

Alteration of regional low-frequency fluctuation in very young autistic children: a sedated-state fMRI study

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Target audience: Radiologist; Neurologist; Pediatrician

Introduction and Purpose: Autism is a neurodevelopment disorder characterized by three core features: impairments in social functioning, difficulties in communication, and restricted and repetitive behaviors. Functional magnetic resonance imaging (fMRI) has been widely applied to detect the functional abnormalities of autism spectrum disorder. This technique has revealed multiple brain regions and networks that are likely responsible for social cognitive deficits of autism in recent studies¹⁻⁴. However, the vast majority of autism-related studies with fMRI are mainly conducted by recruiting autistic patients from high-functioning adult/adolescent subjects. So far, it remains largely unknown how the regional functional patterns are altered in very young autistic children. In this study, we hypothesize that social cognition-associated brain areas have exhibited significant functional changes in autistic patients at very young stage, as compared to normally developing controls. Specifically, sedated-state fMRI (S-fMRI) was applied to examine the brain functional activities in treatment-naïve young autistic children and controls.

Methods: S-fMRI data of 33 male autism (age ranged from 2 to 6 years) and 26 age-matched male controls (age ranged from 2 to 6 years) were collected from a Philips 3T scanner. The autistic patients were diagnosed according to the ADI-R and DSM-IV. The exclusion criteria for controls include nervous system diseases, psychiatric disorders and systemic symptoms by experienced clinicians. Functional images were acquired using an echo-planar imaging (EPI) sequence with the following parameters: repetition time (TR) = 2000 ms; echo time (TE) = 24 ms; flip angle = 60°; number of slices = 33; slice thickness = 3 mm; gap = 1 mm; voxel size = 3.44 × 3.44 × 3 mm³, and matrix = 64 × 64. Our protocol was approved by Beijing Children's Hospital Research Ethics Committee.

To quantify the functional activity across the brain, amplitude of low-frequency fluctuations (ALFF) and fractional ALFF were used⁵⁻⁶. Specifically, the first five volumes were discarded for each subject, leaving 195 images for further analysis. ALFF and fALFF were calculated using REST software⁷ and analyzed in two different frequency bands (slow-5: 0.01–0.027 Hz; slow-4: 0.027–0.073 Hz)⁶. To detect the group difference of ALFF or fALFF between autistic children and controls, a general linear model were applied to all voxels in grey matter, after controlling for age. Statistical significance were determined by a cluster extent threshold of $p < 0.05$ (FWE-corrected), with a height threshold of $p < 0.01$ (uncorrected) at voxel-level.

Results: We have found significant differences of frequency-dependent ALFF/fALFF in multiple brain regions between autistic children and controls.

Specifically, compared to controls, the autistic children showed similar decreased patterns in ALFF of both frequency bands and in fALFF of slow-5 band, including left inferior/middle/superior temporal gyrus, left inferior parietal gyrus, left supramarginal gyrus, left angular gyrus, left fusiform gyrus, left middle occipital gyrus (Fig.1-3). In addition, fALFF in slow-4 band decreased in right inferior/middle/superior temporal gyrus, right supramarginal gyrus, right angular gyrus, right fusiform gyrus and right lateral cerebellum (Fig.4). In contrast, we also observed significantly increased ALFF values of slow-5 band in bilateral brainstem, cerebellar vermis, media cerebellum and left parahippocampal gyrus, as shown in Fig.1 (Blue).

Discussion: Our analysis revealed frequency-specific ALFF/fALFF abnormalities of young autistic children in multiple regions that are associated with social cognition. The affected regions such as bilateral supramarginal gyrus, bilateral angular gyrus, and left parahippocampal gyrus have been repeatedly reported as components of default-mode networks, which were putatively associated with core symptoms in autistic adolescents and adults^{1,3}. Other observed regions such as posterior superior temporal sulcus (pSTS) and temporoparietal junction (TPJ) are among the brain areas

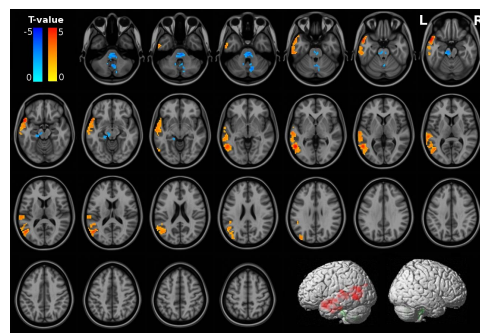


Fig.1: The main effect for group on ALFF of slow-5 band. Hot color represents higher ALFF in the patient group than in the control group, whereas blue color represents lower ALFF.

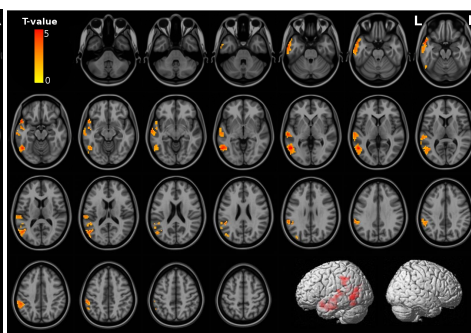


Fig.2: The main effect for group on ALFF of slow-4 band. Hot color represents higher ALFF in the patient group than in the control group.

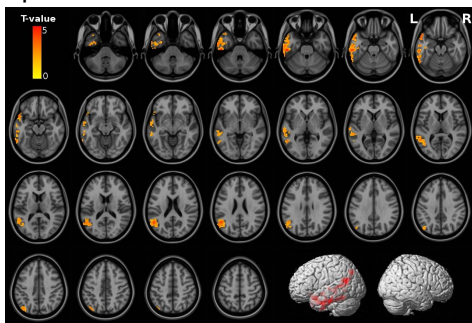


Fig.3: The main effect for group on fALFF of slow-5 band. Hot color represents higher fALFF in the patient group than in the control group.

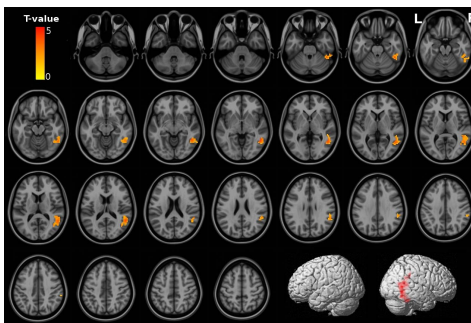


Fig.4: The main effect for group on fALFF of slow-4 band. Hot color represents higher fALFF in the patient group than in the control group.

consistently showing aberrant structure and function in autism^{2,8}. Particularly, autistic children here showed significant decreases of ALFF/fALFF in the fusiform gyrus and the superior temporal gyrus, i.e. the main functional areas of face perception, which could play a role in the deficits of social cognition related with face processing⁴. On the other hand, the increased fALFF values in brain stem, cerebellar vermis may be related with maldevelopment or compensation of functional abnormalities of autism⁹.

Conclusion: Our study reveals the abnormalities of functional activity of very young autistic children (2-6 years) in multiple brain regions, which possibly underlies core symptoms of autism. These results also suggest that the ALFF/fALFF analysis based on sedated-state fMRI can be utilized as a potential method to evaluate brain functional development in very young children.

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