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Weak network efficiency in young children with Autism Spectrum Disorder: Evidence from a functional near-infrared spectroscopy study

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ABSTRACT

Functional near infrared spectroscopy (fNIRS) is particularly suited for the young population and ecological measurement. However, thus far, not enough effort has been given to the clinical diagnosis of young children with Autism Spectrum Disorder (ASD) by using fNIRS. The current study provided some insights into the quantitative analysis of functional networks in young children (ages 4.8–8.0 years old) with and without ASD and, in particular, investigated the network efficiency and lobe-level connectivity of their functional networks while watching a cartoon. The main results included that: (i) Weak network efficiency was observed in young children with ASD, even for a wide range of threshold for the binarization of functional networks; (ii) A maximum classification accuracy rate of 83.3% was obtained for all participants by using the k-means clustering method with network efficiencies as the feature parameters; and (iii) Weak lobe-level inter-region connections were uncovered in the right prefrontal cortex, including its linkages with the left prefrontal cortex and the bilateral temporal cortex. Such results indicate that the right prefrontal cortex might make a major contribution to the psychopathology of young children with ASD at the functional network architecture level, and at the functional lobe-connectivity level, respectively.

1. Introduction

Autism Spectrum Disorder (ASD) describes a range of developmental disabilities that are characterized by persistent impairment in social interaction and communication, stereotyped patterns of behavior, and restricted interests (Woolfenden, Sarkozy, Ridley, & Williams, 2012; Worley & Matson, 2012). According to the latest report released by Centers for Disease Control and Prevention, ASD is one of the fastest growing developmental disabilities (Wingate et al., 2014). The prevalence of ASD in U.S. children increased by 119.4 percent from 2000 (1 in 150) to 2010 (1 in 68). Thus, uncovering of the neural mechanism, early diagnosis, and risk prediction of ASD are of great importance in biomedical sciences.

It is challenging to explore the neurodevelopment of young children (younger than 8 years old) with ASD, because: (i) those young patients are usually unwilling to lay down into a claustrophobic space, which in turn results in unacceptable head movements or a signal acquirement failure during an imaging scan; and (ii) they generally have serious cognitive and social interaction disorders and thereby can't fully understand the experimental tasks or complete complex behavioral responses as expected (Philip et al., 2012). In such a circumstance, some scientists suggested that young children with ASD be scanned after sedation (Walker et al., 2012). However, that is clearly not an ecological measurement. FNIRS, a non-invasive neuroimaging tool using near infrared light to detect the hemoglobin concentrations in the outer cortex, is safe, portable, low cost, relatively insensitive to head movement, and captures relatively higher spatial resolution. Such advantages make it a promising imaging tool in investigating the neurodevelopment of the young and clinical population (Boas, Elwell, Ferrari, & Taga, 2014; Vanderwert & Nelson, 2014). Researchers have utilized fNIRS to explore the neural mechanisms in infants and young children during multiple cognitive tasks (Perlman, Huppert, & Luna, 2015), emotional tasks (Perlman, Luna, Hein, & Huppert, 2014), and other special mental states (Homae et al., 2010; Lloyd-Fox et al., 2014; White, Liao, Ferradal, Inder, & Culver, 2012). Some scientists tried to use fNIRS to uncover the neural abnormalities of ASD (Keehn, Wagner, Tager-Flusberg, & Nelson, 2013; Kikuchi et al., 2013), however, fNIRS is still new to clinicians even in specialized neurological departments.

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Brain functional networks can mathematically be characterized by complex networks which consist of nodes denoting voxels or brain regions that are linked by edges representing functional connections among them (Bullmore & Sporns, 2009). Recent advances in complex networks have been rapidly translated to studies of brain functional networks in ASD by using different imaging tools such as fMRI (Barttfeld et al., 2012; Itahashi et al., 2014), magnetoencephalography (MEG) (Tsiaras et al., 2011), and electroencephalography (EEG) (Barttfeld et al., 2011). For instance, Barttfeld et al. (2012) found that adults with ASD exhibited weak intrinsic connectivity during resting state scanning. Such a result was consistent with previous findings suggesting the altered brain functional networks of the default mode in such population (see reviews, Belmonte et al., 2004; Wass, 2011). Itahashi et al. (2014) pointed out the existence of the aberrant network organization in adults with ASD, suggesting significant deficits in several global indexes (including clustering coefficient and characteristic path length) of the functional topological network. However, the majority of previous reports focused only on adults with ASD. Remarkably, recent advances discovered there were some abnormal neural signs for young children with ASD. Keehn et al. (2013), for instance, found significant functional connectivity differences between infants at a high risk of ASD and healthy controls. Kikuchi et al. (2013) found young children (3–7 year olds) with ASD exhibited higher inter-hemispheric functional connectivity in the anterior prefrontal cortex by using a two-channel-fNIRS. Collectively, this literature suggests participants with ASD exhibit altered brain functional network features. However, few studies have examined the functional network efficiency in young children with ASD.

