European Journal of Radiology 79 (2011) 92–95

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Gray matter abnormalities in Internet addiction: A voxel-based morphometry study

Yan Zhou[a,1], Fu-chun Lin[b,1], Ya-song Du[c,1], Ling-di Qin[a], Zhi-min Zhao[c], Jian-rong Xu[a,*], Hao Lei[b,**]

[a] Department of Radiology, RenJi Hospital, Jiao Tong University Medical School, Shanghai 200127, PR China
[b] State Key Laboratory of Magnetic Resonance and Atomic and Molecular Physics, Wuhan Institute of Physics and Mathematics, Chinese Academy of Sciences, Wuhan 430071, PR China
[c] Department of Child & Adolescent Psychiatry Shanghai Mental Health Center, Shanghai Jiao Tong University, Shanghai 200030, PR China

ARTICLE INFO

Article history:
Received 30 July 2009
Received in revised form 14 October 2009
Accepted 14 October 2009

Keywords:
Internet addiction
Magnetic resonance imaging
Voxel-based morphometry
Gray matter density

ABSTRACT

Background: This study aims to investigate brain gray matter density (GMD) changes in adolescents with Internet addiction (IA) using voxel-based morphometry (VBM) analysis on high-resolution T1-weighted structural magnetic resonance images.
Methods: Eighteen IA adolescents and 15 age- and gender-matched healthy controls took part in this study. High-resolution T1-weighted magnetic resonance imaging scans were performed on the two groups. VBM analysis was used to compare the GMD between the two groups.
Results: Compared with healthy controls, IA adolescents had lower GMD in the left anterior cingulate cortex, left posterior cingulate cortex, left insula, and left lingual gyrus.
Conclusions: Our findings suggested that brain structural changes were present in IA adolescents, and this finding may provide a new insight into the pathogenesis of IA.

1. Introduction

Recently, Internet addiction (IA) has been considered a serious public health issue [1]. IA is a compulsive–impulsive spectrum disorder that involves online and/or offline computer usage and consists of three subtypes, namely, excessive gaming, sexual preoccupations, and e-mail/text messaging [2–4]. These variants share four components: excessive use, withdrawal, tolerance, and negative repercussions [5,6]. Several countries in Asia, particularly China, South Korea, and Taiwan, have been reported to have the highest incidence of computer or Internet addiction among young people [7]. A survey among 5135 adolescents from 16 middle schools of 6 districts of Shanghai reported that the rate of Internet use among the surveyed adolescents was 94.32%, wherein the incidence rate of Internet addiction was 8.78% [8]. Data from the China Internet Network Information Center, as of 30 June 2005, showed that 103 million people had gone online, 15.8% of whom were teenagers below 18 years old [9].

Like other addictions, IA has been linked to a lot of problems, such as little sleep, limited physical activity, and disrupted studies. Furthermore, IA is resistant to treatment, entails significant risks [10], and has high relapse rates. Moreover, it makes comorbid disorders less responsive to therapy [5]. About 86% of IA cases are afflicted with other disorders based on the Diagnostic and Statistical Manual of Mental Disorders-Version IV (DSM-IV) diagnosis [5]. For these reasons, the problem of IA has attracted much attention from psychiatrists, educators, and the public alike.

Voxel-based morphometry (VBM) is a fully automated alternative to the techniques that require volumetric samples to detect the differences between groups [11]. Compared with traditional morphometric approaches which rely on measuring brain volumes manually, VBM is a time-saving technique. In addition, it is not specific to particular brain regions. This measure was developed to detect group differences in the relative concentration of gray matter (GM) tissues across the whole brain in a voxel-wise manner [11,12]. Currently however, there are only a few brain Magnetic Resonance (MR) imaging studies on IA. In relation to this, the aim of this study is to detect the possible brain morphology changes in IA in adolescents and its mechanism.

