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Original article

Enhanced resting-state brain activities in ADHD patients: A fMRI study

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Abstract

Resting-state functional MRI (fMRI) could be an advantageous choice for clinical applications by virtue of its clinical convenience and non-invasiveness. Without explicit stimulus, resting-state brain activity patterns cannot be obtained using any model-driven method. In this study, we advanced a measure named resting-state activity index (RSAI) to evaluate the resting-state brain activities. Using RSAI, we first investigated the resting-state brain activity patterns in normal adolescents to test the validity of this RSAI measure. Then we compared the resting-state brain activity patterns of Attention deficit hyperactivity disorder (ADHD) patients to those of their matched controls. According to the resultant brain activity patterns, we suggest that RSAI could be an applicable measure to evaluate resting-state brain activities. As compared to the controls, the ADHD patients exhibited more significant resting-state activities in basic sensory and sensory-related cortices. This finding was in accordance with ADHD symptoms of inattention.

Keywords: Regional homogeneity; Low-frequency fluctuations; Resting-state activity index (RSAI); Sensory

1. Introduction

Attention deficit hyperactivity disorder (ADHD) is characterized by developmentally inappropriate symptoms of inattention, hyperactivity and impulsivity. It affects nearly 5% of school-aged children and frequently persists into adolescence, or even into adulthood [1]. Many functional neuroimaging studies have been carried out to discover the pathologies underlying the disorder. Convergent evidence has implicated the fronto-striatal network abnormalities as the core deficits of ADHD [2–4].

Blood oxygen level dependent (BOLD) functional MRI (fMRI) is a valuable technique for ADHD pathology analyses. It measures the mismatch between blood flow and oxygen extraction when neuronal activity occurs [5]. Using this technique, the brain activity patterns aroused by certain tasks can be obtained by evaluating the dynamic brain changes between task conditions and baselines. And the pathology underlying the disorder can be assessed by examining the task-aroused brain activity pattern differences between the ADHD patients and their matched controls. To date, most BOLD fMRI studies on ADHD are task-based [6–9].

Conscious resting-state is quite different from task state and thus studies carried out during this state can possibly provide us an alternative perspective on brain

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functional abnormalities in ADHD. Moreover, as compared to task-based fMRI studies, studies carried out during resting-state are easy to perform (without experiment designing and subject training) and comparable across different studies. Based on resting-state BOLD fMRI, Zang et al. found ADHD patients exhibited decreased amplitude of low-frequency fluctuation (ALFF) in the right inferior frontal cortex, the bilateral cerebellum and the vermis as well as increased ALFF in the right anterior cingulated cortex, the left sensorimotor cortex, and the bilateral brainstem [10]; Tian et al. have formerly found that ADHD adolescents had abnormal dorsal anterior cingulated cortex (dACC) functional connectivity patterns [11]; and Cao et al. found the ADHD patients exhibited decreased regional homogeneity (ReHo) in the frontal–striatal–cerebellar circuits, but increased ReHo in the occipital cortex [12]. Resting-state ADHD pathology analyses have also been carried out by using another fMRI technique named T2 relaxometry (other than BOLD) [13,14]. T2 relaxation time measured by T2 relaxometry is directly related to the perfusion of certain brain regions and thus enables a direct evaluation of resting-state brain activity pattern.

