Progress in Neuro-Psychopharmacology & Biological Psychiatry 53 (2014) 116–122

Contents lists available at ScienceDirect

Progress in Neuro-Psychopharmacology & Biological Psychiatry

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

Neural hyperactivity related to working memory in drug-naive boys with attention deficit hyperactivity disorder☆

Yuanyuan Li [a,1], Fei Li [b,1], Ning He [a], Lanting Guo [a,*], Xiaoqi Huang [b], Su Lui [b], Qiyong Gong [b]

[a] Department of Psychiatry, West China Hospital of Sichuan University, Chengdu, Sichuan Province, China
[b] Huaxi MR Research Center (HMRRC), Department of Radiology, West China Hospital of Sichuan University, Chengdu, Sichuan Province, China

ARTICLE INFO

Article history:
Received 15 January 2014
Received in revised form 20 March 2014
Accepted 25 March 2014
Available online 3 April 2014

Keywords:
Attention deficit hyperactivity disorder
Categorical n-back task
Globus pallidus
Hippocampus
Hyperactivation
Working memory

ABSTRACT

Background: Impaired working memory is thought to be a core feature of attention deficit hyperactivity disorder (ADHD). Previous imaging studies investigating working memory in ADHD have used tasks involving different cognitive resources and ignoring the categorical judgments about objects that are essential parts of performance in visual working memory tasks, thus complicating the interpretation of their findings. In the present study, we explored differential neural activation in children and adolescents with ADHD and in healthy controls using functional magnetic resonance imaging (fMRI) with the categorical n-back task (CN-BT), which maximized demands for executive reasoning while holding memory demands constant.
Methods: A total of 33 drug-naive, right-handed male ADHD without comorbidity (mean age 9.9 ± 2.4 years) and 27 right-handed, healthy male controls (mean age 10.9 ± 2.7 years) were recruited in the present study. Event-related fMRI was used to study differences in brain activity during the CN-BT between the two groups.
Results: The two groups did not differ in their accuracy in the CN-BT, although the ADHD patients showed significantly shorter reaction times to correct responses than did the controls. During the CN-BT, both ADHD patients and controls showed significant positive and negative activations by the correct responses, mainly in the sensory-motor pathways and the striato-cerebellum circuit. Additionally, the ADHD patients showed significantly higher activation in the bilateral globus pallidus and the right hippocampus compared with the controls. There was also a positive correlation between hyperactivation of the left globus pallidus and the reaction time to correct responses in ADHD.
Conclusions: In contrast to controls, ADHD patients showed neural hyperactivation in the striatum and mediotemporal areas during a working memory task involving categorization. Hyperfunction in these areas might be the pathophysiological foundation of ADHD, related to the deficits of working memory and the impulsive symptoms.

© 2014 Elsevier Inc. All rights reserved.

1. Introduction

Attention deficit hyperactivity disorder (ADHD) is characterized by developmentally inappropriate symptoms of inattention, impulsiveness, and hyperactivity that arise in childhood and often persist into adolescence and adulthood (Biederman and Faraone, 2005). Previous studies have proposed that deficiencies in cognitive function, and particularly in executive functions, are the core features of children and adolescents with ADHD (Sergeant et al., 2002). Executive functions often include working memory, planning, organization, inhibitory control, sustained attention, and set shifting. Among these executive functions, working memory is one of the most consistently reported deficits and is a crucial cognitive process that is implicated in theoretical models of ADHD (Cortese et al., 2012; Willcutt et al., 2005). Working memory refers to time-limited processes of active representations of information and is accessible for recall or for further manipulation (Martinussen et al., 2005). Working memory is an outcome of sustained attention on task-relevant mental representations and on the suppression of competing distracting events (Sander et al., 2012). Working memory consists of the manipulation, maintenance, and storage of verbal, object, or spatial–visual material, and refers to processes that are involved in the control, regulation, and active representation of information that guides conduct (D'Esposito, 2007). Clinically, working memory impairment is important because it is strongly associated with academic under-achievement (Gathercole and Alloway, 2006). In fact,

Abbreviations: ADHD, attention deficit hyperactivity disorder; fMRI, functional magnetic resonance imaging; CN-BT, categorical n-back task; SCID, Structured Clinical Interview for DSM-IV; WISC-CR, Wechsler Intelligence Scale for Children — Chinese Revision; CPRS-R, revised Conners' Parent Rating Scale; FWHM, full width at half maximum; GLM, general linear model; BA, Brodmann area; DAT, dopamine transporter; RT, reaction time; FWE, family-wise error.

