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Full title: A review of magnetic resonance imaging (MRI) and functional magnetic resonance imaging (fMRI) studies focusing on brain structures and morphologies related to Attention Deficit Hyperactivity Disorder (ADHD)

Short title: A review of MRI and fMRI studies focusing on brain structures related to ADHD

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Abstract

Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder that has unique brain structures associated with it. These brain areas are interspersed throughout the brain and include cortical structures, subcortical structures, and deep brain structures. This review compiles the studies implicated in ADHD from 2011 until the present, 2021. There are main areas that have consistently been reported to be involved in ADHD, such as prefrontal cortex regions, anterior cingulate cortex, basal ganglia, putamen, caudate nucleus, etc. Despite increased research, many areas will need further research before any conclusions can be made as to their involvement in ADHD. This review helps to further support that ADHD is a unique disorder that has specific brain morphologies.

Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) is a form of neurodevelopmental disorder. Neurodevelopmental disorders are characterized by onset during the developmental period that induces deficits that result in impairment of functioning [1]. Neurodevelopmental disorders include autism spectrum disorder (ASD), intellectual disability (ID), and ADHD. There

are many ways to define ADHD. The classification most commonly used is the DSM-V. However, as the DSM-V edition was published in 2013 there are still cases where the diagnosis criteria of the DSM-IV may be used. The DSM-V defines ADHD as a persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development, as characterized by symptoms of inattention and/or hyperactivity. These symptoms need to be present in two or more settings. Several inattention and/or hyperactivity-impulsivity symptoms must have been present prior to age 12 years. Additionally, the symptoms experienced need to interfere with or reduce the quality of social, academic, or occupational functioning [2].

ADHD can be further classified into different presentation types. These presentation types are combined, predominantly inattentive, or predominantly hyperactive/impulsive. The presentation types are determined by the type of symptoms that a person experiences. Combined presentation refers to a person experiencing both inattentive and hyperactive-impulsive symptoms equally. The inattentive presentation can be conceptualized as experiencing or performing "too little". Examples of inattentive symptoms are commonly losing items necessary for a task and/or difficulty with sustained attention. Hyperactive-impulsivity can be conceptualized as experiencing and/or performing "too much"; examples of hyperactive-impulsivity symptoms include being constantly on the go and/or talking excessively. [2] The full list of ADHD symptoms can be found in Table 1.1.

ADHD is not a purely behavioral disorder. ADHD at its core is an impairment of cognitive functioning. These impairments are typical of non-emotional processing such as executive functioning, attention, and reward pathways. Many of these functions have distinct brain areas and structures associated with them. Areas of executive functioning, in general, included the frontal lobe and its projections. The prefrontal cortex (PFC) has long been known to

be involved in attention. The reward pathway has been found to include areas such as the ventral striatum and limbic cortex. [3] ADHD has been shown to have structural abnormalities as well as functional differences in many of these areas.

ADHD is a pervasive chronic disorder that impacts adults and children as well as people of all genders and ethnic backgrounds. The worldwide prevalence of ADHD is 5.29%. [4] The adult prevalence is estimated to be about 4.4%. [5, 15] The childhood prevalence of ADHD in the United States of America is 9.4%. [6] Additional prevalence information to consider is that ADHD is more common in certain demographics. For example, ADHD is more common in males than females. Furthermore, ADHD is more common amongst non-white Hispanic people than other ethnicities. [5]

The prevalence of ADHD is increasing every year in both children and adults. The reason for this increase in children has to do with changes in the diagnostic and treatment practices of ADHD, greater awareness, and better access to healthcare. [7] Additionally, the changes from the DSM-IV to the DSM-V may have resulted in a greater amount of adults being diagnosed with ADHD. [8] These increases reflect the fact that more people are receiving the support that they require. Current studies show that only 44.02% of people with ADHD will receive any form of treatment in their lifetime. This treatment also occurs later in life with the average age of first treatment as 18.65 years. [9] In other words, over half of the people diagnosed with ADHD will receive no support, and the ones that do will receive support will do so years after their initial onset of symptoms and impairment. By highlighting the fact that ADHD is a brain disorder, the number of people who receive a diagnosis, and then treatment, may be increased. This emphasis may also help to reduce the stigma associated with ADHD.