Without explicit stimulus, it is impossible to obtain resting-state brain activity patterns using any model-driven method as most task-based fMRI studies did. However, spatial and temporal characteristics of voxels activated by task stimulus are illuminative for analyzing resting-state brain activities. The temporal characteristic is that effective frequency components of the time series of active voxels should have significant variance. For instance, voxels activated by a block-designed task with a period of 30 s should have time series whose frequency component of 1/30 Hz would exhibit significant variance. That means, we can pick out the frequency component of 1/30 Hz of each time series, and consider only the voxels with significant variance in this component as candidates for active voxels. Low-frequency fluctuations (LFFs, 0.01–0.08 Hz) of BOLD signals have been found to be physiologically meaningful [15] and quite informative [15–18]. Using a method whose essential was to pick out voxels with LFFs of significant variance, Zang et al. [10] and Fransson [19] found significant resting-state brain activities in the precuneus/posterior cingulate cortex (PCC), the medial frontal cortex (MedPFC)/ventral anterior cingulate cortex (vACC) and several other brain regions in normal subjects. PCC and vACC are two important components of the default mode network, which has been suggested to be tonically active during conscious resting-state [20]. So, one reasonable hypothesis for resting-state brain activity analyses may be that voxels with significant resting-state activities should have LFFs of significant variance. The spatial characteristic is that brain activities are more likely to occur as clusters rather than separate voxels. Based on this concept, Zang et al. successfully obtained the brain activity pattern in a finger motion task using a measure named ReHo, which measures the similarity between the time series of a given voxel and those of its nearest neighborhoods [21]. So, another hypothesis for resting-state brain activity pattern analyses may be that voxels with significant resting-state activities should have significant ReHo.

It should be noticed that voxels with significant resting-state activities should simultaneously satisfy these two hypotheses. In the present study, we defined a resting-state activity index (RSAI) to evaluate the significance of resting-state brain activities. For a given voxel, its RSAI was a combination of its ReHo and standard variance of its LFFs. We first obtained the resting-state brain activity patterns in normal adolescents by evaluating RSAIs on a voxel by voxel basis to test the validity of this measure. Then, a comparison of the resting-state brain activity patterns between the ADHD patients and their matched controls was performed to see if there exists any difference between the resting-state brain activity patterns of the two groups.

2. Subjects and methods

2.1. Subjects and imaging methods

The present study used the same dataset as those used in Tain et al. [11]. Twelve ADHD patients (range 11–14.8 years, mean 13.48 ± 1.11 years) and 12 controls (range 12.5–14.1 years, mean 13.19 ± 0.49 years) participated in the study. The ADHD adolescents all met diagnosis of ADHD. Ten of them were of the inattention subtype, and the other two were of the combined subtype. Eleven of the ADHD patients were medication-free for at least half a year, and one was taken off medication for only 48 h. All subjects assented to participate in the study and their parents gave written informed consents. The study was ethically approved by local ethical committee. Due to excessive head motions, functional images of only eight ADHD patients (seven of inattention subtype and one of combined subtype) and 10 controls were available for further analysis. For more details about the subjects, please see Ref. [11].

Functional images were acquired on a SIEMENS TRIO 3-Tesla scanner. During the resting-state, subjects were told not to concentrate on anything in particular, but just to relax with their eyes closed. Functional images were obtained axially using Echo planer imaging (EPI) sequence, and the parameters are: 2000/30 ms (TR/TE), 30 slices, 4.5/0 mm (thickness/gap), 220×220 mm (FOV), 64×64 (resolution), 90° (flip angle). The functional imaging lasted for 480 s. To facilitate the localization of functional images, we also obtained high-resolution T1-weighted spoiled gradient-recalled whole-brain volume sagittally using the following parameters: 1700/3.92 ms (TR/TE), 176 slices, 1.0/

0 mm (thickness/gap), 256 × 256 mm (FOV), 256 × 256 (resolution), 12° (flip angle). Other series have no relation to the present study are not described here.

2.2. Data preprocessing

The functional scans were first preprocessed with slice timing, motion realignment, and then spatially normalized to a standard template (Montreal Neurological Institute), resampled to 3 mm cubic voxels and spatially smoothed with a 4 × 4 × 4 mm full width at half maximum Gaussian kernel. All these processes were conducted by using SPM2 (http://www.fil.ion.ucl.ac.uk/spm/). Finally, the waveform of each voxel was passed through a band-pass filter (0.01–0.08 Hz) to obtain LFFs using AFNI (http://afni.nimh.nih.gov/).

RSAI is sensitive to head motions, whereas severe head motions were observed in most subjects during the scanning processes in the present study. We tried to minimize the head motion effects by picking out 150 continuous volumes with relatively less head motions for further analyses. Specifically, among the 91 possible choices, we chose the one that contains the minimum of the maximum of x, y, or z displacements. The datasets with the maximum displacement in either cardinal direction (x, y, z) greater than 1 mm even within these 150 volumes were discarded. As mentioned above, images of four ADHD patients and two controls were excluded from further analyses due to excessive head motions.