* Corresponding author at: Department of Radiology, RenJi Hospital, Jiao Tong University Medical School, No. 1630 Dongfang Road, Shanghai 200127, PR China. Tel.: +86 21 5875 2345x3059.
** Corresponding author at: State Key Laboratory of Magnetic Resonance and Atomic and Molecular Physics, Wuhan Institute of Physics and Mathematics, Chinese Academy of Sciences, West No. 30 Xiao Hong Shan, Wuhan 430071, PR China. Tel.: +86 27 8719 8542; fax: +86 27 8719 9291.
E-mail addresses: clare1475@hotmail.com (Y. Zhou), fclin@wipm.ac.cn (F.-c. Lin), yasongdu@yahoo.com.cn (Y.-s. Du), flyingfool838@hotmail.com (L.-d. Qin), zmzsky@163.com (Z.-m. Zhao), xujianr@hotmail.com (J.-r. Xu), leihao@wipm.ac.cn (H. Lei).
[1] These authors contributed equally to this work.

0720-048X/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.ejrad.2009.10.025

2. Methods

2.1. Subjects

All the subjects came from the Department of Child and Adolescent Psychiatry Shanghai Mental Health Center. Eighteen subjects (2 females and 16 males, mean age = 17.23 ± 2.60) whose behaviors correspond to DSM-IV criteria for IA according to the modified Diagnostic Questionnaire for Internet addiction (YDQ) criteria by Beard and Wolf [6] were imaged. Eighteen age- and gender-matched healthy individuals with no personal or family history of psychiatric disorders were also imaged as the control group. All the IA subjects and control groups were right-handed. Three healthy subjects were abandoned for their poor imaging quality, so only fifteen members of the control group (2 females, mean age = 17.81 ± 2.58) and 18 IA subjects were used in the VBM analysis. This study was approved by the local Ethics Committee of RenJi Hospital, and full, written, and informed consent was obtained from all the parents before the MR examinations.

The diagnostic questionnaire for Internet addiction was adapted from DSM-IV criteria for pathological gambling by Young [13]. Young's Diagnostic Questionnaire (YDQ) consisting of eight "yes" or "no" questions was translated to Chinese. It includes the following questions: (1) Do you feel absorbed in the Internet (remember previous online activity or the desired next online session)? (2) Do you feel satisfied with Internet use if you increase your amount of online time? (3) Have you failed to control, reduce, or quit Internet use repeatedly? (4) Do you feel nervous, temperamental, depressed, or sensitive when trying to reduce or quit Internet use? (5) Do you stay online longer than originally intended? (6) Have you taken the risk of losing a significant relationship, job, educational or career opportunity because of the Internet? (7) Have you lied to your family members, therapist, or others to hide the truth of your involvement with the Internet? (8) Do you use the Internet as a way of escaping from problems or of relieving an anxious mood (e.g., feelings of helplessness, guilty, anxiety, or depression)? Young asserted that five or more "yes" responses to the eight questions indicate a dependent user. Later, Beard and Wolf [6] modified the YDQ criteria. Respondents who answered "yes" to questions 1 through 5 and at least any one of the remaining three questions were classified as suffering from Internet addiction.

A basic information questionnaire was used to collect demographic information such as gender, age, and year in high school.

2.2. Data acquisition

MR imaging was performed on a 3T MR scanner (3T Achieva, Philips). The optimized MPRAGE pulse sequences for gray matter/white matter contrast (TR = 331 ms, TE = 4.6 ms, FOV = 256 mm × 256 mm, slice thickness = 1 mm, gap = 0, slices = 155, matrix = 256 × 256) were scanned.

2.3. Data analysis

Image analysis was performed with the optimized VBM approach by SPM2 (Welcome Department of Cognitive Neurology, http://www.fil.ion.ucl.ac.uk/spm). Optimized VBM consists of two main steps including the construction of a study-specific brain template and tissue priors, as well as the anatomical properties of the study groups. First, the images from all subjects were normalized to the Montreal Neurological Institute (MNI) template and were segmented into gray matter, white matter, and cerebral spinal fluid (CSF). Then the customized template and tissue priors were constructed. After this, all images were segmented again with the customized template and tissue priors. Finally, the segmented images were smoothed with a 12 mm full-width half-maximum Gaussian kernel for the subsequent statistical analysis.