With the number of people impacted by ADHD increasing, there is a heightened need for further research of this disorder. Despite ADHD being a well-known and well-researched disorder in regard to symptoms and behavioral presentations, much of this disorder's neuronal mechanisms and neurobiology are still unknown. There is little doubt that ADHD is a disorder of the brain; however, the exact areas and their functional significance remain areas of current research. The present research has many conflicting studies and results. These conflicting results are likely due to the different presentations of ADHD not being controlled for in studies. [10] ADHD has a wide variety of clinical presentations and subtypes.

In this review, the morphological and functional differences of brain structure associated with ADHD will be examined. The structures examined have been organized into three broad categories which are cortical structures, subcortical structures, and deep structures. The articles in this review are from 2011 until the present, 2021. The studies used in this review have controlled for the different presentations of ADHD. This review did not exclude articles where comorbidities and/or stimulant use were present in participants as such factors have been found to not result in significant changes in brain structure and/or function. [11]

Cortical structures

Lobar regions

Frontal lobe. The right and left frontal lobes were found to have reduced cortical thickness and lower volumes in combined type ADHD compared to controls. [12] The frontal lobe has cortical thickness differences (CT) associated with ADHD compared to controls, these differences were only present in the right hemisphere. [13] The following areas have reduced cortical thickness in children with ADHD: the superior frontal gyrus, the paracentral lobule, and the rostral middle frontal area. [13] Adolescents with ADHD had decreased cortical thickness on

the lateral surface of the right frontal lobe, this includes the superior frontal gyrus, rostral middle frontal area, and precentral gyrus. [13] When the functional activity of the frontal lobe was examined it was found that there was reduced activation in the bilateral superior frontal gyri and left medial frontal gyri. This result was present while participants performed the N-Back task which measures working memory and inhibition of irrelevant stimuli. [10] In Stop-Tasks, which require response inhibition, children with ADHD activated certain brain areas less than controls; these less activated areas were the bilateral inferior frontal gyrus, right superior frontal gyrus, and the right middle frontal gyri. [10] This abnormal activation in the right superior frontal gyrus decreased in older children with ADHD. [10]. There have been unique functional activations that are associated with ADHD subtypes in the frontal lobe. Inattentive and hyperactive-impulsivity forms of ADHD are linked to decreased activation of the right medial frontal gyrus. On the other hand, combined-type ADHD has been found to have less activation in the right superior frontal gyrus and right inferior frontal gyrus. In Go/no-go tasks that measure response inhibition, people with ADHD were found to have reduced activation in the left medial frontal gyrus. [10]

Temporal lobe. The left temporal lobe was found to have significantly lower volumes and cortical thickness in combined type ADHD compared to controls. [12] The temporal lobe had cortical thickness differences (CT) associated with ADHD compared to controls: this difference was only present in the right hemisphere. [13] Adolescents with ADHD have a greater cortical thickness on the lateral surface of the right temporal lobe. [13] Combined type ADHD is associated with reduced activation of the left fusiform gyrus. [10] The medial temporal gyrus (MTG) has reduced functional connectivity in ADHD when compared to controls. [16]

Parietal lobe. There was the greatest anatomical difference of volume, surface area, and cortical thickness between the control and the ADHD combined group in the bilateral parietal

lobes. This effect was present even after controlling for intracranial volume (ICV). [12] The partial lobes volumes were 9.4 % smaller in the left parietal lobe and 8.4% smaller in the right partial lobe in the ADHD combined group than in the control group. [12] The parietal lobe had cortical thickness differences (CT) associated with ADHD compared to controls, this difference was only present in the right hemisphere. [13] Areas that had increased cortical thickness in children with ADHD was the pericalcarine area. In children with ADHD, the precuneus had reduced cortical thickness compared to neurotypical people. [13]. Adolescents with ADHD were found to have reduced cortical thickness of the superior partial and postcentral areas. Adults with ADHD had increased cortical thickness in the superior parietal surface. [13]

