Cerebellar parcellation in schizophrenia and bipolar disorder

Running title: Cerebellum in psychosis

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Abstract.

Objective. Cerebellum plays a crucial role in the regulation of cognition and emotion processing. Cerebellar alterations could explain symptoms of schizophrenia spectrum disorder (SZ) and bipolar disorder (BD). In addition, literature suggests that lithium might influence cerebellar anatomy. Our aim was to study cerebellar anatomy in SZ and BD, and investigate the effect of lithium. **Methods.** Participants from 7 centers worldwide underwent a 3T MRI. We included 182 patients with SZ, 144 patients with BD and 322 controls. We automatically segmented the cerebellum using the CERES pipeline. All outputs were visually inspected. **Results.** Patients with schizophrenia SZ showed a smaller global cerebellar grey matter volume compared to controls, with most of the changes located to the cognitive part of the cerebellum (Crus II and lobule VIIb). This decrease was present in the subgroup of patients with recent-onset SZ. We did not find any alterations in the cerebellum in patients with BD. However, patients medicated with lithium had a larger size of the anterior cerebellum, compared to patients not treated with lithium. **Conclusion.** Our multicenter study supports a distinct pattern of cerebellar alterations in SZ and BD.

Keywords: Cerebellum, psychosis, parcellation, lithium

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Significant outcomes:

- Cortical grey matter volume in the cognitive part of the cerebellum is smaller in patients with schizophrenia compared to controls.
- Cortical grey matter volume was no different in patients with bipolar disorders compared to controls.
- Lithium increases the volume of the anterior part of the cerebellum

Limitations:

- The design of the study was cross-sectional

1. Introduction

The cerebellum represents 10% of the brain volume but contains more than 50% of its neurons [1]. In humans, the cerebellum and the prefrontal cortex are the two most developed parts in comparison with other non-human primates [2]. Following the seminal work of Leiner et al. [3] suggesting that the cerebellum was involved in non-motor function, Schmahmann et al. described a decade later the cognitive and affective cerebellar syndrome [4]. It is now admitted that the cerebellum is involved in a broad range of cognitive function, including working memory, emotion processing or social cognition [5].

Functional magnetic resonance imaging (fMRI) [6] and lesion studies [7] suggested that the cerebellum can be functionally divided in regions based on their connectivity with the cerebrum. The posterior lobe of the cerebellum is involved in cognition and connected to associative regions such as the prefrontal cortex, whereas the anterior cerebellum likely modulates sensory-motor cortical activity. As the cerebellar architecture is considered to be homogeneous through the cerebellar lobules [8], it has been proposed that the cerebellum regulates in a similar manner the activity of the sensory-motor and the associative cortex. Similarly to the sensorimotor regions of the cerebellum in which damages lead to motor dysmetria [9], abnormalities in cerebellar regions involved in executive functions and affective regulation may have implications for cognitive dysmetria. This concept has been developed to explain symptoms of psychiatric disorders such as schizophrenia [10] and affective symptoms [9].

In schizophrenia, Moberget et al. [11] found in a large sample of 2332 patients and controls a robust reduction of the cerebellar grey matter volume. A more refined analysis within the cerebellar lobules showed that this reduction had a maximum effect size in regions of interest located in the posterior cerebellum.

In contrary to schizophrenia, cerebellar anatomy in BD has been investigated to a lesser extent. In a sample of 115 patients, we did not find any global cerebellar size reduction [12]. However we were not able to perform our analysis at the level of the cerebellar lobules.

Understanding the exact location of the cerebellar alterations in schizophrenia and bipolar disorder is important because of the regional specialization of the cerebellum [13]. Since the first descriptions of Kraepelin, it has been proposed that schizophrenia and bipolar disorder may share common pathophysiological features. Whereas some studies reported overlapping alterations between schizophrenia and bipolar disorder

It has been proposed that lithium may have a neurotrophic effect in the brain (see Hajek et al. for full review [15]). In addition, Johnson et al. [16] [17] reported, using quantitative T1p mapping, cerebellar abnormalities in patients with BD. T1p mapping abnormalities were normalized in patients treated with lithium. Last, lithium is known to affect the cerebellum [18] and cerebellar tremor is a common side effect of this type of medication.

