Universiteit Utrecht

Master Thesis

Implications of cerebellar anatomy and functioning on fluid intelligence and the moderating effects of trait anxiety

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# Abstract

The role of the cerebellum in cognitive performance has started to be investigated in recent years. In particular, experimental data of healthy subjects points towards contributions of Crus I and II in inductive reasoning and problem solving. Data on populations with cerebellar lesions also finds implications of emotional responses, especially related to anxiety.
This two-part study was made up of a dataset from the data-sharing website ABIDE and experimental data that was collected at Utrecht University in the form of a pilot study. In the first part a sample of 45 neurotypical University students were assessed on their cerebellar volumes using structural MRI and scores on the WISC were obtained. In the second part a different student sample received cathodal cerebellar transcranial direct current stimulation (tDCS) while performing the Raven Progressive Matrices (RPM) test. Results of the first study showed no associations between inductive reasoning and Crus I and Crus II volumes as well as total cerebellar volume. There was also no effect of cerebellar tDCS on RPM performance test and participant's reaction times on the RPM. Trait anxiety was assessed to explore its role in the effects of tDCS on inductive reasoning using the STAI. There was no moderating effect of trait anxiety on the relationship between cerebellar disruption through transcranial stimulation and scoring on the Matrices task. The current studies do not provide evidence that cerebellar volume size affects fluid intelligence and that cerebellar tDCS interferes with inductive reasoning. These findings are discussed with regards to the literature and implications for future research.

Key words: Cerebellum, Crus I, Crus II, Inductive reasoning, fluid intelligence, Raven Progressive Matrices, transcranial direct current stimulation, cerebellar tDCS, trait anxiety

Word count: 7325

Introduction

The cerebellum might only make up about 10 % of the brain’s total weight, but it contains roughly half of the brain's neurons (Kandel et al., 2000). It is one of the oldest parts of the brain and its persistence throughout evolution gives credit to its remarkable function in human neuroanatomy (Karamian, 1962). The cerebellar cortex is made up of an extensive three-layered sheet (Pfaff, 2013, p.1149). It is wrapped around three deep cerebellar nuclei. It connects to the brainstem via three peduncles but is also heavily interconnected with the cerebral cortex (Strick et al., 2009). In terms of neurodevelopment, the cerebellum grows more rapidly during the third trimester of pregnancy than any other cerebral structure (Tam et al., 2011).

It used to be assumed that the cerebellum receives information from the four cerebral lobes and converges it through cerebral circuits onto the thalamus (Glickstein & Doron, 2008). From there it performs a sensorimotor transformation on its inputs and conveys the results to the primary motor cortex (Strick et al., 2009). This would mean that the cerebellum and cerebellar impairments purely affect motor functions, in particular the coordination of motor movements and balance (Sullivan et al., 1995). Nowadays research has demonstrated the cerebellum gets information from the cortex via the pontine nuclei in the brainstem (Percheron et al., 1996). Furthermore, the cerebellar cortex projects to the deep cerebellar nuclei and the dorsal cochlear nucleus projects to the thalamus (Purves et al., 2011). This means that the output of the cerebellum targets multiple non-motor areas, namely within the domains of cognition and emotion through the cortico-ponto-cerebellar (feedback projection) and cerebello-thalamo-cortical pathways (feedforward projection, Bugalho et al., 2006).

Evidence for a role of the human cerebellum in cognitive functions comes from anatomical, clinical and neuroimaging data (Buckner, 2013). Which cognitive functions are related to the cerebellum can be best examined when looking at the tasks that show cerebellar activation in functional imaging studies (Yoon et al., 2017). Cerebellar activation has been reported during language and reading tasks such as word generation tasks, but also spatial processing tasks as the line bisection task, working memory tasks (e.g. Sternberg task) and lastly tasks related to executive functioning such as the Wisconsin card sorting task or the Tower Of Hanoi task (Stoodley et al., 2012). Cerebellar volume was moreover found to be significantly correlated with general intelligence and verbal memory (Paradiso et al., 1997). The default-mode network, which is active during daydreaming but also reasoning and planning is functionally connected with Crus I and II of the posterolateral lobes (Yoon et al., 2017). Crus I and II are located in the posterior cerebellum, which forms pathways to lateral prefrontal areas and hence important parts in cognitive processes. A meta-analysis found that while Crus I and II are both related to executive functioning and language, only Crus I is simultaneously also linked to working memory (Keren-Happuch et al., 2014).

While cerebellar involvement in cognitive functions is still not well understood, cognitive deficits related to working memory, language and spatial processing have been linked to certain regions of the cerebellum (Stoodley et al., 2012). In healthy subjects, a higher IQ is associated with continuous larger growth of cerebellar volume (Brouwer et al., 2014). Whether abnormalities to the cerebellum as such or within pathways linked to the cerebellum are responsible for cognitive deficits in neurological and psychiatric disorders that feature simultaneous cerebellar changes is still a topic of debate (Stoodley et al., 2012). One way to understanding the cerebellar role in cognition and in particular intelligence is looking at the cognitive impairments of patient groups with cerebellar abnormalities. Neuropsychological examinations of children with cerebellar hypoplasia revealed intelligence quotient (IQ) values ranging from 30 to 85 (Steinlin, 2008) and ataxia teleangiectasia, which is a neurogenerative disorder affecting the cerebellum and immune system, was related to low verbal IQ scores (Mostofsky et al., 2000). In a sample of patients with temporal lobe epilepsy, a deviation from normal cerebellar volumes towards smaller volumes was related to lower intelligence (Hellwig et al., 2013).

The view that the cerebellum is also involved in cognition has also been supported by clinical studies that focused on the functional impairments of patients, who suffered lesions uniquely to the cerebellum, either through cerebellar stroke, tumour, cerebellitis, or neurodegenerative disorders (Schmahmann et al., 2007). Effects of impairments are also dependent on the part of the cerebellum. Lesions to the anterior cerebellum have been found to result in smaller impairments in executive and visual-spatial function compared to lesions to the posterior cerebellum, lesions to which also resulted in more pronounced behavioural and cognitive deficits (Schmahmann & Sherman, 1998). It can therefore be assumed that the posterior cerebellum is more sensitive to lesions compared to the anterior cerebellum. These studies were largely carried out by Jeremy Schmahmann, who referred to this clinical entity the ‘cerebellar cognitive affective syndrome’. It is important to highlight that the diagnosis of CCAS is only given if the cerebellum is the only neural substrate that exhibited lesions, whereby the effects of other neural parts on impairments could be excluded. Schmahmann termed the cognitive aspects of cerebellar dysfunction “dysmetria of thought”. Symptoms appeared to be pronounced in patients with bilateral and acute disease and improved over time in most instances (Schmahmann & Sherman, 1998).

Prenatal and geriatric developmental factors also seem to influence the cerebellum and its effect on intelligence. Smaller cerebellar volumes are associated with lower cognitive abilities such as IQ and executive functioning in prematurely born adolescents (Brossard-Racine et al., 2015) and lower neuromotor skills in another sample of prematurely born children (Lind et al., 2011). But also aging had an effect on the neuroanatomy of the cerebellum, which in turn had implications on cognitive and reasoning abilities. In particular, gray matter volume of the cerebellum is associated with general cognitive ability in older men, but not in older women (Hogan et al., 2011). This can be explained by the fact that the cerebellum shrinks proportionally more with age in men than women (Xu et al., 2000). Besides the shrinking in cerebellar volume, degraded connections between the cerebral cortex and cerebellar circuitry have a negative impact on task domains within motor function and cognition in ageing (Bernard & Seidler, 2014).

