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Gray matter and white matter abnormalities in online game addiction

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ABSTRACT

Online game addiction (OGA) has attracted greater attention as a serious public mental health issue. However, there are only a few brain magnetic resonance imaging studies on brain structure about OGA. In the current study, we used voxel-based morphometry (VBM) analysis and tract-based spatial statistics (TBSS) to investigate the microstructural changes in OGA and assessed the relationship between these morphology changes and the Young's Internet Addiction Scale (YIAS) scores within the OGA group. Compared with healthy subjects, OGA individuals showed significant gray matter atrophy in the right orbitofrontal cortex, bilateral insula, and right supplementary motor area. According to TBSS analysis, OGA subjects had significantly reduced FA in the right genu of corpus callosum, bilateral frontal lobe white matter, and right external capsule. Gray matter volumes (GMV) of the right orbitofrontal cortex, bilateral insula and FA values of the right external capsule were significantly positively correlated with the YIAS scores in the OGA subjects. Our findings suggested that microstructure abnormalities of gray and white matter were present in OGA subjects. This finding may provide more insights into the understanding of the underlying neural mechanisms of OGA.

1. Introduction

With the rapid development of computer and network technology, online gaming has been considered as a mainstream recreational activity among internet users. Unfortunately, the online gaming also contributed to the creation of a negative habit in the form of online gaming addiction, which was characterized by an individual's inability to control his or her playing online games [1]. Data from a survey about adolescents' online gaming addiction in China, as of 2 February 2010, showed that the incidence of internet addiction among Chinese urban youths was about 14.1%, with the total number of 24 million. It is worth noting that online gaming is the main culprit in cases of adolescents' internet addiction (http://www.zqwx.youth.cn/). The adolescents with online game addiction suffered from a number of serious psychological and social problems, resulting in adverse effects on their social relationships and day-to-day living. A survey among 174 Taiwanese college-age online players reported that the quality of interpersonal relationships worsened and social anxiety increased as the amount of time spent on playing online games increased [2].

Current studies about OGA are primarily based on psychological self-reported questionnaires. These researches have demonstrated exactly the existence of online gamers who have psychological problems and cognitive impairments [3,4]. It is notable that most of these empirical studies have merely focused on proposing potential reasons of OGA, such as players' personal reasons, environmental factors, and characteristics of online games, instead of the underlying reasons of OGA. Furthermore, some researchers point out the necessity of investigating physical injuries of OGA but it is hard to include this dimension by means of a questionnaire. Few neuroimaging studies of internet addiction disorder (IAD) have demonstrated that some aspects of brain structure and function existed changes in IAD [5]. However, as one primary subtype of internet addiction, studies focused on the brain morphology changes of OGA specially have not been conducted. Voxel-based morphometry (VBM) technique and tract-based spatial statistics (TBSS) analysis were two widely used neuroimaging analysis techniques that allow investigation of focal differences in brain anatomy [6,7]. In this study we aimed to investigate the differences in the brain morphology between OGA subjects and healthy controls without OGA and to explore the possible mechanism of OGA by virtue of VBM technique and TBSS analysis.

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Table 1
Regions that showed significant differences in GMV and white matter FA between the OGA and controls.

	MNI coordinates (mm)			Hemisphere	Voxels	Corresponding cortical region	*p*-Value
	X	*Y*	*Z*				
VBM results							
	34	25	−21	R	334	Orbitofrontal cortex	0.02
	−31	−6	−3	L	177	Insula	0.00
	37	−7	−4	R	364	Insula	0.00
	2	−4	59	R	82	Supplementary motor area	0.03
TBSS results							
	14	25	19	R	238	Genu of corpus callosum	0.00
	−33	21	21	L	171	Frontal lobe white matter	0.00
	28	31	19	R	142	Frontal lobe white matter	0.00
	26	18	−7	R	149	External capsule	0.00