The goals of our study were threefold. First, we aimed to replicate previous results on cerebellar anatomy in SZ spectrum disorders. Second, we wanted to understand the specificity of these findings within the psychosis spectrum by studying a sample of patients with BD. Last, we aimed to understand how the cerebellar lobules volumes were influenced by lithium.

2. Material and Methods:

Participants. Patients with SZ spectrum disorder and controls were recruited in 3 different sites located in France (Créteil), Czech Republic (Prague) and the USA (New Mexico). Patients with BD and controls were recruited in 5 different centers in USA (Pittsburgh), Germany (Mannheim), Italy (Udine) and 2 sites in France (Créteil and Grenoble). All details on inclusion criteria are described in Supplementary Material 1. Demographic characteristics are reported in Table 1. Only one center (Créteil, France) recruited patients with SZ, BD and controls. All other centers recruited either SZ and controls or BD and controls.

Data acquisition and data processing. All participants underwent a T1 weighted MRI (T1) with a full coverage of the cerebellum. Details on acquisition sequences are reported in Supplementary Material 1. All T1 images were processed using the CERES pipeline that performs a fully automated segmentation and parcellation of the cerebellum [19] following the protocol described in Park et al. paper [20]. Afterwards, we divided the cerebellar grey matter in 6 regions of interest: lobule I-V, lobule V, Crus I, Crus II, lobule VIIb and the postero-inferior lobe (lobules VIII to X). We chose these regions of interest because the resolution on standard T1 images do not allow to visually differentiate the five first (lobules I to V) and the three last lobules (lobule VIII to X) of the cerebellum. We extracted the grey matter volume of these 6 regions of interest (ROIs) and the global cerebellar grey matter volume.

Quality control. All segmentations were visually inspected by an examiner

(CL) blind of the diagnoses. Each segmented cerebellum (3D volume) was inspected in axial, coronal and sagittal views using Brainvisa/Anatomist software (http://brainvisa.info) (Figure 1). First, the examiner checked the quality of the segmentation, to ensure that no extra cerebellar tissue was labeled as cerebellar tissue and vice-versa. Second, the examiner inspected the quality of the lobular parcellation. Last, CL inspected the global brain segmentation to ensure the validity of the total intracranial measure (ICV), included as a covariate in the statistical analysis. Details on the included subjects and examples of rejected subjects are provided in Supplementary Material 2. All images not meeting our quality criteria were excluded of the study.

Statistical analyses. We used a Chi-square test to test for significant differences in the proportion of males and females and a Student t-test to compare ages between patients and controls (Table 1).

To compare the size of the global cerebellar volume and ROIs in the cerebellum between patients and controls, we performed a linear model with (i) age and ICV as covariates and (ii) sex, diagnosis and site as cofactors. Before performing pairwise comparisons (t-tests) between patients and controls, we ensured that the standardized residuals were normally distributed, as assessed by the Shapiro–Wilk test ($p > 0.05$) and a QQ-plot. We applied a false discover rate correction (FDR – Benjamini Hochberg correction) to control multiple testing. We present both uncorrected (presented as “p” value) and corrected p values (presented as “p corrected”). Results that survived correction for multiple comparisons were considered as significant.

We conducted our statistical analyses separately on the SZ and the BD sample. Similarly, we compared the size of the global cerebellar volume and ROIs in patients with BD medicated vs not medicated with lithium, with a linear model including (i) age and ICV as covariates and (ii) sex, lithium status and site as cofactors.

We conducted several supplementary analyses. Because of the exploratory nature of theses analyses, we did not correct our results for multiple comparisons.