Molinari and Leggio (2007) formulated a general framework of cerebellar involvement in cognition in which the cerebellum played a specific role in both extracting relevant spatial information from the environment and the acquisition of these spatially related procedures. Regarding memory, Chen and Desmond (2005) have hypothesised that the cerebello-frontal loop is involved in visual-to-phonological encoding, while the cerebello-parietal loop is involved in the maintenance and storage of information. These processes are important to consider since they are necessary abilities for cognitive functioning. Another framework of cerebellar functioning in cognitive processes describes the cerebellum's importance in learning and automatization (Raymond et al., 1996). Its function would be particularly relevant during development or later during rehabilitation processes. It is believed that once a learned function is well mastered, it can be done automatically and mostly require activation of the cerebrum. Therefore, the involvement of the cerebellum in this cognitive activity might decline after learning is finalised. Evidence for this also comes from research into dyslexia, which found that cerebellar learning mechanisms are necessary for acquiring literacy skills and cerebellar disruption constitutes one of the neural correlates of developmental dyslexia (Stoodley & Stein, 2013).

In addition to studying cerebellar function with structural and functional neuroimaging, the role of the cerebellum for research purposes can also be assessed in healthy participants specifically by using cerebellar tDCS in an easy, time-effective, cheap and non-invasive way. Studies using this method have found that cerebellar cathodal tDCS modules verbal working memory by reducing the correct responses on a forward digit span test and blocking the practice dependent increase in correct numbers during a backward digit spans (Boeringer et al., 2013). Evaluating the arithmetic aspects of working memory and attention, cathodal tDCS over the right cerebellum improves cognitive performance in the Paced Auditory Serial Subtraction Task, while as sham or anodal cerebellar tDCS did not affect performance (Pope & Miall, 2012). In line with the cerebellar function framework by Raymond et al. (1996), anodal cerebellar tDCS influence procedural learning on a reaction time task in healthy subjects (Ferrucci & Priori, 2014). Although it is widely assumed that anodal tDCS causes functional enhancement and cathodal tDCS leads to functional disruptions, there is only limited evidence for this and a recent study did not find polarity-dependent effects of anodal and cathodal tDCS on improving and disrupting behaviour (Oldrati & Schutter, 2018)

The cerebellum has not just been found to exert an effect on cognition but does also influence emotions (Schmahmann, Weilburg & Sherman, 2007). Cerebellar tDCS improves cognitive reappraisal in an autobiographical social situations' reappraisal task in healthy students with symptoms of social anxiety, indicating that the cerebellum can modulate effects on anxiety perception (Haeems, 2018). There is evidence to suggest that anxiety actually is related to cerebellar activity, as it is one of the emotions which is prevalently heightened next to general emotional dysregulation following CCAS and other cerebellar disorders (Schmahmann et al., 2007; Schmahmann, 2016). Anxiety can be conceptualized as a multifaceted construct, which is comprised of state anger (instances of subjective feelings of tension, worry or fear directly related to adverse situations in a specific moment) and trait anxiety (trait of personality related to individual differences in tendency to present state anxiety) (Van der Veen et al., 2017). Trait anxiety therefore reflects individuals' predisposition towards anxiety in general and were therefore chosen as a more reliable and appropriate indicator for this study. Individuals who score high on anxiety are found to exhibit multiple cognitive distortions such as negative cognitive errors and faulty logical thinking processes which in turn negatively impact reasoning abilities (Maric et al., 2011). The established cerebellar involvement on emotional processing in particular in relation to negative emotion influenced heightened negative mood in an emotion regulation task after administering cerebellar rTMS (Schutter & Van Honk, 2009). The accumulation of these findings supports the evidence for implications of reduced cerebellar size and connectivity to other brain regions in psychopathology and anxiety disorders. In healthy populations intrinsic connectivity between the cerebellum and executive network is influenced by individual differences in anxiety vulnerability (Caulfield et al., 2016). These findings suggest that trait anxiety may play an important role in mediating cerebellar connectivity.

The specific role of the cerebellum in abstract reasoning, also referred to as inductive reasoning has so far only been looked at in psychiatric populations but not in healthy participants. Abstract reasoning refers to a conceptual process in which general rules are derived from the classification and usage of specific examples (Embretson, 2002). This cognitive ability is measured with the Raven's progressive matrices, a task that was originally developed to measure fluid intelligence by John C. Raven in 1938 (Carpenter et al., 1990).

Given the state of the literature, the cerebellum appears to be crucial in processes of learning and cognition of children and the elderly, but its role and importance in healthy young adults has so far been overlooked. Understanding if the cerebellum is actually involved in inductive reasoning in healthy individuals does not just increase our overall understanding of its involvement in cognitive processes, but also provides further evidence for its relevance in clinical work and might give rise to the development of psychiatric medication should focus on targeting the cerebellum. To further address the interrelations between the cerebellum as a whole and its substrates namely Crus I and II and measures of fluid intelligence as the laid-out gap in the literature, this study aims to assess how the anatomy and activity of the cerebellum affects cognitive functioning.

Study 1

The first part of the thesis answers the primary research question how the anatomy of the cerebellum is linked to cognitive functioning. This focus was chosen because of the previously laid out connection between cerebellar volume and intelligence, learning and other cognitive outcomes.

Reduced cerebellar volumes are imminent in many neurological disorders which impact the cerebellum and the cognitive scores of these children tends to be below average (Steinlin, 2008). An example of this are children with paediatric cerebellar astrocytomas, which is a form of benign tumour which develops in brain cells, demonstrate widespread cognitive deficits evident in below average scores on performance and full-scale IQ tests (Beebe et al., 2005). Intelligence is significantly correlated with intracranial cerebral, temporal lobe, hippocampal, and cerebellar volume in neurotypical individuals (Andreasen et al., 1993). Thus, a positive relationship between cerebellar volume and performal IQ is expected.

The primary hypothesis based on previous literature is:

H1: There is a positive relation between cerebellar volumes and performal IQ scores.

Methods

Design

The first part of the thesis is based on a dataset that was published on the data sharing website ABIDE (Autism Brain Imaging Data Exchange), where researchers can use datasets of MRI scans from over 1000 datasets with the aim of promoting discovery science on the brain connectome in Autism Spectrum Disorder (ASD). The ABIDE is a publicly available repository of structural MRI and resting-state fMRI data based on individuals with ASD and typically developing individuals from 17 independent North American and European institutions.[1]

Participants

The dataset consists of 45 neurotypical volunteers who were recruited from the California Institute of Technology and Carnegie Mellon University. 34 participants are males and 11 females, with a mean age of 24.1 years (SD 10.1, age range 9.4 to 56.2 years). Individuals with a history of major neurodevelopmental disorders and below average intelligence scores were excluded from the dataset.

Participants were all of average to above average intelligence, ranging from performal IQ of 90 to 128 with a mean score of 110 (SD 9.7).

Measures

The dependent variable is the performal IQ score measured with the Wechsler Adult Intelligence Scale (WAIS, Wechsler, 1981) and the Wechsler Abbreviated Scale of Intelligence (WASI). They both measure the same abilities using the same subtest, the difference is that the WASI is made up off less subtests than the WAIS. The WAIS is an IQ test originally developed in 1955 by David Wechsler to measure verbal, performal and full-

[1] For a more detailed description, see Appendix 1 and the ABIDE website.

scale IQ in adolescents and adults. The focus on performal IQ was chosen as it is most similar to the cognitive function that is measured in the second study of this thesis.

The independent variables that are analysed for this hypothesis are total cerebellar volume and averaged volume of left/right CRUS I, respectively CRUS II. Cerebellar volumes were assessed using MRI scans at both University sites. A cerebellar segmentation method called CERES[2] was used to parcellate the cerebellum lobules and get estimates on the volume of Crus I and II. CERES is a patch-based multi-atlas segmentation tool, which uses standard resolution magnetic resonance T1-weighted images and the Optimized PatchMatch algorithm to segment the cerebellum into 24 lobules. All measures are taken in cm3.

Intracranial volume, gender and age of the participants are added as control variables.

<u>Data reduction and analysis</u>

Hypothesis 1 was analysed using an OLS linear regression enter method to detect the influence of cerebellar anatomy (IV) on cognition (DV) while controlling for intracranial volume, sex (dummy variable) and age. The independent variables that are analysed for this hypothesis are total cerebellar volume, averaged volume of left/right Crus I, respectively Crus II. An alpha significance levels of 0.05 was chosen to reach a substantial trade-off between alpha and beta errors.

