Title: Brain Functional Correlates of Intelligence Score in ADHD Based on EEG

Running title: Correlation of EEG Power and Intelligence Score in ADHD

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To appear in: Basic and Clinical Neuroscience

Received date: 2020/03/5
Revised date: 2020/09/16
Accepted date: 2020/09/28

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Please cite this article as:
DOI: http://dx.doi.org/10.32598/bcn.2021.1904.1
Abstract

It has been shown that intelligence as a general mental ability is related to structure and function of the brain regions. However, specificity of this regional dependencies to the intelligence scores in the typical and atypical developed individuals needs to be well understood. In this study, we hypothesized that neural correlates of IQ should not have a fixed pattern rather it must follow a dynamic pattern to compensate the functional deficits caused by a neurodevelopmental disorder. Therefore, EEG correlates of normal IQ in various subtypes of attention deficit hyperactive disorder (ADHD) were compared to a group of healthy controls. Sixty-three ADHD subjects comprising of combined, inattentive, and hyperactive individuals diagnosed by a psychiatrist using structural clinical interview for DSM-V, and 46 healthy controls with similar normal IQ scores were recruited in this study. The subjects’ EEG data were then recorded during an eye-closed resting condition. The subjects’ intelligence level was measured by the Raven’s standard progressive matrices. Then, association between IQ and power of EEG signal were computed in the conventional frequency bands. Subsequently, topographical representations of these associations were compared between the groups. Our results demonstrated that association between IQ score and EEG power is not the same in various ADHD subtypes, and healthy controls. This finding suggests a compensatory mechanism in ADHD individuals for changing the regional oscillatory pattern to maintain the IQ within a normal range.

Key words: ADHD, Intelligence score, EEG, Power spectrum analysis, Subtype
1. Introduction

Intelligence is a general mental ability which includes planning, reasoning, comprehension, abstraction and learning (Gottfredson, 1997). Therefore, intelligence scores may be used to predict one's performance (Haier & Jung, 2008). In fact, this cognitive ability is produced by the brain structure and functions which could be traced by the neuroimaging techniques. In this regard, neuroimaging studies have mainly presented a region-specific pattern of anatomy as well as activities associated with the intelligence score. In terms of structure, with the advent of MRI studies researchers have found strong association between intelligence and grey matter density (Narr et al., 2006). For example, association between intelligence and grey matter density has been reported in basal ganglia (Dietrich, 2004), hippocampus (Deary, Penke, & Johnson, 2010), fusiform (Deary, Penke, & Johnson, 2010), posterior region (Heilman, Nadeau, & Beversdorf, 2003), Parietal, frontal (R. W. Thatcher, North, & Biver, 2008), (R. Thatcher, North, & Biver, 2007) and dorsolateral prefrontal cortex (DLPFC) (Cabeza & Nyberg, 2000). Other studies associated global properties of the structural brain network to the general intelligence (Fischer, Wolf, Scheurich, & Fellgiebel, 2014). Similar to structural studies, functional studies also suggest a network for intelligence (Jung & Haier, 2007). In this context about relation between intelligence and function of the brain, a variety of psychophysiological measurement methods ranging from positron emission tomography (PET) (Metz, Yasillo, & Cooper, 1987), (Kane & Engle, 2002), (Gray, Chabris, & Braver, 2003), functional magnetic resonance imaging (fMRI) (Geake & Hansen, 2005), (Burgess, Gray, Conway, & Braver, 2011), (Tang et al., 2010) and Electroencephalography (EEG) (Neubauer, Grabner, Fink, & Neuper, 2005), (Anokhin, Lutzenberger, & Birbaumer, 1999) has been employed. From the all above mentioned methods, EEG is one of the most popular used method because it is cheap, portable, easy to wear and has a
high temporal resolution (Reis, Hebenstreit, Gabsteiger, von Tscharner, & Lochmann, 2014) and proper to use in the applied researches. It has been shown that EEG could present a correlation with intelligence (Mundy-Castle, 1958). Recent studies have demonstrated that high intelligent individuals allocate fewer resources and recruit minimum task relevant brain areas when performing an easy task, while they allocate more resources and recruit several brain areas when the task demand is high. In contrast, low intelligent individuals do not use different resource allocation strategies during easy and hard tasks (Kang & Lee, 2015).

