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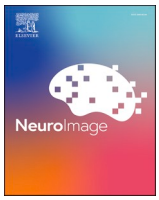

The cognitive cerebellum: linking microstructure to cognitive functions in a healthy population

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ABSTRACT

Background: The cerebellum is recognized for its role in motor control. However, it also plays a crucial part in modulating circuits involved in cognition and affect. While studies conducted on people with cerebellar disorders highlight both structural and functional links with cognition, research on cerebellar structure in the healthy population remains sparse. To better clarify the cerebellum's role and operational mode in cognition, this multi-scale study explores the relationship between cognitive functions and cerebellar macrostructure and micro-structure in healthy individuals. Macrostructural analysis focused on grey matter (GM) and white matter (WM) volumes, while microstructural evaluation used fractional anisotropy (FA) values.

Methods: Using a large normative cohort, the study examined cerebellar GM and WM volumes in 151 participants and FA in 83 participants. Cerebellar GM and WM volumes and FA values were correlated voxel-wise against the following cognitive domains: long-term memory, abstract reasoning, language-related executive functions, processing speed, and impulsive decision-making.

Results: Significant positive correlations were found between FA in specific cerebellar regions and long-term memory ($p = 0.030$), abstract reasoning ($p = 0.048$), and language-related executive functions ($p = 0.043$). Additionally, cerebellar FA values negatively correlated in several clusters with reaction time ($p = 0.001$; $p = 0.026$; $p = 0.045$), indicating faster processing speed with higher FA. No significant associations were found between cerebellar GM/WM volumes and cognitive performance after Family Wise Error correction, except for a positive correlation between WM and reaction time ($p = 0.023$).

Discussion: These findings highlight the cerebellum's microstructure role in cognition. FA may reflect the efficiency of communication between cerebellar and cortical regions, thus allowing the cerebellum to improve cognitive performance by updating internal models and correcting discrepancies between predictions and outcomes.

1. Introduction

The cerebellum's involvement in functions beyond motor control has gained increasing recognition in recent research. Over the past thirty years, studies have established the role of the cerebellum in a wide range of cognitive and affective functions (Leggio and Olivito, 2018; Leggio et al., 2011; Schmahmann, 2004; Stoodley and Schmahmann, 2018; Tedesco et al., 2011; Timmann et al., 2010). Studies involving patients with cerebellar degenerative conditions or cerebellar lesions have shown cognitive deficits across domains including executive functions, verbal fluency, perseverative behaviour, attention, visuospatial abilities, and language (Bellebaum and Daum, 2007; Schmahmann and Sherman, 1998; Tedesco et al., 2011). Moreover, volumetric and resting-state functional MRI studies have revealed that reductions of grey matter (GM) volume within specific regions of the posterior cerebellum, as well as altered functional connections between these regions and cortical areas involved in cognitive and social functions, underlie the observed cognitive and emotional deficits (Lupo et al., 2020; Olivito et al., 2018).

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Supporting the cerebellum's role in cognitive functions, resting-state functional connectivity studies in healthy individuals have also shown connections between the posterior cerebellar hemispheres and brain regions within networks implicated in cognitive functions, such as the fronto-parietal networks involved in executive control, attention networks, and the default mode network (DMN), (Buckner et al., 2011; Habas et al., 2009; Krienen and Buckner, 2009). Additionally, task-based functional connectivity studies have demonstrated activation of posterior cerebellar regions during cognitive tasks in healthy subjects (Guell et al., 2018; Stoodley and Schmahmann, 2009). Notably, King et al. (2019) employed a comprehensive multi-domain task battery to identify distinct functional boundaries within the cerebellar cortex, highlighting subregions selectively engaged in motor, cognitive, and socio-affective processing. Further supporting this view, studies in clinical populations with cerebellar involvement have reported altered functional connectivity at resting-state both between the cerebellum and cortical areas implicated in cognition, and within cerebellar subregions, particularly those associated with attention, language, and memory (Biondi et al., 2024; Marino et al., 2024).

While functional MRI research has uncovered cerebellar mechanisms underlying cognition, in both health and disease, studies examining the macrostructural and microstructural characteristics of the cerebellum in healthy individuals remain relatively sparse. Most research on the relationship between cerebellar structure and cognitive functions has focused on populations with cerebellar pathologies, such as multiple sclerosis, schizophrenia, frontotemporal dementia, autism, and cerebellar ataxias (Akhlaghi et al., 2014; Chang et al., 2022; McKenna et al., 2021; Moroso et al., 2017; Olivito et al., 2023; Savini et al., 2019). From a macrostructural perspective, in healthy individuals GM volume in posterior cerebellar regions – such as crus I, lobules VI, VII, and VIII – correlates positively with cognitive functions like language, working memory, executive functions, and processing speed (Bernard and Seidler, 2013; Grogan et al., 2009; He et al., 2013; Ridler et al., 2006). However, our understanding of how these structural properties relate to cognitive processes remains limited, and further research is needed to explore these links in both healthy and clinical populations.