2. Materials and methods

2.1. Subjects

Seventeen subjects with OGA were recruited from the Department of Psychology, Anhui Provincial Hospital (13 females and 4 males, mean age = 16.25 ± 3.02), all of whom met the modified Young's diagnostic questionnaire (YDQ) for internet addiction criteria by Beard and Wolf [8]. Seventeen age- and gender-matched healthy individuals without OGA were selected as the control group (15 females and 2 males, mean age = 15.54 ± 3.19). The YDQ criteria consisting of eight "yes" or "no" questions were translated into Chinese. Beard and Wolf asserted that respondents who answered "yes" to questions 1 through 5 and at least to any one of the remaining three questions were classified as suffering from internet addiction, which was a universally accepted criterion for screening the subjects in the present study. We confirmed that playing online game was their primary activity when the OGA subjects used internet and verified this by investigating the time per day they spent in playing online games. All the OGA subjects and control groups were right-handed, never used illegal substances, and were native Chinese speakers. Exclusion criteria for both groups included (1) subjects with substance (alcohol, nicotine, or drug) abuse or dependence, (2) existence of neurologic or medical disorders (brain tumor, epilepsy, etc.), and (3) a history or current episode of major psychiatric disorders, such as depression, anxiety disorder, schizophrenia, or psychotic episodes. The demographic information of the subjects included was listed in Table 1.

The Ethics Committee of Anhui Provincial Hospital Affiliated to Anhui Medical University approved all experimental procedure, and informed consent was obtained from all participants after a complete description of the procedure.

2.2. Behavioral data acquisition and assessments

To probe the behavioral characteristics of online game players, we used the Young's Internet Addiction Scale (YIAS) and Barratt Impulsiveness Scale-11 (BIS-11) to assess all subjects. The YIAS was designed to identify the degree of OGA tendency as mildly, moderately or severely addicted, which consisted of 20 items including psychological dependence, compulsive use, withdrawal, and the related problems of school or work, sleep, family, and time management (for each item, a graded response was selected from 1 = "not at all" to 5 = "always"). The total score was in the range of 20–100, and a higher score implies a tendency toward addictive usage: ≤49 is considered normal, 50–79 is considered problematic and 80–100 is classed as significantly problematic [9]. The 11th version of the BIS was a 30-item (the items were scored on a 4-point scale: 1 = "rarely/never", 2 = "occasionally", 3 = "often", and 4 = "almost always/always") self-report measure assessing impulsiveness, or the tendency to lose control over one's thoughts or behaviors. All items were summed, with higher scores indicating greater impulsivity [10].

The differences in demographic characteristics between the OGA group and the control group were performed by means of independent *t*-test and chi-square test. Between-group comparisons of the YIAS and BIS-11 scores were analyzed using independent *t*-test. All tests were two-sided, and a *p* value of less than 0.05 was considered to indicate statistical significance. All analyses were performed with the use of SPSS software, version 12.0.

2.3. MR data acquisition and analysis

2.3.1. Data acquisition

MRI scans were performed using a Philips Intera 3.0 T MR imaging scanner (Philips Medical Systems, Netherlands) with a standard head coil in Anhui Provincial Hospital. 3D T1-weighted images were obtained using the following parameters (magnetization – prepared rapid gradient echo, MPRAGE): TR = 1900 ms, TE = 3.37 ms, field of view = 240 mm × 240 mm, flip angle = 8°, in-plane matrix resolution = 240 × 240, slices = 150, field of view = 240 mm^2. Diffusion tensor images were collected by using a single shot echo planar imaging with a twice-refocused spin echo pulse sequences with diffusion sensitization gradients applied in 30 non-collinear directions and a *b*-value of 1000 s/mm^2: TR = 7200 ms, TE = 104 ms, field of view = 240 mm × 240 mm, acquisition matrix = 128 × 128, 64 slices were acquired with a slice thickness of 2.0 mm and no gap. The same imaging parameters were applied to acquire T2 weighted (*b*-value = 0 s/mm^2) images to use as a reference image for signal attenuation measurement.

