Brain & Development 38 (2016) 893–902

BRAIN & DEVELOPMENT
Official Journal of the Japanese Society of Child Neurology

www.elsevier.com/locate/braindev

Original article

Frequency specific patterns of resting-state networks development from childhood to adolescence: A magnetoencephalography study

Meng Lu [a,b,*], Jing Xiang [b]

[a] College of Information Science and Engineering, Northeastern University, Shenyang, Liaoning 110000, China
[b] MEG Center, Division of Neurology, Cincinnati Children's Hospital Medical Center, 3333 Burnet Avenue, Cincinnati, OH 45220, USA

Received 29 March 2016; received in revised form 14 May 2016; accepted 16 May 2016

Abstract

Objective: The present study investigated frequency dependent developmental patterns of the brain resting-state networks from childhood to adolescence.

Method: Magnetoencephalography (MEG) data were recorded from 20 healthy subjects at resting-state with eyes-open. The resting-state networks (RSNs) was analyzed at source-level. Brain network organization was characterized by mean clustering coefficient and average path length. The correlations between brain network measures and subjects' age during development from childhood to adolescence were statistically analyzed in delta (1–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), and beta (12–30 Hz) frequency bands.

Results: A significant positive correlation between functional connectivity with age was found in alpha and beta frequency bands. A significant negative correlation between average path lengths with age was found in beta frequency band.

Conclusions: The results suggest that there are significant developmental changes of resting-state networks from childhood to adolescence, which matures from a lattice network to a small-world network.

Keywords: MEG; Resting-state networks; Development; Graph theory

1. Introduction

It has been shown that the blood oxygen level-dependent (BOLD) signal fluctuations can be detected in the absence of an explicit task (resting state). This phenomenon is most easily demonstrated in quietly resting humans, therefore, the associated spatially separate brain regions are now widely known as resting-state networks (RSNs) [1]. RSNs is unique in terms of its high resting metabolism, deactivation profile during cognitively demanding tasks [2,3], and increased activity during high-level social cognitive tasks [4]. Though precise functions of RSNs are still largely unknown, it has been shown that brain regions of RSNs are involved in the integration of autobiographical, self-monitoring and social cognitive functions [5,6]. The available evidences suggest that RSNs reflect slow, synchronous, spontaneous fluctuations of spatially organized neural signaling, which may be involved in the construction or development of neural networks.

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* Corresponding author at: College of Information Science and Engineering, Northeastern University, Shenyang, Liaoning 110000, China.

E-mail address: menglu1982@gmail.com (L. Meng).

http://dx.doi.org/10.1016/j.braindev.2016.05.004

The synchronization of activity between distributed brain regions is assumed to reflect functional interactions between brain regions and is referred to as functional connectivity [7]. Brain is increasingly seen as a complex network of dynamical systems with functional connectivity between local and remote brain regions. There are several motivations for using network to characterize the brain [8]. First, network analysis promises to reliably quantify the brain with a small number of neurobiologically meaningful and easily computable measures [9–13]. Second, by explicitly defining anatomical and functional connections on the same map of brain regions, network analysis may be a useful setting for exploring structural–functional connectivity relationships [14,15]. Third, comparisons of structural or functional network topologies between subject populations appear to reveal presumed connectivity abnormalities in neurological and psychiatric disorders [16,17]. To characterize the brain network, mean clustering coefficient and average path length are the most frequently used measures in the network analysis. Mean clustering coefficient measures how well connected the neighbors of a node are to one another, which is a measure of functional segregation. Average path length measures the average number of steps needed to go between any two nodes, which is a measure of functional integration.

Previous fMRI studies have shown that the horizontal interhemispheric functional connections were already established in preadolescent children [18]. The RSNs is only sparsely connected in children aged 7–9 years [19]. Over adolescence, short range correlation tends to weaken, whereas long-range, especially anterior-posterior connection starts to strengthen [20]. The long-range connections increased over development to form complete networks like the RSNs in adults [21,22]. However, fMRI mainly detect brain activity at a very low frequency range (nominally, <0.1 Hz) by measuring BOLD signals.

Magnetoencephalography (MEG) has also been used to study RSNs. de Pasquale et al. [22] showed correlation between resting state temporal MEG signals originating in nodes of the default mode network (DMN) and the "task positive" or dorsal attention network (DAN). Liu et al. [23] examined correlations between oscillatory power envelopes at the sensor level showing that significant envelope correlation could be measured across hemispheres. Brookes et al. [24] used seed-based envelope correlation in conjunction with beamformer spatial filtering methods to show interhemispheric motor cortex connectivity in source space.

The objective of the present study was to investigate RSNs with MEG at source-level in multiple-frequency ranges. Our central hypothesis is that the structure of RSNs changes with age in multiple frequency ranges. A better understanding about the developmental changes of RSNs will provide novel insight into the functional maturation of the brain and help us to identify functional impairments and/or developmental delay in children with a variety of disorders.

2. Materials and methods

2.1. Subjects

Twenty volunteers who met the inclusion criteria (age: 6–16 years; mean age: 11 years; girls: 13; boys: 7), participated in this study. A written informed consent, at Cincinnati Children's Hospital Medical Center (CCHMC), was obtained from each child and from the parent/legal guardian of each child. This study was approved by the Institutional Review Board (IRB) at CCHMC. The inclusion criteria for participation were: (1) healthy (i.e., without history of neurological disorder, psychiatric disease, or brain injury); (2) normal hearing, vision, and hand movement; (3) age at appointment time between 6 and 16 years old; (4) completion of a questionnaire based on the Edinburgh Handedness Inventory (Oldfield, 1971) to indicate dominant hand. The exclusion criteria for participation were: (1) subject data contained excessive motion artifacts (difference in head localization before and after was greater than 5 mm); (2) subjects with excessive unidentifiable magnetic noise during recording; (3) subjects with claustrophobic tendencies or (4) pregnancy.

2.2. MEG recordings

The MEG data were recorded using a whole-head CTF 275-Channel MEG system (VSM Medical Technology Company, Canada) in a magnetically shielded room (MSR), which is dim light. Before MEG recording, three small coils were attached to the nasion, and the left and right pre-auricular points of each subject. The subject's head positions were measured relative to the MEG sensors for every 2 min block using the three coils. The large head movement during MEG recordings might affect the accuracy of source localization. If head movement during a recording was beyond 5 mm, that dataset was indicated as "bad" and an additional dataset was recorded. MEG signal was acquired at a sampling rate of 6000 Hz with a noise cancelation of third order gradients. To identify system and environmental noise, we routinely recorded one MEG dataset without patient just before the experiment.

Subjects were asked to lie on a bed, keep their eyes open and stay still (avoid swallowing or teeth clenching). Continuous MEG recordings were completed in 2 min time blocks and repeated 2 times for a 4 min total recording. The segments of MEG data with artifacts were set as "bad segments", which were automatically excluded from network analysis in our software package.