

Neuroradiological changes in patients with attention deficit hyperactivity disorder: Presentation of 3 cases and literature update

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ABSTRACT

Introduction: Attention deficit/hyperactivity disorder (ADHD) is thought to be caused by structural and functional abnormalities in the frontal-striatal circuitry of the brain. The dorsolateral prefrontal cortex, caudate, pallidum, corpus callosum, and cerebellum all have significantly smaller volumes in children with ADHD. According to recent reports, other cortical and cerebellar regions generally suffer impairment.

Case Series: Multiple nodes of dysfunction at the frontostriatal and mesocorticolimbic networks in attention-deficit/hyperactivity disorder (ADHD) have been identified through functional neuroimaging studies. We present a group of three ADHD patients and review the clinical findings and potential connections to neuroimaging tests. **DISCUSSION:** Adults with ADHD

have different brain volume patterns in the areas of the brain responsible for attention and executive function.

Conclusion: Among other neuroradiological findings, the ADHD patients in the current study showed changes in the frontal and prefrontal cortex, thickening of the corpus callosum, and elevated levels of glutamine and glutamate in the cerebellum. New studies are required to understand better the clinical finding with potential neuroanatomical and functional changes. Attention-deficit/hyperactivity disorder, brain, and neuroimage are keywords.

Keywords: ADHD, Cerebellum, MRI, Structural brain imaging

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INTRODUCTION

Few studies have examined the relationship between these networks' structural and functional connectivity and the behavioral symptoms of ADHD [1]. Studies using diffusion tensor imaging show that ADHD is linked to essential variations in white matter microstructure,

particularly in frontostriatal and specific corticocortical tracts. Resting-state functional magnetic resonance imaging studies point to disrupted interactions between this network and frontostriatal attentional systems and altered connectivity within a default mode network of structures active during introspective, task-free processes. More recent research suggests that the primary symptoms of ADHD may be caused by an uncontrolled process of brain plasticity, which peaks during development. As in the cases of the adults and adolescents in the examples above, such altered connectivity patterns may last into adulthood [2, 3].

This study will present the clinical picture (main manifestations) and look for a correlation with described areas of the central nervous system that are allegedly abnormal in thickness or even dysfunctional. We will also talk about the function of glutamine and glutamate as indicators of potential clinical effects, particularly in the cerebellum [4, 5].

Involvement of the cerebellum in cognitive and affective processes has been demonstrated by discoveries over the past 20 years. Neuroimaging data that show the same is active in a variety of cognitive tasks aside from motor control, which is its primary function, support this [6, 7].

CASE SERIES

Case 1

Male, 32 years old, tradesman, without co-morbidities. No past history of possible fetal distress or other disorders, such as central nervous system infections. Apart from the first consultation in November 2022 with complaints about running over thoughts, leaving activities half-functioning was considered invasive and inconvenient. It is difficult for him to stabilize himself in services due to the extreme lack of attention. He reaffirms that he has a low attention span, emotional outbursts, and troubled lines of thought in strategies regarding tasks and behaviors. The magnetic resonance imaging (MRI) points to an increase in glutamine and glutamate in the right frontal lobe—a finding with high prevalence in ADHD. Makes Ritalin 10 mg—twice a day; sodium valproate 250 mg—night (Figures 1 and 2).

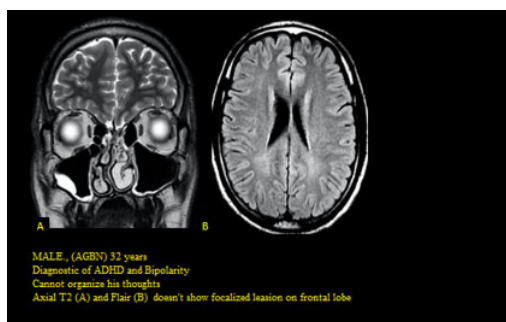


Figure 1: Axial T2 (A) and flair (B).

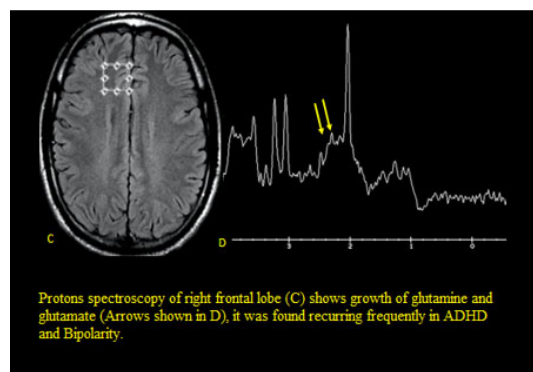


Figure 2: Growth of glutamine and glutamate.