Occipital lobe. One study using a voxel-based-meta-analyses (VBM) comparison when covarying for age and sex found that the left occipital lobe showed a reduction of GMV in the ADHD group compared to both the control group and the OCD group; this result was disorder specific to ADHD. [15] The occipital lobe had cortical thickness differences (CT) associated with ADHD compared to controls, this difference was only present in the right hemisphere. [13] Areas that had increased cortical thickness in children with ADHD are the right occipital lobe, lingual gyrus, and cuneus. [13] Adolescents with ADHD have a greater cortical thickness of the occipital lobes. [13] Combined type ADHD in Adults and children is correlated with a negative difference in the left inferior occipital gyrus. [10] Furthermore, combined type ADHD is linked to greater activation of the right lingual gyrus. [10]

Pre-Frontal cortex (PFC)

Dorsolateral prefrontal cortex and Dorsomedial prefrontal cortex. The study Bayard et. al 2020, found that there was a decrease in GMV in the dm/dl PFC in people with ADHD. The study also found the surface areas in dl/dm PFC was negatively correlated with ADHD. These

results were still present for ADHD when Conduct disorder (CD) scores were controlled for. [14] The study done by Bayard et al., 2020 divided ADHD scales into Hyperactivity/Impulsivity scores and Inattention scores; this showed that both subtypes contributed to the structural effects in the dl/dm PFC. An additional result of the study was that no cortical thickness differences in the dl/dm PFC were correlated with ADHD traits. [14]

Ventrolateral prefrontal cortex (vl-PFC). The vl-PFC was not found to have any significant anatomical morphologies related to ADHD traits. [14] When using FMRI the ADHD group was found to have bilateral underactivation in the vl-PFC when compared to healthy controls and the OCD group. [15] In other words, although the vl-PFC was not found to have any structural features associated with ADHD; there were functional differences present unique to ADHD.

Medial prefrontal cortex MPFC. While using a VBM comparison, one study found that the ADHD group had decreased GMV in MPFC compared to controls. [15]

Orbital frontal cortex. One study found that ADHD traits were significantly correlated to smaller GMV in the orbital frontal cortex after controlling for CD trait. [14] Another study found that when using VBM people with ADHD had decreased GMV in the ventral medial OFC when comparing ADHD to controls. This result was not unique to ADHD as this result of decreased GMV in the vm-OFC was present in the OCD group as well. [15]

Limbic lobe

Anterior cingulate cortex. When examining function studies, it was found the ACC has reduced activation in ADHD inattentive type children during go/no-go tasks and reading fluency tasks. This reduced activation could be due to the ACC's involvement in error monitoring. [16] A disorder-specific finding of ADHD is a reduced surface area and gray matter volume in the

caudal anterior cingulate cortex (cACC). These results were found after controlling for CD scores. [14] The study Bayard et al. 2020, divided ADHD scales into Hyperactivity/Impulsivity scores and Inattention scores; the results showed that both subtypes contributed to the structural effects in the cACC. [14] This study did not find any cortical thickness differences that were correlated with ADHD traits. (14) A different study by Norman et al. used VBM to find that the rostral anterior cingulate cortex (rACC) of the ADHD group had decreased GMV when compared to controls. [15]. These VBM results conflict with the results from the Bayard et al., 2020 study. These conflicting results can be explained by methodological differences between the two studies. The Norman et al., 2016 study was comparing ADHD and OCD groups, while the Bayard et al., 2020 study compared ADHD and CD groups. The Norman study did not control for Conduct disorder comorbidities within the ADHD group; therefore, the rACC result is not due to ADHD but rather to CD. Overall, the cACC reduced GMV is a disorder specific finding associated with ADHD, while the rACC decreased GMV is a disorder-specific finding of CD. These disorder-specific findings can be best summarized in the Figure 1.1 in the Tables and Figures section of this paper.