More generally, recent advances in MRI techniques, particularly diffusion MRI, have enabled the study of the microstructural properties of tissue, including the white matter (WM) tracts, which are critical for signal transmission between brain regions (Filley and Fields, 2016; Mayeli et al., 2018; Seyedmirzaei et al., 2022). As diffusion MRI is sensitive to the microscopic molecular motion within tissue, it is influenced by the orientation and density of individual axons and their myelination, producing voxel-level metrics that reflect microstructural organisation beyond image resolution. The most popular approach to analyse diffusion MRI data, known as diffusion tensor imaging (DTI) provides indices such as mean diffusivity (MD) and fractional anisotropy (FA), which reflect tissue composition and organisation. Consistent with the assumption that efficient signal transmission between brain regions is essential for executing cognitive processes effectively (Parsaei et al., 2025), in healthy individuals, higher WM microstructural organisation assessed by diffusion MRI correlates with better cognitive performance (Madden et al., 2012). This relationship extends to the cerebellum, which acts as an optimizer of neural processes by modulating the activity of brain areas involved in cognition. Effective modulation depends on optimal information transfer both between the cerebral and cerebellar areas and within the cerebellum itself (Mannarelli et al., 2019; Schmahmann, 2019).

Recent diffusion MRI studies have investigated cerebellar microstructure in patients with spinocerebellar ataxia (SCA), revealing widespread reductions in FA in cerebellar and brainstem white matter tracts and a correlation between cerebellar microstructure and motor scores (Al-Arab and Hannoun, 2024; Mascalchi et al., 2015; Meira et al., 2020; Olivito et al., 2017; Park et al., 2020). Moreover, studies conducted on patients with SCA have found a correlation between cerebellar FA and measures of social cognition, as well as between brainstem FA and performance on the digit span test (Clausi et al., 2021; Lopes et al., 2013). In healthy individuals, a recent study by Parsei and colleagues (2025) analysed the relationship between whole-brain quantitative anisotropy (QA – a measure similar to FA, but estimated from a different model of diffusion) and cognitive functions such as attention, executive functions, episodic memory, and working memory. Notably, QA values in the cerebellar WM were found to correlate with all the aforementioned cognitive functions (Parsaei et al., 2025). Furthermore, two other studies have demonstrated that other microstructural measures, such as MD and FA, also link cerebellar white matter microstructure to personality traits and cognitive empathy in healthy individuals (Picerni et al., 2021, 2013).

Despite these findings, which reinforce the importance of investigating this relationship, the role of cerebellar microstructure in cognitive functioning among healthy individuals remains poorly understood due to limited evidence. This gap in knowledge also restricts our understanding of the cerebellum's contribution to the cognitive deficits observed in various psychopathologies, such as cerebellar ataxias, schizophrenia, depression, and autism. To bridge this gap, here we investigate the association between cerebellar macrostructural (GM and WM volume) and microstructural (FA) measures and a broad range of cognitive functions in a large sample of healthy individuals. The rationale for this investigation is that the structural characteristics of the cerebellum should mediate its interactions with cortical and subcortical regions thus impacting on higher order functions. The cognitive functions examined include long-term memory, abstract reasoning, language-related executive functions, processing speed, and impulsive decision-making. We examined whether these functions correlated with cerebellar GM and WM volumes from a macrostructural perspective and with cerebellar FA values from a microstructural perspective. Based on prior evidence of cerebellar involvement in cognition, we hypothesize that greater GM and WM volumes and higher FA values in posterior cerebellar regions (crus I–II, lobules VI–VIII) would correlate with better performance in long-term memory, abstract reasoning, language-related executive functions, and processing speed. Given the role of the cerebellum in affective and reward-related modulation (Clausi et al., 2015; Schmahmann, 2019; Stoodley and Schmahmann, 2009), we also expect correlations between cerebellar structural measures and impulsive decision-making. These hypotheses are supported by previous studies linking cerebellar microstructure to cognitive tests (Parsaei et al., 2025; Picerni et al., 2021) and cerebellar GM volume to functions such as language and executive control (Bernard and Seidler, 2013; Grogan et al., 2009).

To the best of our knowledge, this is the first study investigating specifically cerebellar macro- and microstructure by FA values together with cerebellar GM and WM and their correlation with a broad spectrum of cognitive functions in a large cohort of healthy subjects, across a broad range of ages, including young adults.