☆ All the authors report no financial relationships with commercial interests.

* Corresponding author at: Department of Psychiatry, West China Hospital of Sichuan University, Guo Xue Xiang No. 37, Chengdu, Sichuan Province 610041, China. Tel./fax: +86 28 8542 2633.
E-mail address: guolanting@sina.com (L. Guo).

[1] Yuanyuan Li and Fei Li contributed equally to this work.

http://dx.doi.org/10.1016/j.pnpbp.2014.03.013
0278-5846/© 2014 Elsevier Inc. All rights reserved.

there is evidence that poor academic achievement is more related to working memory impairment than to the behavioral symptoms of inattention and hyperactivity/impulsiveness in ADHD patients (Rapport et al., 1999).

Various functional magnetic resonance imaging (fMRI) studies have been used to investigate the neural basis of working memory in children and adolescents (Fassbender et al., 2011; Silk et al., 2005; Vance et al., 2007). The neural patterns associated with working memory in healthy children involve the frontoparietal network in the classical n-back task (Owen et al., 2005). Deficits in working memory among children with ADHD are robust, with the largest impairments in tasks that require executive control in dealing with visual and spatial information (Martinussen et al., 2005; Willcutt et al., 2005). Previous studies indicate differential working memory-related activation patterns in distributed regions within the fronto-striato-parieto-cerebellar network of ADHD compared to healthy controls (Fassbender et al., 2011; Silk et al., 2005; Vance et al., 2007). However, these studies are characterized by inconsistent results, such as less activation in the right parieto-occipital areas of ADHD (Silk et al., 2005; Vance et al., 2007) or ADHD patients did not display working memory modulated brain activation that might be complicated by the medication exposure (Fassbender et al., 2011). Neuroimaging findings have shown a different location and amount of sustained activity dependent on the type of information held in working memory (Grossman et al., 2002; Zimmer, 2008), and previous spatial and verbal working memory studies (Massat et al., 2012, Vance et al., 2007) could not reflect the neural mechanism of visual-object working memory in ADHD.

Furthermore, categorical judgments about objects are essential parts of performance in visual working memory tasks. A new variant of the traditional n-back task, named the categorical n-back task (CN-BT), has been designed as a complex visual-object working memory paradigm comprising stringent attention focusing, active memory encoding, cognitive categorical judgment, and fast motor response. This visual working memory based paradigm maximizes demands for executive reasoning while holding memory demands constant (Ciesielski et al., 2006, 2010; Sander et al., 2012). Previous studies have shown that the CN-BT is more sensitive in detecting impairments in the executive domain of working memory (Ciesielski et al., 2006, 2010). To our knowledge, altered brain activation related to the CN-BT has not previously been reported in children and adolescents with ADHD.

The current study aimed to investigate the neural mechanisms of visual-object working memory in ADHD children during the early illness course without the confounding factor of medication using CN-BT. We hypothesized the following: that (i) ADHD patients would show hyperactivation involved in fronto-striatal and mediotemporal patterns, which may underlie the pathophysiology subtending working memory-related processes; and that (ii) the altered neural activation would associate with the expression of clinical symptoms of ADHD.