3. RSAI analyses

The preprocessed images were then evaluated for RSAI on a voxel by voxel basis. The RSAI of a given voxel was here defined as the multiplication of the standard deviation of its LFFs and its Kendall's coefficient of concordance (KCC) that measures the regional homogeneity of the voxel:

$$\mathrm{RSAI} = \mathrm{KCC} \times \mathrm{std}_{\mathrm{LFFs}} \quad (1)$$

KCC of a given voxel was defined as follows [22]:

$$\mathrm{KCC} = \frac{\sum_{i=1}^{n}(R_i)^2 - n(\overline{R})^2}{\frac{1}{12}K^2(n^3 - n)} \quad (2)$$

where n is the number of time points, here $n = 150$; K is the number of voxels selected as its nearest neighbors, and here, we select the given voxel together with its nearest 26 neighbors, that is, $K = 27$; R_i is the sum of the rank of all the 27 voxels at the ith time point; $\overline{R}$ is the mean of R_i. The RSAI was calculated under Matlab circumstance (The MathWorks, Inc.). The resulting RSAI maps was masked by a grey matter map that was obtained by segmenting the mean normalized high-resolution T1-weighted images of all the subjects, to include only the voxels falling in grey matter.

4. Statistical analyses

Within-group resting-state brain activity patterns and between-group resting-state brain activity pattern differences were obtained by two-sample Wilcoxon–Mann–Whitney rank-sum test using AFNI software package (http://afni.nimh.nih.gov/). For within-group analyses, average-RSAI maps for each subject were first obtained by setting all the voxels within the formerly used grey matter mask to the average of all RSAIs within this mask, and within-group activity patterns were then obtained by comparing the 10 RSAI maps to these 10 average-RSAI maps. Here, we chose non-parametric statistical analyses for two reasons. The first was that the distribution of RSAI differed significantly from normal distribution, or any distribution closely related to normal. The second, non-parametric statistical techniques are more robust than parametric ones considering the presence of "outliers" in the RSAI maps.

A combined threshold and clustering approach was performed to correct for multiple comparisons. The random distribution of cluster sizes for a given per voxel threshold was determined by Monte Carlo simulations. According to this distribution, for within-group resting-state brain activity pattern analysis, we selected a per voxel threshold of $P < 0.01$ ($Z > 2.58$) and a cluster size of at least 16 continuous voxels (432 mm^3) to achieve a corrected P-value of $P < 0.01$. The threshold for between-group activity pattern difference analysis was $P < 0.05$ (corrected, before correction $Z > 1.96$, per voxel threshold $P < 0.05$, cluster size >1188 mm^3). Statistical map were superimposed on the mean normalized high-resolution T1-weighted images of all the subjects.

5. Results

5.1. Resting-state brain activity pattern of the controls

Significant resting-state brain activities were found in the controls in the following regions: a large cluster of the PCC/Precuneus (BA 23/31/7), the bilateral vACC/MedFC (BA 25/9/10/32), the bilateral fusiform gyrus (BA 19), the bilateral superior temporal gyrus (STG, BA 42), the bilateral thalamus, and the left inferior parietal lobe (IPL, BA 40/7) (Fig. 1 and Table 1). The right IPL (BA 40) also tended to show significant resting-state brain activity for it had the largest cluster size among the brain regions that did not survive the threshold for cluster size.