Results

Table 1 shows the descriptive statistics for the variables included.

Table 1. legend

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Dev.
Performal IQ	45	90	128	110.38	9.8
Average Crus I	45	12.1	19.719	15.56	1.84
Average Crus II	45	7.14	14.15	9.53	1.63
Cerebellar mean Volume	45	120.44	172.74	145.43	13.15
Intracranial Volume	45	1249.35	16067.89	2415.59	3455.01
Sex (1 = male)	45	1	2	1.24	0.435
Age	45	9.44	56.20	24.1240	10.13727

[2] For a more detailed description on CERES, look up Romero et al., (2017)

In the multiple OLS regression (F (6, 38) = 1.59, p = 0.177) with an adjusted R^2 of 0.075, hypothesis 1 is not confirmed. The coefficients of total cerebellar volume, Crus I and II are not significant on a 5% level. The control variables sex, age and intracranial volume do not significantly explain the dependent variable.

Table 2 legend

Multiple Ordinary least squares Regression

	B	Std. Error	Beta	t value	p value
(Constant)	79.66	22.66		3.52	0.001
Total Cerebellar Volume	0.48	0.32	0.65	1.54	0.133
Average Crus I	-1.45	1.44	-0.27	-1.01	0.322
Average Crus II	-2.99	1.86	-0.5	-1.6	0.117
Intracranial Volume	0.01	0.00	0.23	1.54	0.131
Sex	5.04	3.79	0.22	1.33	0.192
Age	0.15	0.15	0.15	0.971	0.337

a. Dependent Variable: Performal IQ, adjusted R^2 is 0.075.

As an illustration, the partial correlation graph displayed in figure 1 shows that cerebellar volume and IQ scores are marginally correlated, t(3, 41) = 1.54, p = 0.133.
Since the cofounding variables sex and age did not have an influence on the correlation, they were only controlled for in the first graph (residuals of variables were calculated), while as the second and third scatter plot did not include them.

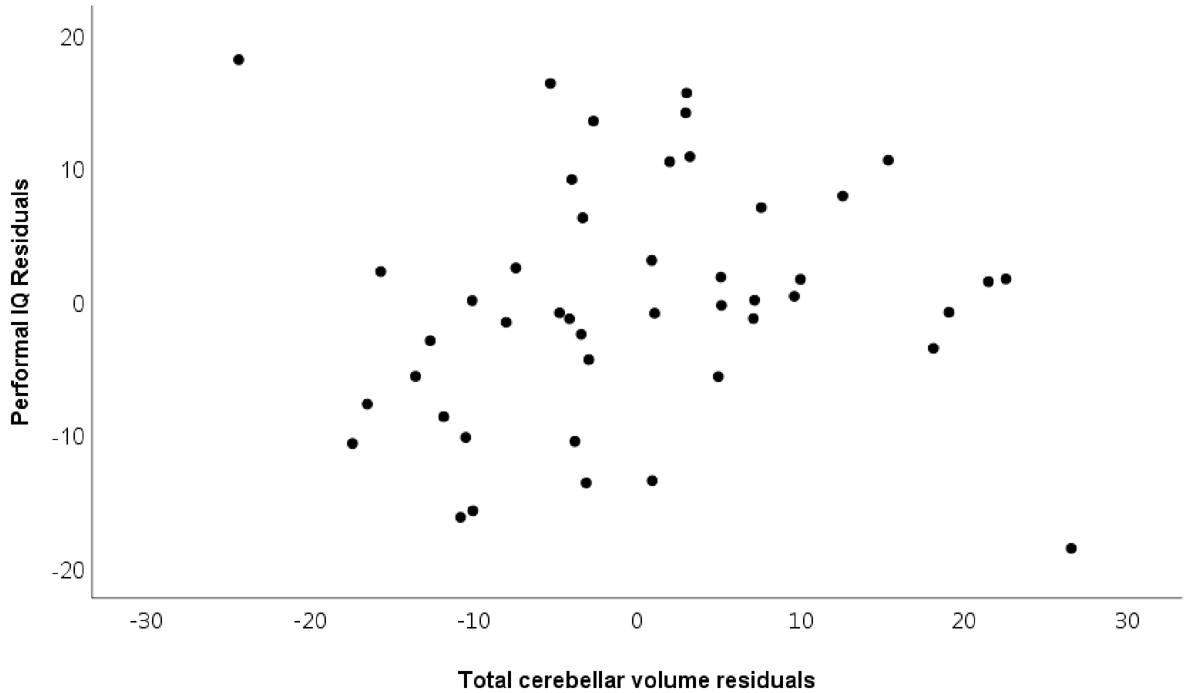

Figure 1: Distribution of performal IQ and total cerebellar volume while controlling for age, sex and intracranial volume

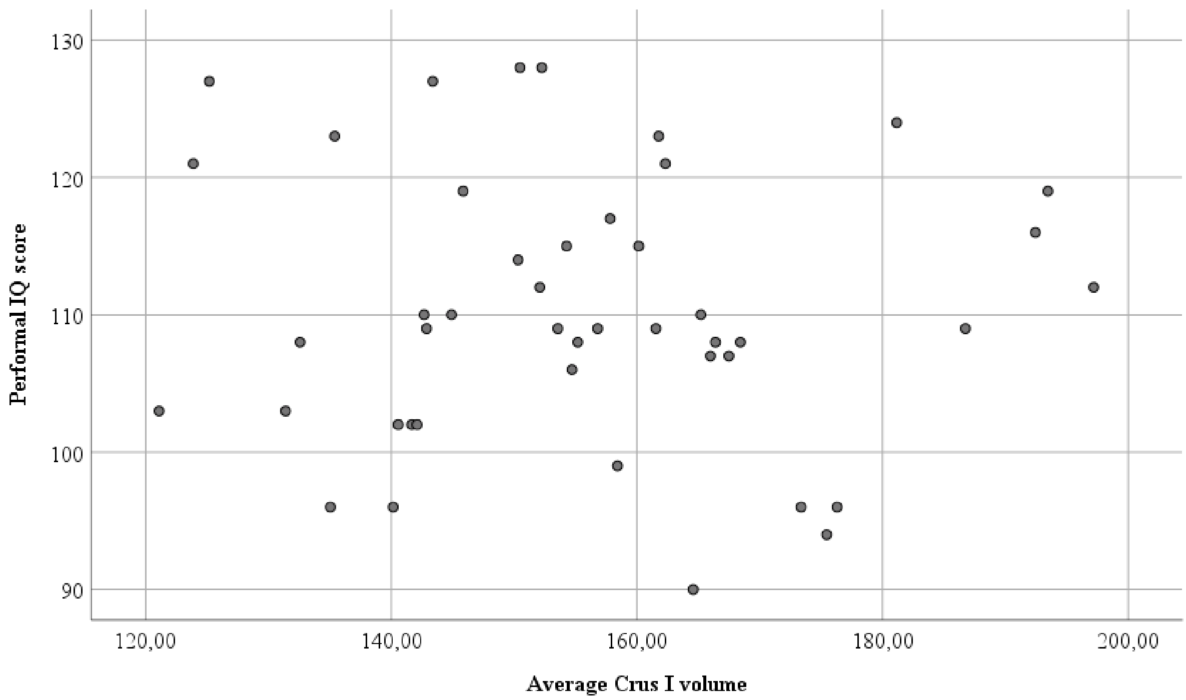

Figure 2: Distribution of performal IQ scores and Average Crus I volume

Figure 2 visually demonstrates that performal IQ scores and average Crus I volume (in $cm^{3})$ are not correlated t (3, 41) = -1.01, p = 0.322.

