic online game play would be similar to those observed in patients with substance abuser.

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REFERENCES

Abe, M., Hanakawa, T., Takayama, Y., Kuroki, C., Ogawa, S. & Fukuyama, H. (2007). Functional coupling of human prefrontal and premotor areas during cognitive manipulation. *The Journal of Neuroscience, 27*(13), 3429–3438.

Beard, K. W. & Wolf, E. M. (2001). Modification in the proposed diagnostic criteria for Internet addiction. *Cyberpsychology and Behavior 4*(3), 377–383.

Beck, A. T., Ward, C. H., Mendelson, M., Mock, J. & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry, 4,* 561–571.

Brown, S. A., Tapert, S. F., Granholm, E. & Delis, D. C. (2000). Neurocognitive functioning of adolescents: Effects of protracted alcohol use. *Alcoholism, Clinical and Experimental Research, 24*(2), 164–171.

Burgess, P. W., Veitch, E., de Lacy Costello, A. & Shallice, T. (2000). The cognitive and neuroanatomical correlates of multitasking. *Neuropsychologia, 38*(6), 848–863.

Crockford, D. N., Goodyear, B., Edwards, J., Quickfall, J. & el-Guebaly, N. (2005). Cue-induced brain activity in pathological gamblers. *Biological Psychiatry, 58*(10), 787–795.

di Pellegrino, G. & Wise, S. P. (1993). Visuospatial versus visuomotor activity in the premotor and prefrontal cortex of a primate. *The Journal of Neuroscience, 13*(3), 1227–1243.

Feigenbaum, J. D., Polkey, C. E. & Morris, R. G. (1996). Deficits in spatial working memory after unilateral temporal lobectomy in man. *Neuropsychologia, 34*(3), 163–176.

Fitzpatrick, J. J. (2008). Internet addiction: Recognition and interventions. *Archives of Psychiatric Nursing, 22*(2), 59–60.

Franken, I. H. (2003). Drug craving and addiction: Integrating psychological and neuropsychopharmacological approaches. *Progress in Neuro-psychopharmacology & Biological Psychiatry, 27*(4), 563–579.

Goel, V. & Dolan, R. J. (2000). Anatomical segregation of component processes in an inductive inference task. *Journal of Cognitive Neuroscience, 12*(1), 110–119.

Goel, V. & Grafman, J. (1995). Are the frontal lobes implicated in "planning" functions? Interpreting data from the Tower of Hanoi. *Neuropsychologia, 33*(5), 623–642.

Goldberg, E., Podell, K., Harner, R., Riggio, S. & Lovell, M. (1994). Cognitive bias, functional cortical geometry, and the frontal lobes: Laterality, sex, and handedness. *Journal of Cognitive Neuroscience, 6,* 276–296.

Goudriaan, A. E., de Ruiter, M. B., van den Brink, W., Oosterlaan, J. & Veltman, D. J. (2010). Brain activation patterns associated with cue reactivity and craving in abstinent problem gamblers, heavy smokers and healthy controls: An fMRI study. *Addiction Biology, 15*(4), 491–503.

Goudriaan, A. E., Oosterlaan, J., de Beurs, E. & van den Brink, W. (2006). Neurocognitive functions in pathological gambling: A comparison with alcohol dependence, Tourette syndrome and normal controls. *Addiction, 101*(4), 534–547.

Ha, J. H., Yoo, H. J., Cho, I. H., Chin, B., Shin, D. & Kim, J. H. (2006). Psychiatric comorbidity assessed in Korean children and adolescents who screen positive for Internet addiction. *The Journal of Clinical Psychiatry, 67*(5), 821–826.

Han, D. H., Bolo, N., Daniels, M. A., Arenella, L., Lyoo, I. K. & Renshaw, P. F. (2011). Brain activity and desire for Internet video game play. *Comprehensive Psychiatry, 52*(1), 88–95.

Han, D. H., Daniels, M. A., Bolo, N., Arenella, L. S. & Lyoo, I. K. (2008). *The correlation between cue-induced craving for internet video game play and brain activation.* Paper presented at The College on Problems of Drug Dependence, San Juan, Puerto Rico.

Han, D. H., Hwang, J. W. & Renshaw, P. F. (2010). Bupropion sustained release treatment decreases craving for video games and cue-induced brain activity in patients with Internet video game addiction. *Experimental and Clinical Psychopharmacology, 18*(4), 297–304.