Case 2

A woman, 36 years old lawyer, reported that he has had absence seizures since adolescence. She had already undergone numerous treatments for attenuation and resolution of the condition; however, only in February of that year she was submitted for an MRI of the skull with diffusion. She was medicated with lamotrigine, lacosamide, and levetiracetam. During the initial consultation, she drew attention to acrylic, mental confusion, attention deficit during the examiner's speech, and extreme difficulty focusing on the medical prescription. She had been explained countless times how to take the medication; however, after a few minutes, he was asked again about the time, doses, and names. She pointed out that she cannot be pleasant company, as she interrupted friends during get-togethers, often preventing them from expressing themselves and putting their points of view. She alternated depression with anxiety and eventually showed unmotivated crying and laughter. On MRI of the skull, it was possible to identify an increase in glutamine and glutamate in the cerebellum—findings of high prevalence in ADHD. The absence of seizures could be explained by right hippocampal sclerosis. However, a rounded and globose appearance in the left hippocampus was consistent with a rotational anomaly (Figures 3 and 4).

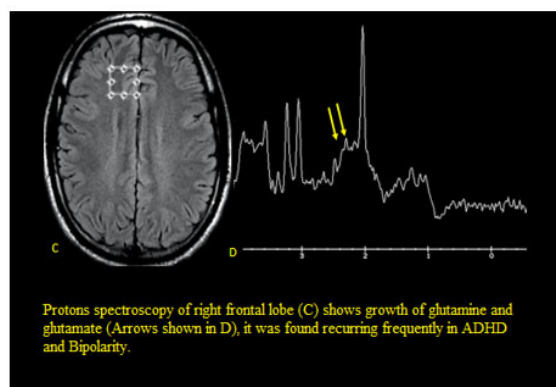


Figure 3: Protons spectroscopy of the right frontal lobe shows the growth of glutamine and glutamate.

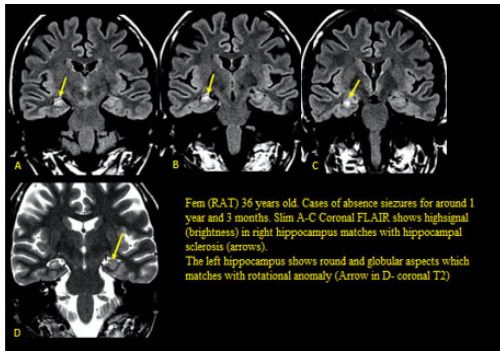


Figure 4: Coronal flair shows a high signal in the right hippocampus (A–C) and Coronal T2 (D).

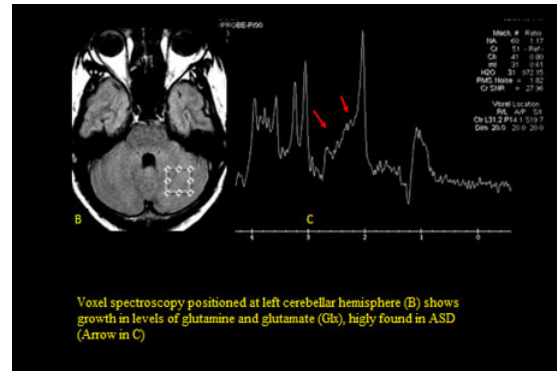


Figure 6: Protons spectroscopy of the left cerebellar hemisphere shows the growth of glutamine and glutamate.

Case 3

Male, 18 years old, with a clinical diagnosis of ADHD and autistic spectrum disorder. The clinical picture is marked by extreme difficulty in maintaining focus, attention, and organization in basic and instrumental tasks of daily life. The patient needs help to choose which activity is most timely and important—trying to do them all simultaneously. He considers himself impulsive, he does not wait his turn, only reads college test questions at the end, interrupts teachers and colleagues, and acts before thinking. Their performance always seems lower than expected for their intellectual capacity. He states that the problems faced from an academic point of view, be it behavior or performance (grades). It presents neurodevelopment characterized by atypical development, behavioral manifestations, communication and social interaction deficits, and repetitive and stereotyped behavior patterns. It is important to emphasize that specific clinical characteristics overlap the two conditions skull MRI with diffusion shows diffuse thickening of the corpus callosum. Voxel spectroscopy positioned in the left cerebellar hemisphere and frontal lobe shows increased levels of glutamine and glutamate, findings frequently found in patients with ASD and ADHD (Figures 5–7).

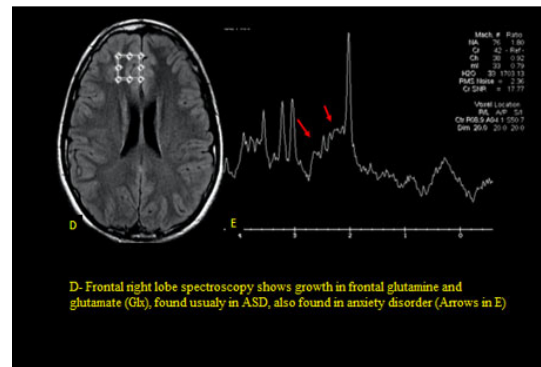


Figure 7: Frontal right lobe spectroscopy shows the growth of glutamine and glutamate.

