Title: Brain Structural Correlates of INTELLIGENCE in ADHD Individuals

Running title: Grey Matter Density Correlates of Intelligence in ADHD

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Abstract

Neuroimaging evidences have shown the association of intelligence with several structural brain properties in normal individuals. However, this association for attention deficit hyperactivity disorder (ADHD) is need to be investigated. we estimated grey matter density of the brain using MRI scanning on 56 ADHD individuals comprising 30 combined (age=10.44±2.41, IQ=112.13±13.15, male, 24 right hand) and 26 inattentive (age=11.39±2.1, IQ=107.44±13.98, male, 28 right hand) as well as 30 IQ matched healthy control (age=11.08±2.15, IQ=115±13.56, male, 23 right hand). In this study, two statistical approaches were used. At the first approach, region based as well as whole pattern of association between full scale IQ and grey matter were computed and compared between groups. The second approach was to look at the differential pattern of grey matter density whithout considering IQ in three groups. Results showed significant differences between ADHD group and control. This finding could suggest that intelligence is not purely grounded on the density of grey matter in certain brain regions; it is a dynamic phenomenon and drastically changes in the neurodevelopmental disorders.

Keywords: ADHD, MRI, Intelligence, Grey matter density

1.Introduction

Intelligence is the capacity which involves planning, reasoning, comprehension, abstraction and learning (Gottfredson, 1997) which can predict important outcomes of the life (Deary, Johnson, & Houlihan, 2009). Therefore, understanding the biological systems taking apart intelligence could be necessary for psychological science (Deary et al., 2009). The neural basis of intelligence has been investigated by a range of neuroimaging studies including MRI (McDaniel, 2005), EEG (Thatcher, North, & Biver, 2005), PET (Tang et al., 2014), task based fMRI (Jung & Haier, 2007) and resting state fMRI (Li & Tian, 2014). Most of structural studies associated IQ with frontal and parietal lobe (Anderson et al., 2004), (Basten, Hilger, & Fiebach, 2015), (Vakhtin, Ryman, Flores, & Jung, 2014), (Jung & Haier, 2007). For instance, association between grey matter volume in the posterior cingulate cortex (PCC) and intelligence has been reported (Deary, Penke, & Johnson, 2010). Moreover, involvement of subcortical regions such as right striatum (Burgaleta et al., 2014), basal ganglia (McNab & Klingberg, 2008), hippocampus(Burgess, Maguire, & O'Keefe, 2002) and caudate (Grazioplene et al., 2015) has also been observed. In addition, the association between grey matter (GM) volume and cognitive deficits have been investigated in lesion studies as well (Karussis, Leker, & Abramsky, 2000), (Pinter, Eliez, Schmitt, Capone, & Reiss, 2001). Despite these findings, studies addressing the relationship between structures of the brain with intelligence in ADHD population are rare. In this study, we hypothesized that structural based of intelligence should not be different in normal and ADHD individuals. Therefore, 56 ADHD individuals including 30 from combined and 26 from inattentive subcategory and 30 healthy controls were scanned by magnetic resonance imaging (MRI). Then, GM densities of anatomically separated brain regions were estimated from the brain images. Subsequently, Pearson’s correlation analysis was employed to detect association between the GM densities of the brain regions and IQ. Whole pattern of association is also estimated. Then, group level analysis was performed and correlation of IQ and GM densities in ADHD groups were compared with each other as well as the healthy controls. Furthermore, differential pattern of grey matter density in three groups was observed. The main aim of the study was to know whether the association between GM density and IQ in ADHD is similar with healthy individuals or it is aligned by the disorder.

2. Method

2.1. Subjects

A number of 56 ADHD including 30 combined and 26 inattentive, as well as 30 healthy control, with similar age and IQ range underwent a session of MRI scanning. Demographic information of each group is shown in Table1. Considering age, IQ and handedness, there were no significant differences among the groups ($P<0.05$).

Table1. Demographic information

Children in the ADHD group had to meet diagnostic criteria defined by the diagnostic and statistical manual 4th edition text revision (DSM- IV-TR) for the ADHD as well as determination by parent and child answers to the KSADS-PL confirmed by a psychiatrist to be involved in this study. Exclusion criteria were comorbid mood or anxiety disorder, autistic or Asperger's disorder, medical illness that was unstable or could cause psychiatric symptoms, or substance abuse within 2 months of participation.