Neuroscience studies have pointed out that network efficiency is a promising measure describing how information transfers across neural networks (Latora & Marchiori, 2001). Such network feature can be used to quantify both local and global features of networks with only one single measure, even if it is dealing with disconnected graphs, non-sparse, or both. Therefore, compared with the conventional use of clustering coefficient and shortest path length, network efficiency is easier to use numerically (Watts & Strogatz, 1998). It also has technical and conceptual advantages. Previous research has confirmed network efficiency is related to behavioral, psychological and biological dysfunction. Achard and Bullmore (2007), for instance, discovered that economical small-world network in human brain was damaged by aging, with decreased global and local network efficiency in older adults. Additionally, they found a single dose of sulpiride, which would lead to the blockade of dopamine neurotransmission, could also weaken global and local network efficiency in younger and older adults. Wang et al. (2009) investigated the alteration of the topological architectures in children with Attention-Deficit/Hyperactivity Disorder (ADHD), providing direct evidence that brain functional network in children could be adversely affected by psychopathology. They found the network efficiency in children with ADHD was altered, with higher local efficiencies but lower global efficiencies when compared with healthy controls. These results provide new perspectives in the clinical diagnosis of psychopathological disorders by using functional brain networks. If, as hypothesized, the functional network efficiency could particularly reflect psychopathology at the neural level, it logically follows that individuals with ASD might show significant differences of network efficiency when compared with healthy controls. To the best of our knowledge, the current study is the first to investigate the global metrics of functional network efficiency in young children with ASD by using fNIRS.

The current study had two main goals. First, we aimed to examine the functional network efficiency (global and local efficiency) in young children with and without ASD using a non-invasive fNIRS technique. We hypothesized that the functional network efficiency in young children with ASD would be altered compared with that in typically developing children, which meant there might be a deficit in the information exchange across the functional networks. Second, since k-means clustering is widely used in identifying distinct phenotypic groups in human disease (Haldar et al., 2008; Yu, 2013), we sought to detect whether network efficiency could be considered as a promising feature for the clinical diagnosis of young children with ASD by using a k-means clustering method at the individual subject level. Based on the k-means clustering results, we further analyzed the lobe-level intra and inner functional connectivity differences between the two groups to see which brain areas were closely related to the alteration of the functional network in children with ASD.

2. Methods

2.1. Participants

Sixteen children with ASD were recruited for the current study. Four ASD participants were excluded from the analysis due to failure of fNIRS data collection. Therefore, 12 children with ASD (9 boys; ages 4.8–8.0 years old, mean age 6.1 ± 1.1 years) were used for data analysis. For statistical purposes, 12 age- and gender-matched typically developing (TD) children, as a control group, were also recruited to participate in the current research. Parents of each participant were requested to report their child's behavior using the Autism Behavior Checklist (ABC) (Yirmiya, Sigman, & Freeman, 1994). All children with ASD came from a local special school (NANJING MINGXIN Intelligence-Promoting School, NJMXIPS) and were diagnosed with ASD in the past two years by a local hospital (NANJING Brain Hospital). It should be noted that those subjects with ASD had never been diagnosed with the comorbidity of ADHD, and were identified as high-functioning autism (within the near normal or normal range of intelligence) according to their teachers' reports. It was further confirmed that none of the TD participants had a history of psychiatric or neurological disorder. Parents of all participants signed the written informed consent for this study, which was approved by the Ethics Committee of the Southeast University.

2.2. Behavior questionnaires

The Autism Behavior Checklist (ABC) (Yirmiya et al., 1994), a parental report questionnaire, was used to confirm the clinical diagnosis of ASD. 57 items describing typical behaviors in different areas of children with ASD were included and divided into five subscales (sensory, relating, body and object use, language, and social and self-help skills). The score assigned for each item varies from 1 to 4, depending on its importance when correlated with the diagnosis of ASD. The subscale scores were produced by adding the weights of all endorsed items for each area, and those were in turn summed up to represent the total score of ABC. It has been suggested that children with a total score equal to or higher than 68 points may have a high risk to be identified as ASD (Yirmiya et al., 1994). Table 1 summarizes the means and standard

Table 1
Means and standard deviations of ABC scores for ASD and TD subjects.

	ASD (Mean ± SD)	TD (Mean ± SD)
Sensory	12.8 ± 4.8	1.8 ± 2.9
Relating	21.0 ± 6.7	1.7 ± 2.6
Body and object use	18.8 ± 5.7	2.9 ± 2.8
Language	17.6 ± 6.5	0.3 ± 0.8
Social and self-help skills	14.8 ± 2.8	1.8 ± 2.4
Total score	85.0 ± 10.9	8.5 ± 9.0