2.4. Statistical analysis

Voxel-wise comparisons of GMD were performed between the groups using the two-sample *t*-test with SPM2. The significance of group differences was estimated by the theory of random Gaussian fields, and significance levels were set at $P < 0.05$ (FDR corrected), while the cluster size was set at >100 voxels. We only found significant change in the control group > IA group in the GMD map.

3. Result

As shown in Table 1 and Fig. 1, the VBM of the MRI data illustrated that the IA group had lower GMD in the left anterior cingulate cortex (ACC), left posterior cingulate cortex (PCC), left insula, and left lingulate gyrus. No significant difference was found in the white matter change between the two groups.

4. Discussion

We supposed that some special changes in brain structure may be associated with the behavioral and emotional problems of IA adolescents. The use of VBM has allowed the detection of structural changes in gray matter and white matter in some psychiatric disorders [14–16]. Previous studies suggested the reported structural changes reflected the underlying pathology of the disease and may determine clinical phenomenology especially in "idiopathic" disease [14]. VBM permitted rapid voxel-wise comparison of local concentrations of gray and white matter regions between subject cohorts without the need for a priori selection of the region of interest (ROI) [17]. We found gray matter change between the IA and control groups. Compared with the control group, IA adolescents showed lower gray matter volume in left ACC, left PCC, left insula, and left lingulate gyrus.

The regions where reductions in GM were found between the IA and control groups were conceptually linked by the areas which are responsible for modulating emotional behavior. Although we do not know the exact histological change, some studies suggested the histopathological correlates of these volume reductions which include loss of synaptic contacts, increased neuronal density, and reductions in glial cells and glial markers [18]. The volumetric change in left ACC, left PCC, and insula should influence the function of these areas. This was in line with the clinical psychological features of the IA group. As shown by other studies, IA adolescents often had more behavioral or emotional problems [19–23].

Recently, the insula has been highlighted as a region that plays a crucial part in addiction. Many studies have shown that activity within the insula is correlated with the subject's ratings of urge [24–27]. Naqvi and Antoine's study [24] provided the first evidence in humans that the insula played a crucial part in addiction. The results of their study suggested that the insula was a region that integrated the interoceptive state into conscious feelings and into decision-making processes that involve certain risks and rewards. Functional imaging data, together with the lesion and inactivation findings in humans and rats, provide evidence that the insula is necessary for the explicit motivation to take drugs, and this function is common among drug abusers [28,29]. 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 [30]. This finding is of note because of the well-known increase in the prevalence of cigarette smoking among schizophrenics, who also have a reduction in insula gray matter [31]. Therefore, our study's result is in agreement with previous

Table 1
Significant differences in GM density between the IA and control groups.

Cluster-level	*T* scores	*Z* scores	Coordinates			Location
			X	*Y*	*Z*	
431	6.09	4.87	−10	29	20	Anterior cingulate cortex (L)
2264	5.86	4.75	−32	−56	6	Lateral ventricle (L)
	5.54	4.56	−25	−63	5	Extra-nuclear (L)
	5.3	4.42	−19	−68	8	Posterior cingulate cortex (L)
290	5.49	4.53	−37	−29	22	Insula (L)
147	4.84	4.13	−3	−88	11	Lingual gyrus (L)

L: left.

findings and supported that the insula played a great role in addiction.

It is a known fact that the cingulated gyrus is the key part of the limbic system. This is in charge of controlling emotions, mood, motivation, and other emotional states [32]. The cingulate gyrus provides a pathway from the thalamus to the hippocampus, which is seemingly responsible for focusing attention on emotionally significant events and regulating aggressive behavior. The anterior cingulated region has been implicated in motor control, cognition, and arousal/drive state [33]. On the other hand, the posterior cingulated regions participate in visual-spatial and sensorimotor processes [32]. The posterior cingulated, which is also a part of a larger “default system” of cortical areas, has been implicated in self-referential functions [34]. Dysfunction within and between structures in this circuit may induce disturbances in the emotional behavior in humans. Goldstein et al. [35] found