In general, association of IQ scores and EEG properties have been studied using the power or amplitude (Klimesch, 1999b) (Giannitrapani & Liberson, 1985), (Martín-Loeches, Muñoz-Ruata, Martínez-Lebrusant, & Gómez-Jarabo, 2001), and the functional connectivity networks extracted with coherence and phase delays (R. W. Thatcher, North, & Biver, 2005) (R. Thatcher et al., 2007). Moreover, the brain works in a frequency specific manner, therefore association between IQ scores and EEG parameters have also been investigated in the conventional frequency bands as well. The conventional frequency bands in EEG include delta (slowest), theta, alpha, beta and gamma (fastest) bands. These frequency bands have been shown to have a critical role for performing the cognitive tasks (Klimesch, Schimke, & Pfurtscheller, 1993), (Moretti, 2015). In addition, cognitive disabilities have also been related to changes in the neural oscillatory pattern (frequency specific activities). For instance, it has been shown that increasing of a task demand increases the theta power and causes more synchronization in this band. In contrast, increase of a task demand decreases the alpha power and causes desynchronization in this band. (Schacter, 1977), (J. G. Webster, 1978) (Marosi et al., 1999) (Fogel, Nader, Cote, & Smith, 2007). In fact, EEG wave forms are caused by large numbers of neurons firing in synchrony. Synchronization behavior of EEG signals is important for decoding information processing in human brain.
In terms of IQ index of EEG, it has been shown that alpha power is most closely correlated with IQ score (Stankova & Myshkin, 2016). In addition, high-IQ individuals present higher modularity in their brain functional connectivity network (FCN) and have different patterns of activations between short-range and long-range connections in the FCN (Hearne, Mattingley, & Cocchi, 2016), (Song et al., 2008). The above-mentioned studies have mainly focused on the normal individual.

As a matter of fact, neurodevelopmental disorders such as attention deficit and hyperactive disorder (ADHD) could influence the pattern of brain activities. For instance, studies have reported greater fronto-central theta activity, lower beta activity, and higher theta/beta ratio in ADHD subjects as compared to healthy controls (Clarke, Barry, McCARTHY, & Selikowitz, 2001b; Loo et al., 2010) and (Bresnahan & Barry, 2002) (Arns, Conners, & Kraemer, 2013)(Loo et al., 2010). However, there is inconsistency in the previous studies in terms of effect of IQ on EEG power in ADHD. For instance, Clark et al. reported IQ does not impact the EEG power in ADHD individuals as compared to their matched control subject (Clarke et al., 2006) While Chabot and Serfontein (1996) showed that there is a different oscillatory pattern in EEG of ADHD children with high and low IQ. They suggested that children with low IQ show lower alpha and beta band (Chabot & Serfontein, 1996). Other studies have also highlighted the importance of IQ on any potential group's differences in ADHD with high and low IQ (Kitsune et al., 2015). Therefore, it seems that studies should try to control effects of IQ on their data. In this study, we hypothesized that neural correlates of intelligence should not have a fixed pattern rather it must follow a dynamic pattern to compensate the deficits caused by the disorder.
Therefore, in this study, EEG was recorded from three ADHD subtypes and a control group in eye closed condition. Then correlation of EEG spectral bands using estimates of absolute and ratio with IQ and significant differences within groups were computed at specific brain region. We also estimated whole pattern of association at each absolute frequency bands. Details of the experimental design and data analysis are explained in the next section.

2. Method

Schematic of experimental design is presented in figure 1.