2.1. Assessment of cognitive performance: IQ scores

All participants completed the Wechsler Abbreviated scale of intelligence (WASI) presented in Table1. The WASI is a general intelligence, or IQ test intended to measure overall cognitive abilities or a specific cognitive capability in individuals in the age range of 6-89. (http://psycnet.apa.org/record/1955-07334-000)

The experimental validation of our proposed method was performed on a dataset gathered from 4 data centers including Kennedy Krieger institute (KKI), Oregon Health and science University (OHSU), Peking university (PEK) and New York University (NYU). These data are related to ADHD-200 global completion and publically available at "http://fcon_1000.projects.nitrc.org/indi/adhd200/".

2.2. MRI data acquisition

All participants underwent a T1-weighted high-resolution MRI scanning using a siemens3T scanner system. The imaging data were collected using the following protocols, KKI (T1: contrast enhancement, TE: shortest, TR: shortest, Flip angle: 8deg, FOV: 256mm, slice thickness: 1mm); OHSU (T1: 900 ms, TE:3.58 ms, TR: 2300 ms, flip angle: 10deg, FOV: 256 mm, slice thickness: 1.1 mm); PEK (T1: 1100 ms, TE: 3.45 ms, TR:2530 ms, flip angle: 7deg, FOV: 256mm, slice thickness: 1mm); NYU (T1: 1100 ms, TE: 3.25 ms, TR:2530 ms, flip angle: 7 deg, FOV: 256 mm, slice thickness: 1.33mm).

2.3. MRI data processing

Standard processing pipeline was performed on the MRI data using FMRIB software library (FSL: https://www.fmrib.ox.ac.uk/fsl) and analysis of functional neuroimaging (AFNI: https://afni.nimh.nih.gov/). The brain MRI images were first deobliqued, then reoriented and skull strip was removed. Then, images were registered to the MNI space. After that, MRI images were segmented into different tissue types and were parcellated either into 392 regions of interest (ROI) using MNI normalized Craddock atlas(Craddock, James, Holtzheimer, Hu, & Mayberg, 2012) or 116 regions using automated anatomical labeling AAL:(Tzourio-Mazoyer et al., 2002).

Results of Craddock method is presented in the main text body and results of the AAL parcellation is provided in the supplementary materials.

2.6. Statistical analysis

Pearsons'correlation was calculated between IQ and GM Densities of separate brain regions and significant associations were recognized by putting a threshold of $p<0.05$. Then statistical analysis was performed using 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). Then, the Brain Net viewer (Xia, Wang, & He, 2013) was used for visualization of the significant results. Whole pattern of association is also acquired using SPSS. We also observed differential pattern of grey matter density in groups as second approach. (see Figure1)

Fig1. Schematic of experimental design.

It should be mentioned that suggested ROIS in the Craddock atlas were too fragmented (392 regions), so for the ease of presentation, the significant results were re indexed to the frontal, occipital, temporal, parietal, cerebellum and subcortical structures.

3. Results

3.1 Significant structural correlates of IQ

Association between IQ scores and grey matter densities were found in several brain regions. Detailed information of significant results ($p<0.05$) are demonstrated in Table2-4, and Fig2-4. Significant positive associations between grey matter density and intelligence are shown in red and negative association are shown in blue.

In ADHD combined group, positive correlation between IQ scores and grey matter density was observed in the frontal region (inferior operculum and orbitofrontal at the right side), temporal region (Superior parts in the left hemisphere, inferior part in the right hemisphere and middle part bilaterally) , occipital region (inferior part bilaterally), cerebellum (CRB 4-5 in the left hemisphere and CRB-Crus1, in the right side and CRB-Crus2 bilaterally), angular gyrus in the right side, fusiform in the right side, and the precentral region on the right side. In addition, negative correlations were also observed in the left inferior temporal region and left fusiform area (Fig2, Table2).

Fig2. Significant association between grey matter density and intelligence in ADHD combined group
Abbreviation: PreC: Precentral; ANG: Angular; Te-Mid: Middle Temporal; Te-Inf: Inferior Temporal; Te-Sup: Superior Temporal; Oc-Inf: Inferior Occipital; CRB: Cerebellum; CEB-Crus1: Cerebellum Crus1; CRB-Crus2: Cerebellum- Crus2; Fr-Inf-Oper: Inferior Operculum; Fr-Inf-Orb: Inferior Orbito frontal; FF: Fusiform.