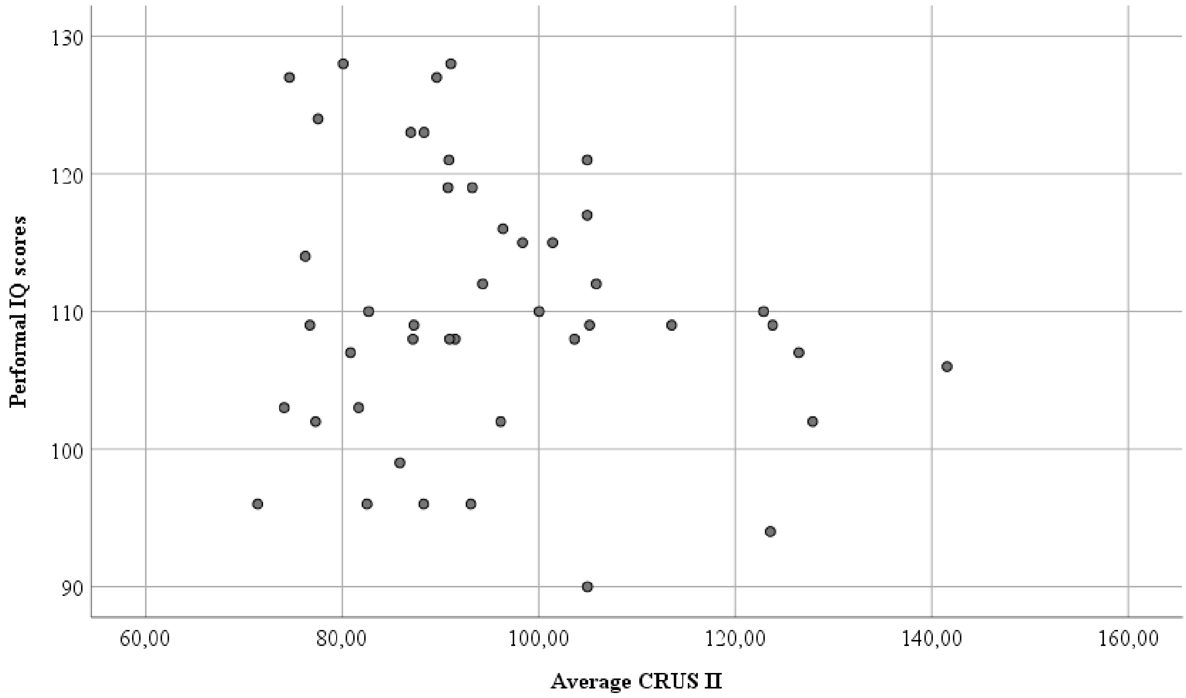

Figure 3: Distribution of performal IQ scores correlated with average Crus II volumes.

There was only a marginal correlation between performal IQ scores and average Crus II volume t (41, 3) = -1.6, p = 0.117

Interim discussion

The aim of study 1 was to examine associations between cerebellar volumes and fluid intelligence. This forms a foundation of how the anatomy of the cerebellum is related to intelligence in neurotypical participants.

Results showed that total cerebellar volume was not correlated with performal IQ scores. This is not in line with the literature, because the importance of cerebellar volume and the negative impact of small cerebellar volume in various neurological disorders which impact the cerebellum has been shown extensively (Hellwig et al., 2013; Stoodley et al., 2012). Also in adolescents born very pre-term smaller cerebellar volumes were found to be significantly related to lower scores on various intelligence tests, such as the WISC and K-ABC, indicating that cerebellar pathology may underlie cognitive impairments (Allin et al., 2001).

Studies that focused on the role of cerebellar vermis volume found that after controlling for prefrontal volume, the relationships between cognitive function and vermian volumes were eliminated, suggesting that prefrontal volumes are better indicators of cognitive performance than cerebellar volumes (Paul et al., 2009). This would be consistent with the frontal ageing hypothesis which states that cognitive declines related to advanced age are consistent with alterations in frontal size and functions (West, 2000).

Intracranial volume, Crus I and Crus II did also not correlate with performal IQ scores. Given that previous neuroimaging studies have found the close connectivity between Crus I and II and the prefrontal cortex in capuchin monkeys and the important role the activity in the prefrontal cortex plays for performal intelligence, our finding that Crus I and II volumes are not correlated to performal IQ is surprising (Balsters et al., 2009). Since cerebellar dissemination is quite rare, few studies have specifically looked at the role of these cerebellar substrates in performal intelligence, so this can be regarded as a novel finding. Given the role of Crus I and II in the default mode network and learning, it would be interesting to investigate if there is indeed an effect for newly learned skills, as the ones measured on this IQ test are expected to be recall of previously learned skills (Yoon et al., 2017). Furthermore, regarding the importance of Crus I in working memory, it is unexpected that Crus I is even less correlated with IQ scores (an indicator of working memory function) than Crus II (Keren-Happuch et al., 2014).

Lastly, it is important to keep in mind that although MRI data can reveal associations, it is not possible to infer causal relationships from them. This means that although non-invasive cerebellar stimulation provides a means to perturb activity in the cerebellum and examine the relation between the cerebellum and aspects of intelligence more directly, these results are only measures of correlation and should be used to further understanding and increase the willingness to research into the topic. Inferring with cerebellar functioning using transcranial direct current stimulation and study its effects on abstract reasoning as a measure of fluid intelligence was the aim of the second part of this study.

Study 2

The secondary part of this thesis is based on the experimental data that was acquired by the master student's own research in the laboratory of Utrecht University from January to March 2020 until the outbreak of the coronavirus made the continuation of data collection impossible. As the aim for 60 participants was reduced into a dataset of only 14 participants, the study was turned into a pilot study. The research questions of the second study analyse the effect of disturbed cerebellar functioning on cognitive functioning. Previous experimental studies have used cathodal cerebellar tDCS as a measure to disrupt cerebellar activity and therefore negatively affect performance, such as motor adaptation during gait (Fernandez et al., 2017).

Given the cerebellar activation during cognitive tasks, it is to be expected that cerebellar disturbance will lead to a decline in inductive reasoning.

H2.1: Disruption of cerebellar activity through cathodal cerebellar tDCS will lead to worse inductive reasoning measured by total score of correct items on the Raven Progressive Matrices.

Patients with psychiatric disorders such as depression and anxiety tend to have difficulties regulating their emotions and exhibit higher levels of trait anxiety and anger (Maric et al., 2011). Given that they oft have simultaneous abnormalities in cerebellar anatomy or functioning and exhibit cognitive impairments, it can be expected that individuals who also exhibit heightened emotional responses show the same pattern (Schutter & Van Honk, 2009).

H2.2: Disparity between cerebellar disruption and performance on the matrices test will be greater for individuals scoring high in trait anxiety than those with low scorings.

Methods

Design

The current study used a double-blind sham controlled cross-over design. The original study was planned as a within-participants, two-part study with 60 participants, but was now turned into a pilot study with 5 participants.

Participants

5 healthy participants (three females, two males, ranging from 21-29 years, mean age = 24.15, SD = 2.51) participated in a double-blind sham-controlled between-subject design in exchange for course credit or a monetary reward (1.5 PPU or 12€). They did not have a psychiatric or neurological history, did not use medication (except for women using oral contraceptives), showed no contradictions for non-invasive brain stimulation and did not have a skin disease or skin allergy. Participants were unaware of the aim of the study and were naive to the tDCS. Written informed consent was obtained. The experiment was approved by the local ethics committee of the Faculty of Social and Behavioural Sciences of Utrecht University.

Measures

The independent variable was the cerebellar disruption and the dependent variable was the number of correct items on the Raven Progressive Matrices test. For H2.2., trait anxiety as the moderator was included.