[figure 1 about here]

2.1. Subjects

One hundred nine boy participants comprising of 22 combined (age=9.13±0.99, IQ=103.13±11.02), 27 inattentive (age=8.62±1.30, IQ=104.37±10.22), 14 hyperactive (age=9.42±1.74, IQ=107.5±9.27), and 46 healthy controls (age=9.41±1.42, IQ=102.39±10.83) were recruited in this study. All subjects were right handed and there was no significant differences in age and IQ between the groups (see Table 1). Diagnostic assessment was performed by psychiatrist and a senior clinical psychologist, comprised the Persian version of the Structural Clinical Interview for DSM-V (SCID). Average DSM-V symptoms scores of inattentive, hyperactive and combined were 7 (SD=1.3), 8.2 (SD=2.9) and 6.3 (SD=1.3), respectively.

Children with brain damage, neurological disorder, and epilepsy as well as children who consume stimulants or were under neurotherapy were excluded. All parents completed the consent form. The research protocol was approved by the Iran University of Medical Science Ethics Committee and all parents signed an informed consent.

[Table 1 about here]
2.2. IQ scores

All participants completed the Ravan’s Standard Progressive Matrices test (SPM). This multiple-choice test is used to assess abstract reasoning and nonverbal ability (Raven, 2000b). It has also been considered to be the best measure of spearman’s g factor (Reynolds & Brown, 1984) and intelligence (Raven, 2000a).

2.3. EEG data recording and analysis

EEG data was recorded during eyes-closed resting state for 4 minutes while children were seated on a comfortable chair. All subjects were asked to sit still, relax and try not to blink. The EEG data was registered using a 19-electrode Mitsar amplifier (www.mitsar-medical.com) with sampling rate of 250 Hz. Electrodes were placed on the scalp using a standard 10-20 montage (Fp1, Fp2, Fz, F3, F4, F7, F8, Cz, C3, C4, T3, T4, T5, T6, Pz, P3, P4, O1, O2) with average of ears channels used as reference and FPz as the ground electrode. Electrode impedances were kept below 5 kΩ. After recording, a self-written program using Matlab (https://www.mathworks.com) and EEGLab functions (https://sccn.ucsd.edu/eeeglab/) were used to process the data. Standard pre-processing included band-pass filtering (1-40 Hz), segmenting the data into epochs of 1 second duration, automatic rejection of disturbed channels using probability (artifact rejection was carried out using both to single electrodes and the collection of all electrodes), spectrum (thresholds are expressed in terms of amplitude changes relative to baseline in dB) and kurtosis (technically called the 4 first cumulates of the distribution) of the signal (Arnaud et al., 2006), interpolation of rejected channels by averaging its spherical neighbours, removing unreliable epochs, and referencing to the average. Subsequently, the pre-processed EEG data was transformed to the frequency domain using Fast Fourier Transform (FFT), and absolute power of the data was then calculated in Delta (1-4 Hz),
Theta (4-8 Hz), Alpha (8-13 Hz), Alpha1 (8-10), Alpha2 (10-12) and Beta (13-30Hz) frequency bands. After that, the power ratio was estimated for the theta/beta and theta/alpha frequency bands.

2.4. Statistical analysis

Pearsons’ correlation was calculated between score of SPM and the spectral of each frequency band. Spectral power was calculated in absolute and ratio style from the cleaned data. Then p values of each correlation score was considered and significant associations were recognized by putting a threshold of 0.05 for the p values. This analysis was performed using the statistical analysis toolbox of MATLAB 2015 (www.mathworks.com). Later, the group comparison of correlation values was performed using the cocor package (Diedenhofen & Musch, 2015).

3. Results

Detailed information of significant results (p<0.05) for absolute and ratio power are presented at Tables 2-7, Figures 2-6 and whole pattern analysis has been shown in Table8, Figure7. Correlation maps were scaled between -1 and 1. Only significant correlations (p<0.05) were plotted. Hot color indicates positive and cold color shows negative correlation.