Table2. Significant association between grey matter density and intelligence in ADHD combined group

In ADHD inattentive group, no significant negative correlation was observed between IQ and grey matter density of the brain regions. While, positive correlation was identified in bilateral fusiform areas, caudate and cerebellum crus1 and inferior parietal region at the right hemisphere (Fig3, Table3)

Fig3. Significant association between grey matter density and intelligence in ADHD inattentive group
Abbreviation: Pa-Inf: Inferior Parietal; FF: Fusiform; CAD: Caudate; CRB-Crus1: Cerebellum Crus1

Table3. Significant association between grey matter density and intelligence in ADHD inattentive group

In the healthy control group, significant positive correlations were observed bilaterally in the precuneus, and fusiform. In the left hemisphere, positive association was seen at the temporal regions (inferior and superior part of temporal pole), calcarine, superior occipital, middle frontal regions. In the right hemisphere, positive association was observed at cerebellum 6, frontal inferior operculum, cingulate cortex. Moreover, negative correlation was also identified in in the left side of superior medial frontal cortex (Fig.4, Table4).

Fig4. Significant association between grey matter density and intelligence in healthy control group
Abbreviation: PreCUN: Precuneus; CG-Mid: Middle Cingululate; Fr-Inf-Oper: Frontal inferior operculum; CRB6: Cerebellum6; Oc-Superior: Superior Occipital; CAL: Calcarine; FF: Fusiform; Te-Inf: Inferior Temporal; Te-Pol-Sup: Superior Temporal Pole; Fr-Mid: Middle Frontal; Fr-Sup-Med: Medial Superior Frontal

Table4. Significant association between grey matter density and intelligence in healthy control group

Comparing cluster size of each section showed that the most significant association for the ADHD-combined group, are located in the temporal, cerebellum, and frontal regions. In ADHD-inattentive group the most significant association was located at the temporal, subcortical region and cerebellum. And in the health control group the most significant association was observed in the temporal, frontal and parietal regions (Table5).

Table5. Total significant associated cluster size with intelligence in brain lobes as well as cerebellum and subcortical region

Results of association between grey matter density and intelligence via AAL parcellations are presented in the supplementary materials (Fig8-10, Table8)

3.2. Group comparison

Significant results of comparing associations (correlations) observed in each group are illustrated in the Fig 5-7, and Table 6 (Significant P values have been bolded in Table6). Significant increased associations between grey matter density and intelligence are shown in red and decreased association are shown in blue.

Table6. Comparing association between grey matter density and intelligence in ADHD combined, ADHD inattentive and health control groups

Comparing ADHD combined versus ADHD inattentive showed significantly increased associated grey matter density with intelligence at superior temporal and cerebellum-6 in the left hemisphere and angular region in the right hemisphere. Decreased associated grey matter density with intelligence were observed at middle cingulate in right side (Figure5).

Fig5. Comparing significant association between grey matter density and intelligence in ADHD combined versus ADHD inattentive group
Abbreviation: Te-Sup: Superior Temporal; ANG: Angular; CG-Mid: Middle Cingulate; CRB-6: Cerebelum6

ADHD combined as compare to healthy control had increased association of grey matter density with intelligence at middle temporal and middle orbitofrontal in right hemisphere as well as rectus and superior parietal in left side. Decreased association of grey matter density were seen at inferior occipital, medial orbitofrontal and superior frontal in right hemisphere (Figure6).

Fig6. Comparing significant association between grey matter density and intelligence in ADHD combined versus health control group
Abbreviation: Te-Mid: Middle Temporal; Oc-Inf: Inferior Occipital; Pa-Sup: Superior Parietal; Fr-Mid-Orb: Middle orbito frontal; Fr-Sup: Superior frontal; REC: Rectus

ADHD inattentive as compare to health control group showed Increased associated gray matter density with intelligence at middle and anterior cingulate and superior motor area in right hemisphere as well as precuneus, superior parietal and rectus in left side. Decreased association of grey matter density with intelligence was observed at inferior occipital, putamen, caudate, medial orbitofrontal and precentral region in right hemisphere as well as middle occipital and cerebellum6 in left side (Figure7).