2. Materials and methods

Neuroimaging, cognitive and behavioural data were obtained from The Welsh Advanced Neuroimaging Database (WAND), a multiscale, multimodal imaging database of the healthy human brain (McNabb et al., 2025). WAND includes data collected from 170 healthy volunteers (18–63 years) at the Cardiff University Brain Research Imaging Centre, UK, between 2019 and 2023. The WAND study was approved by the Cardiff University School of Psychology Ethics Committee. All participants gave permission for their anonymised data to be shared with researchers in other organisations and deposited in publicly accessible databases. Inclusion criteria were: age between 18 and 65 years and suitability for MRI scanning. Exclusion criteria included: (i) diagnosis of any heart or breathing problem (ii) high blood pressure (iii) nerve issues, including carpal tunnel syndrome and nerve damage (iv) history of stroke, brain tumour or brain injury (v) dizziness, palpitations or fainting (vi) diabetes (vii) current or previous diagnosis of psychiatric

condition (viii) use of medication known to alter breathing, blood pressure or mood (ix) pregnancy or breast-feeding (x) heavy use of tobacco (xi) frequent migraines (xii) epilepsy (xiii) history of concussion resulting in loss of consciousness. More details are provided in (McNabb et al., 2025).

2.1. Participants

For the current study, we first selected participants in the WAND database who matched the following criteria: (i) had diffusion MRI and T1-weighted volumetric MRI obtained at 3T (ii) the cerebellum had been adequately covered in the diffusion MRI acquisition (iii) had completed the cognitive test battery. As not all datasets complied with criterion ii, the sample sizes included in the VBM and DTI analyses were of different size. Specifically, for the cerebellar VBM analyses, 151 healthy subjects were selected (M/F: 61/90; mean age ± SD: 29.08 ± 10.64; range: 18–63; mean educational level ± SD: 15.21 ± 2.17). For the cerebellar FA analysis, a subsample of 83 subjects was included (M/F: 23/60; mean age ± SD: 28.36 ± 10.93; range: 18–63; mean educational level ± SD: 14.96 ± 2.06). Histograms of the VBM and FA groups age distribution are respectively shown in Fig. 1a and Fig. 1b

2.2. Cognitive assessment and factor analysis

The cognitive tests considered in this study were drawn from the WAND database and include the following:

- Choice reaction-time task: This computerized test comprises two distinct tasks. In the first task, participants are required to rapidly differentiate between images of faces and other scenes. In the second task, participants observe four circles on the screen and must press a button corresponding to the circle that turns white during a trial.
- The logical memory task from the Wechsler Memory Scale IV (WMS-IV; Wechsler, 2009), subdivided into logical memory immediate task and logical memory recall task.
- Matrix reasoning from the Wechsler Abbreviated Scale of Intelligence-II (WASI-II; Wechsler, 2011).
- Vocabulary test from the WASI-II (Wechsler, 2011).
- Verbal fluency test: This test is divided into four tasks, each focusing on a different category of words (words beginning with the letter "f", animals, names of friends, items present in the bedroom). Participants are instructed to produce as many words as possible within 60 s for each task.
- Balloon Analogue Risk Task (BART; Lejuez et al., 2002), a measure of impulsive decision-making.

For the choice reaction-time task, the mean reaction time (RT) was considered as a measure for each of the two tasks, and the average was calculated for each subject to obtain a single RT measure. In the BART, the measure used for statistical analyses was the adjusted average pumps. For the purpose of this task, participants inflated an on-screen balloon by pressing the space bar. Each balloon had a pre-determined bursting point that was unknown to the participant. Participants earned five points for each pump and could choose to "bank" the points earned for that balloon at any point. If the balloon burst, then participants would earn no points from that trial. The measure we considered is the average number of pumps on the unexploded balloons, which is considered indicative of risk-taking behaviour. Regarding the other cognitive measures, since several of them assessed similar constructs, a factor analysis using principal component analysis (PCA) via SPSS (Statistical Package for the Social Sciences, version 27) was conducted to group them into factors.

Initially, a PCA was performed to examine data collinearity using the following measures: logical memory immediate, logical memory recall, matrix reasoning, vocabulary, and verbal fluency (across four categories). Three factors emerged from this analysis considering eigenvalues above one. The first factor, which included both logical memory measures, was excluded due to a multicollinearity violation, as their correlation exceeded 0.9. Consequently, only the logical memory recall measure was retained for further analysis.