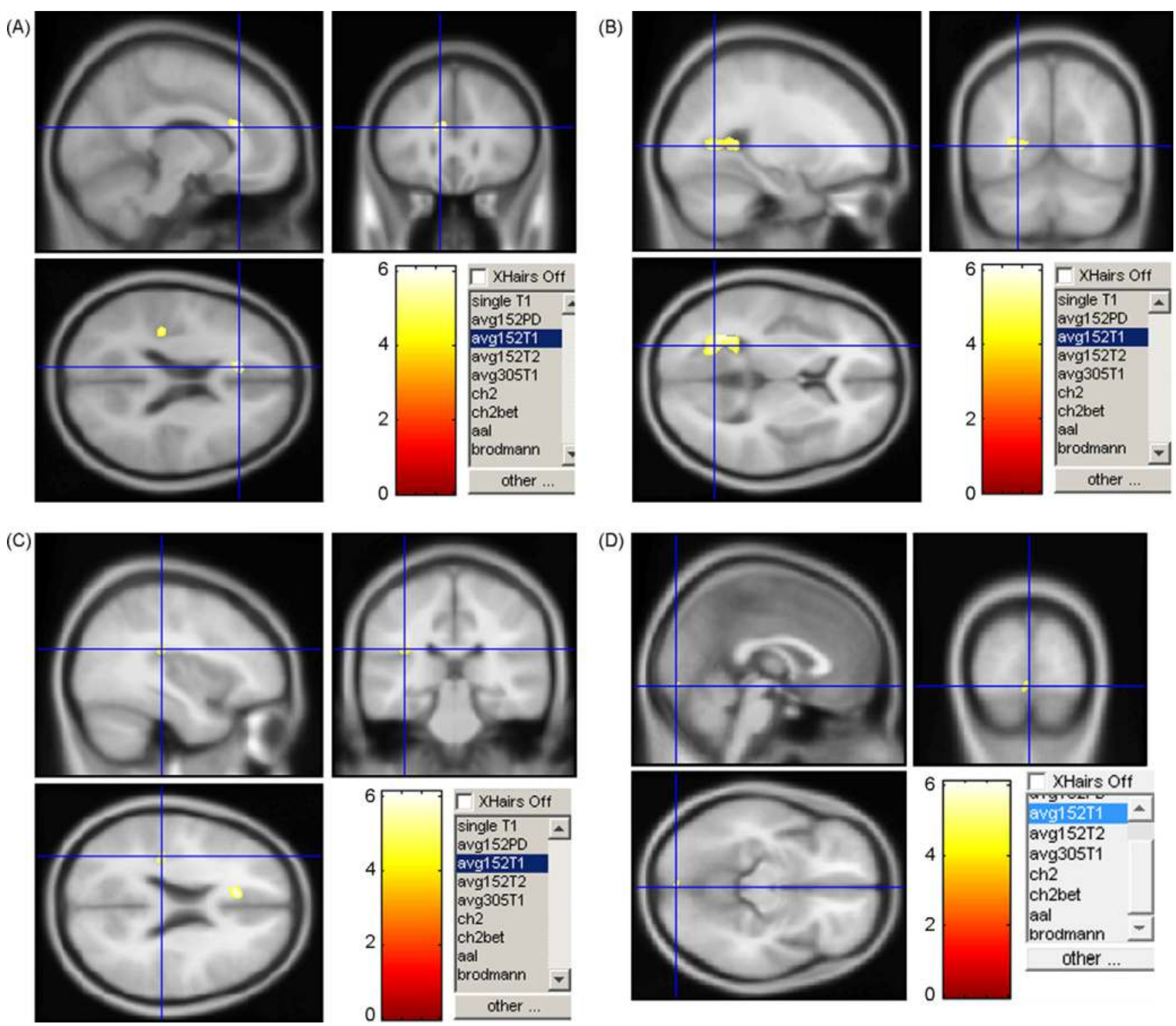

Fig. 1. Regions of decreased GM shown on the template in the left anterior cingulate cortex (A), left posterior cingulate cortex (B), left insula (C), and left lingual gyrus (D) in IA subjects compared with the controls.