Fig7. Comparing significant association between grey matter density and intelligence in ADHD inattentive versus health control group

Abbreviation: CG-Ant: Anterior Cingulate; CG-Mid: Middle Cingulate; Oc-Inf: Inferior Occipital; Oc-Mid: Middle Occipital; PUT: Putamen; SMA: Superior Motor Area; CAD: Caudate; PreCUN: Precuneus; Pa-Sup: Superior parietal; Fr-Med-Orb: Medial orbito frontal; CRB6: Cerebelum6; REC: Rectus; PreC: Precentral

As compare to healthy control, both ADHD groups (combined and inattentive) had increased associated grey matter density with intelligence at superior parietal and rectus in left hemisphere, while decreased associated grey matter density with intelligence was seen at inferior occipital and medial frontal in right side. Results from comparing association between grey matter density and intelligence via AAL are presented in supplementary materials (Figure 11-13, Table9).

Multiple comparison of whole pattern of association in brain also showed differences between groups. Although ADHD combined had significant difference with other groups, this was not in case for ADHD inattentive group (Table7), (Figure21in supplementary materials).

Table7. Multiple comparison of whole pattern of association

We also compare raw data of grey matter density to show structural differences in terms of grey matter density whithin groups. Results from CC400 are shown in Table 10, Figure 15-17 and those of AAL116 are presented in Table 11, Figures 18-20 in supplementary material).

4. Discussion

The attention deficit and hyperactivity disorder is suggested to be a heritable phenotype which could be influenced by the genetic factors. Therefore, the genetic could influence morphometric properties of the brain in ADHD which has been reported in the previous studies (Bellgrove et al., 2005; Swanson et al., 2007). In fact, the intelligence is also a heritable phenotype and overlapping effects of genetic on the intelligence score and the ADHD also could be investigated. In the case that IQ score is only related to the morphometry properties of the brain, there should not be any significant differences between IQ matched ADHD and control individuals. Otherwise relationship between IQ score and the brain anatomy follows another mechanism which we are investigating in this study. In this study, the regional GM density and full-scale IQ were compared between two groups of ADHD subtypes including combined and inattentive, and a healthy control group. Two different parcellation strategies including functionally separated regions (CC400) and anatomically separated regions (AAL116) were applied to detach the brain to 392 and 116 regions, respectively. After statistical analysis, it was observed that association of IQ with regional GM density is mainly positive and located at the right hemisphere. The right hemisphere plays an important role in the cognition (Robertson, 2014), language (Gainotti, 2013), arithmetic (Knops & Willmes, 2014) and visuospatial attention (Longo, Trippier, Vagnoni, & Lourenco, 2015). Interestingly, these findings are not impressed by the parcellation technique and the results of CC400 were almost the same of AAL116.

The changes of grey matter density may alter behavior and cognitive functions that are discussed in the following. Our findings of healthy control group, showed significant positive association between grey matter density and IQ score at inferior and middle frontal, precuneus, fusiform, inferior temporal, calcarine, superior occipital, middle cingulum and cerebelum6. The inferior frontal, is involved in selecting responses under uncertain situations (Frangou, Chitins, & Williams, 2004) and reasoning ability (Goel, Gold, Kapur, & Houle, 1997) and association of frontal and parietal with intelligence has been shown in previous studies (Jung & Haier, 2007). Another finding was the inferior part of temporal lobe which has been shown that plays a role in the analysis of visual form, motion and representation of individuals and is directly related to the intelligence score (Frangou et al., 2004). Our results about fusiform may also reflects its role in the language skill (Tan et al., 2011), recognition and elaboration on the visual inputs (Colom et al., 2009). Furthermore, significant association between cingulum grey matter density and IQ, observed in this study, in the healthy control group may also reflect its role in spatial learning and memory (Aggleton, Neave, Nagle, & Sahgal, 1995). Last but not least, the association of cerebellum GM density with the intelligence has also been reported in the previous studies (Stoodley & Schmahmann, 2009). These findings present a confirmation on the results as compare to the previous studies.

On the other hand, the ADHDs showed a significant different mechanism, pattern of association between GM density and intelligence, as compare to the healthy controls. Comparing whole pattern of association, also suggest discrepancy whithin groups. Differences between ADHD combined and control group was more significant than those of between ADHD inattentive and control, which seems rational because of more severe symptoms of deficiency in ADHD combined.