5.2. Between-group resting-state brain activity pattern differences

As compared to the control, the ADHD patients exhibited more significant resting-state brain activities

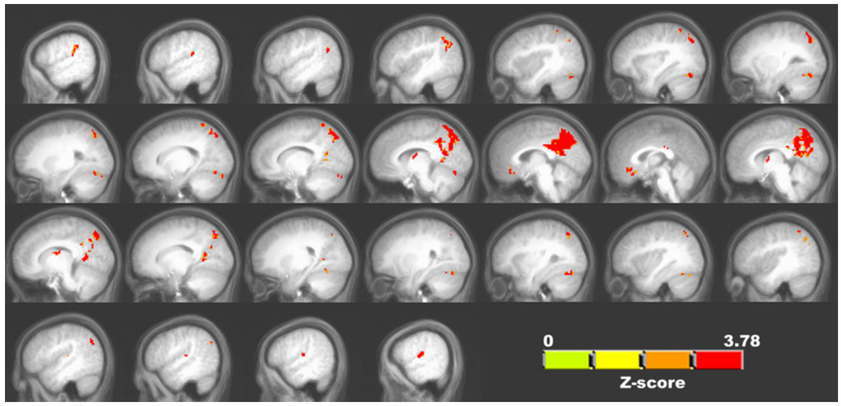

Fig. 1. Map of the resting-state brain activity pattern in the controls. Maps are superimposed on sagittal sections of the group-average 3D images from $x = -59$ mm to $x = 61$ mm in Talairach and Tournoux system, between slice coordinate increment is 5 mm. Threshold is $P < 0.01$, corrected for multiple comparisons. Z-score scale is shown on the lower right.

Table 1
Resting-state brain activity pattern in the controls

Area	Cluster size, mm^3	BA	Talairach (peak)			Z-score (peak)
B PCC/Precuneus	30,564	23/31/7	3	−48	27	3.78
L FG	1782	19	−36	−76	−14	3.63
R IPL	1701	39	48	−65	34	3.63
B vACC	972	25	0	28	−19	3.33
R FG	945	19	30	−62	−15	3.25
R STG	918	42	62	−17	12	3.55
L STG	810	42	−56	−31	15	3.55
L FG	756	18	−12	−88	−16	3.55
B MedFC	675	9/10/32	3	50	17	3.70
L PCC	648	18/30	−12	−52	5	3.78
Thalamus	540		9	1	14	3.78
Thalamus	486		−6	0	6	3.78
L IPL	486	40/7	−36	−52	58	3.63
R IPL[a]	405	40	48	−53	47	3.78

The threshold is $P < 0.01$, corrected for multiple comparisons. BA, Brodmann's area; PCC, posterior cingulate cortex; vACC, ventral anterior cingulated cortex; FG, fusiform gyrus; IPL, inferior parietal lobe; STG, superior temporal gyrus; Med FC, medial frontal cortex; L, left; R, right; B, bilateral.

[a] The right inferior parietal lobe has the largest cluster size among the brain regions that did not survive the threshold for cluster size.

in the bilateral VI/VII (BA 17/18/19), the left SI (BA 3), the left AII (BA 22), the bilateral thalamus, and the left dorsal brainstem, midbrain (Fig. 2 and Table 2). No more significant activity was found in the controls.

6. Discussion

In the present study, we hypothesized that voxels with significant resting-state activities should simultaneously exhibit significant ReHo and have LFFs of significant variance. Based on this hypothesis, we developed a RSAI to evaluate resting-state brain activities, and then analysed the resting-state brain activity pattern differences between the ADHD patients and their matched controls.

The controls exhibited the most significant resting-state brain activity in the bilateral PCC/Precuneus, with a cluster size of as large as 30,564 mm^3 (Table 1). The PCC has been found to be one of the most metabolically active brain regions during conscious resting-state [20,23]. Greicius et al. paid their particular attention to the "default mode network", which has been suggested to be tonically active during conscious resting-state, and suggested that the PCC would play a central role in this network [23]. Our result of PCC/Precuneus' most significant resting-state activity was in consistence with these former findings. Two other brain regions exhibited significant resting-state activities in the controls in the present study, the bilateral IPL and the MdFC/vACC, have also been suggested to be important components of the default mode network [20,23].

