The Cerebellum and Attention Deficit Hyperactivity Disorder
A Case Study of a Cerebellar Chiari 1 Malformation

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Abstract

The cerebellum is the most consistently implicated and the most robustly deviant brain structure in the pathophysiology of Attention-Deficit/Hyperactivity Disorder (ADHD). Its role in the neurobiology of ADHD is also buttressed by many recent anatomical, functional neuroimaging, and human lesion studies that have implicated it in the neural network that mediates selective attention. This article may add to the evidence for the role of the cerebellum in the pathophysiology of ADHD by presenting a case history of a young female adult with a cerebellar disorder called a Chiari Malformation type 1. She developed a severe impairment in selective attention, which resulted in an adult onset of ADHD. This case study provides a unique exploration of the pathophysiology of ADHD because all prior clinical findings from human lesion studies implicating the involvement of the cerebellum in the neural circuit for selective attention have overlooked the relevance of Chiari Malformation type 1.

Attention-Deficit/Hyperactivity Disorder (ADHD) is characterized by developmentally inappropriate levels of inattention and hyperactivity/impulsivity, which adversely affects many facets of an individual's life, and tends to be chronic (American Academy of Pediatrics, 2011; Barkley, 2006, Barkley, Murphy & Fischer, 2008). Its importance is also underscored by the fact that it is the most commonly diagnosed juvenile neurodevelopment disorder, with a prevalence of approximately 8% of juveniles between the ages of 5-17 in the United States (American Academy of Pediatrics, 2011). Its adult prevalence is approximately 5% (Barkley et al., 2008).

It is generally accepted that genetic and neurological factors are the most common causes of ADHD (Barkley, 2006; Nigg, 2006). Structural, functional, and clinical findings indicate that these factors affect multiple brain structures and neural circuits that are involved in the pathophysiology of ADHD (Bledsoe, Semrud-Clikeman, & Pliska, 2011; Durston, van Belle, & de Zeeuw, 2011; Nigg, 2006, 2010; Sonuga-Barke, 2010). Although the cerebellum which has historically been thought of as a structure involved primarily if not exclusively in motor control, it is the most consistently implicated and also the most robustly abnormal structure in the pathophysiology of ADHD (Bledsoe, Semrud-Clikeman, & Pliska, 2011; Kieling et al., 2008; Krain & Castellanos, 2006; Mackie et al., 2007).[1] Its involvement beyond that of a simple controller of motor acts stems from the fact that it is second in size to only the cerebral cortex, contains more neurons than the rest of the brain combined, and is massively connected to the cerebral cortex (Bower & Parsons, 2003; Stick, Dum, & Fiez, 2009). Its role in the neurobiology of ADHD is also buttressed by many recent anatomical, functional neuroimaging, and human lesion studies of individuals without ADHD that have implicated it in numerous non-motor functions (e.g. ex-

[1] Note that neuroimaging techniques that study brain structures implicated in the pathophysiology of ADHD such as the cerebellum cannot currently be used in clinical diagnosis (Zametkin, Schroth, & Faden, 2005).

ecutive control, language, working memory) as well as selective attention (Casey & Riddle, 2012; Cherkasova & Hechtman, 2009; Strick, Dum, & Fiez, 2009; Stoodley, 2011; Timmann & Daum, 2007).

The purpose of this article is to add to the evidence for the role of the cerebellum in the pathophysiology of ADHD by presenting the case history of an individual with a cerebellar disorder called a Chiari Malformation type I (CMI). It will do so by first briefly reviewing the evidence establishing a selective attention network and the role of the cerebellum in this network. It will then discuss the onset of CM1 in young adulthood that so adversely affected the selective attention that it resulted in a secondary attention-deficit/hyperactivity disorder (SADHD) which is the term that was coined for ADHD that develops after traumatic brain injuries (Max, 2011). This clinical case study provides a unique exploration to the pathophysiology of ADHD because all prior clinical findings from human lesion studies implicating the involvement of the cerebellum in the neural circuit for selective attention have overlooked the relevance of this disorder (National Institute of Neurological Disorders and Strokes, NINDS, 2011; Timmann & Daum, 2007).

Selective Attention and the Cerebellum

Cognitive neuroscience has resoundingly rejected the previously held view that attention is a uniform, monolithic concept (Raz & Buhle, 2006). It is now recognized that attention, like any other aspect of human cognition, is a multilevel phenomenon and that there are different kinds of attention mediated by different discreet, independent, though overlapping neural circuits (Raz & Buhle, 2006; Wang, Liu, & Fan, 2012). The Posner three-network model of attention has the most empirical support (Raz & Buhle, 2006). In this model, there is compelling evidence at both a functional and anatomical level for a selective attention network (Raz & Buhle, 2006).