In fact, the IQ score represents a score for verbal and visual abilities, fluid reasoning, working memory, and the processing speed (Wechsler, 1949). In previous studies, strengths and weakness of ADHD individuals in these cognitive functions have been reported (Frazier, Demaree, & Youngstrom, 2004). Mayes group has tried to suggest a neurobiological basis for ADHD by emphasizing on the strengths of ADHD in verbal and visual reasoning and their weakness in attention, processing speed and graph motor skill (Mayes & Calhoun, 2006). Given that the ADHD and healthy control groups in our study are IQ matched, observed differences of associated GM density with IQ between ADHD and healthy control group, may suggest a compensatory mechanism in ADHD to maintain an adequate performance. This mechanism could be discussed on the finding of our investigation. In ADHD groups, both combined and inattentive, a decreased association between grey matter density and intelligence score was observed at the right inferior occipital and right medial frontal regions. The inferior occipital region involves in visual imaging (Goldenberg et al., 1989) and medial frontal engages in the switching tasks (Rushworth, Hadland, Paus, & Sipila, 2002). In contrast, an increased association was observed at the left superior parietal and the left rectus. The superior parietal region involves in the manipulation of information in working memory (Koenigs, Barbey, Postle, & Grafman, 2009) and the rectus is engaged in the paradigm of reward learning (Kringelbach, 2005). Therefore, lessened association between GM density and intelligence in the right hemisphere (inferior occipital and medial frontal) could be considered to be compensated with increase of association in the left hemisphere (superior parietal and rectus). This mechanism will help the ADHD subject to maintain in an adequate level of cognitive performance.

Comparing row data of grey matter density in groups also reinforced the idea of compensatory mechanism. In that, grey matter differences between ADHD inattentive and control group in our study was more than that of between ADHD combined and control. This alteration in grey matter density may help ADHD inattentive individuals to compensate their brain deficiency and better performance as compare to ADHD combined.

Previous studies have shown that cortical compensatory mechanism can cope with deficit in several cognitive process in ADHD (Ma et al., 2012). Hence, different association between regional grey matter density with the IQ score in the ADHD and control group may indicate that brain structure is not the single determiner of intelligence; rather intelligence may also be underpinned by neural dynamics of the brain.

4.1. limitation

The results of this study had a number of limitations; for example, correlation was done for full scale IQ and WISC subtests were not analyzed. Moreover, this study only focused on the age range of 8 to 13 years on the male participants which could be extended in future works. Therefore, a developmental study on both genders could provide additional insights into the mechanism of structural changes in brain involved with intelligence.

5. Conclusion

To our knowledge this is the first study that investigates brain structural correlates of IQ in the ADHD individuals. The study provides an evidence that IQ may be closely related to GM density of particular brain regions but the pattern could be influenced by a disorder. Significant changes observed in the association scores of the ADHD individuals as compare to the healthy controls suggests a compensatory mechanism to hold a suitable cognitive performance (IQ). Our findings indicate that, IQ score may be affected by the neural dynamics, therefore, the structural covariates could be a better alternative for the GM density. We hope that these findings could provide additional information to pave the way to better understand relationship between the brain morphometry and the intelligence.

Conflict of interest

The authors declare no conflict of interest.

Author contribution

All authors contributed in data analysis. F.F wrote the manuscript and R. K edited and prepared it for submission.

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References

Aggleton, J. P., Neave, N., Nagle, S., & Sahgal, A. (1995). A comparison of the effects of medial prefrontal, cingulate cortex, and cingulum bundle lesions on tests of spatial memory: evidence of a double dissociation between frontal and cingulum bundle contributions. *Journal of Neuroscience, 15*(11), 7270-7281.

Anderson, J. R., Bothell, D., Byrne, M. D., Douglass, S., Lebiere, C., & Qin, Y. (2004). An integrated theory of the mind. *Psychological review, 111*(4), 1036.

Basten, U., Hilger, K., & Fiebach, C. J. (2015). Where smart brains are different: a quantitative meta-analysis of functional and structural brain imaging studies on intelligence. *Intelligence, 51*, 10-27.

Bellgrove, M. A., Hawi, Z., Lowe, N., Kirley, A., Robertson, I. H., & Gill, M. (2005). DRD4 gene variants and sustained attention in attention deficit hyperactivity disorder (ADHD): effects of associated alleles at the VNTR and− 521 SNP. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, 136*(1), 81-86.

