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Altered brain network topology in left-behind children: A resting-state functional magnetic resonance imaging study

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A B S T R A C T

Whether a lack of direct parental care affects brain function in children is an important question, particularly in developing countries where hundreds of millions of children are left behind when their parents migrate for economic or political reasons. In this study, we investigated changes in the topological architectures of brain functional networks in left-behind children (LBC). Resting-state functional magnetic resonance imaging data were obtained from 26 LBC and 21 children living within their nuclear family (non-LBC). LBC showed a significant increase in the normalized characteristic path length (λ), suggesting a decrease in efficiency in information access, and altered nodal centralities in the fronto-limbic regions and motor and sensory systems. Moreover, a decreased nodal degree and the nodal betweenness of the right rectus gyrus were positively correlated with annual family income. The present study provides the first empirical evidence that suggests that a lack of direct parental care could affect brain functional development in children, particularly involving emotional networks.

1. Introduction

Parental care can affect not only child behavior but also the maturation of the brain systems that support psychological and emotional development in human beings (Callaghan & Tottenham, 2016; Rifkin-Graboi et al., 2015). Numerous animal experiments have provided evidence that maternal deprivation can lead to the deterioration of emotional and cognitive processes during adulthood (Akillioglu, Yilmaz, Boga, Binokay, & Kocaturk-Sel, 2015; Marco et al., 2015; Xiong, Yang, Cao, Mao, & Xu, 2015). However, it remains unclear whether and how the lack of direct parental care can affect brain function in children.

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This issue is potentially of considerable public health significance. Millions of parents in developing countries migrate to other countries for economic or political reasons, leaving their children behind (Liu et al., 2015; Lu, 2015; Siriwardhana et al., 2015). In China, for example, there are more than 60 million left-behind children (LBC) (China Women's Federation, 2013), and among these LBC, there is a significantly higher prevalence of negligence (Zhao et al., 2014), higher level of suicidal ideation (Gao et al., 2010) and greater risk of developing depression and anxiety (Cheng & Sun, 2015; Wang et al., 2015) than there is among children living within their nuclear family (non-LBC). However, the effect of a lack of parental care on brain function in LBC largely remains unknown.

In the past few years, neuroimaging technologies have been increasingly used to study the neurobiological mechanism underlying the effects of adverse psychosocial experiences on brain development (Bick et al., 2015). Neglected children and adolescents have demonstrated impaired functioning in the dorsal executive regions (Mueller et al., 2010) and hyperactivation in the amygdala and hippocampus in response to seeing fearful and angry faces (Maheu et al., 2010). Early institutional care has been shown to be associated with long-lasting effects on neuroanatomic development, such as reduced total grey and white matter volumes (Sheridan, Fox, Zeanah, McLaughlin, & Nelson, 2012) and diminished white matter connectivity in the uncinate fasciculus region (Eluvathingal et al., 2006) in institutionalized children in comparison with non-institutionalized controls. Furthermore, removal from conditions of negligence in early life and entry into a high-quality family environment has been reported to normalize the trajectory of white matter growth (Bick et al., 2015). In addition, children who experienced early maternal deprivation have exhibited acceleration in the maturation of amygdala–prefrontal connectivity, which is considered an ontogenetic adaptation in humans in response to early adversity (Gee et al., 2013). These results support the notion that separation from the primary caregiver may have an adverse effect on children (Mueller et al., 2010) and influence brain development. However, the conditions faced by institutionalized children are at times more dire and extreme than the conditions faced by LBC in the care of relatives.

The human brain is a complex network, and recent advances in graph-based theoretical approaches have allowed the noninvasive characterization of its topological properties; this has proven to be an effective and informative way to explore brain function and human behavior (Bullmore & Bassett, 2011; Bullmore & Sporns, 2009). In this approach, the brain is modeled as a network composed of a number of nodes connected by edges. For instance, a normal brain is functionally organized in a small-world fashion (characterized by high local specialization and high global integration between brain regions), a prominent feature shared by various social, economic, and biological networks (Bullmore & Bassett, 2011). That is, the nodes of the network have greater local interconnectivity or cliquishness than a random network, but the minimum path length between any pair of nodes is smaller than a regular network or lattice (He, Chen, & Evans, 2007; Watts & Strogatz, 1998). Furthermore, such an organization pattern is disrupted in neuropsychiatric disorders, such as major depressive disorder (Zhang et al., 2011) and schizophrenia (Liu et al., 2008). Although different brain diseases show different changes, the topology of the functional network of an abnormal brain can be regarded as less optimal when it deviates more from the small-world network topology, suggesting both a possible role in pathophysiology and a potential biomarker. However, the topological centralities of the functional connectomes in LBC have not yet been investigated.

In general, we hypothesized that both global and local topological features would differ significantly between LBC and non-LBC. To test our hypothesis, we collected resting-state functional magnetic resonance imaging (r-fMRI) data from 26 LBC and 21 non-LBC and analyzed their intrinsic brain connectivity networks using graph theoretical approaches. Between-group differences and relationships with clinical variables were also investigated.

2. Materials and methods

2.1. Participants

A total of 47 subjects were recruited, including 26 LBC and 21 age and sex-matched non-LBC. All subjects were classmates or schoolmates from the same local primary schools with similar educational environments in a town of southeastern China. All LBC subjects were living with their grandparents as their parents had immigrated abroad for work. They communicated with their parents occasionally over the phone or via internet audiovisual software. In contrast, non-LBC lived with their nuclear family throughout their childhood. Subjects' intelligence quotient (IQ) was measured using the Chinese Wechsler Intelligence Scale for Children (C-WISC), administered by an experienced child psychologist. All subjects were screened by an experienced child psychiatrist using the Chinese modified version of SCID-I (Non-patient Edition) (Wang, Yang, Jiang, & Michael, 2009) to exclude any Axis I psychiatric diagnoses, and all of their first-degree relatives were free of psychiatric illness. Exclusion criteria for all subjects included the presence of (a) head trauma; (b) a history of organic brain disorders, neurological disorders, or cardiovascular diseases; (c) any physical illness, as assessed by personal history and laboratory analysis; (d) MRI contraindications; and (e) recent medication that might affect brain function. The demographic and clinical characteristics of these subjects are summarized in Table 1.

MR images of all subjects were first reviewed by a neuroradiologist to ensure that there were no structural abnormalities or data quality flaws. This study was approved by the Research Ethics Committee of the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University. The guardians of the children were provided with a detailed information