Selective or focused attention is the ability to select target information from a broad field of stimuli and inhibit irrelevant stimuli (Nigg, 2006). It receives its classic description from William James: “Everyone know what attention is…the taking possession by the mind, in clear and vivid form, of one out of what seem several simultaneously possible objects or trains of thought. Focalization, concentration, of consciousness is of its essence “(cited in Bisley & Goldberg, 2010, p.2).

The possibility that the cerebellum might be part of an attentional network was first seriously considered in the late 1980s (Haarmeier & Thier, 2007). Since then numerous anatomical studies have demonstrated that the cerebellum is connected to brain structures that are part of the selective attention network such as the parietal lobe and prefrontal cortex (Casey & Riddle, 2012; Cherkasova & Hechtman, 2009; Posner & Rothbart, 2007; Stoodley, 2011; Strick, Dum, & Fiez, 2009). In addition, studies of patients with various cerebellar abnormalities have found various cognitive deficits including disorders of attention control (Schmanmann, Weilburg, & Sherman, 2007). However, as previously mentioned, none of these patient studies has included cases of CM1.

Case History

Erin was a 25 year old graduate first year student in a doctoral program of clinical psychology when she was granted a leave of absence from the program because she developed a number of physical symptoms that made it impossible for her to function in the program. Prior to the onset of the symptoms she was in excellent physical and mental health, had no prior significant medical or psychological problems, and was functioning as a straight “A” student. There

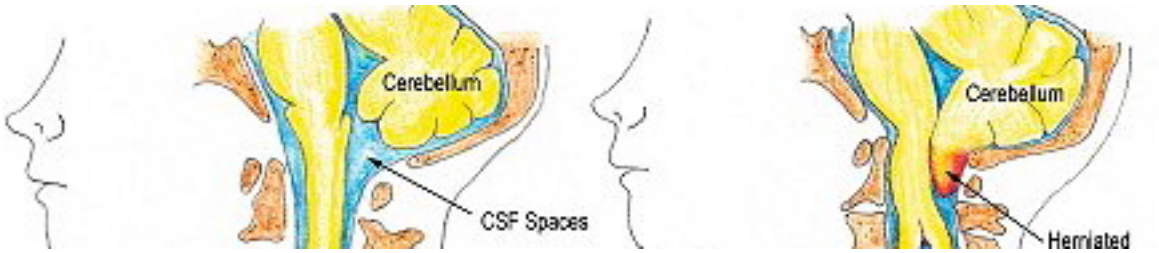
was no family history of CM1 which is not an uncommon finding because the extent to which genes are implicated in the etiology of the disorder is still not clear (Labuda, Loth, & Slavin, 2011).

The symptoms included:

- Severe, excruciating, daily headaches which she reported felt like an "ice pick going through my skull" and often forced her to go to the emergency room to manage the pain
- Burning neck pain at the base of her skull
- Burning pain in shoulders and behind shoulder blades
- Random jerking throughout her body

She was referred by her physician for a neurological evaluation which included a magnetic resonance imaging (MRI) scan and was subsequently diagnosed with a "Chiari I" malformation (CM1). Chiari malformations (CMs), which have a prevalence of less than 1% among adults (Benjjani & Cockerham, 2001), refer to a spectrum of abnormal hindbrain abnormalities affecting the relationship between the cerebellum, brain stem, upper cervical cord, and the bony skull base (Ramkumar et al., 2010). They are named for Hans von Chiari, who in 1891 while studying the effects of hydrocephalus (an abnormal accumulation of cerebrospinal fluid [CSF] within the four ventricles of the brain), described various alterations of the cerebellum which came to bear his name (Bejjani & Cockerham, 2001). The adult form, type 1, involves the herniation (extension) of the cerebellar tonsils (the lower part of the cerebellum) into cone shaped projections into the foramen magnum (an opening at the bottom of the skull) without involving the brain stem (National Institute of Neurological Disorders [NINDS], 2011). Most CMs are congenital disorders that develop when the posterior fossa (the lower part of the skull on which the cerebellum rests) is too small to accommodate the cerebellar tonsils (Labuda, Loth, & Slavin, 2011). Consequently, because not enough room is provided for the cerebellum, the cerebellar tonsils are forced to protrude into the foramen magnum. [See Figure 1.]. This protrusion can also disrupt the natural flow of cerebrospinal fluid across the cranioverterbal junction which can lead to a build-up of cerebral spinal fluid in the brain and an increase in intracranial pressure (Benjjani & Cockerham, 2001;Labuda, Loth, & Slavin, 2011). In addition, CM1 may also be associated with microstructural abnormalities in other brain regions (Kumar et al., 2011). Thus in cases of CM1, as well as virtually all other cases involving various other cerebellar abnormalities, extracerebellar abnormalities may also be involved. (Timmann & Daum, 2007).