Han, D. H., Lee, Y. S., Yang, K. C., Kim, E. Y., Lyoo, I. K. & Renshaw, P. F. (2007). Dopamine genes and reward dependence in adolescents with excessive internet video game play. *Journal of Addiction Medicine, 1*(3), 133–138.

Jacobsen, L. K., Pugh, K. R., Constable, R. T., Westerveld, M. & Mencl, W. E. (2007). Functional correlates of verbal memory deficits emerging during nicotine withdrawal in abstinent adolescent cannabis users. *Biological Psychiatry, 61*(1), 31–40.

Kane, M. J. & Engle, R. W. (2002). The role of prefrontal cortex in working-memory capacity, executive attention, and general fluid intelligence: An individual-differences perspective. *Psychonomic Bulletin & Review, 9*(4), 637–671.

Khazaal, Y., Chatton, A., Atwi, K., Zullino, D., Khan, R. & Billieux, J. (2011). Arabic validation of the Compulsive Internet Use Scale (CIUS). *Substance Abuse Treatment, Prevention, and Policy, 6,* 32.

Ko, C. H., Liu, G. C., Hsiao, S., Yen, J. Y., Yang, M. J., Lin, W. C. et al. (2009). Brain activities associated with gaming urge of online gaming addiction. *Journal of Psychiatric Research, 43*(7), 739–747.

Korea Agency for Digital Opportunity & Promotion [KADO] (2009). National Survey of Internet Use in Korea. Retrieved December 1, 2010 from http://www.kado.or.kr

Korean Statistical Information Service [KOSIS] (2009). High Speed Internet Market Penetration. Retrieved December 1, 2010 from http://kostat.go.kr

Lazeron, R. H., Rombouts, S. A., Machielsen, W. C., Scheltens, P., Witter, M. P., Uylings, H. B. et al. (2000). Visualizing brain activation during planning: The Tower of London test adapted for functional MR imaging. *American Journal of Neuroradiology, 21*(8), 1407–1414.

Lee, Y. S., Han, D. H., Yang, K. C., Daniels, M. A., Na, C., Kee, B. S. et al. (2008). Depression like characteristics of 5HTTLPR polymorphism and temperament in excessive internet users. *Journal of Affective Disorders, 109*(1–2), 165–169.

Leiserson, V. & Pihl, R. O. (2007). Reward-sensitivity, inhibition of reward-seeking, and dorsolateral prefrontal working memory function in problem gamblers not in treatment. *Journal of Gambling Studies, 23*(4), 435–455.

Maas, L. C., Lukas, S. E., Kaufman, M. J., Weiss, R. D., Daniels, S. L., Rogers, V. W. et al. (1998). Functional magnetic resonance imaging of human brain activation during cue-induced cocaine craving. *The American Journal of Psychiatry, 155*(1), 124–126.

Miotto, E. C., Bullock, P., Polkey, C. E. & Morris, R. G. (1996). Spatial working memory and strategy formation in patients with frontal lobe excisions. *Cortex, 32*(4), 613–630.

Morris, R. G., Miotto, E. C., Feigenbaum, J. D., Bullock, P. & Polkey, C. E. (1997). The effect of goal-subgoal conflict on planning ability after frontal- and temporal-lobe lesions in humans. *Neuropsychologia, 35*(8), 1147–1157.

Moss, H. B., Kirisci, L., Gordon, H. W. & Tarter, R. E. (1994). A neuropsychologic profile of adolescent alcoholics. *Alcoholism, Clinical and Experimental Research, 18*(1), 159–163.

Newman, S. D., Carpenter, P. A., Varma, S. & Just, M. A. (2003). Frontal and parietal participation in problem solving in the Tower of London: fMRI and computational modeling of planning and high-level perception. *Neuropsychologia, 41*(12), 1668–1682.

Park, H. S., Kim, S. H., Bang, S. A., Yoon, E. J., Cho, S. S. & Kim, S. E. (2010). Altered regional cerebral glucose metabolism in internet game overusers: A 18F-fluorodeoxyglucose positron emission tomography study. *CNS Spectrums, 15*(3), 159–166.

Park, M. H., Park, E. J., Choi, J., Chai, S., Lee, J. H., Lee, C. et al. (2011). Preliminary study of Internet addiction and cognitive function in adolescents based on IQ tests. *Psychiatry Research, 190*(2–3), 275–281.