Other cortex areas

Insula. There was disorder-specific GMV reduction in the anterior posterior insula in the ADHD group when compared to the OCD group after covarying for age and sex. [15] When using VBM to examine anatomical differences associated with ADHD, a decrease in GMV in both the anterior and posterior insula was observed when compared to controls. [15] When comparing the ADHD group to the OCD group using VBM it was found that there was decreased GMV in the ADHD group. The OCD group presented with an opposite result and an increase in GMV. When using fMRI , it was reported that the ADHD group had bilateral

underactivation of the insula when compared to the healthy controls. [15] An additional result using fMRI data was that the ADHD group had bilateral underactivation in the posterior insula when compared to OCD. [15] Although both comparisons showed an underactivation, there seems to be a unique involvement with the posterior insula which is disorder-specific to ADHD. Overall, the differences in structure and function further demonstrate the differences between ADHD and similar disorders of impaired inhibition such as OCD. The ADHD forms inattentive and hyperactivity-impulsivity have been found to have decreased activation in the right insula. [10]

Supplementary motor area SMA. The supplementary motor area (SMA) has been found to have underactivation in people with ADHD when compared to controls. [15] In children with predominantly inattentive type of ADHD, the SMA was found to have reduced activation while performing executive functioning tasks such as the go/no-go tasks and during reading fluency tasks. [16] This reduced activation during go/no-go tasks is a disorder-specific result, as this underactivation is present in children with ADHD diagnosis and children with a comorbid diagnosis of ADHD and reading disability. [16] If a child only has a diagnosis of reading disability, then the underactivation in the SMA is not present.

Subcortical Structures

Limbic system: Amygdala. When using VBM and covarying for age there has been a bilateral GMV reduction in the amygdala in the ADHD group compared to the OCD group. [15] The amygdala has been found to have decreased volume when compared to neurotypical controls. [11] This result has clinical importance as it links emotional regulation problems to ADHD. [11] Emotional dysfunction is not currently included with the DSM-V symptomatic definitions of ADHD.

Diencephalon: Thalamus. The thalamus does not have any anatomical morphologies associated with ADHD. There have been function differences with ADHD associated with this area. In both inattentive and hyperactive-impulsivity ADHD types, the left thalamus had decreased activation. [10] Within the right thalamus, older people with ADHD had lower activation compared to their younger ADHD counterparts. [10] This change could be explained through the change in clinical symptoms that occur in the transition from childhood to adulthood. Adults with ADHD typically have less pronounced hyperactive-impulsive symptoms while inattentive symptoms persist. [10]

Deep brain structures

Basal ganglia. The basal ganglia is a collection of structures; therefore, studies have different classifications of the basal ganglia. Using VBM and covarying for age, a bilateral reduction in GMV had been found in the ADHD group compared to the OCD group. This result is disorder-specific to ADHD. [15] Using VBM, the ADHD group had been found to have decreased GMV in the right basal ganglia when compared to controls. [15] Basal ganglia had reduction in total surface area and volume in people with ADHD. [3]

Dorsal Striatum: Putamen. The putamen has been found to have reduced volume in people with ADHD. [11] Using VBM to compare the ADHD and OCD groups, results found were that the ADHD group had decreased GMV in the right while this area had an increase in GMV in the OCD group. [15] Using FMRI data, the ADHD group was found to have bilateral underactivation of the putamen when compared to both controls and the OCD group. [15] These results were compiled and used to complete a multimodal analysis which showed an overlapping cluster in the right putamen that had decreased GMV and decreased activation in people with ADHD compared to controls. This was a disorder-specific to ADHD and showed no overlap with OCD. [15] The reduction of surface area of the putamen is only demonstrated in certain

areas, the anterior-superior putamen, the mid-body putamen, and the posterior-inferior putamen. [3] This reduction is caused by a fixed surface areas reduction which can be first detected in childhood and then persists throughout life. [3]

Dorsal striatum: Caudate. Using FMRI, the ADHD group was found to have underactivation in the right caudate nucleus compared to the controls. [15] In Go/no-go tasks that measure response inhibition, people with ADHD were found to have reduced activation in the right caudate compared to neurotypical controls. [10] The lateral caudate has the most prominent reduction in surface area and volume of the basal ganglia. [3, 11]

Ventral striatum: The ventral striatum has been found to have progressive surface constriction in ADHD, which is atypical for development. [3] A structure in the ventral striatum is the nucleus accumbens. The nucleus accumbens has been reported to have reduced volume in people with ADHD. [11] The nucleus accumbens has been thought to be involved with reward processing, motivation, and emotional regulation.