To validate the PCA, we ensured the Kaiser-Meyer-Olkin (KMO) test value was above 0.5 and that Bartlett's test of sphericity was significant. We then conducted a parallel analysis using the parallel analysis engine software (Patil et al., 2017) to determine which eigenvalues surpassed the corresponding random eigenvalues (Horn, 1965). Only the first of the remaining two factors had an eigenvalue high enough to be retained, leading to the exclusion of the second factor.

The retained factor, named language-related executive functions, encompasses the variance explained by the vocabulary test and the four verbal fluency tasks. To further evaluate the internal consistency of this factor, we calculated Cronbach's alpha, which yielded a value of α=0.68. Although this value falls slightly below the conventional, albeit arbitrary, threshold of 0.70 (Nunnally, 1978) we chose to retain the factor based on both theoretical and empirical considerations. There is precedent for interpreting these measures as indicators of higher-order cognitive functions. For instance, verbal fluency tasks are included in the Delis-Kaplan Executive Function System neuropsychological battery ((Delis et al., 2001)) and our vocabulary measure was derived from a general intelligence assessment. Furthermore, Cronbach's alpha is sensitive to the number of items contributing to a scale (Nunnally, 1978). Given that only five tasks load onto this component and considering that language-related executive functions encompass a broad range of processes, we considered an alpha of 0.68 to be sufficient (see John et al., 2023 for a similar rationale). The component matrix with loadings of each task can be found in Table S1 of the Supplementary Materials. The matrix reasoning measure, not loading on any factor, was analysed individually.

Overall, the measures subjected to subsequent comparative analyses and the relative cognitive functions are as follows:

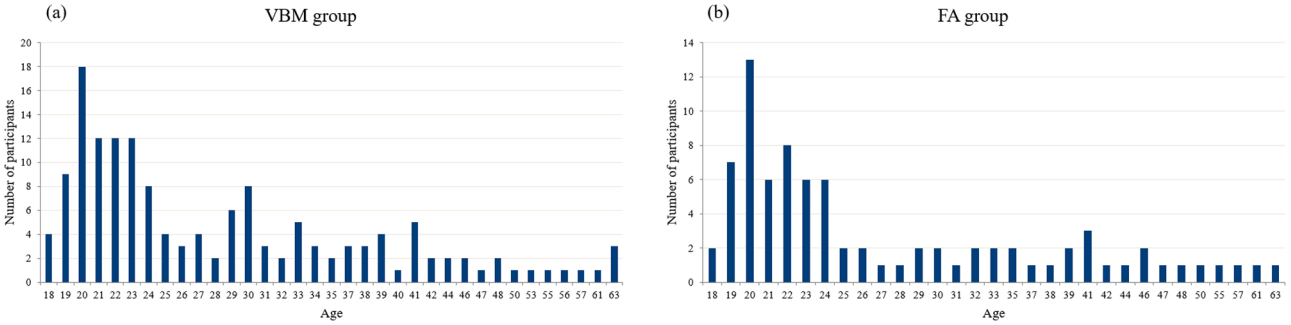

Fig. 1. Age distribution across participants. (a) age distribution of the 151 participants considered for VBM analysis; (b) age distribution of the 83 participants considered for FA analysis.

- Logical memory recall, a measure of long-term memory.
- Matrix reasoning, indicative of fluid intelligence and abstract reasoning.
- Language-related executive functions, assessing the ability in executive functions by means of verbal-content tests.
- Mean reaction time, a measure of processing speed.
- Adjusted average pumps (BART), indicating impulsive decision-making.

2.3. Imaging data acquisition

WAND diffusion MRI data were acquired using a 3T Connectom MRI scanner, modified from a 3T MAGNETOM Skyra (Siemens Healthcare, Erlangen, Germany), and equipped with ultra-strong magnetic field gradients (up to 300 mT/m). A 32-channel head coil was used for signal reception. A single-shot pulsed gradient spin echo sequence was used to collect 6 diffusion-weighted shells, with a variable number of diffusion directions per shell, and a maximum b value of 6000 smm^{-2}. Other parameters were: TE=59 ms, TR=3000 ms, resolution=2 mm isotropic. Data were preprocessed using standard correction methods, including correction for Gibbs ringing, drift, susceptibility and eddy current distortions, and gradient non-uniformity, using tools from FSL and MRtrix. Only shells with $b \leq 2400$ smm^{-2} were used for the diffusion tensor estimation, and the B-matrix was adjusted voxel-wise to account for the effects of gradient nonlinearities (Rudrapatna et al., 2021). The diffusion tensor was estimated voxel-wise using in-house code developed in MATLAB (MathWorks, Natick, MA), implementing a weighted least squares (WLS) approach (Basser et al., 1994) to improve the robustness of the fit to noise. FA was then computed from the tensor's eigenvalues (Pierpaoli and Basser, 1996), and FA maps were retained for the voxel-wise analysis.