Figure 1



The onset of symptoms is typically slow and insidious. Most cases are not detected until the third or fourth decades and 15% to 30% remain asymptomatic (Bejjani & Cockerham, 2001). CM1 results in a number of physical symptoms including headache, neck pain, dizziness, and

impaired balance (NINDS, 2011). It can also result in a severe impairment in selective attention, as the case history will document. Additional support for this causal relationship will be discussed subsequent to the case history presentation.

Selective Attention Impairment

After finally discovering a medication (a 2-year quest) that successfully treated the pain, Erin returned to the program. She had decided against a surgical procedure because of the risks involved. Pain free for the first time in two years, she was happy and excited to return to her doctoral program. However, despite the absence of pain, she experienced grave difficulties in resuming her high level of cognitive functioning because of a severe impairment in selective attention. She reported that she was constantly being bombarded by inner and outer stimuli, which she could not filter out and which affected her in many ways. Her major symptoms were

- Severe difficulty in filtering out external extraneous sounds, which, for example, made it painful for her to be in situations with a lot of noise (e.g., graduation reception for her MA in clinical psychology).
- Severe difficulty in filtering out internal stimuli such that her mind was constantly full of racing, random thoughts. These difficulties caused her to
    - become exhausted taking exams because of the tremendous amount of energy required to concentrate.
    - have grave difficulty listening to someone or learning as she reported that the new information is "*added to the internal mass of information and usually gets lost right away*."
    - have significant word retrieval problems.
- Severe difficulty in task persistence and reengagement because of the distractibility.

Because of these symptoms, she struggled with academic demands that she previously had accomplished rather effortlessly and with great success. For example, accurate note taking became virtually impossible and she had to resort to taping lectures and then laboriously reviewing them to extract the relevant information. Likewise, the multiple reading demands required much more time as she constantly had to struggle with focus and continually needed to reread.

Erin's grave deficit in selective attention was by no means a unique finding with regard to CM1. Despite the failure of the authoritative NINDS (2011) fact sheet to list an attention impairment as a common symptom in CM1, there is significant anecdotal evidence of patients reporting "*foggy thinking, poor memory and concentration*" (Wisconsin Chiari Center, 2011, p.2) a direct quote needs a page or paragraph number). There is also some scientific support, though in general this issue has not been studied. Frim (2010) evaluated 17 adult patients with a battery of neuropsychological tests prior to surgery for the disorder and reported finding 'subtle' attention deficits compared to a control group. In Erin's case however, these deficits in selective attention were so severe that she was diagnosed with SADHD.

SADHD

As previously discussed, despite the successful management of her pain, which enabled an enthusiastic return to her doctoral studies, she experienced grave difficulties in resuming her high level of cognitive functioning because of the severe impairment in selective attention. Be-

cause impaired attention very commonly occurs after traumatic brain injury (McCullagh & Feinstein, 2011) with the result that 20% to 50% of individuals who sustain a severe brain injury develop SADHD (Yeates et al., 2005), this prompted a referral to a neurologist for an evaluation. Erin was diagnosed with Attention Deficit/Hyperactivity Disorder Not Otherwise Specified which is given to individuals whose symptoms and impairment meet the criteria for Attention-Deficit/Hyperactivity Disorder, Predominantly Inattentive Type but whose age at onset is beyond 7 years (American Psychiatric Association, 2000). Because impairment of selective attention, as indexed by the criterion "*is easily distracted by extraneous stimuli or irrelevant thoughts,"* is the single most sensitive indicator of adult ADHD (Barkley, Murphy, & Fischer, 2008, p. 113), it is not surprising that she was so diagnosed.

Following the diagnosis, she was treated with stimulant medication (Adderall) for the SADHD. This treatment was very successful as it greatly enhanced her ability to concentrate and remain on task as it typically does in most cases (Swanson, Baler, Volow, 2011). She returned to her prior high level of academic functioning as a straight "A" student, which she has maintained for a period of three years as of this writing.

Conclusion

This case study may provide additional support for the involvement of the cerebellum in the pathophysiology of ADHD from an overlooked domain of human lesion studies of the cerebellum. Future research with CM1 cases needs to focus on two areas. First, the symptom of impairment in selective attention warrants much greater study to investigate in a methodologically sophisticated way the numerous patient reports of such impairment. Second, because CM1 involves not only cerebellar impairment (i.e., compression) but also associated extra-cerebellar impairments, a better understanding of the exact mechanisms, which result in a deficit in selective attention, is needed. You discuss implications for future research, what about implications for practice? Here it is

Lastly, with regard to practice, the most important implication is that the case study provides an important reminder that although ADHD is a highly hereditable disorder, there are a number of biological non-genetic risk factors associated with ADHD (Nigg, 2006) such as lead ingestion (Nigg et al., 2010), prenatal exposure to alcohol (Eme & Millard, 2012), and severe traumatic brain injury (Eme, 2012). Hence, an evidence-based assessment for ADHD requires that a clinician be highly knowledgeable regarding the non-genetic biological risks factors associated with ADHD and conduct an evaluation that is informed by this knowledge.

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