Independent Variable: Cerebellar tDCS

Cerebellar disruption was achieved through cathodal transcranial direct-current Stimulation (tDCS), which is a form of neuromodulation where electrodes are placed across the lower parts scalp and generate low direct currents. A battery-driven Magstim Eldith DC-stimulator Plus (NeuroConn, GmbH, Ilmenau, Germany) was used for stimulation. One of the two conducive-rubber electrodes of 5 x 7 cm was placed in a wet sponge embedded in electrode gel over the medial cerebellum (35cm^2) and the reference electrode was placed over the right deltoid muscle (25cm^2). The sponges containing the electrodes were placed under an EEG cap for appropriate localization and fixation.[3]

Cathodal tDCS leads to decreased neuronal excitability by decreasing the spontaneous cell firing and hyperpolarizing the resting membrane potential (Ferrucci et al., 2015). There were no cortical changes during and after the stimulation has ended given the intensity of 2mA and duration of 20 minutes. This type of tDCS has been chosen to achieve cerebellar disruption instead of enhancement. The stimulating electrode is placed over the cerebellum and the return electrode over the right shoulders in order to target the posterior cerebellum (Ferrucci et al., 2015). Stimulation in the sessions comprises either: (1) cathodal tDCS (2 mA, 30s ramp up and 30s ramp-down); and (2) placebo (SHAM) tDCS (0 mA, 30s ramp up and 30s ramp-down). In both cathodal tDCS and SHAM, the current was initially increased for several seconds until reaching 2 mA. In SHAM, the stimulator was turned off after 30 seconds. The perceived sensations on the skin, such as itching, usually fade out in the first 30s of tDCS so the participants did not know whether they were in the real of sham tDCS condition. Moreover, in all sessions both, subjects and investigator, were blinded to the intervention type.

Throughout the study, stimulation was well tolerated, and no adverse events occurred.

Dependent Variable: Fluid intelligence – Raven Progressive Matrices

Cognitive performance was measured through the Raven Progressive Matrices test. It is regarded as a measure of abstract and inductive reasoning which are part of fluid intelligence.

[3] Further details on the application of cerebellar tDCS are explained by Ferrucci et al., 2014

It consists of 60 items which are listed in order of difficulty. To solve the matrix, participants must identify the missing element to complete a pattern. This test has been used in research for years and was also found to score high in terms of validity and reliability (Burke, 1985).

Moderator: Trait Anxiety

The State-Trait Anxiety Inventory (STAI) is a commonly used measure of trait anxiety (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). It is a 40-item self-report measure which is also based on a 4-point Likert scale. It is comprised into three scales: trait anxiety, state anxiety and anxiety as a personal characteristic. This questionnaire has been investigated in terms of its reliability and validity and is considered as high in both (Lievaart et al, 2016; Metzger, 1976). Trait emotions are different to state emotions in that they persist on a day-to-day basis and are not the reactions in exceptional but everyday situations. Since trait emotions seem to be better constant measures, they were chosen over state emotions.

Procedure

Participants were recruited both offline and online through the distribution of a poster which briefly laid out the most important parts of the study and explained who was eligible. Participants who were interested were then able to contact the research student via email and request a time slot to take part. The study was advertised through research participation groups on Facebook as well as the University’s online research website SONA where psychology bachelor students can sign up in order to receive credits towards their degree.

In the first email contact, participants were presented with more detailed information on the study through the study information sheet and consent form. They were also reminded of the eligibility criteria, specifically the need to be free of any illness or medication at the time of participation. Once the study participation could be confirmed on both sides, they were invited into the lab on two occasions, which had to be at the same time of the day (+/- 1 hour) on two executive days within one week. On their first time in the lab, they were provided with the physical copies of the information sheet and consent form which they had to sign and were asked again if they had any more questions. After filling out the consent form the had to fill in the electronic version of the STAI. Upon completion the tDCS was applied to their scalp, the machine was turned on and the random code with the condition was added. In the next step the instruction of the Raven Progressive Matrices was read out to participants and they had to complete two example trials to see if they understood how it worked. If they did, they got to proceed on to the actual test. The test took about 15 minutes and up to 20 minutes per participant depending on how long they took for each matrix. Afterwards the tDCS machine was turned off and taken off participants heads. They were thanked and a second appointment was made. On this second appointment, participants went through a similar procedure, but this time they did not have to sign the consent form or fill out the questionnaire. This is also why the first session took roughly 30-40 minutes and the second one about 20 minutes. Upon completion of the second part participants got to fill in their bank details if they wished to receive a monetary compensation for their participation. The demographic and research data were kept in separate files at all times and not on same computer.

Data-reduction and analysis

Hypothesis 2.1 is analysed using a paired samples t-test while hypotheses 2.2 uses a repeated measures t-test as a moderator analysis. Anxiety is the moderator under investigation. For the repeated measures t-test the corrected Greenhouse Geisser test was chosen as the most appropriate test, because sphericity could not be assumed.

Results

Stimulation was well tolerated, and no adverse events occurred.

Table 3 shows the descriptive statistics of the variables included in study 2.

Table 3 legend

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
real	5	9	13	11.40	1.82
sham	5	8	15	11.80	2.86
Reaction Time during real stimulation	5	19.47	37.87	28.27	6517.27
Reaction Time during sham stimulation	5	19.82	39.37	30.13	7181.74
Trait anxiety	5	29	46	36.80	6.9

Table 4 legend

Paired Samples Statistics – Scores on Raven's Progressive Matrices

		Mean	N	Std. Deviation	Std. Error Mean
Scores on Raven's Matrices	Real	11.40	5	1.82	0.81
	Sham	11.80	5	2.86	1.28

Table 4 compares the means of correct items participants got right on the Raven Progressive matrices task while receiving the real and a sham tDCS. H 2.1 was not confirmed, because participants who received the real tDCS (mean = 11.4, SD = 1.82) did not do worse on the Raven Progressive Matrices test, but they even did slightly better than those in the sham condition (mean = 11.8, SD = 2.86), with a t-value of -0.78 (p = 0.477). These results suggest that receiving cerebellar tDCS did not significantly impact inductive reasoning.

To assess whether the reaction time as an indicator of effort or even ability differed in the sham and real stimulation, a further paired samples t-test was carried out. The reaction time states how long participants took on average per matrix on all of the 21 matrices they had to solve in each condition.

Table 5 legend

Paired Samples Statistics - Reaction times

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Reaction Time during real stimulation	28.27	5	6517.27	29.14
	Reaction Time during sham stimulation	30.13	5	7181.74	32.11

Table 5 depicts the differences in reaction times that participants took while doing the matrices test under the real and sham stimulation. Participants had slightly shorter reaction times when receiving the real stimulation (mean = 29.14 seconds) versus the sham stimulation (mean = 32.11 seconds), t = -0.67, p = .538.

Table 6 legend

Tests of Within-Subjects Effects

Measure: Raven's Progressive Matrices

Factors		Type III Sum of Squares	df	Mean Square	F	Sig.
tDCS	Greenhouse-Geisser	1.19	1.00	1.19	2.25	0.230
tDCS * trait anxiety	Greenhouse-Geisser	1.01	1.00	1.01	1.89	0.262

A one-way within subjects (or repeated measures) ANOVA was conducted to compare the effect of trait anxiety on the relationship between performance on the matrices test in both the real and sham stimulation. As sphericity cannot be assumed (Mauchly's test = 1.00), the corrected Greenhouse-Geissler test shows that the tDCS stimulation did not have a significant effect with F(1,8) = 2.25 (p = 0.230).

Trait anxiety did not have a moderating effect on performance during either stimulation with F(1,8) = 1.896 (p = 0.262).

As sphericity cannot be assumed, the corrected Greenhouse-Geissler test shows that the tDCS stimulation did not have a significant effect. Sphericity not assumed = 1.2, F (1,9) = 2.25, p = 0.23.
Post hoc tests were not run since the results were non-significant. These results suggest that trait anxiety did not influence participants' performance depending on receiving tDCS.

Interim discussion

Contrary to our hypothesis, receiving cerebellar tDCS (real stimulation) while undertaking the Raven progressive matrices did not lead to worse performance on the cognitive test. Instead, there was no significant difference between conditions and participants scored almost identically regardless of the fact if they received stimulation or not. There were differences between participants, which indicate differences in fluid intelligence and inductive reasoning on an intra-individual level. This is not in line with previous research, which found that cerebellar tDCS can modulate cognition, in particular verbal working memory, procedural learning and reaction times (Boeringer et al., 2013; Ferrucci & Priori, 2014).