2.3.2. VBM data preprocessing and analysis

Structural data was processed with a FSL-VBM [6], a VBM style analysis carried out with FSL 4.1.4 (FSL 4.1.4; www.fmrib.ox.ac.uk/fsl) tools. First, all structural images were brain-extracted and tissue-type segmented to produce gray matter, white matter and cerebrospinal fluid. The gray matter partial volume images were aligned to MNI152 standard space, followed by nonlinear registration, which used a *b*-spline representation of registration warp filed. The resulting images were averaged to create a study-specific template, and the native gray matter images were nonlinearly re-registered to the template images. The registered partial volume images were then modulated by dividing the Jacobian of the warp field to correct for local expansion or contraction. All the modulated registered gray matter images were smoothed by a range of Gaussian kernel with a sigma of 3.0 mm for the threshold-free cluster enhancement (TFCE) based analysis. Regional changes in gray matter between the OGA group and control were assessed using permutation-based non-parametric testing with 5000 random permutations; in addition, age and gender effects were used for analysis of covariance (ANCOVA). Cluster-size shareholding at

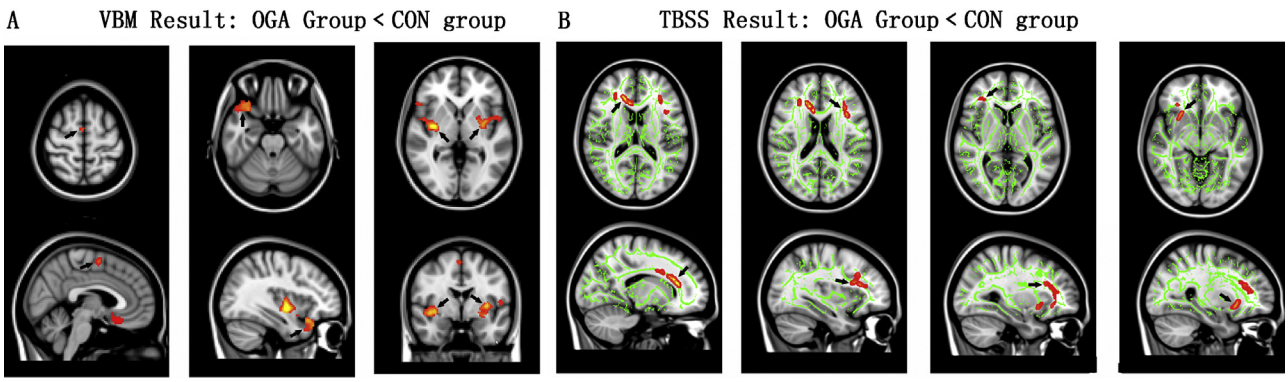

Fig. 1. VBM results and TBSS results.

$p < 0.05$, correcting for multiline comparisons across space, was used.

2.3.3. TBSS data preprocessing and analysis

Raw diffusion images were analyzed using FMRIB's diffusion toolbox for data preprocessing. The DTI dataset were aligned to its corresponding b_0 image (non-diffusion-weighted image) to correct for subject head motion artifacts and the effects of eddy currents distortions. After this process, we used a volume without diffusion weighting (i.e., b_0 image) to generate a brain mask and created FA by fitting diffusion tensor to each voxel. The output FA images were used as input for TBSS analysis [7]. The first TBSS script ran the nonlinear registration, aligning all the FA data to an FMRIB58_FA template and the aligned FA volumes were normalized to a 1 mm × 1 mm × 1 mm Montreal Neurological Institute (MNI 152) standard space. Next, all subjects' standard space nonlinearly aligned images were averaged to generate a cross-subject mean FA image, and this then fed FA skeletonization program to create a mean FA skeleton (using a threshold of 0.3), which represented the centers of all tracts the group had in common. Following the thresholding of the mean FA skeleton, the aligned FA data of each participant was projected onto the mean skeleton to create a skeletonized FA map for further statistical analysis. Two contrasts, OGA subjects greater than controls and controls greater than OGA subjects, were estimated by a voxel by voxel permutation nonparametric test (5000 permutations). The significance threshold for between-group difference was set at $p < 0.05$ using the threshold-free cluster enhancement (TFCE) after family-wise error rate (FWE) correcting for multiple comparisons.

2.3.4. Regions of interest (ROI) analysis

Each participant's GMV and FA values were extracted in the OGA group. To do so, the brain regions where OGA subjects showed significantly different GMV and FA values from the controls were first extracted as ROI masks. These ROI masks were then back-projected to the original images of each subject, and the GMV values and FA values of each participant were calculated. Finally, correlation analysis was performed to investigate the relationship among the YIAS scores and the GMV values and FA values of each subject. The correlation was considered to be significant at $p < 0.05$.