Burgaleta, M., MacDonald, P. A., Martínez, K., Roman, F. J., Álvarez-Linera, J., González, A. R., . . . Colom, R. (2014). Subcortical regional morphology correlates with fluid and spatial intelligence. *Human brain mapping, 35*(5), 1957-1968.

Burgess, N., Maguire, E. A., & O'Keefe, J. (2002). The human hippocampus and spatial and episodic memory. *Neuron, 35*(4), 625-641.

Colom, R., Haier, R. J., Head, K., Álvarez-Linera, J., Quiroga, M. Á., Shih, P. C., & Jung, R. E. (2009). Gray matter correlates of fluid, crystallized, and spatial intelligence: Testing the P-FIT model. *Intelligence, 37*(2), 124-135.

Craddock, R. C., James, G. A., Holtzheimer, P. E., Hu, X. P., & Mayberg, H. S. (2012). A whole brain fMRI atlas generated via spatially constrained spectral clustering. *Human brain mapping, 33*(8), 1914-1928.

Deary, I. J., Johnson, W., & Houlihan, L. M. (2009). Genetic foundations of human intelligence. *Human genetics, 126*(1), 215-232.

Deary, I. J., Penke, L., & Johnson, W. (2010). The neuroscience of human intelligence differences. *Nature reviews. Neuroscience, 11*(3), 201.

Diedenhofen, B., & Musch, J. (2015). cocor: A comprehensive solution for the statistical comparison of correlations. *PloS one, 10*(4), e0121945.

Frangou, S., Chitins, X., & Williams, S. C. (2004). Mapping IQ and gray matter density in healthy young people. *Neuroimage, 23*(3), 800-805.

Frazier, T. W., Demaree, H. A., & Youngstrom, E. A. (2004). Meta-analysis of intellectual and neuropsychological test performance in attention-deficit/hyperactivity disorder. In: American Psychological Association.

Gainotti, G. (2013). The contribution of language to the right-hemisphere conceptual representations: A selective survey. *Journal of clinical and experimental neuropsychology, 35*(6), 563-572.

Goel, V., Gold, B., Kapur, S., & Houle, S. (1997). The seats of reason? An imaging study of deductive and inductive reasoning. *NeuroReport, 8*(5), 1305-1310.

Goldenberg, G., Podreka, I., Steiner, M., Willmes, K., Suess, E., & Deecke, L. (1989). Regional cerebral blood flow patterns in visual imagery. *Neuropsychologia, 27*(5), 641-664.

Gottfredson, L. S. (1997). Mainstream science on intelligence: An editorial with 52 signatories, history, and bibliography. In: JAI.

Grazioplene, R. G., G Ryman, S., Gray, J. R., Rustichini, A., Jung, R. E., & DeYoung, C. G. (2015). Subcortical intelligence: Caudate volume predicts IQ in healthy adults. *Human brain mapping, 36*(4), 1407-1416.

Jung, R. E., & Haier, R. J. (2007). The Parieto-Frontal Integration Theory (P-FIT) of intelligence: converging neuroimaging evidence. *Behavioral and Brain Sciences, 30*(2), 135-154.

Karussis, D., Leker, R., & Abramsky, O. (2000). Cognitive dysfunction following thalamic stroke: a study of 16 cases and review of the literature. *Journal of the neurological sciences, 172*(1), 25-29.

Knops, A., & Willmes, K. (2014). Numerical ordering and symbolic arithmetic share frontal and parietal circuits in the right hemisphere. *Neuroimage, 84*, 786-795.

Koenigs, M., Barbey, A. K., Postle, B. R., & Grafman, J. (2009). Superior parietal cortex is critical for the manipulation of information in working memory. *Journal of Neuroscience, 29*(47), 14980-14986.

Kringelbach, M. L. (2005). The human orbitofrontal cortex: linking reward to hedonic experience. *Nature Reviews Neuroscience, 6*(9), 691-702.

Li, C., & Tian, L. (2014). Association between resting-state coactivation in the parieto-frontal network and intelligence during late childhood and adolescence. *American Journal of Neuroradiology, 35*(6), 1150-1156.