However, there are also other studies, which did not find effects of cerebellar tDCS, which are in line with hypothesis 2.1. In one of them, participants received anodal, cathodal, and sham cerebellar tDCS over the right cerebellum and there were no significant differences in performance between conditions while undertaking a working memory task (van Wessel et al., 2016). They propose an explanation for their findings in which the task that they used, the N-back task, requires more explicit than implicit memory. However cerebellar functioning has been linked to implicit memory, while as the PFC relates to explicit memory. This would explain why there are no real effects applying the cerebellar tDCS, since the task mostly relies on activity in the PFC.

Another interesting perspective is that the effects of cerebellar tDCS on cognition are likely to be task- and/or load-specific. This comes from a study which only found effects of cathodal cerebellar tDCS on tasks which were rated as difficult and it made response times shorter in a task on verbal fluency (Pope, 2015).

Regarding hypothesis 2.2, trait anxiety did not moderate the relationship between cerebellar tDCS and scoring on the matrices task. How anxiety as an emotional response influences inductive reasoning as a cognitive response under the influence of tDCS is a novel approach which so far has not been looked at specifically. Previous research has found links between cerebellar functioning and anxiety without its relation to cognitive functioning. One example of this is the mediating effect of anxiety vulnerability on the intrinsic connectivity between the cerebellum and executive network (Caulfield et al., 2016).

Psychiatric populations with diverse anxiety disorders also exhibit differences in cerebellar volume size and cerebellar functional connectivity (Laricchiuta et al., 2014). A systematic review could link cerebellar abnormalities to anxiety disorders, depression, autism, ADHD, bipolar disorder and schizophrenia (Phillips at al., 2015). The cerebellar anatomy and functioning depend on the type of anxiety disorder, but an adult PTSD sample demonstrated higher blood flow in the cerebellum compared to healthy controls (Bonne et al., 2003). There was also hyperactivity in the fear network and significantly higher levels of glucose uptake in the cerebellum in patients with panic disorder (Sakai et al., 2005).

These could be explained through impairments in cerebellar anatomy and functioning which may result in decreased cognitive and affective information processing (i.e., the dysmetria of thought hypothesis), giving rise to emotional dysregulation and subsequently symptoms of depression and anxiety (Schmahmann, 2007).

General discussion

Both studies have investigated the extent the cerebellum, both in terms of its volume and functioning, is implicated in cognition. For Study 1, structural brain images of total cerebellar volume, average Crus I and Crus II volumes were compared with performal IQ scores on the WISC. Results of this study could not find a correlation between cerebellar substrate volumes and IQ scores. This is not in line with previous literature, which highlights the importance of cerebral as well as cerebellar volumes for cognitive performance (Allin et al., 2001; Hellwig et al., 2013). It is important to note that the two named studies both focused on clinical groups, the first one on pre-term born adolescents and the second on adolescents with temporal lobe epilepsy. The scope of the literature on the connection between cerebellar volumes and lower intelligence is mainly based on somatic and psychiatric patients (Parmeggiani et al., 2003).

This is in contrast to this study, which has used only healthy participants and purposely excluded participants with preconditions. A meta-analysis establishing the functional topography in the human cerebellum in neurotypical individuals (Stoodley, Valera & Schmahmann, 2012). They found that spatial processing was predominantly left-lateralized and localized to lobule VI, language related skills activated predominantly right-hemisphere regions of lobules VI, Crus I and Crus II, tasks requiring working memory activated bilateral regions of lobules VI, Crus I, and VIIIA, executive function paradigms demonstrated converging activation in lobules VI, Crus I and left VIIB and lastly tasks involving emotional processing paradigms activated bilateral clusters in VI-Crus I in healthy young adults

(Stoodley, Valera & Schmahmann, 2012). But not only preconditions but also age seems to be an indicator of how much cerebellar volumes affect cognitive functioning (Paul et al., 2009). This has been emphasised in studies which found cerebellar gray matter volume decline as well as degraded connections between the cerebral cortex and cerebellar circuitry in the elderly being correlated with cognitive decline (Hogan et al., 2011).

Given the role the cerebellum plays in learning, its role in childhood cognitive development is also more relevant than in this population, which were young adults. Besides their age, the sample was specific in that they were recruited as students from Universities, meaning that their cognitive abilities and intelligence can be expected to be above average, which is in line with their IQ scoring (between 90 and 128). It can therefore be reasoned that the scores on intelligence tests of our population require activity mostly based on the PFC and its connectivity to the cerebellum despite variability of cerebellar volumes (mean = 145.43cm^3 , SD = 13.15) between participants to identify correlations between cerebellar volume and IQ scores. This is however specific to this dataset and hence the results should be replicated with a larger sample of a more diverse social background, which is likely to exhibit bigger differences in cerebellar volume as well as higher disparities in IQ scores.

Furthermore, given that this sample did not have neurological preconditions, which might have impacted their neurological development and potentially harmed cerebellar volumes, the cerebellar volume of our sample was slightly higher than average. What would have been of interest would be to control for week of gestation to see if being born preterm might have a negative impact on cerebellar volumes and potentially cognition (Brossard-Racine et al., 2015). Besides cerebellar volumes, other neural substrates might have had an effect on cognition, such as the volumes of gray and white matter as well as different structures of the cerebral cortex. Intracranial volume of the cerebellum was one of the factors controlled for in this study and it did not influence performal IQ scores. There might even be positive correlations in that subjects who have higher cerebral volumes and IQ scores also have higher cerebellar volumes, but these are ideas which need further exploration. Future research could also focus on investigating the implications of the cerebral-cerebellar pathway on reasoning abilities through functional magnetic imaging.

Limitations of the first study constitute its small sample size as well as potential not-included factors influencing brain activity, such as menstrual cycle phase, which was not controlled for, and might influence female brain activity during performance on the WISC (Comasco and Sundström-Poromaa, 2015).

Study 2 found that cerebellar cathodal tDCS did not influence correct scores and reaction times during inductive reasoning, nor did trait anxiety have an effect. These findings were contradictory to previous studies, which found that tDCS does not just influence inductive reasoning abilities in terms of scoring, but also prolong reaction times (Ferrucci & Priori, 2014; Pope, 2015). Interpretations of our pilot study must be made with caution though, given the extremely small sample size, which was unfortunately due to the closure of Utrecht University following the pandemic of Covid-19.

Another factor which might explain why tDCS did not influence the performance of participants might be that the stimulation might have not been done long enough to measure significant effects. Participants were stimulated for up to 20 minutes while solving the 21 matrices, however many of them finished before the time was up and ended up only being stimulation for roughly half of the time. Even though stimulation was started 60 seconds before participants were asked to start the Raven test, this might have not been long enough for either the machine to stimulate fully and reach its intensity. The chosen intensity of 2mA matches those of other studies which did find differences in scoring, hence missing differences is less likely to be due to intensity of stimulation (van Wessel et al., 2016). Instead, there are many other intraindividual factors influencing stimulation, such as fatigue and stress levels.

As with the first study, the small sample size can be named as the biggest limitation of the second study. Statistical effects as well as reliability, validity and generalizability cannot be taken as granted with the sample size. Another limitation might be the fact that only one test was used to measure inductive reasoning, as more tests might have provided a more reliable index of inductive reasoning.

The small sample size also partially explains why trait anxiety did not moderate the relationship between cerebellar disruption and inductive reasoning. Given the fact that patients with anxiety disorders often exhibit cerebellar functioning abnormalities, it would be expected that this also influences their cognitive performance (Sakai et al., 2005). What would serve as an explanation of why heightened trait anxiety did not impact cognitive performance may be that anxiety influenced how participants felt about receiving brain stimulation as worry and fear of tDCS as well as the fear of not performing well on the task are expected to be bigger than in those scoring high on trait anxiety. At the same time individuals high in trait anxiety also tend to have higher pleasing tendencies and conscientiousness than others, which might have balanced out the increased worries (Karsten et al., 2012). This might have been controlled for by surveying participants about their worries related to low performance and brain stimulation and later on controlling for them separately in the analysis.