2. Methods

2.1. Participants

The study was approved by the local research ethics committee, and written informed consent was obtained from the guardians of all participants. A total of 33 drug-naive, right-handed male children and adolescents with ADHD (mean age 9.9 ± 2.4 years, range 6–15 years) and 27 right-handed, healthy control males (mean age 10.9 ± 2.7 years, range 8–16 years) were recruited at the Mental Health Center of West China Hospital. The Structured Clinical Interview for DSM-IV (SCID), patient edition, was used to determine and establish a diagnosis of ADHD without conduct disorder, oppositional defiant disorder and Tourette's disorder, or any other Axis I psychiatric comorbid disorder. Three experienced clinical psychiatrists (L.G., Y.L., N.H.) performed the psychiatric examination for all patients to diagnose ADHD and to make sure they were drug-naive to be eligible for the study. There were 22 combined-subtype and 11 inattentive-subtype ADHD patients in the present study. Healthy controls were recruited from the local area by means of a poster advertisement and were screened using the SCID, non-patient edition. The selected healthy controls had no known history of psychiatric illness in first-degree relatives. Handedness was assessed with Annett's Hand Preference Questionnaire (Dragovic and Hammond, 2007) The ADHD patients and healthy controls had a full-scale IQ above 90 according to an age-appropriate Wechsler Intelligence Scale for Children — Chinese Revision (WISC-CR) (Dai and Gong, 1990), and there was no significant difference in IQ between ADHD patients and healthy controls ($P > 0.05$). Primary behavioral measures were assessed using the impulsivity–hyperactivity factor and the hyperactivity index from the revised Conners' Parent Rating Scale (CPRS-R) (Conners et al., 1998) for all of the participants in the present study. The CPRS-R offered flexible administration options while also allowing the collection of varying perspectives on a child's behavior from parents to help assess ADHD and to evaluate problematic behavior in children and adolescents.

The following exclusion criteria were applied to all subjects: any neurologic disorders; psychosurgery; any substantial physical illness, such as a brain tumor, epilepsy, or hepatitis, as assessed on the basis of clinical evaluation and medical records; and magnetic resonance (MR) contraindications. Conventional MR images were inspected by two experienced neuroradiologists, and no gross abnormalities were observed for any participant.

2.2. CN-BT

The present CN-BT involved 57 commercially available color drawings of inanimate objects (buildings, cars, fruits, and plants) and animals (mammals, birds, reptiles, fish, and insects), which were presented consecutively and in random order. Small crosses were pseudo-randomly intermixed with the picture stimuli to provide a fixation point and an irregularity of timing to be as a control detection baseline. A drawing of a panda served as the n-back target. When the panda was presented, the subject was required to press a button with his/her right thumb only if at least two drawings prior to the panda belonged to the category of animals; alternatively, he/she was required to press a button with the left thumb for any other combinations of stimuli preceding the panda (Figure S1) (details in the Supplementary material according to the previous studies (Ciesielski et al., 2006, 2010)). All subjects were trained using a demo program before the scans and confirmed that they fully understood the procedures.

Visual stimuli were displayed on a white background using the E-prime 2.0 software package (http://www.pstnet.com/eprime.cfm) and were projected on a screen behind the MRI scanner. The subjects viewed the visual stimuli through a mirror attached to a head coil. Each run consisted of 124 stimuli (25% pandas, 23% other animals, 22% non-animals, and 30% crosses). Each stimulus of animals and non-animals lasted 500 ms, each stimulus of 18 crosses lasted 6 s, and each stimulus of 19 crosses lasted 4 s to provide time for the participants to press the button. In total, each run lasted 227.5 s.

2.3. fMRI data acquisition

All subjects underwent an fMRI scan using a 3 T Siemens Trio MRI system with an eight-channel phased-array head coil. A daily quality assessment was used to evaluate the stability of the MRI system and involved scanning a water phantom to achieve data quality assurance indexes. MR images sensitized to changes in blood-oxygen-level-dependent signal levels were obtained with a gradient-echo echo-planar imaging sequence: repetition time/echo time (TR/TE), 2000/30 ms; flip angle, 90°; slice thickness, 5 mm (no slice gap); matrix, 64 × 64; FOV, 240 × 240 mm^2; and voxel size, 3.75 × 3.75 × 5 mm^3. Each brain volume comprised 30 axial slices, and each functional run contained 114 image volumes, resulting in a total scan time of 228 s.

Download English Version:

https://daneshyari.com/en/article/5844436

Download Persian Version:

https://daneshyari.com/article/5844436

Daneshyari.com