among cocaine users that the more classical color-word Stroop design had bilateral activations in the caudal-dorsal ACC (cdACC) and hypoactivations in the rostro-ventral ACC/medial orbitofrontal cortex (mOFC) (rACC/mOFC). This neural network also appears to participate in the executive cognitive function (ECF) which governs the resolution of conflict, response inhibition, performance monitoring, implementation of control, and error monitoring. Disruption of these functions could impair an individual's ability to monitor and inhibit inappropriate behavior.

It was more difficult to interpret gray matter volume decreased in IA group as compared to healthy subjects in left lingual gyrus. This visual associative area has been less commonly implicated in articles about schizophrenia [36,37]. However, as mentioned above, Mane et al. [36] observed an excessive increase volume in bilateral lingual gyrus and were inversely related to functional outcome in schizophrenia. Up to now, we cannot determine the definite meaning of this finding in IA adolescent.

5. Conclusion

To our knowledge, this was the first study that reported the morphometric abnormalities in IA adolescents in the regions of GM of the left ACC, left PCC, left insula, and left lingual gyrus. These findings provide new insights into the pathogenesis of IA.

Conflict of interest statement

The authors declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work, there is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the position presented in, or the review of, the manuscript.

Acknowledgment

This research was supported by the Shanghai Leading Academic Discipline Project (Project Number S30203).