Despite the brain regions in common such as the PCC, the IPL, and the MdFC/vACC, there were also slight differences between the brain activity pattern in the controls in the present study and the default mode network [20,23]. Three facts may be in favour of the

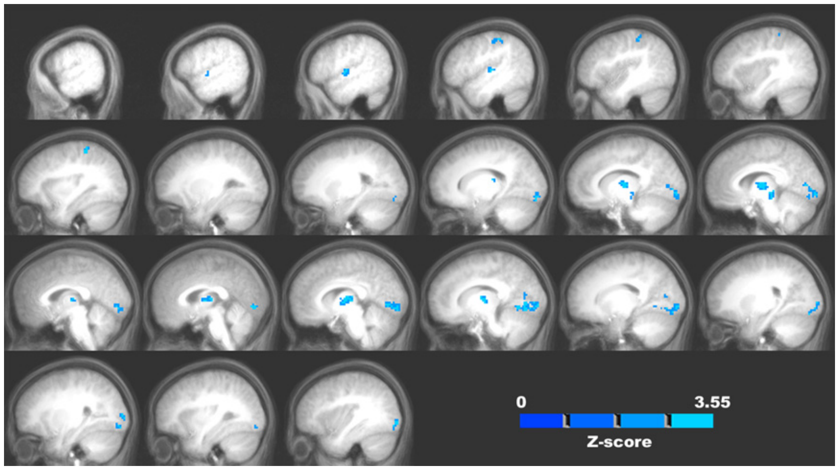

Fig. 2. Map of the resting-state brain activity pattern differences between the ADHD patients and the controls. Maps are superimposed on sagittal sections of the group-average structural images from $x = -64$ mm to $x = 36$ mm in Talairach and Tournoux system, between slice coordinate increment is 5 mm. The threshold is $P < 0.05$, corrected for multiple comparisons. Z-score scale is shown on the lower right. Blue color means the ADHD patients exhibited more significant resting-state brain activity then did the controls. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 2
Resting-state brain activity pattern differences between the ADHD patients and the controls

Area	Cluster size, mm^3	BA	Talairach (peak)			Z-score (peak)
B VI/VII	10,503	17/18/19	−9	−93	0	−3.47
B[a] Thalamus/dorsal brainstem, midbrain	4752		−6	−29	−1	−3.55
L SI	1539	3	−45	−32	51	−3.29
L AII	1242	22	−53	−11	3	−3.11

The threshold is $P < 0.05$, corrected for multiple comparisons. Negative Z-scores indicates that more significant resting-state brain activities were found in ADHD patients. BA, Brodmann's area; L, left; B, bilateral.
[a] More significant activity was found in ADHD patients in bilateral thalamus, but only in left dorsal brainstem, midbrain.

validity of the present results. One is that these brain regions exhibited significant resting-state activities only in the present study lies in exact (for thalamus and fusiform gyrus) or nearly (for STG) symmetric positions of the two hemispheres, while fake brain activity patterns would less likely to appear in this way. The second, in the present study, we adopted a more conservative statistical method, non-parametric statistical analysis, and this perhaps exclude some brain regions in the default mode network that had less significant activity. The third, the significant brain activities found in the bilateral fusiform gyrus, the thalamus, and the STG were functionally meaningful: the excessive noise of MRI scanners may arouse brain activity in the STG, while none of the methods adopted by former studies on the default mode network are suitable for sorting out this activity [20,23,24]; the fusiform gyrus, despite its predominant role in face recognition [25,26], has also been found to be active in a lot of semantic retrieval situations [27,28], which may occur reasonably during conscious resting-state [19,23]; and the thalamus, as a relay centre of sensory information, may also be activated by frequent somatosensory and auditory inputs during fMRI scanning. So we suggest that RSAI could be an applicable measure to evaluate resting-state brain activities.

