Biomedical Signal Processing and Control 40 (2018) 351–358

Contents lists available at ScienceDirect

Biomedical Signal Processing and Control

journal homepage: www.elsevier.com/locate/bspc

# Investigation of brain networks in children with attention deficit/hyperactivity disorder using a graph theoretical approach

Jianqin Cao[a,1], Yang Li[a,1], Hong Yu[a], Xiwu Zhao[a], Yingli Li[a], Suhong Wang[b,*]

[a] Department of Nursing, Harbin Medical University (Daqing), Xinyang Road No.39, Daqing 163319, China
[b] Department of Neuroscience, The Third Affiliated Hospital of Soochow University, Juqian Road No.185, Changzhou 213003, China

A R T I C L E I N F O

*Article history:*
Received 18 April 2017
Received in revised form 31 August 2017
Accepted 7 October 2017

*Keywords:*
Graph theory
Attention deficit hyperactivity disorder (ADHD)
Brain network

A B S T R A C T

In this study, brain networks in children with attention-deficit/hyperactivity disorder (ADHD) were investigated. Electroencephalogram (EEG) data were collected from 16 children with ADHD (ADHD group) and 16 healthy children (control group) while they performed an improved visual continuous performance test. A combination coherence and graph theory method was used to construct each subject's nerve conduction network using EEG signal data. Differences in brain network topology parameters between the two groups were then compared (two-sample *t* test). Results revealed the following: when performing functional tasks, alpha bands can be used as an important parameter in ADHD research; the shortest path length can be used as a reference to assess ADHD; and ADHD brains exhibit significant defects in left lateralization of neural networks. These results support the conclusions of the cognitive-energetic model.



## 1. Introduction

Attention deficit/hyperactivity disorder (ADHD) is a neurological condition that often occurs in school-age children and may continue to develop into adulthood. Clinically, this disorder primarily manifests as attention deficit inconsistent with age, impulsivity/hyperactivity, and other symptoms. Based on varying symptoms, the American Psychiatric Association has classified ADHD into three subtypes: attention deficit (ADHD-In); impulsivity or hyperactivity disorder (ADHD-Hyp); or a combination of both (ADHD-com) [1]. ADHD seriously affects academic achievement, and familial and social relationships of affected children; therefore, finding the underlying causes of ADHD is important and a primary focus of research [2].

Presently, there is no consensus regarding the causes of ADHD [3]; however, the literature has suggested that abnormalities in the striatal network of the frontal, parietal and temporal lobes, the cerebellum, and other areas of the brain in children with ADHD play a crucial role in its onset and development [4–9]. These studies have provided a solid foundation for researchers to understand and analyze ADHD. Recently, some studies investigating neural networks in the brain have been based on the Default Mode Network (DMN) [10], which is a functional network composed of spontaneous low-frequency electroencephalogram (EEG) activity within many areas of the human brain. Selected studies examining the DMN include Liang et al. [11], who studied brain networks using a Pearson correlation graph theory network construction method and found that the brain network of children with ADHD tended to develop into a normal network. Fair et al. [12] found that atypical integration in the network was an important factor in the development and progression of ADHD. Finally, Ahmadlou et al. [13] constructed a network using nonlinear Fuzzy synchronization likelihood and found that the shortest path length "L" and the clustering coefficient "C" in the delta bands could be used to distinguish ADHD groups from control groups. These studies have added a specific neural network perspective to ADHD research. It is not counterintuitive to find that the DMN in certain areas of ADHD brains may be dysfunctional, resulting in information processing disorders in the network. The majority of studies investigating DMN require test subjects to be in the resting state; therefore, external stimuli presented to the subjects are relatively small. In addition, surveys examining particular nerve conduction networks in subjects encountering various stimuli in daily life are lacking. Are there similar obstacles in the nerve conduction networks in the brains of children with ADHD during the execution of these stimulus tasks? Unfortunately, related research investigating this question is currently scarce. Accordingly, this study constructed a nerve conduction network based on graph theory using an improved visual-continuous performance test (visual-CPT) to collect electroencephalogram (EEG) data from

* Corresponding author.
*E-mail address:* 11787227@qq.com (S. Wang).
[1] Same contribution to this work.

https://doi.org/10.1016/j.bspc.2017.10.005
1746-8094/

subjects while they performed attention execution and inhibition control tasks [9,14]. Abnormalities in the nerve conduction networks in the brains of children with ADHD in different bands were subsequently examined. In designing our study, we considered previous research that used this paradigm. A functional magnetic resonance imaging study reported disorders in the striatal network of the frontal, parietal and temporal lobes, the cerebellum, and other areas of the brain in individuals with ADHD [9]. A study investigating event-related potentials (ERPs) in the frontal area found that the magnitude of ERPs in the frontal area of individuals with ADHD was abnormal during execution of attention and inhibition control tasks [14]. Based on this paradigm, we hypothesized that the following outcomes would be observed:

1. Normal children would show more long-range connections than children with ADHD;
2. Compared with control brains, the brain neural networks in children with ADHD would exhibit connection abnormities in the frontal, parietal, and temporal lobes; and
3. The brain nerve conduction networks in normal children would be more effective in conveying information than children with ADHD during execution of attention and inhibition control tasks.