3. Results

3.1. Demographic and behavioral performance

The two groups did not differ significantly in age, sex ratio, or education. The mean amount of time spent on the internet per week of the OGA group was 49.62 ± 7.35 h which was significantly higher than the control group (18.12 ± 2.51 h) ($p < 0.001$). Significantly higher YIAS (OGA: 66.53 ± 12.45, CON: 36.52 ± 10.43, $p < 0.001$) and BIS-11 (OGA: 68.85 ± 13.66, CON: 65.94 ± 6.65, $p < 0.05$) scores for the OGA group were also observed.

3.2. VBM and TBSS results

VBM and TBSS results were shown in Table 1 and Fig. 1.

Fig. 1A shows the VBM results: areas in red–yellow are regions where GMV is significantly lower in OGA relative to controls. The background image is the standard MNI 152_T1_1mm_brain template in FSL.

Fig. 1B shows the TBSS results: areas in red–yellow are regions where FA is significantly lower in OGA relative to controls. The background image is the standard MNI 152_TI_5mm_brain template in FSL and the mean FA skeleton (green).

The left side of the image corresponds to the right hemisphere of the brain.

3.3. ROI results

Significant positive correlations were observed between GMVs and the YIAS scores in the right orbitofrontal cortex ($r = -0.65$, $p < 0.001$) and bilateral insula ($r = -0.78$, $p < 0.001$). Furthermore, the FA values tended to correlate positively with the YIAS scores in the right external capsule ($r = -0.66$, $p < 0.001$) (see Fig. 2).

4. Discussion

A number of recent findings suggested that the prefrontal cortex of the brain implicated in alcohol, cocaine, nicotine and some behavior addiction [5,11,12]. A hypothesis argued for the prefrontal cortex impairments in addiction resulted in executive dysfunction in the brain, which was considered been important to the cognitive control of behavior, contributed directly to the addiction process [13]. The executive system is a theorized cognitive system in psychology that controls and manages other cognitive processes in our daily life, which consists of the dorsolateral prefrontal cortex (DLPFC), anterior cingulate cortex (ACC) and the orbitofrontal cortex (OFC) of the prefrontal regions, and has a major impact on our ability to perform such tasks as planning, prioritizing, organizing, paying attention to and remembering details, and controlling our emotional reactions [14]. Behavioral studies showed that internet addiction was an impulse disorder or at least to impulse control. Now it is commonly held that the OFC plays a key role in impulse control and monitoring ongoing behavior and lesions can cause disinhibition, impulsivity. Our finding that OGA impaired gray and white matter integrity in the OFC and the prefrontal cortex was consistent with these precious results [15,16]. Impaired gray and white matter integrity in the prefrontal cortex resulted in

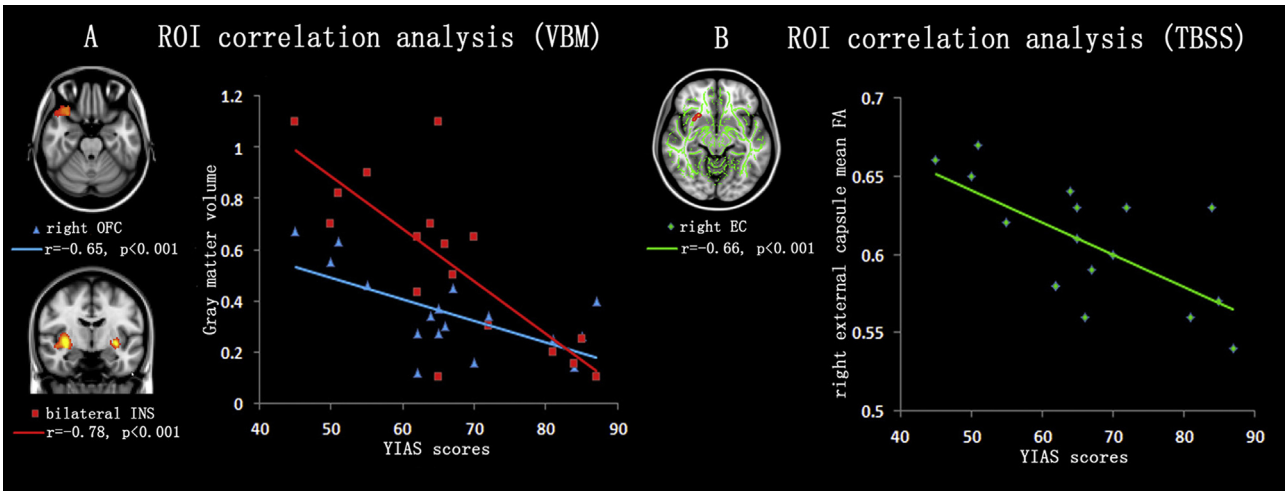

Fig. 2. ROI correlation analysis.