Park, S. K., Kim, J. Y. & Cho, C. B. (2008). Prevalence of Internet addiction and correlations with family factors among South Korean adolescents. *Adolescence, 43*(172), 895–909.

Pope, H. G., Jr., Gruber, A. J., Hudson, J. I., Huestis, M. A. & Yurgelun-Todd, D. (2001). Neuropsychological performance in long-term cannabis users. *Archives of General Psychiatry, 58*(10), 909–915.

Potenza, M. N., Steinberg, M. A., Skudlarski, P., Fulbright, R. K., Lacadie, C. M., Wilber, M. K. et al. (2003). Gambling urges in pathological gambling: A functional magnetic resonance imaging study. *Archives of General Psychiatry, 60*(8), 828–836.

Schwartz, R. H., Gruenewald, P. J., Klitzner, M. & Fedio, P. (1989). Short-term memory impairment in cannabis-dependent adolescents. *American Journal of Diseases of Children, 143*(10), 1214–1219.

Schweinsburg, A. D., Nagel, B. J., Schweinsburg, B. C., Park, A., Theilmann, R. J. & Tapert, S. F. (2008). Abstinent adolescent marijuana users show altered fMRI response during spatial working memory. *Psychiatry Research, 163*(1), 40–51.

Shallice, T. (1982). Specific impairments of planning. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences, 298*(1089), 199–209.

Talairach, J. & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain: 3-dimensional proportional system: An approach to cerebral imaging*. New York: Thieme Medical Publishers.

Tapert, S. F., Granholm, E., Leedy, N. G. & Brown, S. A. (2002). Substance use and withdrawal: Neuropsychological functioning over 8 years in youth. *Journal of the International Neuropsychological Society, 8*(7), 873–883.

Tapert, S. F., Schweinsburg, A. D., Barlett, V. C., Brown, S. A., Frank, L. R., Brown, G. G. et al. (2004). Blood oxygen level dependent response and spatial working memory in adolescents with alcohol use disorders. *Alcoholism, Clinical and Experimental Research, 28*(10), 1577–1586.

Van den Heuvel, O. A., Groenewegen, H. J., Barkhof, F., Lazeron, R. H., van Dyck, R. & Veltman, D. J. (2003). Frontostriatal system in planning complexity: A parametric functional magnetic resonance version of Tower of London task. *Neuroimage, 18*(2), 367–374.

van Holst, R. J., van den Brink, W., Veltman, D. J. & Goudriaan, A. E. (2010). Brain imaging studies in pathological gambling. *Current Psychiatry Reports, 12*(5), 418–425.

Walker, M. B. (1989). Some problems with the concept of "gambling addiction": Should theories of addiction be generalized to include excessive gambling? *Journal of Gambling Studies, 5*(3), 179–200.

Wallis, J. D. & Miller, E. K. (2003). Neuronal activity in primate dorsolateral and orbital prefrontal cortex during performance of a reward preference task. *The European Journal of Neuroscience, 18*(7), 2069–2081.

Watanabe, M., Cromwell, H. C., Tremblay, L., Hollerman, J. R., Hikosaka, K. & Schultz, W. (2001). Behavioral reactions reflecting differential reward expectations in monkeys. *Experimental Brain Research, 140*(4), 511–518.

Wilson, S. J., Sayette, M. A. & Fiez, J. A. (2004). Prefrontal responses to drug cues: A neurocognitive analysis. *Nature Neuroscience, 7*(3), 211–214.

Young, K. S. (1996). Psychology of computer use: XL. Addictive use of the Internet: A case that breaks the stereotype. *Psychological Reports, 79*(3 Pt 1), 899–902.

Young, K. S. (1998). *Caught in the Net: How to recognize the signs of Internet addiction and a winning strategy for recovery*. New York, NY: John Wiley & Sons.

Yuan, K., Qin, W., Liu, Y. & Tian, J. (2011). Internet addiction: Neuroimaging findings. *Communicative and Integrative Biology, 4*(6), 637–639.

Yurgelun-Todd, D. A., Gruber, S. A., Hanson, R. A., Baird, A. A., Renshaw, P. F. & Pope, H. G., Jr. (1998). *Residual effects of marijuana use: An fMRI study.* In *Problems of drug dependence.* Paper presented at the 60th Annual Scientific Meeting, the College on Problems of Drug Dependence, Bethesda.