DISCUSSION

Prefrontal cortical thickness has been found to be abnormally thin in children with attention-deficit/hyperactivity disorder (ADHD) in previous morphological research. Greater accuracy can be achieved in defining the brain areas most affected by ADHD using analytical methods, with meta-analyses emphasizing the basal ganglia's vulnerability. Cortical abnormalities are also frequently observed, especially in the lateral prefrontal and parietal cortex, albeit there is less agreement on the precise site of structural change. The limbic system and frontostriatal loops are implicated in the illness due to abnormalities in the form of subcortical structures, particularly the basal ganglia, hippocampus, and amygdala [5, 6].

The primary abnormalities associated with those described in the literature in patients with ADHD were described in the frontal lobe, corpus callosum, cerebellum, and the temporal region—in this, there was a bias, as the patient also had an absence of seizure (corroborating with the neuroradiological finding).

The main abnormalities associated with those described in the literature in patients with ADHD were described in the frontal lobe, corpus callosum, cerebellum, and temporal region—in this, there was a bias, as the patient also had an absence seizure (corroborating with the neuroradiological finding). Cerebellar parallel-fiber

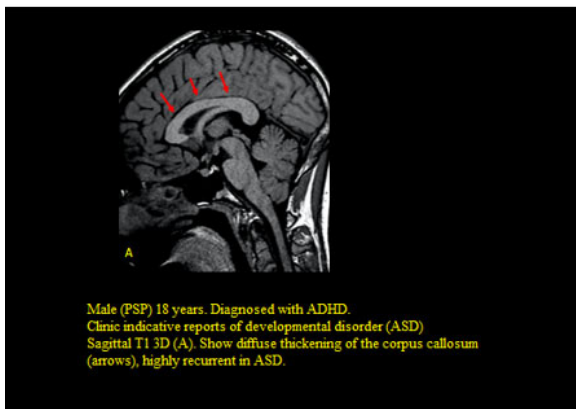


Figure 5: Sagittal T1 shows diffuse thickening of the corpus callosum.

terminals contain a glutaminase activity enabling them to synthesize glutamate from glutamine [7]. Convergent data from neuroimaging, neuropsychology, genetics, and neurochemical studies consistently point to the involvement of the frontostriatal network as a likely contributor to the pathophysiology of ADHD. This network includes the putamen, caudate nucleus, dorsal anterior cingulate cortex, and lateral prefrontal cortex. Additionally, a growing body of evidence shows that the cerebellum and other cortical regions are also affected by abnormalities [4, 7].

Numerous studies associate dysfunctions in the frontal lobe with repercussions related to social behavior, with moments of introspection and others of euphoria. Such findings are compatible with those presented in our series of cases. Brain areas in the frontal lobe have been implicated in behavioral flexibility and control [8–10].

The cerebellum's functional topology makes it easier to modulate scattered networks that serve a variety of diverse tasks. There are three distinct topographic representations in the cognitive/limbic cerebellum, which is located in the posterior cerebellar lobe; their exact nature is yet unknown. The cerebellar cognitive affective syndrome (CCAS), brought on by posterior lobe lesions, is characterized by deficiencies in executive function, visual-spatial processing, linguistic ability, and affect regulation. Autism spectrum diseases, psychotic spectrum disorders, and disorders of emotional regulation, attentional control, and social skill set are all examples of affective dyscontrol [11–13].

Our patients have alterations (increased levels of glutamine and glutamate in the cerebellum). This is possibly one of the factors related to cerebellar cognitive affective syndrome. Recent studies now implicate the cerebellum in anxiety. Here, we examine the evidence that suggests the cerebellum may play a role in anxiety. This evidence, which includes clinical studies and experimental manipulation of neural activity, collectively suggests that the cerebellum, and perhaps a particular topographical locus within the cerebellum, is one of the orchestrators of anxiety responses [10, 12].

Authors also consider it an organ related to motor learning, although with projections to other centers mediating depression.

The corpus callosum is a connecting structure between the two cerebral hemispheres. Its development occurs between the 8th and 20th week of gestation—a crucial structure for transferring and integrating information, including attention processes, across the brain. In our case series, one patient had diffuse thickening of the corpus callosum [13].

CONCLUSION

Given this series of case reports, it is possible to observe the importance of neuroimaging evaluations as a factor that corroborates the diagnosis of ADHD, which is

currently still strictly clinical. Because surgical transection of the corpus callosum does not reproduce the cognitive and behavioral abnormalities observed in patients with agenesis of the corpus callosum (AgCC), it is possible that additional anatomical changes are responsible for the observed clinical outcomes. New studies are necessary to better elucidate the functioning of systems that are directly/indirectly related in patients with ADHD and also such neuroradiological changes.

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Author Contributions

Daniel Antunes Pereira – Conception of the work, Interpretation of data, Drafting the work, Final approval

of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Marcela de Moraes Mesquita – Conception of the work, Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Marco Antônio Orsini Neves – Conception of the work, Design of the work, Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Lara Alexandre Brandão Toomassini – Conception of the work, Design of the work, Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Antônio Marcos da Silva Catharino – Conception of the work, Design of the work, Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Adalgiza Mafra Moreno – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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