3.1 Association between EEG power spectrum and IQ score

Absolute power

Figure2, Table2 present the significant correlation between absolute power and intelligence in ADHD subtypes and healthy control group. ADHD-combined group, showed significant positive correlations between IQ score mainly at P4 in alpha band, and at Fp1, C3, T5 in beta band. Negative correlations in this group were also found between IQ score and delta power at F8, and
theta power at Cz. ADHD-inattentive group showed significant positive correlation between IQ and delta power at F3, and alpha power at P4. Negative correlation in this group was also observed between IQ score and delta power at C4, and theta power at T3. ADHD-hyperactive/impulsive group, showed positive correlation between IQ score and theta power at Cz and negative correlation between IQ score and delta power at T3, and alpha power at C4. Healthy control group did not show any negative correlation between IQ and EEG bands, while positive correlations were observed between IQ score and theta power at F3 and F7, and alpha1 power at T5 and O1.

[Figure1 about here]

[Table1 about here]

Association between ratio power (theta/alpha, theta/beta) and intelligence score presented in Table3, and Figure3. ADHD-combined group showed negative correlations between IQ score and theta/alpha at Cz, and O2 as well as theta/beta at F3, and Cz areas. ADHD-inattentive group revealed positive correlation between IQ score and theta/beta at Fp2, and negative correlation between IQ score and theta/alpha at P4. ADHD-hyperactive group and healthy control group did not show any significant correlation between IQ score and above-mentioned power ratios.

[Figure3 about here]

[Table3 about here]

3.2. Differential patterns of association between IQ scores and EEG power spectrum in ADHD subtypes and healthy control groups
Topographical differences of association between IQ score and absolute power in various frequency bands in ADHD subtypes were compared to healthy control group (see Table4, Figure4). As compared to healthy control group, ADHD-combined showed increased alpha power at P3, and decreased delta at F8 and Fz, and theta at F3 and Cz, and alpha1 power at F3, C4, T4 locations. ADHD-inattentive, revealed increased theta power at F8 and T3, and increased alpha power at P4, and decreased beta power at P3. In addition, ADHD-hyperactive also showed decreased theta power at F8 and Fz, and decreased alpha power at T5, and decreased power of lower alpha band at F4 and C4 areas.

[Figure4 about here]

[Table4 about here]

Subsequently, comparison between patterns of ADHD subtypes were also performed that results are shown in Table5, Figure5. Elevated alpha2 power at F7 and Cz, and decreased delta power at F8 and T6, and decreased theta power at O1 were observed in ADHD-combined as compared to ADHD-inattentive group. Moreover, ADHD-combined group showed increased alpha power at C4 and T5, and increased beta power at Fp2, F3 and O1, together with decreased theta power at Cz as compared to the ADHD-hyperactive group. In addition, ADHD-inattentive group was also compared to ADHD-hyperactive group and presented increased theta power at F7, and alpha power at T5, and lower alpha power at F4, and beta power at O1.

[Figure5 about here]

[Table5 about here]
Topographical differences of association between intelligence and patterns of ratio power for ADHD subtypes as well as control group are presented in Table 6, 7 and Figure 6. In comparison with the healthy control group, ADHD-combined as compare to control group, showed decreased theta/alpha at f3, cz, o1, o2, and decreased theta/beta at f3, c3, cz. ADHD-inattentive also showed decreased theta/alpha at f3, and ADHD-hyperactive presented decreased theta/beta at f3 (Table 6, Figure 6). In addition, ADHD-combined group as compared to ADHD-inattentive present decreased theta/alpha at o1 and theta/beta at cz. Decrease of theta/beta at cz were also observed in ADHD-combined as compared to ADHD-hyperactive (Table 7, Figure 6).

In the second phase of analysis, comparisons of whole-brain patterns of association between IQ scores and EEG power were performed to discriminate patterns of EEG power related to IQ scores in ADHD subtypes from healthy controls (Table 8, Figure 7). ADHD-combined revealed increased correlation of IQ score with whole brain pattern of beta power, and decreased correlation of IQ score with whole-brain pattern of power at theta and alpha1 bands. ADHD-inattentive showed no significant differences, and ADHD-hyperactive/impulsive group showed decreased correlation of IQ score with whole-brain pattern of power at theta, alpha1, and beta bands as compared to the healthy control group.