Longo, M. R., Trippier, S., Vagnoni, E., & Lourenco, S. F. (2015). Right hemisphere control of visuospatial attention in near space. *Neuropsychologia, 70*, 350-357.

Ma, J., Lei, D., Jin, X., Du, X., Jiang, F., Li, F., . . . Shen, X. (2012). Compensatory brain activation in children with attention deficit/hyperactivity disorder during a simplified Go/No-go task. *Journal of neural transmission, 119*(5), 613-619.

Mayes, S. D., & Calhoun, S. L. (2006). WISC-IV and WISC-III profiles in children with ADHD. *Journal of Attention Disorders, 9*(3), 486-493.

McDaniel, M. A. (2005). Big-brained people are smarter: A meta-analysis of the relationship between in vivo brain volume and intelligence. *Intelligence, 33*(4), 337-346.

McNab, F., & Klingberg, T. (2008). Prefrontal cortex and basal ganglia control access to working memory. *Nature neuroscience, 11*(1), 103.

Pinter, J. D., Eliez, S., Schmitt, J. E., Capone, G. T., & Reiss, A. L. (2001). Neuroanatomy of Down's syndrome: a high-resolution MRI study. *American Journal of Psychiatry, 158*(10), 1659-1665.

Robertson, I. H. (2014). A right hemisphere role in cognitive reserve. *Neurobiology of Aging, 35*(6), 1375-1385.

Rushworth, M., Hadland, K., Paus, T., & Sipila, P. (2002). Role of the human medial frontal cortex in task switching: a combined fMRI and TMS study. *Journal of neurophysiology, 87*(5), 2577-2592.

Stoodley, C. J., & Schmahmann, J. D. (2009). Functional topography in the human cerebellum: a meta-analysis of neuroimaging studies. *Neuroimage, 44*(2), 489-501.

Swanson, J. M., Kinsbourne, M., Nigg, J., Lanphear, B., Stefanatos, G. A., Volkow, N., . . . Wadhwa, P. D. (2007). Etiologic subtypes of attention-deficit/hyperactivity disorder: brain imaging, molecular genetic and environmental factors and the dopamine hypothesis. *Neuropsychology review, 17*(1), 39-59.

Tan, L. H., Chen, L., Yip, V., Chan, A. H., Yang, J., Gao, J.-H., & Siok, W. T. (2011). Activity levels in the left hemisphere caudate–fusiform circuit predict how well a second language will be learned. *Proceedings of the National Academy of Sciences, 108*(6), 2540-2544.

Tang, Z., Chen, Z., Zhai, Q., Hao, Y., Zhang, Y., & Zeng, X. (2014). Correlation between interictal cerebral glucose hypometabolism and IQ in children with epilepsy. *Epilepsy & Behavior, 31*, 15-18.

Thatcher, R. W., North, D., & Biver, C. (2005). EEG and intelligence: relations between EEG coherence, EEG phase delay and power. *Clinical neurophysiology, 116*(9), 2129-2141.

Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., . . . Joliot, M. (2002). Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage, 15*(1), 273-289.

Vakhtin, A. A., Ryman, S. G., Flores, R. A., & Jung, R. E. (2014). Functional brain networks contributing to the parieto-frontal integration theory of intelligence. *Neuroimage, 103*, 349-354.

Wechsler, D. (1949). Wechsler intelligence scale for children.

Xia, M., Wang, J., & He, Y. (2013). BrainNet Viewer: a network visualization tool for human brain connectomics. *PloS one, 8*(7), e68910.

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Table2. significant association between grey matter density and intelligence in ADHD combined group

Table3. Significant association between grey matter density and intelligence in ADHD inattentive group

Table4. Significant association between grey matter density and intelligence in healthy control group

Table5. Total significant associated cluster size with intelligence in brain lobes as well as cerebellum and subcortical region

Table6. Comparing association between grey matter density and intelligence in ADHD combined, ADHD inattentive and healthy control groups

Table7. Multiple comparison of whole pattern of association

Table8. Significant association between grey matter density and intelligence in ADHD combined, ADHD inattentive and healthy control groups (AAL)

Table9. Comparing association between grey matter density and intelligence in ADHD combined, ADHD inattentive and healthy control groups (AAL)

Table10. Comparing grey matter density in ADHD combined, ADHD inattentive and health control group (CC400)

Table11. Comparing grey matter density in ADHD combined, ADHD inattentive and health control group (AAL)