Changes in cerebellar volume could be related to the lifetime dose of medication or to the duration of the illness. We thus repeated our analysis on the significant regions previously identified in the subsample of first episode patients with SZ spectrum disorder and controls recruited in Czech Republic (n = 174).

We studied the association between the severity of schizophrenia (assessed with the Positive and Negative Symptoms Schizophrenia (PANSS) scale) and the regions of interest in the cerebellum. The PANSS scale was available in patients recruited in France (n = 35) and Czech Republic (n = 79). Tests were conducted with the Z-score of PANSS total, negative, positive and general psychopathology scores. We performed linear models with (i) age, ICV and PANSS Z scores as covariates and (ii) sex and site as cofactors.

Clinical, genetic and neuroimaging studies [21] suggested that there might be distinct patterns between patients with BD (n = 53) with and without psychotic features (n = 56). We thus repeated our analysis on patients with BD with and without psychotic features. In this analysis, patients were recruited in Créteil,

France (n = 19), Germany (n = 34), USA (n = 39), Grenoble, France (n = 13) and Italy (n = 4).

Alcohol dependence is known to have a damaging effect on the cerebellum: cerebellar ataxia is frequent in alcoholics and prenatal exposure to alcohol affects the cerebellum [22]. Thus, alcohol dependence might be a confounding factor in our study. We repeated our analysis to ensure that our results remained significant when considering only patients without alcohol dependence.

Likewise, it has been proposed that cannabis could affect the structure of the cerebellum [23]. Thus, we conducted an analysis in the sample recruited in Czech Republic to study the effect of cannabis consumption, during the month prior to the inclusion, on the cerebellum. We performed a linear model, considering age and intracranial volume as covariates and sex and cannabis status as cofactors.

Antipsychotics are known to affect brain structures and could be also a potential confounding factor, explaining the structure differences in the cerebellum between patients with schizophrenia and controls. To address this question, we repeated our analyses in a sample of first episode patients with schizophrenia, with limited exposure to antipsychotics. In addition we conducted a linear model, in our population of patients with schizophrenia recruited in Czech Republic (Supplementary Material 4) to study the effect of medication load (computed in chlorpromazine equivalent dose) on our regions of interest in the cerebellum. We considered age, ICV and medication load as covariates and sex as a cofactor.

We conducted all statistical analyses with the python statsmodels open source library [24].

3. Results

3.1 Total cerebellar volume and lobular analysis in schizophrenia

One hundred and eighty-two patients with SZ and 198 controls were included in this analysis. Demographic characteristics are reported in Table 1.A.

The global cerebellar volume, Crus II and lobule VIIb were significantly smaller in patients compared to controls (Table 2 and Figure 2).

3.2 Total cerebellar volume and lobular analysis in bipolar disorder

One hundred and forty four patients with type I BD and 176 controls were included in this analysis. Demographic characteristics are reported in Table 1.B.

We did not find any significant difference between patients and controls for any of the regions of interest. Results are reported in Table 2.

BD participants treated with Li at the time of scanning (n=56) had significantly larger volume of the left anterior cerebellum grey matter volume than participants not treated with Li (n = 86), see Table 3.

3.3 Exploratory analyses

Cerebellar volume in the sample of first episode patients with schizophrenia

We found a decreased volume in patients compared to controls in the total cerebellar volume (p= 0.0005), Crus II (p = 0.0006) and lobule VIIb (p = 0.0036). This suggests that the size reduction in the cerebellum is present since the beginning of the illness and is not related to its evolution.

Influence of PANSS score in patients with schizophrenia

We found a negative correlation between the volume of Crus I and the PANSS general psychopathology score (p = 0.007). In addition, we found a negative correlation between the volume of Crus I and the PANSS total score (p = 0.047) (Supplementary Material 3).