uncontrolled behavior and internet gambling urges which may be one possible underlying mechanism of OGA.

The insular cortex is divided into two parts: the larger anterior insula and the smaller posterior insula. The smaller posterior insula has been ascribed a role in somatosensory, vestibular and motor integration. The larger anterior insula, especially agranular regions has been ascribed a role in the integration of autonomic and visceral information into emotional and motivational functions which support its role in motivation, emotion and addiction. Naqvi and Bechara [17] study provided the first evidence in humans that the insula played a crucial part in addiction. The result of their study suggested that the insula was a region that integrated the interoceptive state into conscious feeling and into decision-making processes that involved certain risks and rewards. A number of functional brain imaging studies have shown that the insular cortex is activated when drug abusers are exposed to environmental cues that trigger cravings or during the administration of drugs abuse. This has been shown for a variety of drugs, including cocaine, alcohol, cigarettes and heroin. Recent researches have shown that cigarette smokers who suffered damage to the insular cortex, from a stroke for instance, had their addiction to cigarettes practically eliminated. This suggested a significant role for the insular cortex in the neurological mechanisms underlying addiction to nicotine and other drugs, which making this area of the brain a possible target for novel anti-addiction medication [18]. The idea that insula dysfunction underlies drug addiction is also supported by a study showing that chronic cocaine users have reduced gray/white matter ratios in the insula [19]. Therefore, our findings were in agreement with previous finding and verified the necessary role of insula for addiction.

The supplementary motor area (SMA) is a part of the primate cerebral cortex that contributes to the postural stabilization of the body, the coordination of both sides of the body such as during bimanual action, the control of movements that are internally generated rather than triggered by sensory events, and the control of sequences of movements [20]. The possible reason for the lower GMV in SMA was that the OGA subjects spent more time playing computer games and the repetitive motor actions such as clicking the mouse and keyboard typing maybe make the structure of the SMA changes.

Moreover, our studies also found OGA subjects had significantly reduced FA in the right genu of corpus callosum and right external capsule. Moreover, these results were similar to other forms of addiction (such as alcohol, cocaine, methamphetamine, and ketamine) and provided evidences of OGA also having deficits in white matter integrity and reflected a disruption in the organization of white matter tracts in OGA [21,22]. Corpus callosum is the largest white matter fiber beneath the cortex in the eutherian brain at the longitudinal fissure, which connects the left and right cerebral hemispheres and facilitates interhemispheric communication. Decreased FA in the genu of corpus callosum is a common finding in cocaine-dependent subjects, methamphetamine abusers, alcoholism, and opiate-dependent patients [23]. External capsule connects the ventral and medial prefrontal cortex to the striatum and its white matter alterations also have been reported in opiate addiction. Our findings suggested that heavy internet overuse, similar to substance abuses, may damage white matter microstructure of the brain.

Of course, there are several limitations in this study and some of which should be mentioned. The sample size in this study is relatively small, which has only 17 subjects from each group. Because of the small sample size, statistical power is very limited. Owing to this limitation, these results should to be considered preliminary, which need to be replicated in future studies with a larger sample size. In addition, the application of VBM for examination of the atrophied brain is still controversial. There are limitations to VBM, including sensitivity to methodological choices in normalization, smoothing kernel and the robustness of standard parametric tests. Therefore, more extensive experiment on this topic should be carried out in future.

5. Conclusion

We used VBM and TBSS analysis to investigate the microstructure of gray and white matter among OGA subjects. The results provided evidence indicating that OGA subjects had multiple structural changes in the gray matter and white matter. These findings suggested OGA may share the some mechanisms with substance addiction and provided more insights into the pathogenesis of OGA.