As compared to the controls, the ADHD patients exhibited an overall more significant brain activity pattern during conscious resting-state. More significant brain activities were found in the ADHD patients in the bilateral VI/VII, the bilateral thalamus, the left brainstem, the left SI, and the left AII. The VI/VII, a recognized brain region for visual processing, exhibited more significant activity in the ADHD patients with the largest cluster size. One reasonable explanation for this was that the ADHD patients may be more apt to disobey the instruction of "rest with eyes closed" and thus received more visual stimuli. Unfortunately, we neglected either to monitor their behaviours during the scanning processes or to obtain after-scanning inquiries. The SI was responsible for receiving and processing information about the body senses, touch, pressure, temperature, and pain. The enhanced SI activities in the ADHD patients may suggest that they are more apt to be involved in somatosensory processing during resting-state. In the resting-state single photon emission computerized tomography (SPECT) study by Lee et al., ADHD children were also found to exhibit enhanced

CBF in the somatosensory cortex [29]. The AII has been thought to be crucial for the processing of auditory spatial information as well as auditory short-term memories [30,31]. Combining with the fact that the thalamus receives auditory, somatosensory, and visual signals and relays sensory signals to the cerebral cortex, and the brainstem (midbrain) contains auditory and visual reflex centres, we suggest that the ADHD patients were more apt to be involved in sensory information processing during conscious resting-state.

Our results of ADHD patients' participating in more sensory information processing during conscious resting-state was in consistence with ADHD symptoms of inattention. As is known, ADHD patients, especially those of inattention subtype as was predominant in the present study, are more apt to be distracted by environmental stimulus. Perhaps this is the reason why more significant brain activities were found in the basic sensory and sensory-related cortices in these patients.

An immediate question now arise is why the ADHD patients are more apt to be involved in sensory information processing during conscious resting state. The present results seem to be insufficient for answering this question, for they seem to be much related to symptoms rather than pathologies of ADHD. The fronto-striatal network abnormalities have been suggested to be the core deficits of ADHD [2–4]. Whether these fronto-striatal network abnormalities in ADHD patients could be the basis of the present more resting-state sensory information processing in them need to be further studied.

The present findings of enhanced resting-state sensory processing in the ADHD patients provide a supplement to the delay aversion (DEL) model for ADHD pathology [32–34]. In this model, the ADHD patients were suggested to be excessively sensitive to delays and more apt to allocate their attention to the environment to avoid or to escape the subjective experience of delay [32–34]. In the present study, the ADHD patients were told simply to rest, that is, there were no prospective outcomes for them. One possibility for the excessive resting-state basic sensory processing in these patients was that they may be averse not only to "delay", but also to the "steady state" they were told to keep.

As has been mentioned, based on resting-state fMRI, Zang et al. [10] and Cao et al. [12] found abnormal resting-state brain activity patterns in the ADHD patients. In the present study, using resting-state fMRI, though we found similar enhanced activities in the ADHD patients in the occipital cortex, the somatosensory cortex, as well as the brainstem, as were found in either the study by Zang et al. [10] or that by Cao et al. [12], discrepancies between the results of the three studies exist. We suggest that the discrepancies mainly result from the fact that RSAI employed in the present study considered both the spatial characteristic (ReHo) and the temporal characteristic (the standard deviation of its LFFs) of voxels, and both of these characteristics are necessary for active voxels, while the methods used in the two former studies considered only one characteristic, that is, either the spatial characteristic [12] or the temporal characteristic [10].

In the study by Teicher et al., reduced resting-state brain activities were found in the bilateral putamen in the ADHD patients, and no significant activity differences were found in the bilateral thalamus [13]. In the study by Anderson et al., ADHD patients exhibited reduced activity in the cerebellar vermis [14]. While in the present study, significant activity pattern differences were found in neither the putamen nor the cerebellum, and the ADHD patients exhibited more significant resting-state activity in the bilateral thalamus. The occurrence of this difference perhaps results from the fact that both these two former studies emphasized particularly on motor related functional deficits in ADHD patients, so their findings may be more suitable for ADHD patients of hyperactivity subtype. While in the present study, most ADHD patients were of the inattention subtype, whose motor related cortices may be intact.

Further studies can increase the applicability of this research. For instance, based on the knowledge that the ADHD patients exhibited more significant resting-state activities in basic sensory and sensory related cortices, a classifier could be developed by a study of larger sample size to facilitate ADHD diagnosis by introducing a more objective criterion based on RSAI; a consideration of subtypes could also be beneficial for finding out whether ADHD patients of other subtypes (other than the inattention subtype) would exhibit abnormal resting-state brain activity patterns; simultaneously recording the physiological data and whole-brain imaging data would enable a reduction of the influence caused by the cardiac and respiratory fluctuation effects that aliased into the LFFs [35,36].