Influence of psychotic features in patients with bipolar disorder

We compared patients with BD with and without psychotic features. We did not find any significant difference between the two groups for any of our regions of interest.

Influence of alcohol dependence

Patients recruited in France and Czech Republic did not suffer from alcohol dependence (Supplementary Material 4). However this information was lacking in patients recruited in the USA. Thus, we repeated our analyses in patients with schizophrenia recruited in France and Czech Republic. Our

results remained significant in the total cerebellar (p = 0.0001; t-value = - 3.9), Crus II (p = 0.0002; t-value = - 3.8) and lobule VIIb (p = 0.0004; t-value = -3.6) volumes.

Influence of cannabis use

Sixteen patients with schizophrenia recruited in Czech Republic had a history of cannabis consumption in the month prior to the inclusion (Supplementary Material 4). However, there was no effect of cannabis history in the last month prior to the inclusion on the volume of the total cerebellar (p-value = 0.60; t-value = - 0.57), Crus II (p-value = 0.12; t-value = -1.57) and lobule VIIb (p-value =0.41; t-value = - 0.81) volumes.

Influence of medication load in patients with schizophrenia

There was no significant effect of medication load on the volume of the total cerebellar (p = 0.41; t-value = - 0.82), Crus II (p=0.79; t-value = - 0.26) and lobule VIIb (p = 0.19; t-value = 1.33) volumes.

4. Discussion

We conducted a volumetric MRI study in 648 participants to study the cerebellar anatomy of patients with SZ and BD.
We found a decreased volume of the total cerebellar volume, Crus II and the lobule VIIb in patients with SZ compared to controls. There was no significant difference between patients with BD and controls per se, but BD patients treated with lithium had a larger anterior cerebellar volume compared to controls. To date, this is the first multicenter study probing cerebellar differences at a lobular level in both patients with SZ and BD.

Our results are in line with findings from the recent Moberget et al. study [11] and with our previous study [12]. Moberget et al. found in a large sample of 983 patients with SZ and 1349 controls, a global volume reduction of the cerebellum compared to controls. In addition, the authors reported in a voxel and vertex wise mega analysis, a reduction of volume within the cerebellum, mostly located in lobule VIIb, Crus II, Crus I and lobule VI. The extent to which our findings replicate the previous results, despite the differences in methods of measuring cerebellar morphometry (voxel based morphometry, versus parcellation into lobules), is remarkable. Such a strong replication is relatively rare in a field which is known for preponderance of false positive findings [25]. Jointly, these findings suggest that smaller volumes of cerebellum are among

the most robust findings in schizophrenia, replicable with different methodological approaches. These findings may be specific to schizophrenia, as we did not find size reduction in bipolar disorder. Similarly, Traut et al., [26] did not reported cerebellar alterations in autism in a large scale study.

Moreover, we found a decreased volume in two cerebellar lobules (Crus II and lobule VIIb, adjacent to Crus II) located in the cognitive part of the cerebellum. The Crus II region is connected to the prefrontal cortex, a region that has been linked to schizophrenia. Our result supports the hypothesis of a cognitive dysmetria in schizophrenia, where the cortical-subcortical circuit between the cerebellum and the prefrontal cortex might be altered [10]. A disruption in this circuit may lead to difficulty in prioritizing, processing and responding to information, which could account for the wide range of symptoms.

This result may also have therapeutic implications. The cerebellum is connected to almost every region of the brain, with the exception of the visual cortex and might represent a potential therapeutic target. For example, trans cranial direct current stimulation (tDCS) has been applied in patients with non-clinical psychosis to improve their skills in procedural learning [14]. Understanding the exact location of the cerebellar alterations in schizophrenia and bipolar disorder is important since the location of the cerebellar stimulation influence the effect of brain stimulation in the cerebellum and distant cortical regions [27].