[Table 6 about here]

[Table 7 about here]

[Figure 6 about here]

[Table 8 about here]
In addition, comparisons of ADHD subtypes also showed that ADHD-combined as compared to ADHD-inattentive present increased correlation of IQ score with whole-brain pattern of power at alpha2 and beta bands, while the correlation decreased at alpha1. ADHD-combined as compared to ADHD-hyperactive showed increased correlation at alpha and beta bands. ADHD-inattentive as compared to ADHD-hyperactive showed increased correlation of alpha and alpha1 to IQ scores.

4. Discussion

The present study primarily investigated association between brain functions based on absolute, and ratio power of EEG and IQ scores in various individuals within a normal range of IQ. The association pattern was then compared between three ADHD subtypes and a healthy control group. The absolute, and ratio powers were calculated in the conventional EEG frequency bands including delta, theta, alpha with its sub-bands alpha1 and alpha2, and beta. Then, association between IQ score and EEG powers was compared within the groups. Calculation of absolute power index provides reliable method to differentiate clinical and normal group (Dumermuth & Molinari, 1987). This study also represented theta/alpha and theta/beta power ratio since these ratio powers can differentiate ADHD individual from healthy control group (Clarke, Barry, McCarthy, & Selikowitz, 2002).

The association between IQ score and EEG power have shown cognitive implication which is discussed in the following. In our healthy control group association between IQ score and EEG bands showed a pattern of lateralization, more significant at the left hemisphere (frontal, temporal
and occipital regions). Several studies has associated the left hemisphere with intelligence and working memory (Basso, Spinnler, Vallar, & Zanobio, 1982), (Paulraj, Schendel, Curran, Dronkers, & Baldo, 2018), (Basso, Capitani, Luzzatti, & Spinnler, 1981). Our finding in healthy control group also showed significant association between IQ score and EEG power at theta, and alpha bands which is nicely fit with the previous studies (Klimesch, 1999a), (Yılmaz, Korkmaz, Arslan, Güngör, & Asyalı, 2014). The association was mainly observed at frontal and temporal regions. Frontal region involves in many functions such as cognition, emotional behavior, memory, language (Mundy-Castle & Nelson, 1960) and temporal region has been shown to associate with vocabulary score of Wechsler test (Dobbins & Russell, 1990) and arithmetic score as well (Inouye, Shinosaki, Iyama, & Matsumoto, 1993).

Nevertheless, pattern of association between IQ score of Ravan test and EEG power was completely different in ADHD individuals as compared to healthy control group. Our ADHD group showed decreased association between EEG bands and IQ score acquired by Ravan test as compared to healthy control group. In fact, Ravan test mainly estimates novel problem solving which is defined by solving the problems that cannot be answered directly by referring to a store of long term knowledge, but instead require analytic or fluid reasoning (Prabhakaran, Smith, Desmond, Glover, & Gabrieli, 1997). The network of brain regions involved in fluid reasoning is comprised of the fronto-polar, middle and inferior frontal gyri and parietal region (Rapport et al., 2008). These regions, more specifically frontal, also associate with working memory which is weak in ADHD’s (Rapport et al., 2008). Therefore, decreased association between EEG bands and IQ score at frontal regions in our ADHD groups is nicely fit with the deficiency of working memory and fluid reasoning acquired by Raven test in the past studies (Tamm & Juranek, 2012). In addition, our finding has implication in terms of default mode network (DMN). This network is
comprised of medial prefrontal, precuneus and angular gyrus (Raichle et al., 2001). DMN which is typically activated during resting state conditions and deactivated during task performance (Broyd et al., 2009), was reported to be an underlying cause of inadequate performance in ADHD (Sonuga-Barke & Castellanos, 2007). Decreased correlation between IQ and EEG bands in our ADHD individuals as compared to healthy control group at anterior region, plays an important role in working memory and attention (Castellanos et al., 2008), that may imply as deficits in anterior part of default mode network (DMN) in ADHD patients as reported in previous studies (Castellanos et al., 2008). In this study, patterns of correlation between IQ score and EEG power in ADHD-combined and ADHD-inattentive were similar. This finding is corroborated by former studies, suggesting similar EEG abnormality in combined and inattentive subtypes (Clarke, Barry, McCarthy, & Selikowitz, 2001a). However, the pattern for our ADHD-hyperactive is different from two other subtypes, which might be implied by small sample size of this group in the current study.