To verify our hypothesis, the EEG signals of subjects were collected using a 128-channel EEG acquisition apparatus, in which 32-channel signals were selected for further analysis and research. During construction of the graph theory network, 32 channel locations were regarded as apexes in the graph theory network, and the coherence (also amplitude square coherence) value between two EEG signals was taken as a reference of the connection edge between the two locations (a threshold was set; if the value exceeded this threshold, there was a connection edge between the two channel signals; or, there was no connection edge). Finally, the network was comprehensively studied using a graph theoretical approach.

## 2. Materials and methods

### 2.1. Subjects

A total of 32 subjects (16 ADHD, 16 control) were enrolled. All subjects were right-hand dominant, their mother language was Chinese, and their vision was normal or corrected to normal. The ADHD subjects comprised out-patients (children) from the Department of Psychology of the Third Affiliated Hospital of Suzhou University (Changzhou, China), while subjects in the control group were from an ordinary primary school in the Changzhou prefecture (Jiangsu, China). The IQ of all subjects was $\geq$85, without significant difference between the groups. Children in the ADHD group met the diagnostic criteria published in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* [1] and were diagnosed with ADHD-com by a pediatric psychiatrist. All subjects were otherwise disease free and did not undergo any type of treatment before the test. Additionally, all subjects were asked to not eat or drink any caffeine-containing food or beverages that could affect nerve activity within 24 h before the test. The present study was performed with the informed written consent of the children and their guardians. Additionally, this study was approved by the Ethics Committee of the Third Affiliated Hospital of Suzhou University. After the test, each subject received a gift or small reward.

### 2.2. Test protocol

The improved Visual-CPT protocol used in this study included three main conditions: Go, No-go and Lure (Fig. 1). Stimuli were presented to the subjects in the center of a cathode ray tube (CRT) display as the Arabic numerals 0–9. The presentation mode was pseudorandom, and only one character was presented at a time (black and white). Each character remained on display for 300 ms, followed by a black screen for 1200 ms. In the test, the numeral “1” represents a clue, and each trail consists of two stimuli (“prompt” and “target”, respectively). Conventions are as follows: when the prompt stimulus is the numeral “1” and the target stimulus is the numeral “9”, subjects are required to press a key (Go condition, accounting for approximately 12% of the total number of stimuli); when the prompt stimulus is the numeral “1” and the target stimulus is not the numeral “9”, subjects are not required to press any key (No-go condition, accounting for approximately 12% of the total number of stimuli); when the prompt stimulus is not the numeral “1” and the target stimulus is the numeral “9”, subjects are also not required to press any key (Lure condition, accounting for approximately 12% of the total number of stimuli); finally, apart from Go, No-go and Lure, no action is required from the subjects (background condition, accounting for approximately 64% of the total number of stimuli). Each subject was required to complete a total of approximately 600 trials. Presentation of the experimental stimuli was controlled by E-prime software (Psychology Software Tools, Inc., Sharpsburg, PA, USA), and the behavioral results were recorded automatically.

### 2.3. Data collection

In the test, 128-channel high-density EEG data from the subjects were collected using an EEG acquisition device (Geodesic EEG System 300, Electrical Geodesics Inc., Eugene, OR, USA), in which the sampling frequency was 500 Hz, the band pass was set at 0.5 Hz to 30 Hz, and CZ was the reference electrode. The left and right mastoid signals were also recorded. The entire collection process in the test was performed in a dark, electromagnetically shielded room. The subjects wore 128-channel electrode caps that were disposed in a 10/10 manner, and sat on comfortable chairs with armrests. The CRT screen was placed approximately 80 cm from the subjects' eyes, and the right index finger placed on buttons pre-fixed to the armrests. To ensure a normal testing procedure, subjects were given approximately 10 min to familiarize themselves with the experimental procedure before the formal experiment, so as to help them understand the entire process. Experimental data collected during the learning stage were not considered in the final data analysis.

### 2.4. Network analysis based on graph theory

After the data had been acquired, it was discovered that some electrodes recorded insufficient signals due to poor contact in 3 ADHD and 1 control subject. Considering the integrity of data and for calculating convenience, 32-channel data were selected for further processing. The channel locations are shown in Fig. 2. The data were segmented for processing (one section of experimental data was from 450 ms before the target stimulus to 1500 ms after the target stimulus), and then classified according to each subject under the Go or No-go conditions. Next, the data were re-referenced according to the bilateral mastoid process, and test data with artificial artifacts were removed manually. Data segments with obvious ocular and electromyographic artifacts were removed using an independent components analysis method.

#### 2.4.1. Construction of brain neural network

The brain neural network was constructed according to the following steps.