We did not find difference in the cerebellar anatomy when comparing patients with bipolar disorder and controls. Previous key studies from Hibar et al. [28] [29] investigated the cortical and subcortical anatomy of patients with bipolar disorder in multicentric samples from the ENIGMA consortium. However the anatomy of the cerebellum was not investigated in these studies.

Lithium is the gold standard treatment for BD. We investigated the effect of Lithium on cerebellar morphology for several reasons. First, Lithium shows neuroprotective effects (see [15] for full review) and is much more often used in BD than in SZ. Consequently, it is possible that the absence of cerebellar changes in BD and their presence in SZ could be related to differential exposure to Lithium. Second, Johnson et al. [16] [17] reported, using quantitative T1p mapping, cerebellar abnormalities in patients with BD. T1p mapping abnormalities were normalized in patients treated with lithium. Last, 5 cases of a lithium induced long-lasting cerebellar toxicity [30] [18] have been reported and intention tremor, also known as cerebellar tremor, is a common side effect of lithium.

We found an increased volume in the anterior cerebellum in patients with BD medicated with lithium compared to BD patients not medicated with lithium. The anterior cerebellum is connected to the sensori-motor cortex [31], which could explain the cerebellar motor syndrome described in patients medicated with lithium. However, we did not see effects of Lithium on the posterior cerebellum, which showed abnormalities in SZ. Therefore, it is unlikely that the absence of cerebellar changes in BD was related to neuroprotective effects of Lithium.

We investigated if confounding factors could explain our results.

Chronic consumption of alcohol in well known to affect the cerebellum [32] and can lead to its size reduction [32] [33]. Thus, our results might have been related to alcohol dependence in patients with schizophrenia. However, when repeating our analyses in a sub-sample of patients with schizophrenia without alcohol dependence, our results remained significant.

Likewise, there is evidence that cannabis could affect the cerebellar structure [23] . However, our analyses suggested that there was no effect of cannabis on our results.

Antipsychotics are known to affect brain structures and could be also a potential confounding factor, explaining the structure differences in the cerebellum between patients with schizophrenia and controls. However, when repeating our analyses in a sample of first episode patients, with limited exposure to antipsychotics, our results remained significant. In addition we did not find any association between the regions differing between patients with schizophrenia and control and the medication load.

Our study comes with several strengths. First, we processed a large sample of 648 patients with SZ, BD and controls using the same state of the art method. Second, we visually inspected every cerebellar parcellation to ensure the quality of the segmentation and we compared cerebellar volumes in the subjects' native space. We used the CERES pipeline [19] based on a multi-atlas framework using the segmentation protocol defined in Park et al. paper [20]. A recent publication [34] suggested that the CERES pipeline outperformed various

automated segmentation methods, including a voxel-based morphometry based pipeline. The manual segmentations of the used atlas have been carefully validated and automated segmentation based on these atlases have been compared to manual tracing [32]. Third, we conducted several additional analyses to assess the effect of potential confounding factors, such as the treatment with antipsychotics, alcohol dependence and cannabis. Last, our results remained significant in a population of patients with a first episode of schizophrenia, suggesting that cerebellar alterations are present at the beginning of the illness.

Several limitations should be considered before interpreting our results. Our study is cross sectional and subjects were recruited in centers using different acquisitions parameters. For the most part, individual centers recruited participants only with schizophrenia or only with BD, thus making a direct transdiagnostic comparison difficult. There is an overlap with our previous study conducted in a sample of patient with SZ, BD and controls [12]. However our current study was conducted in a larger sample, with different software, allowing us to investigate the morphometry of the cerebellum at a lobular level.

Our results suggest that Lithium has an effect on the size of the anterior cerebellum in patients with bipolar disorder. However, due to the cross-sectional nature of this study, it is not possible to draw any firm conclusion on the effect of lithium on the cerebellum. Further studies with a longitudinal design are warranted to better understand the effect of lithium on the cerebellum.