Globus pallidus: internal and external segment. The globus pallidus has a reduction of surface area in the posterior-inferior region associated with ADHD. [3]

Results and conclusions

ADHD is a complex disorder with multiple clinical presentations; this complexity is also present in the neural anatomy associated with ADHD. Despite this complexity, there are general conclusions that can be made about the ADHD brain. There is a negative correlation between gray matter volume and ADHD traits. [14] There has also been an overall pattern of reduced overall volume in the brains of people with ADHD. The cause of this reduction is due to both decreased gray matter volume, cortical thickness reduction, and reduced surface area. [12, 15, 14] There have also been findings of increased cortical thickness in some posterior brain areas.

This increase in cortical thickness may be due to compensatory mechanisms; such a mechanism allows a person with ADHD to have improved functioning in their life. [13]

Some hypotheses of ADHD suggest that it could be a type of delayed development; other hypotheses suggest that ADHD is a type of abnormal development. [13] The evidence seems to support that ADHD is an abnormal form of development, especially as many anatomical and functional brain morphologies are present both in children and adults. If ADHD was purely a developmental delay, then such abnormalities should decrease with age; however, this is not the case.

Comparing ADHD to other disorders helps to provide further insight into the neural presentation of ADHD. In this review, ADHD has been compared to OCD, CD, and LD. ADHD and CD have large amounts of overlap in brain structures; however, they also have disorder-specific areas and activations. [14] The differences between CD and ADHD have been hypothesis to correspond to cool executive functioning (EF) and hot EF, with ADHD being found to be involved with the cool non-emotional EF. When comparing ADHD to OCD, one of the main structural differences between the disorders is that people with ADHD have reduced GMV in their right putamen and insula while OCD has an increase of GMV in these areas. [15] The main structural similarity between the two disorders is that both areas have reduced GMV in the vm-OFC. Furthermore, ADHD and OCD have different functional presentations with ADHD being characterized by underactivation and OCD characterized by overactivation. [15] When comparing ADHD inattentive type to reading disability (RD), it was found that the two disorders are distinct but can be comorbid. The SMA/ACC have been indicated in executive functioning and are commonly implicated in ADHD while the planum temporal and inferior frontal gyrus are implicated in RD. [16] Overall, ADHD may have overlap with similar disorders

such as CD, OCD, and LD. However, due to the unique functional activations and anatomy that are associated with ADHD, it is necessary to consider ADHD to be its own unique disorder and not a different presentation of other disorders.

The finding in this review can be used to further improve the understanding and possible interventions for ADHD. The amount of people diagnosed with ADHD has increased every year. For example, from 2003 to 2011 the prevalence of children diagnosed with ADHD increased by 42%. [17] With such a large amount of people impacted by this disorder, the importance of better understanding and treatments for ADHD have become increasingly evident. By understanding ADHD neural presentation, the external clinical presentations are better able to be understood.

Figures and/or tables

Table 1.1

Attention-Deficit/Hyperactivity Disorder (ADHD) 314.0X (F90.X)

A. A persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development, as characterized by (1) and/or (2):

1. Inattention: Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities: Note: The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or failure to understand tasks or instructions. For older adolescents and adults (age 17 and older), at least five symptoms are required.

   a. Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities (e.g., overlooks or misses details, work is inaccurate).
   b. Often has difficulty sustaining attention in tasks or play activities (e.g., has difficulty remaining focused during lectures, conversations, or lengthy reading).
   c. Often does not seem to listen when spoken to directly (e.g., mind seems elsewhere, even in the absence of any obvious distraction).
   d. Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (e.g., starts tasks but quickly loses focus and is easily sidetracked).
   e. Often has difficulty organizing tasks and activities (e.g., difficulty managing sequential tasks; difficulty keeping materials and belongings in order; messy, disorganized work; has poor time management; fails to meet deadlines).

f. Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (e.g., schoolwork or homework; for older adolescents and adults, preparing reports, completing forms, reviewing lengthy papers).

g. Often loses things necessary for tasks or activities (e.g., school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones).

h. Is often easily distracted by extraneous stimuli (for older adolescents and adults, may include unrelated thoughts).

i. i. Is often forgetful in daily activities (e.g., doing chores, running errands; for older adolescents and adults, returning calls, paying bills, keeping appointments).