Conflicts of interest

There is no conflict of interest for each author including employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding.

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References

[1] Kim J, Haridakis PM. The role of internet user characteristics and motives in explaining three dimensions of internet addiction. Journal of Computer-Mediated Communication 2009;14:988–1015.
[2] Lo SK, Wang CC, Fang W. Physical interpersonal relationships and social anxiety among online game players. Cyberpsychology & Behavior 2005;8:15–20.
[3] Shapira NA, Goldsmith TD, Keck Jr PE, et al. Psychiatric features of individuals with problematic internet use. Journal of Affective Disorders 2000;5:726772.
[4] Whang LS, Lee S, Chang G. Internet over-users' psychological profiles: a behavior sampling analysis on internet addiction. Cyberpsychology & Behavior 2003;6:143e50.
[5] Han DH, Bolo N, Daniels MA, et al. Brain activity and desire for internet video game play. Comprehensive Psychiatry 2011;52:88–95.
[6] Ashburner J, Friston KJ. Voxel-based morphometry – the methods. NeuroImage 2000;11:805–21.
[7] Smith SM, Jenkinson M, Johansen-Berg H, et al. Tract-based spatial statistics: voxelwise analysis of multi-subject diffusion data. NeuroImage 2006;31:1487–505.
[8] Beard KW, Wolf EM. Modification in the proposed diagnostic criteria for internet addiction. Cyberpsychology & Behavior 2001;4:377–83.
[9] Young KS. Internet addiction: symptoms, evaluation and treatment. In: Vande Creek L, Jackson T, editors. Innovation in clinical practice: a source book. Sarasota: Professional Resource Press; 1999. p. 19e31.
[10] Patton JH, Stanford MS, Barratt ES. Factor structure of the Barratt impulsiveness scale. Journal of Clinical Psychology 1995;51:768–74.
[11] Filbey FM, Claus E, Audette AR, et al. Exposure to the taste of alcohol elicits activation of the mesocorticolimbic neurocircuitry. Neuropsychopharmacology 2008;33:1391–401.
[12] Maas LC, Lukas SE, Kaufman MJ, et al. Functional magnetic resonance imaging of human brain activation during cue-induced cocaine craving. American Journal of Psychiatry 1998;155:124–6.
[13] Hester R, Garavan H. Executive dysfunction in cocaine addiction: evidence for discordant frontal, cingulate, and cerebellar activity. Journal of Neuroscience 2004;24:11017–22.
[14] Chan RC, Shum D, Toulopoulou T, et al. Assessment of executive functions: review of instruments and identification of critical issues. Archives of Clinical Neuropsychology 2008;23:201–16.
[15] Alvarez JA, Emory E. Executive function and the frontal lobes: a meta-analytic review. Neuropsychology 2006;16:17–42.
[16] Rolls ET, Grabenhorst F. The orbitofrontal cortex and beyond: from affect to decision-making. Progress in Neurobiology 2008;86:216–44.
[17] Naqvi NH, Bechara A. The hidden island of addiction: the insula. Trends in Neurosciences 2009;32:56–67.
[18] Naqvi NH, Rudrauf D, Damasio H, et al. Damage to the insula disrupts addiction to cigarette smoking. Science 2007;26:531–4.
[19] Franklin TR, Acton PD, Maldjian JA, et al. Decreased gray matter concentration in the insular, orbitofrontal, cingulate, and temporal cortices of cocaine patients. Biological Psychiatry 2002;51:134–42.
[20] Zhang S, Ide JS, Li CS. Resting-state functional connectivity of the medial superior frontal cortex. Cerebral Cortex 2012;22:99–111.
[21] Bora E, Harrison BJ, Fornito A, et al. White matter microstructure in patients with obsessive–compulsive disorder. Journal of Psychiatry & Neuroscience 2011;36:42–6.
[22] Yeh PH, Simpson K, Durazzo TC, et al. Tractbased spatial statistics (TBSS) of diffusion tensor imaging data in alcohol dependence: abnormalities of the motivational neurocircuitry. Psychiatry Research 2009;173:22–30.
[23] Arnone D, Abou-Saleh MT, Barrick TR. Diffusion tensor imaging of the corpus callosum in addiction. Neuropsychobiology 2006;54:107–13.