On the other hand, the ADHD individuals revealed decreased association between IQ score and power of EEG at the theta band. While, the association between IQ score and alpha power increased as compared to healthy control group. This finding shows an existence of a compensatory mechanism such that decreased theta can be compensated by increased alpha in ADHD group to keep adequate intellectual function. ADHD-combined group also showed positive association at the beta band. It has been shown that active attention and psychomotor (Polunina & Davydov, 2006) have been related to brain activities at the beta band. Therefore, positive association of EEG beta power with intelligence, in our findings, seems to be a logical pattern. There was more number of association between IQ and beta as compare to that of with alpha in our ADHD-combined group. We think this finding of combined group is in the same line with
Webster theory who suggested that in condition of serious mental activity beta replaced alpha’s place (J. G. Webster, 1978).

Moreover, unlike the healthy control group, no specific lateralization pattern was found in ADHD subtypes. The recent finding may provide additional support for the presence of a compensatory mechanism such that deficiencies in the right hemisphere are compensated by the left hemisphere to have an adequate intellectual performance.

Our findings of different association between EEG bands and IQ between the healthy controls and the ADHD groups were not limited to some specific brain regions and significant differences were also observed at the global pattern extracted from the whole brain regions. Decreased theta in all subtypes of ADHD has been shown in whole brain regions. The differential patterns of associations in local and global measures potentially implies that a dynamic change in the brain regional functions towards increasing the alpha (or beta) band activities and decreasing the laterality effect could be a compensatory mechanism to maintain a normal intelligence score in the ADHD individuals.

At ratio power our results showed a decreased theta/alpha ratio in the ADHD group (all subtypes) as compared to the healthy control group. Assuming that, theta/alpha power ratio has been introduced as a criteria for the intelligence (Markowitsch & Pritzel, 1985), it is expected that theta/alpha ratio should not be different in the IQ matched individuals. While, our findings put a question mark on the validity of the above-mentioned criteria for the intelligence in the ADHD individuals.
4.1. Limitation

The results of this study had a number of limitations. First, it was limited to a few number of ADHD-hyperactivity/impulsivity subjects as compared to other subtypes of ADHD and control group. Second, the study focused on the age range of 8-12. Since, EEG activity shifts from less to high frequency bands during maturation, more detailed developmental analysis may provide a better insight into the relationship between intelligence and EEG oscillations. Furthermore, the study performed in the eyes-close resting state, therefore, a further investigation on the task-based EEG will be helpful to strengthen the results. Although the findings are inspiring, more studies are required to test the reliability and validity of the results.

5. Conclusion

Significant changes observed in the score of association between IQ and EEG power in the ADHD individuals as compared to the IQ matched healthy control group, suggests the existence of a compensatory mechanism to hold a suitable cognitive performance (IQ) in the ADHD subjects. We conclude that the dynamic of the brain activities in addition to the specific brain structure plays a great role in intelligence. Discrepancy of theta/alpha ratio in groups with similar IQ score, may suggest weakness of this marker for intelligence. We hope that these findings could provide additional information to pave the way to better understanding of relationship between the brain functions and the intelligence.

Conflict of interest

The authors declare no financial interest.
Acknowledgment

We would like to thank Dr. Reza Rostami, Dr. Masoud Nosrat-abadi and their colleagues for their generous help on the data collection. We also would like to thank Iranian council of cognitive science and technologies for their financial support on this study.
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