2. Hyperactivity and impulsivity: Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities:

Note: The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or a failure to understand tasks or instructions. For older adolescents and adults (age 17 and older), at least five symptoms are required.

a. Often fidgets with or taps hands or feet or squirms in seat.

b. Often leaves seat in situations when remaining seated is expected (e.g., leaves his or her place in the classroom, in the office or other workplace, or in other situations that require remaining in place).

c. Often runs about or climbs in situations where it is inappropriate. (Note: In adolescents or adults, may be limited to feeling restless.)

d. Often unable to play or engage in leisure activities quietly.

e. Is often "on the go," acting as if "driven by a motor" (e.g., is unable to be or uncomfortable being still for extended time, as in restaurants, meetings; may be experienced by others as being restless or difficult to keep up with).

f. Often talks excessively.

g. Often blurts out an answer before a question has been completed (e.g., completes people's sentences; cannot wait for turn in conversation)

h. h. Often has difficulty waiting his or her turn (e.g., while waiting in line).

i. Often interrupts or intrudes on others (e.g., butts into conversations, games, or activities; may start using other people's things without asking or receiving permission; for adolescents and adults, may intrude into or take over what others are doing).

B. Several inattentive or hyperactive-impulsive symptoms were present prior to age 12 years.

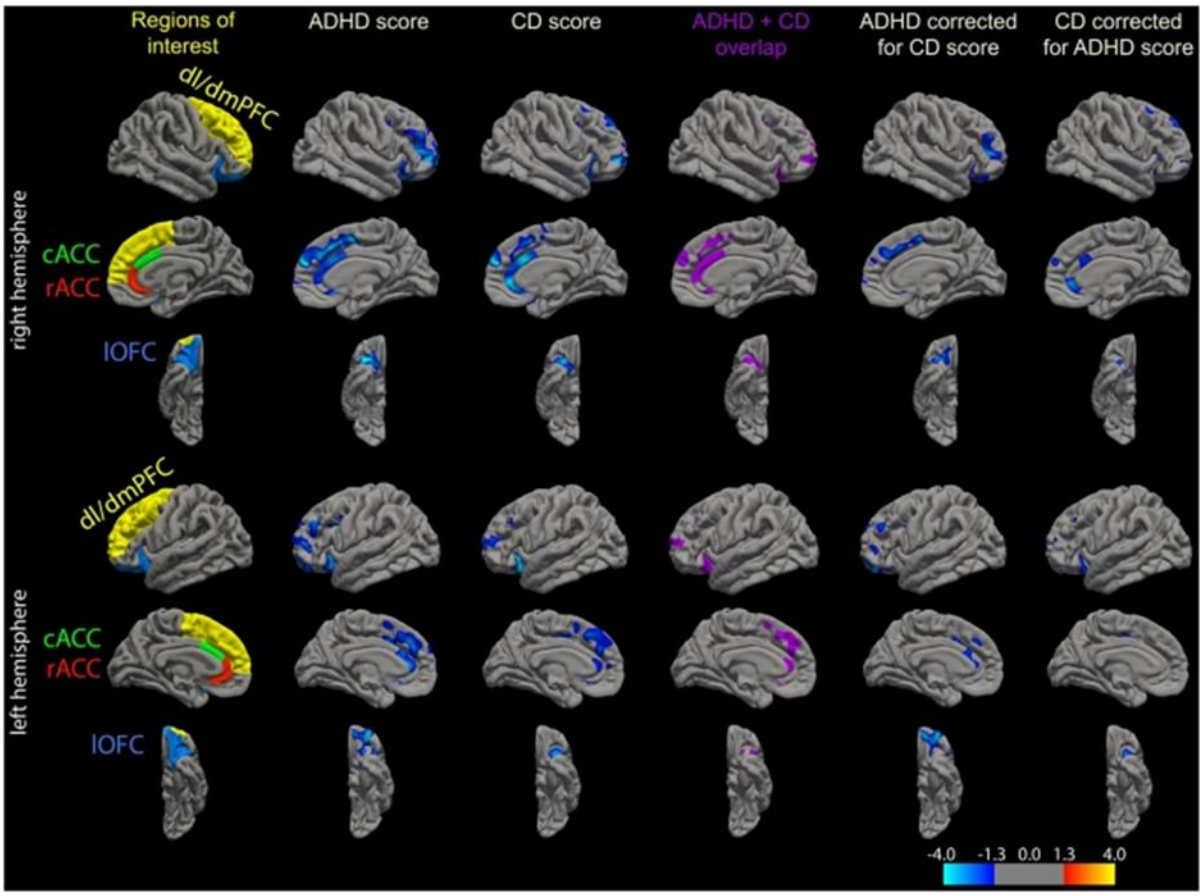
C. Several inattentive or hyperactive-impulsive symptoms are present in two or more settings (e.g., at home, school, or work; with friends or relatives; in other activities).