T1-weighted images were acquired on a 3T MAGNETOM Prisma scanner (Siemens Healthcare, Erlangen, Germany) using a 3D magnetization prepared rapid acquisition with gradient echo (MPRAGE) sequence with the following key parameters: voxel size 1 mm × 1 mm × 1 mm, TI/TR = 850/2100 ms, TE = 3.24 ms, flip angle = 8°, field-of-view = 256 × 256 × 176 mm, for a scan time of approximately 8 min.

WAND data are available from https://gin.g-node.org/CUBRIC/WAND (McNabb et al., 2025).

2.4. Preprocessing

Image preprocessing was conducted using Statistical Parametric Mapping version 12 (SPM12, http://www.fil.ion.ucl.ac.uk/spm, Wellcome Trust Centre for Neuroimaging, Institute of Neurology, University College London, UK). The Spatially Unbiased Infratentorial Template (SUIT) toolbox (Diedrichsen et al., 2009) was employed for cerebellum preprocessing. Each T1-weighted image underwent inspection for Left Posterior Inferior (LPI)-orientation and subsequent adjustment of the image origin to the anterior commissure. Segmentation into GM, WM, and cerebrospinal fluid (CSF) was performed, with the cerebellum being isolated. Normalization into SUIT space and reslicing were achieved using Diffeomorphic Anatomical Registration Through Exponentiated Lie algebra (DARTEL, Ashburner, 2007) a suite of tools facilitating more precise inter-subject registration of brain images. Smoothing of images was conducted using an 8 mm FWHM Gaussian kernel. Following these analyses, cerebellar modulated GM and WM volumes maps were obtained.

FA images were coregistered onto T1-weighted images using the SPM interface. Subsequently, the cerebellum was isolated utilizing the previously created cerebellar mask. FA cerebellar images were resliced into SUIT space using DARTEL and smoothed using an 8 mm FWHM Gaussian kernel.

2.5. Statistical analyses

Statistical analyses were conducted using SPM12. The segmented, normalized, modulated, and smoothed cerebellar GM, WM, and FA images were utilized for analyses. For the cerebellar VBM analysis, we investigated the voxel-level relationship between the volumes of cerebellar GM and WM and the aforementioned cognitive measures (logical memory recall, matrix reasoning, language-related executive functions, mean RT, adjusted average pumps - BART) by applying a General Linear Model (GLM). The SPM design "one-sample *t*-test" was employed, specifying the variable of interest as covariate, effectively implementing a linear regression model. An absolute masking with a threshold of 0.2 was applied. Additionally, the analysis was corrected for total intracranial volume (ICV) values – inserted as global values – and a global normalization via ANCOVA was performed. This normalization effectively treats the global values as a covariate, adjusting for ICV. A similar design was used to analyse the cerebellar FA maps. Relative masking with a threshold of 0.8 was applied. In both analyses, sex was included as a covariate, and only results surviving Family-Wise Error (FWE) correction at the peak voxel level ($p < 0.05$) were considered significant.

3. Results

3.1. VBM analyses

Neither grey nor white matter voxel-wise cerebellar volume showed any association with cognitive measures after FWE correction, except for a positive correlation between WM volume in the left superior cerebellar peduncle and mean RT ($p = 0.023$, FWE). The other significant associations found at an uncorrected level ($p < 0.001$) between cerebellar GM and WM volumes and cognitive measures are available in Table S2 of the Supplementary Materials. By contrast, the analysis between cerebellar FA maps and cognitive measures revealed several significant associations. Specifically, a significant positive association was identified between language-related executive functions and the right crus I/right middle cerebellar peduncle ($p = 0.009$, FWE). Additionally, the logical memory recall measure was significantly positively correlated with the vermis IX/right lobule IX area ($p = 0.008$, FWE). Another significant positive association was found between matrix reasoning and the left lobule V ($p = 0.043$, FWE). The relationship between the BART measure and cerebellar FA images revealed no significant results after FWE correction. Finally, three clusters showed a significant negative association with mean RT. Specifically, one peak was located in the brainstem/right corticospinal tract area ($p = 0.001$, FWE); another peak voxel was found in the right lobule IX/right inferior cerebellar peduncle ($p = 0.023$, FWE); and the final peak voxel was in the right corticospinal tract ($p = 0.045$, FWE). Significant associations found at the uncorrected threshold ($p < 0.001$) between cerebellar FA volumes and cognitive measures are reported in Table S3 of the Supplementary Materials. The significant results of the comparisons between GM, WM, and FA volumes and cognitive measures are detailed in Table 1. Fig. 2 illustrates the clusters showing significant associations between GM, WM, and FA volumes and cognitive measures, while Fig. 3 presents scatterplots between mean FA and WM volumes within the significant clusters and cognitive performance.