A strength of this study which needs to be mentioned is the choice of a within-subjects over a between-subjects design so that differences in both performance and anxiety were not due to differences in intelligence and personality between participants, but instead these were kept stable by testing the same individual twice.

Future research could focus on stimulating different substrates of the cerebellum separately to assess, which has the biggest implication on inductive reasoning. This has been mostly done by stimulating only the cerebellar vermis, but with the development of more specific stimulation methods it might even be possible someday to only stimulate for instance Crus I and II or just one of the cerebellar hemispheres. That way focality would be improved by using different montages such as high density with the aim of focusing on lateralisation of function.

Investigating the precise role of the cerebellum in cognition is a task that will keep on being a challenge to explore in future research given its cognitive, motor and emotional implications for somatic and psychiatric patient populations. tDCS can be seen as a novel and exciting method to explore its functioning as well as being used as its rehabilitative measure to achieve the best possible treatment for patients and outcome in research.

References

Allin, M., Matsumoto, H., Santhouse, A. M., Nosarti, C., AlAsady, M. H., Stewart, A. L., ... & Murray, R. M. (2001). Cognitive and motor function and the size of the cerebellum in adolescents born very pre-term. Brain, 124(1), 60-66.

Andreasen, N. C., Flaum, M., Swayze, V., O'Leary, D. S., Alliger, R., Cohen, G., ... & Yuh, W. T. (1993). Intelligence and brain structure in normal individuals. American Journal of Psychiatry, 150, 130-130.

Balsters, J. H., Cussans, E., Diedrichsen, J., Phillips, K. A., Preuss, T. M., Rilling, J. K., & Ramnani, N. (2010). Evolution of the cerebellar cortex: the selective expansion of prefrontal-projecting cerebellar lobules. Neuroimage, 49(3), 2045-2052.

Beebe, D. W., Ris, M. D., Armstrong, F. D., Fontanesi, J., Mulhern, R., Holmes, E., & Wisoff, J. H. (2005). Cognitive and adaptive outcome in low-grade pediatric cerebellar astrocytomas: evidence of diminished cognitive and adaptive functioning in National

Collaborative Research Studies (CCG 9891/POG 9130). Journal of Clinical Oncology, 23(22), 5198-5204.

Ben-Yehudah, G., Guediche, S., & Fiez, J. A. (2007). Cerebellar contributions to verbal working memory: beyond cognitive theory. The Cerebellum, 6(3), 193.

Bernard, J. A., & Seidler, R. D. (2014). Moving forward: age effects on the cerebellum underlie cognitive and motor declines. Neuroscience & Biobehavioral Reviews, 42, 193-207.

Boehringer, A., Macher, K., Dukart, J., Villringer, A., & Pleger, B. (2013). Cerebellar transcranial direct current stimulation modulates verbal working memory. Brain stimulation, 6(4), 649-653.

Brossard-Racine, M., Du Plessis, A. J., & Limperopoulos, C. (2015). Developmental cerebellar cognitive affective syndrome in ex-preterm survivors following cerebellar injury. The Cerebellum, 14(2), 151-164.

Brouwer, R. M., Hedman, A. M., van Haren, N. E., Schnack, H. G., Brans, R. G., Smit, D. J., ... & Pol, H. E. H. (2014). Heritability of brain volume change and its relation to intelligence. Neuroimage, 100, 676-683.

Buckner, R. L. (2013). The cerebellum and cognitive function: 25 years of insight from anatomy and neuroimaging. Neuron, 80(3), 807-815.

Bugalho, P., Correa, B., & Viana-Baptista, M. (2006). Role of the cerebellum in cognitive and behavioural control: scientific basis and investigation models. Acta medica portuguesa, 19(3), 257-67.

Carpenter, P. A., Just, M. A., & Shell, P. (1990). What one intelligence test measures: a theoretical account of the processing in the Raven Progressive Matrices Test. Psychological review, 97(3), 404.

Caulfield, M. D., Zhu, D. C., McAuley, J. D., & Servatius, R. J. (2016). Individual differences in resting-state functional connectivity with the executive network: support for a cerebellar role in anxiety vulnerability. Brain Structure and Function, 221(6), 3081-3093.

Chen, S. A., & Desmond, J. E. (2005). Cerebrocerebellar networks during articulatory rehearsal and verbal working memory tasks. Neuroimage, 24(2), 332-338.

Comasco, E., and Sundström-Poromaa, I. (2015). Neuroimaging the menstrual cycle and premenstrual dysphoric disorder. Curr. Psychiatry Rep. 17, 77. doi: 10.1007/s11920-015-0619-4

DeYoung, C. G., Hirsh, J. B., Shane, M. S., Papademetris, X., Rajeevan, N., & Gray, J. R. (2010). Testing predictions from personality neuroscience: Brain structure and the big five. Psychological science, 21(6), 820-828.

Embretson, S. E. (2002). Generating abstract reasoning items with cognitive theory. Item generation for test development, 219-250.

Fernandez, L., Albein-Urios, N., Kirkovski, M., McGinley, J. L., Murphy, A. T., Hyde, C., ... & Enticott, P. G. (2017). Cathodal transcranial direct current stimulation (tDCS) to the right cerebellar hemisphere affects motor adaptation during gait. The Cerebellum, 16(1), 168-177.

Ferrucci, R., Cortese, F., & Priori, A. (2015). Cerebellar tDCS: how to do it. The Cerebellum, 14(1), 27-30.

Ferrucci, R., & Priori, A. (2014). Transcranial cerebellar direct current stimulation (tcDCS): motor control, cognition, learning and emotions. Neuroimage, 85, 918-923.

Kandel, J. H. Schwartz, & Jessell T.M. (2000). Principles of neural science (Vol. 4, pp. 1227-1246). E. R. (Eds.). New York: McGraw-hill.

Glickstein M, Doron K. (2008) Cerebellum: connections and functions. Cerebellum 7:589–94

Haeems, G. B. (2018). Emotion regulation in social anxiety disorder: exploration and neuro-modulation of underlying neural mechanisms of cognitive reappraisal (Doctoral dissertation, University of Southampton).

Heit, E. (2015). Brain imaging, forward inference, and theories of reasoning. Frontiers in human neuroscience, 8, 1056.

Hellwig, S., Gutmann, V., Trimble, M. R., & van Elst, L. T. (2013). Cerebellar volume is linked to cognitive function in temporal lobe epilepsy: a quantitative MRI study. Epilepsy & Behavior, 28(2), 156-162.

Hogan, M. J., Staff, R. T., Bunting, B. P., Murray, A. D., Ahearn, T. S., Deary, I. J., & Whalley, L. J. (2011). Cerebellar brain volume accounts for variance in cognitive performance in older adults. Cortex, 47(4), 441-450.

Ismail, Z., Gatchel, J., Bateman, D. R., Barcelos-Ferreira, R., Cantillon, M., Jaeger, J., ... & Mortby, M. E. (2018). Affective and emotional dysregulation as pre-dementia risk markers: exploring the mild behavioral impairment symptoms of depression, anxiety, irritability, and euphoria. International psychogeriatrics, 30(2), 185-196.

Karamian, A.I. (1962) *Evolution of the function of the cerebellum and cerebral hemispheres*. Jerusalem: Israel Program for Scientific Translations.

Karsten, J., Penninx, B. W., Riese, H., Ormel, J., Nolen, W. A., & Hartman, C. A. (2012). The state effect of depressive and anxiety disorders on big five personality traits. Journal of psychiatric research, 46(5), 644-650.

Keren-Happuch, E., Chen, S. H. A., Ho, M. H. R., & Desmond, J. E. (2014). A meta-analysis of cerebellar contributions to higher cognition from PET and fMRI studies. Human brain mapping, 35(2), 593.