7. Conclusion

In this study, we developed a new measure RSAI to detect resting-state brain activity pattern differences between the ADHD patients and their matched controls. We found that the ADHD patients exhibited more significant resting-state brain activities in basic sensory and sensory-related cortices. By virtue of its non-invasiveness, high-spatial, and temporal resolution, low-expense (as compared to PET) and clinical convenience (as compared to task-based studies), RSAI based on resting-state LFFs could be an advantageous choice for diagnosis of ADHD and other mental disorders.

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References

[1] Biederman J. Attention-deficit/hyperactivity disorder: a life-span perspective. J Clin Psychiatry 1998;59(Suppl. 7):4–16.
[2] Castellanos FX. Toward a pathophysiology of attention-deficit/hyperactivity disorder. Clin Pediatr (Phila) 1997;36:381–93.
[3] Seidman LJ, Biederman J, Weber W, Hatch M, Faraone SV. Neuropsychological function in adults with attention-deficit hyperactivity disorder. Biol Psychiatry 1998;44:260–8.
[4] Swanson J, Castellanos FX, Murias M, LaHoste G, Kennedy J. Cognitive neuroscience of attention deficit hyperactivity disorder and hyperkinetic disorder. Curr Opin Neurobiol 1998;8:263–71.
[5] Ogawa S, Tank DW, Menon R, Ellermann JM, Kim S, Merkle H, et al. Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging. Proc Natl Acad Sci USA 1992;89:5951–5.
[6] Bush G, Frazier JA, Rauch SL, Seidman LJ, Whalen PJ, Jenike MA, et al. Anteri cingulate cortex dysfunction in attention-deficit/hyperactivity disorder revealed by fMRI and the Counting Stroop. Biol Psychiatry 1999;45:1542–52.
[7] Rubia K, Overmeyer S, Taylor E, Brammer M, Williams SCR, Simmons A, et al. Hypofrontality in attention deficit hyperactivity disorder in high order motor control: a study with functional MRI. Am J Psychiatry 1999;156:891–6.
[8] Durston S, Tottenham NT, Thomas KM, Davidson MC, Eigsti IM, Yang Y, et al. Differential patterns of striatal activation in young children with and without ADHD. Biol. Psychiatry 2003;53:871–8.
[9] Schulz KP, Fan J, Tang CY, Newcorn JH, Buchsbaum MS, Cheung AM, et al. Response inhibition in adolescents diagnosed with attention deficit hyperactivity disorder during childhood: an event-related fMRI study. Am J Psychiatry 2004;161:1650–7.
[10] Zang YF, He Y, Zhu CZ, Cao QJ, Sui MQ, Liang M, et al. Altered baseline brain activity in children with ADHD revealed by resting-state functional MRI. Brain Dev 2007;29:83–91.
[11] Tian L, Jiang T, Wang Y, Zang Y, He Y, Liang M, et al. Altered resting state functional connectivity patterns of anterior cingulate cortex in adolescents with attention deficit hyperactivity disorder. Neurosci Lett 2006;400:39–43.
[12] Cao Q, Zang Y, Sun L, Sui M, Long X, Zou Q, et al. Abnormal neural activity in children with attention deficit hyperactivity disorder: a resting-state functional magnetic resonance imaging study. Neuroreport 2006;17:1033–6.
[13] Teicher MH, Anderson CM, Polcari A, Glod CA, Maas LC, Renshaw PF. Functional deficits in basal ganglia of children with attention deficit/hyperactivity disorder shown with functional magnetic resonance imaging relaxometry. Nat Med 2000;6:470–3.
[14] Anderson CM, Polcari A, Lowen SB, Renshaw PF, Teicher MH. Effects of methylphenidate on functional magnetic relaxometry of the cerebellar virmis in boys with ADHD. Am J Psychiatry 2002;159:1322–8.