D. There is clear evidence that the symptoms interfere with, or reduce the quality of, social, academic, or occupational functioning.

E. The symptoms do not occur exclusively during the course of schizophrenia or another psychotic disorder and are not better explained by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, personality disorder, substance intoxication or withdrawal).

[2]

Figure 1.1



"Fig. 3 ROIs as defined by the Desikan atlas that are used for the main analysis are shown in the left column. The other columns contain results of the exploratory analysis showing correlations within those ROIs on a vertex-level. In column 2–3 correlations between GMV and ADHD and CD scores, respectively, are shown. Their regional overlap is shown in column 4 (purple areas). Both ADHD and CD score revealed negative correlations with GMV within a sub-region of the left and right dl/dmPFC. Those were mainly localized in a cluster comprising the rostral middle frontal and lateral superior frontal cortex, extending to medial portions of the prefrontal cortex. Similar focal associations were observed in posterior and anterior sub-regions of the left and right lOFC. Correlations observed in the ACC were spread over right caudal and rostral ACC ROIs, whereas a correlation of more focal nature was observed in the left ACC. When correcting

for CD trait, the ADHD scores were negatively correlated with the GMV in right rostral middle frontal cortex, right rostral dmPFC, left cACC and bilateral anterior lOFC (column 5). In contrast, when correcting for ADHD trait, CD scores were negatively correlated with the GMV in right rACC (column 6). Moreover, right cACC and posterior lOFC also showed this relation to a certain extent (column 6). Thus, on a vertex-level there seemed to be a more complex and unique relation between local GMV and the different traits: While GMV in left cACC was more negatively related to ADHD scores, GMV in right cACC and rACC was more related to CD scores. Likewise, while the negative relation between ADHD scores in lOFC GMV was more widespread and anterior when controlling for CD, the negative relation between CD scores in lOFC GMV was more ventrolateral (spreading into ventrolateral PFC). Overall, no positive correlations were observed. Significance is represented on a log(p-value) scale, where positive values (warm colors) are assigned to positive associations, and negative values (cold colors) to negative associations. For explorative reasons the display threshold was set to 1.3, corresponding to p = .05 (uncorrected)" [15]

References:

1) Morris-Rosendahl DJ, Crocq MA. Neurodevelopmental disorders-the history and future of a diagnostic concept. Dialogues Clin Neurosci. 2020;22(1):65-72. doi:10.31887/DCNS.2020.22.1/macrocq
2) American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). https://doi.org/10.1176/appi.books.9780890425596
3) Shaw P, De Rossi P, Watson B, et al. Mapping the development of the basal ganglia in children with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2014;53(7):780-9.e11. doi:10.1016/j.jaac.2014.05.003
4) Polanczyk, G., de Lima, M.S., Horta, B.L., Biederman, J. & Rohde, L.A. 2007, "The Worldwide Prevalence of ADHD: A Systematic Review and Metaregression Analysis", The American journal of psychiatry, vol. 164, no. 6, pp. 942-948.
5) Kessler RC, Adler L, Barkley R, et al. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. Am J Psychiatry. 2006;163(4):716-723. doi:10.1176/ajp.2006.163.4.716
6) Melissa L. Danielson, Rebecca H. Bitsko, Reem M. Ghandour, Joseph R. Holbrook, Michael D. Kogan & Stephen J. Blumberg (2018) Prevalence of Parent-Reported ADHD Diagnosis and Associated Treatment Among U.S. Children and Adolescents, 2016, Journal of Clinical Child & Adolescent Psychology, 47:2, 199-212, DOI: 10.1080/15374416.2017.1417860
7) Rydell, M., Lundström, S., Gillberg, C., et al. Gillberg Neuropsychiatry Centre, Centre for Ethics, Law, and Mental Health, Göteborgs universitet, Gothenburg University, Gillbergcentrum, Sahlgrenska Academy, Sahlgrenska akademin, Centrum för etik, juridik