We did not find size reduction in patients with bipolar disorder compared to controls. Although we investigated the cerebellar anatomy in a multicenter sample of 144 patients, we cannot exclude that this negative finding might be related to a lack of power. In addition, the number of inclusion centers and the variability in the imaging acquisition protocols might as well explain our negative findings. We conducted several exploratory analyses in sub-samples of our study. Because of the lack of power, our results (in particular negative findings) must be interpreted with caution.

In conclusion, our study confirms that the size of the total cerebellar grey matter volume is decreased in SZ and that this size reduction is located within the cognitive, posterior parts of the cerebellum including Crus II and lobule VIIb. Association between schizophrenia and smaller cerebellar volumes is one of the most robust and replicated brain imaging findings in this disorder. In line with other studies, we did not find any alterations in the cerebellum in bipolar patients. However BD patients medicated with Lithium had an increased size of the anterior part of the cerebellum, compared to BD patients not treated with Lithium. Our study supports a distinct pattern of cerebellar alterations in SZ and BD.

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Tables

Table 1. Demographic characteristics of participants

Table 1. A: Patients with schizophrenia and controls

	Patients (n = 182)	Controls (n = 198)	Statistical test	Statistics, p-value
Mean age (std)	32 (11)	33 (11)	Student t-test	t = - 0.16, p = 0.87
Sex: Male / Female	122 / 60	96 / 102	Chi-2 test	q = 13.3, p < 0.001
Site of Inclusion	COB = 57 PRA = 86 CRE = 39*	COB = 58 PRA = 88 CRE = 52	-	-

COB = COBRE dataset
PRA = Prague, Czech Republic
CRE = Créteil, France
*: including 3 patients with schizo-affective disorder

Table 1. B: Patients with bipolar disorder and controls

	Patients (n = 144)	Controls (n = 176)	Statistical test	Statistics, p-value
Mean age (std)	38 (11)	35 (10)	Student t-test	t = 2.41, p = 0.02
Sex: Male / Female	53 / 91	68 / 108	Chi-2 test	q = 0.11, p = 0.73
Site of Inclusion	CRE = 31 MAN = 37 PIT = 51 GRE = 13 UDI = 12	CRE = 52 MAN = 36 PIT = 23 GRE = 10 UDI = 55	-	-

CRE = Créteil, France
MAN = Mannheim, Germany
PIT = Pittsburgh, USA
GRE = Grenoble, France
UDI = Udine, Italy

Table 2. Effect of diagnosis on cerebellar anatomy

Table 2. A: Effect of diagnosis in patients with SZ compared to controls

Grey matter volumes (cm3)	pval	FDR corr. P value	tval	[95% conf. inter.]	dof	Effect size for diagnosis ; sex ; age ; site ; ICV (η^2 effect size)
Total cerebellum	0.0003	**0.001 ***	-3.62	[-4.16 ; -1.23]	6	0.034 ; 0.071 ; 0.079 ; 0.025 ; 0.312
Lobule I-V	0.0828	0.097	-1.74	[-0.48 ; 0.03]	6	0.008 ; 0.043 ; 0.011 ; 0.018 ; 0.147
Lobule VI	0.0459	0.074	-2.00	[-0.81 ; -0.01]	6	0.011 ; 0.002 ; 0.017 ; 0.024 ; 0.225
Crus I	0.1928	0.19	-1.30	[-1.03 ; 0.21]	6	0.005 ; 0.020 ; 0.050 ; 0.020 ; 0.139
Crus II	0.0008	**0.002 ***	-3.38	[-1.06 ; -0.28]	6	0.030 ; 0.022 ; 0.065 ; 0.048 ; 0.060
Lobule VIIb	0.0000	**0.0001 ***	-4.33	[-0.64 ; -0.24]	6	0.048 ; 0.025 ; 0.029 ; 0.021 ; 0.065
Lobule VIII - X	0.0535	0.074	-1.94	[-1.09 ; 0.01]	6	0.010 ; 0.073 ; 0.016 ; 0.002 ; 0.183