[15] Biswal B, Yetkin FZ, Haughton VM, Hyde JS. Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. Magn Reson Med 1995;34:537–41.
[16] Lowe MJ, Mock BJ, Sorenson JA. Functional connectivity in single and multislice echoplanar imaging using resting-state fluctuations. Neuroimage 1998;7:119–32.
[17] Cordes D, Haughton VM, Arfanakis K, Carew JD, Turski PA, Moritz CH, et al. Frequencies contributing to functional connectivity in the cerebral cortex in "resting-state" data. AJNR Am J Neuroradiol 2001;22:1326–33.
[18] Hampson M, Peterson BS, Skudlarski P, Gatenby JC, Gore JC, et al. Detection of functional connectivity using temporal correlations in MR images. Hum Brain Mapp 2002;15:247–62.
[19] Fransson P. Spontaneous low-frequency BOLD signal fluctuations – an fMRI investigation of the resting-state default mode of brain function hypothesis. Hum Brain Mapp 2005;26:15–29.
[20] Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA, Shulman GL. A default mode of brain function. Proc Natl Acad Sci USA 2001;98:676–82.
[21] Zang Y, Jiang T, Lv Y, He Y, Tian L. Regional homogeneity approach to fMRI data analysis. Neuroimage 2004;22:394–400.
[22] Kendall M, Gibbons JD. Rank correlation methods. Oxford: Oxford University Press; 1990.
[23] Greicius MD, Krasnow B, Reiss AL, Menon V. Functional connectivity in the resting brain: a network analysis of the default mode hypothesis. Proc Natl Acad Sci USA 2003;100:253–8.
[24] Shulman GL, Fiez JA, Corbetta M, Buckner RL, Miezin FM, Raichle ME, et al. Common blood flow changes across visual tasks: II. Decreases in cerebral cortex. J Cognit Neurosci 1997;9:648–63.
[25] Kanwisher N, McDermott J, Chun MM. The fusiform face area: a module in human extrastriate cortex specialized for face perception. J Neurosci 1997;17:4302–11.
[26] McCarthy G, Puce A, Gore JC, Allison T. Face specific processing in the human fusiform gyrus. J Cogn Neurosci 1997;9:605–10.
[27] Martin A, Haxby JV, Lalonde FM, Wiggs CL, Ungerleider LG. Discrete cortical regions associated with knowledge of color and knowledge of action. Science 1995;270:102–5.
[28] Thompson-Schill SL, Aguirre GK, Desposito M, Farah MJ. A neural basis for category and modality specificity of semantic knowledge. Neuropsychologia 1999;37:671–6.
[29] Lee JS, Kim BN, Kang E, Lee DS, Kim YK, Chung JK, et al. Regional cerebral blood flow in children with attention deficit hyperactivity disorder: comparison before and after methylphenidate treatment. Hum Brain Mapp 2005;24:157–64.
[30] Colombo M, D'Amato MR, Rodman HR, Gross CG. Auditory association cortex lesions impair auditory short-term memory in monkeys. Science 1990;247:336–8.
[31] Rauschecker JP, Tian B. Mechanisms and streams for processing of "what" and "where" in auditory cortex. Proc Natl Acad Sci USA 2000;97:11800–6.
[32] Sonuga-Barke EJ, Taylor E, Sembi S, Smith J. Hyperactivity and delay aversion-I. The effect of delay choice. J Child Psychol Psychiatry 1992;33:387–98.
[33] Sonuga-Barke EJ. On dysfunction and function in psychological theories of childhood disorder. J Child Psychol Psychiatry 1994;35:801–15.
[34] Sonuga-Barke EJ, Saxton T, Hall M. The role of interval underestimation in hyperactive children's failure to suppress responses over time. Behav Brain Res 1998;94:45–50.
[35] Dagli MS, Ingeholm JE, Haxby JV. Localization of cardiac-induced signal change in fMRI. Neuroimage 1999;9:407–15.
[36] Bhattacharyya PK, Lowe MJ. Cardiac-induced physiologic noise in tissue is a direct observation of cardiac-induced fluctuations. Magn Reson Imaging 2004;22:9–13.