och mental hälsa, Karolinska Institutet, Dept of Medical Epidemiology and Biostatistics & Inst för medicinsk epidemiologi och biostatistik 2018, "Has the attention deficit hyperactivity disorder phenotype become more common in children between 2004 and 2014? Trends over 10 years from a Swedish general population sample", Journal of child psychology and psychiatry, vol. 59, no. 8, pp. 863-871.

8) Matte B, Anselmi L, Salum GA, Kieling C, Gonçalves H, Menezes A, et al. ADHD in DSM-5: a field trial in a large, representative sample of 18- to 19-year-old adults. Psychol Med 2015 01;45(2):361-373.

9) Bernardi S, Faraone SV, Cortese S, Kerridge BT, Pallanti S, Wang S, et al. The lifetime impact of attention deficit hyperactivity disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Psychol Med 2012 04;42(4):875-87.

10) McCarthy, H., Skokauskas, N. & Frodl, T. 2014, "Identifying a consistent pattern of neural function in attention deficit hyperactivity disorder: a meta-analysis", Psychological medicine, vol. 44, no. 4, pp. 869-880.

11) Hoogman M, Bralten J, Hibar DP et al. Subcortical brain volume differences in participants with attention deficit hyperactivity disorder in children and adults: a cross-sectional mega-analysis. Lancet Psychiatry. 2017 Apr;4(4):310-319. Available From: https://pubmed.ncbi.nlm.nih.gov/28 219628/

12) Silk TJ, Beare R, Malpas C, et al. Cortical morphometry in attention deficit/hyperactivity disorder: Contribution of thickness and surface area to volume. Cortex. 2016;82:1-10.

13) Almeida Montes, L. G. et al. (2013) 'Brain Cortical Thickness in ADHD: Age, Sex, and Clinical Correlations', Journal of Attention Disorders, 17(8), pp. 641–654. doi: 10.1177/1087054711434351.

14) Bayard, F., Nymberg Thunell, C., Abé, C. et al. Distinct brain structure and behavior related to ADHD and conduct disorder traits. Mol Psychiatry.2020; 25(11): 3020–3033. Available from: https://doi.org/10.1038/s41380-018-0202-6

15) Norman LJ, Carlisi C, Lukito S, et al. Structural and Functional Brain Abnormalities in Attention-Deficit/Hyperactivity Disorder and Obsessive-Compulsive Disorder: A Comparative Meta-analysis [published correction appears in JAMA Psychiatry. 2017 Oct 1;74(10):1079] [published correction appears in JAMA Psychiatry. 2018 Mar 1;75(3):303]. JAMA Psychiatry. 2016;73(8):815-825. doi:10.1001/jamapsychiatry.2016.0700

16) Langer, N, Benjamin, C, Becker, BLC, Gaab, N. Comorbidity of reading disabilities and ADHD: Structural and functional brain characteristics. Hum Brain app. 2019; 40(9): 2677– 2698. Available From: https://doi.org/10.1002/hbm.24552

17) National Institute of Mental Health, NIH. Attention-Deficit/Hyperactivity Disorder [Internet]. The National Institute of Mental Health Information Resource Center: [2017 November]. Available from: https://www.nimh.nih.gov/health/statistics/attention-deficit-hyperactivity-disorder-adhd