4. Discussion

This is the first exploration of the relationship between cerebellar macrostructure and microstructure, as quantified through GM and WM volumes and FA values, and a comprehensive battery of cognitive functions in a large cohort of healthy individuals. The findings revealed that cerebellar FA values are significantly correlated with performance across a range of cognitive functions, enabling the identification of specific cerebellar regions where the microstructure of WM appears to influence cognitive task performance. In contrast, comparative analyses

Table 1
Detailed statistics of significant results of voxel wise comparison between cerebellar GM and WM volumes, FA maps and cognitive measures after FWE correction.

Cognitive Measures	Contrast	*p*	Cluster size (NoV)	Peak coordinates (x y z)	Peak z-score	Cerebellar region
FA – Language-related executive functions	positive	0.043	4	40 − 54 − 38	4.16	R crus I/middle cerebellar peduncle
FA – Logical memory recall	positive	0.030	30	3 − 55 − 35	4.23	vermis IX/R lobule IX
FA – Matrix reasoning	positive	0.048	1	−5 − 58 − 10	4.10	L lobule V
		0.001	231	7 − 33 − 43	5.05	brainstem/R corticospinal tract
FA – Mean RT	negative	0.026	74	10 − 44 − 41	4.28	R lobule IX/ R inferior cerebellar peduncle
		0.045	6	17 − 24 − 6	4.12	R corticospinal tract
WM – Mean RT	positive	0.023	46	−4 − 43 − 25	3.77	L superior cerebellar peduncle

Results are corrected at peak voxel level FWE correction. Coordinates are in Montreal Neurological Institute (MNI) space. p = significance (corrected at peak-level); NoV = Number of Voxels; R = Right; L = Left.

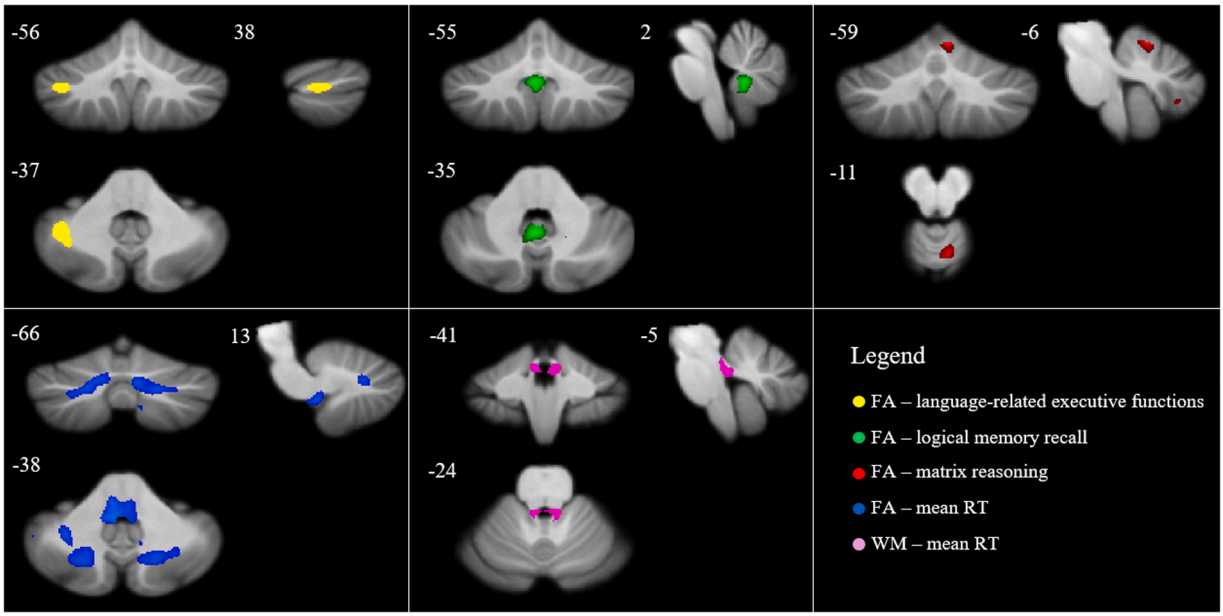

Fig. 2. Clusters of significant association between cerebellar GM, WM, FA and Cognitive Measures. The clusters are superimposed on the Spatially Unbiased Infratentorial Template (SUIT; Diedrichsen et al., 2009). Coordinates are in Montreal Neurological Institute (MNI) space. For representation purposes, all voxels significant at an uncorrected level ($p < 0.001$) are shown, while peak voxel coordinates (significant after FWE correction at $p < 0.05$) are reported in Table 1.