References

[1] Koh YS. Development and application of K-scale as diagnostic scale for Korean Internet addiction. In: 2007 International symposium on the counselling and treatment of youth Internet addiction. Seoul, Korea: National Youth Commission; 2007. p. 294.
[2] Block JJ. Issues for DSM-V: Internet addiction. Am J Psychiatry 2008;165:306–7.
[3] Dell'Osso B, Altamura AC, Allen A, et al. Epidemiologic and clinical updates on impulse control disorders: a critical review. Eur Arch Psychiatry Clin Neurosci 2006;256:464–75.
[4] Hollander E, Stein DJ, editors. Clinical manual of impulse-control disorders. Arlington, VA: American Psychiatric Publishing; 2006.
[5] Block JJ. Pathological computer use in the USA. In: 2007 International symposium on the counselling and treatment of youth Internet addiction. Seoul, Korea: National Youth Commission; 2007. p. 433.
[6] Beard KW, Wolf EM. Modification in the proposed diagnostic criteria for Internet addiction. Cyberpsychol Behav 2001;4:377–83.
[7] Fitzpatrick JJ. Internet addiction: recognition and interventions. Arch Psychiatr Nurs 2008;22:59–60.
[8] Xu J, Shen LX, Yan CH, et al. Internet addiction among Shanghai adolescents: prevalence and epidemiological features. Zhonghua Yu Fang Yi Xue Za Zhi 2008;42:735–8.
[9] Cao F, Su L. Internet addiction among Chinese adolescents: prevalence and psychological features. Child Care Health Dev 2007;33:275–81.
[10] Block JJ. Lessons from Columbine: virtual and real rage. Am J Forensic Psychiatry 2007;28:5–33.
[11] Ashburner J, Friston KJ. Voxel-based morphometry – the methods. NeuroImage 2000;11:805–21.
[12] Segall JM, Turner JA, van Erp TG, et al. Voxel-based morphometric multisite collaborative study on schizophrenia. Schizophr Bull 2009;35:82–95.
[13] Young KS. Internet addiction: the emergence of a new clinical disorder [On-Line]. Bradford, USA: Center for On-Line Addictions; 1996. Available at: http://www.netaddiction.com/articles/newdisorder.html.
[14] May A, Gaser C. Magnetic resonance-based morphometry: a window into structural plasticity of the brain. Curr Opin Neurol 2006;19:407–11.
[15] Fornito A, Yucel M, Patti J, et al. Mapping gray matter reductions in schizophrenia: an anatomical likelihood estimation analysis of voxel-based morphometry studies. Schizophr Res 2009;108:104–413.
[16] Drevets WC, Price JL, Furey ML. Furey brain structural and functional abnormalities in mood disorders: implications for neurocircuitry models of depression. Brain Struct Funct 2008;213:93–118.
[17] Tapp PD, Head K, Head E, et al. Application of an automated voxel-based morphometry technique to assess regional gray and white matter brain atrophy in a canine model of aging. NeuroImage 2006;29:234–44.
[18] Drevets WC. Neuroplasticity in mood disorders. Dialog Clin Neurosci 2004;6:199–216.
[19] Min J, Du YS. The clinical application of screen for anxiety related emotional disorders. Shanghai Arch Psychiatry 2005;17:72–4.
[20] Zhu YH, Du YS, Jiang WQ. Emotional correlation of internet addiction disorder among middle-school students in Shanghai. Shanghai Arch Psychiatry 2006;18:69–71.
[21] Du YS, Jiang WQ. The relationship between overuse and time management disposition among middle school students in Shanghai. Shanghai Arch Psychiatry 2006;18:129–33.
[22] Whang LS, Lee S, Chang G. Internet over-users' psychological profiles: a behavior sampling analysis on internet addiction. Cyberpsychol Behav 2003;6:143–50.
[23] Wu HR, Zhu K. Path analysis on related factors causing internet addiction disorder in college students. Chin J Public Health 2004;20:1363–4.
[24] Naqvi HN, Antoine B. The hidden island of addiction: the insula. Trends Neurosci 2008;32:56–67.
[25] McBride D, Barrett SP, Kelly JT, et al. Effects of expectancy and abstinence on the neural response to smoking cues in cigarette smokers: an fMRI study. Neuropsychopharmacology 2006;31:2728–38.
[26] Franklin TR, Wang Z, Wang J, et al. Limbic activation to cigarette smoking cues independent of nicotine withdrawal: a perfusion fMRI study. Neuropsychopharmacology 2007;32:2301–9.
[27] Wang Z, Faith M, Patterson F, et al. Neural substrates of abstinence-induced cigarette cravings in chronic smokers. J Neurosci 2007;27:14035–40.
[28] Naqvi NH, David R, Hanna D, et al. Damage to the insula disrupts addiction to cigarette smoking. Science 2007;315:531–4.
[29] Marco C, Francisco C, Fernando T, et al. Inactivation of the interoceptive insula disrupts drug craving and malaise induced by lithium. Science 2007;318: 655–8.
[30] Franklin TR, Acton PD, Maldjian JA, et al. Decreased gray matter concentration in the insula, orbitofrontal, cingulate, and temporal cortices of cocaine patients. Biol Psychiatry 2002;51:134–42.
[31] Crespo-Facorro B, Kim J, Andreasen NC, et al. Insula cortex abnormalities in schizophrenia: a structural magnetic resonance imaging study of first-episode patients. Schizophr Res 2000;46:35–43.
[32] Mayberg HS. Limbic-cortical dysregulation: a proposed model of depression. J Neuropsychiatry Clin Neurosci 1997;9:471–81.
[33] Paus T. Primate anterior cingulate cortex: where motor control, drive and cognition interface. Nat Rev Neurosci 2001;2:417–24.
[34] Bush G, Luu P, Posner MI. Cognitive and emotional influences in anterior cingulate cortex. Trends Cogn Sci 2000;4:215–22.
[35] Goldstein RZ, Tomasi D, Rajaram S, et al. Role of the anterior cingulate and medial orbitofrontal cortex in processing drug cues in cocaine addiction. Neuroscience 2007;144:1153–9.
[36] Mane A, Falcon C, Mateos JJ, et al. Progressive gray matter changes in first episode schizophrenia: a 4-year longitudinal magnetic resonance study using VBM. Schizophr Res 2009;114:136–43.
[37] Bangalore SS, Goradia DD, Nutche J, et al. Untreated illness duration correlates with gray matter loss in first-episode psychoses. Am J Psychiatry 2009;166:196–205.