*, significant results after FDR correction
pval: p - value
tval: t - value
conf. inter.: confidence interval
dof: degrees of freedom

Table 2. B: Effect of diagnosis in patients with BD compared to controls

Grey matter volumes (cm3)	pval	FDR corr. P value	tval	[95% conf. inter.]	dof	Effect size for diagnosis ; sex ; age ; site ; ICV (η^2 effect size)
Total cerebellum	0.2273	0.5754	1.21	[-0.66 ; 2.76]	8	0.005 ; 0.016 ; 0.124 ; 0.115 ; 0.304
Lobule I-V	0.3288	0.5754	0.98	[-0.15 ; 0.45]	8	0.003 ; 0.016 ; 0.042 ; 0.025 ; 0.157
Lobule VI	0.6841	0.6841	0.41	[-0.37 ; 0.57]	8	0.001 ; 0.000 ; 0.034 ; 0.012 ; 0.135
Crus I	0.4217	0.5904	0.80	[-0.37 ; 0.89]	8	0.002 ; 0.021 ; 0.089 ; 0.212 ; 0.095
Crus II	0.3044	0.5754	1.03	[-0.22 ; 0.71]	8	0.003 ; 0.001 ; 0.045 ; 0.171 ; 0.150
Lobule VIIb	0.1756	0.5754	1.36	[-0.07 ; 0.40]	8	0.006 ; 0.000 ; 0.025 ; 0.048 ; 0.200
Lobule VIII - X	0.5801	0.6768	0.55	[-0.42 ; 0.74]	8	0.001 ; 0.025 ; 0.068 ; 0.031 ; 0.202

*, significant results after FDR correction
pval: p - value
tval: t - value
conf. inter.: confidence interval
dof: degrees of freedom

Table 3. Effect of Lithium on cerebellar morphology in patients with BD

Grey matter volumes (cm3)	pval	FDR corr. p value	tval	[95% conf. inter.]	dof	Effect size for diagnosis ; sex ; age ; site ; ICV (η^2 effect size)
Global cerebellar volume	0.0322	0.095	2.17	[0.25 ; 5.43]	8	0.034 ; 0.001 ; 0.103 ; 0.070 ; 0.367
Lobule I-V	0.0042	0.029*	2.92	[0.21 ; 1.11]	8	0.060 ; 0.000 ; 0.033 ; 0.029 ; 0.190
Lobule VI	0.0668	0.12	1.85	[-0.05 ; 1.42]	8	0.025 ; 0.021 ; 0.019 ; 0.022 ; 0.223
Crus I	0.5434	0.63	0.61	[-0.64 ; 1.20]	8	0.003 ; 0.023 ; 0.112 ; 0.053 ; 0.118
Crus II	0.8163	0.81	0.23	[-0.63 ; 0.80]	8	0.000 ; 0.004 ; 0.047 ; 0.104 ; 0.151
Lobule VIIb	0.2955	0.41	1.05	[-0.18 ; 0.58]	8	0.008 ; 0.004 ; 0.023 ; 0.064 ; 0.212
Lobule VIII - X	0.0408	0.10	2.07	[0.04 ; 1.68]	8	0.031 ; 0.000 ; 0.031 ; 0.109 ; 0.290

*, significant results after FDR correction
pval: p - value
tval: t - value
conf. inter.: confidence interval
dof: degrees of freedom

Figures

Figure 1: Cerebellar segmentation with the CERES pipeline

Figure 2: Grey matter volume of the cerebellum, Crus II and lobule VIIb in patients with SZ and controls: partial residual plot

Legends: hs, healthy subjects; sz, patients with schizophrenia; comparison of studentized residuals after regressing the effect of site, age, sex and intra cranial volume. Hashed lines delineate quartiles of the distribution; the central hashed lines refer to the mean of the distribution