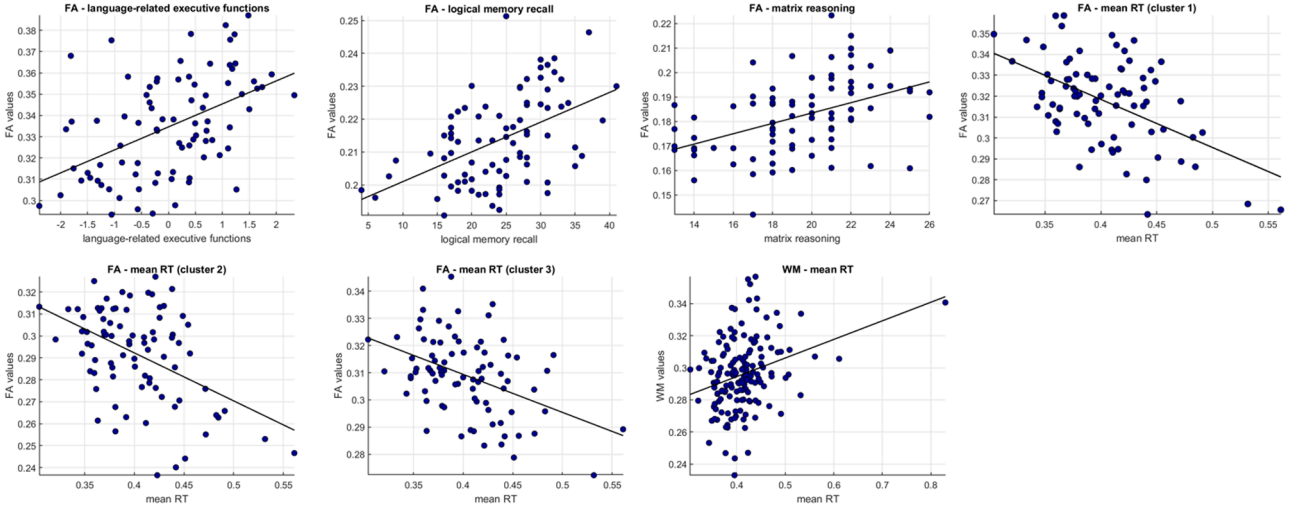

Fig. 3. Scatterplots of mean FA and WM values in the significant clusters and cognitive performance. Mean FA and WM values were computed by averaging the values within the significant clusters identified in the voxel-wise analyses investigating the associations between GM, WM, and FA maps and cognitive measures.

between cerebellar GM and WM volumes and the administered cognitive test battery yielded only one significant association, highlighting a less prominent role of these macrostructural measures in determining cognitive functions. Specifically, the analyses revealed a positive correlation between white matter in the left superior cerebellar peduncle and mean reaction time. This finding aligns with existing literature, considering that the superior cerebellar peduncle represents the primary efferent pathway from the cerebellum to the cerebral cortex and is therefore crucial for motor control required by tasks of this nature. Moreover, recent studies have shown that the amount of white matter in this region is associated with motor learning and processing speed in healthy adults (Della-Maggiore et al., 2009; Magistro et al., 2015).

Considering FA results, language-related executive functions showed a positive correlation with the cerebellar FA in the right crus I and the right middle cerebellar peduncle. This result seems to indicate that higher levels of WM microstructure in these cerebellar areas contribute to a better performance in executive functions, especially when considering language related material. This finding aligns with our hypothesis and with previous research, where resting-state and task-based functional connectivity studies have identified the crus I region as central to speech production, listening, verbal fluency tasks, and executive functions, alongside regions such as crus II, lobules VI, and VIIIab (Callan et al., 2007; Grimaldi and Manto, 2012; Molinari and Leggio, 2016; Muller and Meyer, 2014; Reineberg et al., 2015; Stoodley and Schmahmann, 2015). The crus I area is also part of the functional cerebellar regions involved in linguistic and executive tasks, as described by Nettekoven and colleagues (2024) in their updated functional cerebellar atlases, which are based on the latest literature. The middle cerebellar peduncle facilitates the transfer of information from associative cortices to cerebellar areas (Habas et al., 2013). This suggests that the integrity of this WM tract might enhance efficient exchanges between cortical and cerebellar regions involved in executing language-related tasks, thereby supporting improved performance. Furthermore, the lateralization observed aligns with literature findings that implicate the right cerebellum and – particularly – the right crus I area more heavily in these functions due to its contralateral relationship with language-related cortical regions (Callan et al., 2007; King et al., 2019).