Laricchiuta, D., Petrosini, L., Piras, F., Macci, E., Cutuli, D., Chiapponi, C., ... & Tamorri, S. M. (2014). Linking novelty seeking and harm avoidance personality traits to cerebellar volumes. Human brain mapping, 35(1), 285-296.

Lind, A., Parkkola, R., Lehtonen, L., Munck, P., Maunu, J., Lapinleimu, H., ... & PIPARI Study Group. (2011). Associations between regional brain volumes at term-equivalent age and development at 2 years of age in preterm children. Pediatric radiology, 41(8), 953-961.

Maric, M., Heyne, D. A., van Widenfelt, B. M., & Westenberg, P. M. (2011). Distorted cognitive processing in youth: the structure of negative cognitive errors and their associations with anxiety. Cognitive therapy and research, 35(1), 11-20.

Molinari, M., & Leggio, M. G. (2007). Cerebellar information processing and visuospatial functions. The cerebellum, 6(3), 214-220.

Mostofsky, S. H., Kunze, J. C., Cutting, L. E., Lederman, H. M., & Denckla, M. B. (2000). Judgment of duration in individuals with ataxia-telangiectasia. Developmental neuropsychology, 17(1), 63-74.

Oldrati, V., & Schutter, D. J. L. G. (2018). Targeting the human cerebellum with transcranial direct current stimulation to modulate behavior: A meta-analysis. The Cerebellum, 17(2), 228–236.

Paradiso, S., Andreasen, N. C., O'Leary, D. S., Arndt, S., & Robinson, R. G. (1997). Cerebellar size and cognition: correlations with IQ, verbal memory and motor dexterity. Cognitive and Behavioral Neurology, 10(1), 1-8.

Parmeggiani, A., Posar, A., Scaduto, M. C., Chiodo, S., & Giovanardi-Rossi, P. (2003). Epilepsy, intelligence, and psychiatric disorders in patients with cerebellar hypoplasia. Journal of child neurology, 18(1), 1-4.

Paul, R., Grieve, S. M., Chaudary, B., Gordon, N., Lawrence, J., Cooper, N., ... & Gordon, E. (2009). Relative contributions of the cerebellar vermis and prefrontal lobe volumes on cognitive function across the adult lifespan. Neurobiology of aging, 30(3), 457-465.

Pfaff, D.W. (2013) *Neuroscience in the 21st century: from basic to clinical*. Cerebellum Anatomy and Function (p.1149-1167) New York: Springer.

Percheron, G., Francois C., Talbi B., Yelnik J. & Fenelon G. (1996*) The primate motor thalamus*. Brain Res Rev, 22, 93-181.

Petrosini, L., Cutuli, D., Picerni, E., & Laricchiuta, D. (2015). Cerebellum and personality traits. The Cerebellum, 14(1), 43-46.

Pope, P. A. (2015). Modulating cognition using transcranial direct current stimulation of the cerebellum. JoVE (Journal of Visualized Experiments), (96), e52302.

Pope, P. A., & Miall, R. C. (2012). Task-specific facilitation of cognition by cathodal transcranial direct current stimulation of the cerebellum. Brain stimulation, 5(2), 84-94.

Purves D., Augustine G. J., Fitzpatrick D., et al., (2011). Projections from the cerebellum. editors. Neuroscience. 2nd edition. Sunderland (MA): Sinauer Associates.

Raymond, J. L., Lisberger, S. G., & Mauk, M. D. (1996). The cerebellum: a neuronal learning machine?. Science, 272(5265), 1126-1131.

Romero, J. E., Coupé, P., Giraud, R., Ta, V. T., Fonov, V., Park, M. T. M., ... & Manjón, J. V. (2017). CERES: a new cerebellum lobule segmentation method. Neuroimage, 147, 916-924.

Sakai, Y., Kumano, H., Nishikawa, M., Sakano, Y., Kaiya, H., Imabayashi, E., ... & Diksic, M. (2005). Cerebral glucose metabolism associated with a fear network in panic disorder. Neuroreport, 16(9), 927-931.

Schmahmann, J. D. (2016). The Cerebellar Cognitive Affective Syndrome and the Neuropsychiatry of the Cerebellum. In Essentials of Cerebellum and Cerebellar Disorders (pp. 499-511). Springer, Cham.

Schmahmann, J. D., & Sherman, J. C. (1998). The cerebellar cognitive affective syndrome. Brain: a journal of neurology, 121(4), 561-579.

Schmahmann, J. D., Weilburg, J. B., & Sherman, J. C. (2007). The neuropsychiatry of the cerebellum—insights from the clinic. The cerebellum, 6(3), 254-267.

Schutter, D. J., Koolschijn, P. C. M., Peper, J. S., & Crone, E. A. (2012). The cerebellum link to neuroticism: a volumetric MRI association study in healthy volunteers. PLoS One, 7(5).

Schutter, D. J., & van Honk, J. (2009). The cerebellum in emotion regulation: a repetitive transcranial magnetic stimulation study. The Cerebellum, 8(1), 28-34.

Stoodley, C. J. (2012). The cerebellum and cognition: evidence from functional imaging studies. The Cerebellum, 11(2), 352-365.

Stoodley, C. J., & Stein, J. F. (2013). Cerebellar function in developmental dyslexia. The Cerebellum, 12(2), 267-276.

Stoodley, C. J., Valera, E. M., & Schmahmann, J. D. (2012). Functional topography of the cerebellum for motor and cognitive tasks: an fMRI study. Neuroimage, 59(2), 1560-1570.

Strick, P. L., Dum, R. P., & Fiez, J. A. (2009). *Cerebellum and nonmotor function*. Annual review of neuroscience, 32, 413-434.

Sullivan, E. V., Rosenbloom, M. J., Deshmukh, A., Desmond, J. E., & Pfefferbaum, A. (1995). Alcohol and the cerebellum: effects on balance, motor coordination, and cognition. Alcohol health and research world, 19(2), 138.

Tam, E. W., Chau, V., Ferriero, D. M., Barkovich, A. J., Poskitt, K. J., Studholme, C., ... & Miller, S. P. (2011). Preterm cerebellar growth impairment after postnatal exposure to glucocorticoids. Science translational medicine, 3(105), 105ra105-105ra105.

van der Veen, D. C., van Dijk, S. D., Comijs, H. C., van Zelst, W. H., Schoevers, R. A., & Oude Voshaar, R. C. (2017). The importance of personality and life-events in anxious depression: from trait to state anxiety. Aging & mental health, 21(11), 1177-1183.

van Wessel, B. W., Claire Verhage, M., Holland, P., Frens, M. A., & van der Geest, J. N. (2016). Cerebellar tDCS does not affect performance in the N-back task. Journal of clinical and experimental neuropsychology, 38(3), 319-326.

Wechsler, David, 1896-1981. (1981). WAIS-R : Wechsler adult intelligence scale-revised. New York, N.Y.: Psychological Corporation.

West, R. (2000). In defense of the frontal lobe hypothesis of cognitive aging. Journal of the International Neuropsychological Society, 6(6), 727-729.

Xu, J., Kobayashi, S., Yamaguchi, S., Iijima, K. I., Okada, K., & Yamashita, K. (2000). Gender effects on age-related changes in brain structure. American journal of neuroradiology, 21(1), 112-118.

Yoon, Y. B., Shin, W. G., Lee, T. Y., Hur, J. W., Cho, K. I. K., Sohn, W. S., ... & Kwon, J. S. (2017). Brain structural networks associated with intelligence and visuomotor ability. Scientific reports, 7(1), 1-9.

Appendix

ABIDE Website

Overall, the data platform consists of cross-sectional and longitudinal data of a total of 539 individuals with ASD and 573 neurotypical individuals ranging from the ages of 5 to 64. The data sets are completely anonymised and coordination of publication of datasets are controlled by the project directors Adriana Di Martino and Michael Milham. Their project is financially supported by an award of the National Institute of Mental Health and the New York University School of Medicine.