The positive correlation between cerebellar FA in the right vermis IX and the right lobule IX and performance in logical memory recall, measuring long-term memory, aligns with existing literature, which generally identifies memory as a cognitive capacity often impacted by cerebellar damage. Examining specific areas, vermis IX and lobule IX are more commonly linked to affective and emotional processes, reflecting their connections with limbic regions and, in the case of lobule IX, with the DMN (Leggio and Olivito, 2018; Stoodley and Schmahmann, 2009). However, studies involving patients with SCA have specifically associated vermis IX and the right lobule IX with performance in verbal working memory as well as in short- and long-term verbal memory, thus supporting our findings (Cooper et al., 2012; Olivito et al., 2018). Moreover, the vermal portion of lobule IX and lobule IX itself are also part of the functional cerebellar regions involved in executive and linguistic functions, particularly in tasks related to recall and working memory (Nettekoven et al., 2024). Given the verbal nature of this memory task, it is possible that a more organized microstructure in this area contributes to better performance in verbal memory.

In analysing the association between matrix reasoning performance and cerebellar FA, a correlation emerged with the left lobule V, highlighting how greater integrity of WM tracts in this cerebellar area is associated with better nonverbal intelligence and abstract reasoning. Generally, previous literature identifies the cerebellum's posterior regions, particularly crus I and II and lobule VII, as strongly implicated in cognitive tasks due to their bidirectional connections with frontal and parietal cortices (Kelly and Strick, 2003). However, lobule V, part of the anterior cerebellum spanning lobules I-V, is traditionally associated with motor control due to its connections with motor cortical areas (Habas et al., 2013; King et al., 2019; Schmahmann, 2019; Stoodley and Schmahmann, 2018). One hypothesis for this result could relate to lobule V's role in sequencing, as identified in a task-based fMRI study on non-social sequencing tasks in healthy subjects (Li et al., 2023). Given the sequential nature of the matrix reasoning task, it is plausible that participants employed sequential strategies to determine the stimuli that best completed the matrix.

No relationship between cerebellar FA and BART scores was observed. Generally, studies on the relationship between cerebellar structure and risk-taking behaviours remain limited, a gap that stimulated our particular interest in this measure. Nonetheless, a 2022 study from Quan and colleagues found a correlation between left cerebellar GM volume and risk tolerance, as well as age-related changes in risk-taking behaviour (Quan et al., 2022). Likely, our measures may not have been optimally suited for a comprehensive investigation of this function and would benefit from refinement for more precise analyses.

Examining the results of the association between cerebellar FA and mean RT, a negative correlation emerged between this measure and three specific cerebellar areas. Two of these regions span the brainstem and the right corticospinal tract. Both areas participate in the motor responses required for reaction time tasks, given their roles in motor control circuits responsible for locomotion, postural control, and sensory information processing (Natali et al., 2023; Noga et al., 2020). The corticospinal tract specifically transmits information from motor cortices to the spinal cord (Natali et al., 2023). Similarly, the brainstem receives inputs from motor cortices and subsequently relays them to the spinal cord via the corticospinal tract (Kandel et al., 2012). The second cerebellar area where WM integrity is associated with shorter RTs is at the intersection of the right lobule IX and the right inferior cerebellar peduncle. The inferior cerebellar peduncle transmits information from the inferior olive nucleus, spinal cord, and vestibular nuclei to the cerebellar cortex, thereby contributing to motor control (Colin et al., 2002; Loyola et al., 2019). This finding is consistent with the prior result concerning the brainstem and right corticospinal tract, as all these regions form part of a shared motor control circuit. Meanwhile, lobule IX is generally associated with social functions, including social cognition and action sequencing (Haihambo et al., 2023; Leggio and Olivito, 2018). However, this region also contributes to the internal connectivity of cortical networks such as the DMN and dorsal attentional network (DAN), (Habas et al., 2009; Stephen et al., 2018). In both networks, intrinsic connectivity correlates with RTs in tasks similar to those employed in our study (Machner et al., 2022; Vatansever et al., 2015).

Altogether, the results presented so far indicate a relationship between cerebellar FA and cognitive functions in healthy individuals. Specifically, considering the tests analysed, this study has demonstrated an association between the microstructure of WM tracts within the cerebellum, as well as those connecting it to cortical structures, and a range of cognitive functions, including language-related executive functions, processing speed, fluid intelligence and abstract reasoning, and long-term memory. Having established this, the question remains how the cerebellum is expected to be involved in the regulation of these functions.

The cerebellum is regarded as a sophisticated processor that, through its extensive connections with specific cortical centres, influences functions that extend beyond sensorimotor processing to encompass cognitive and affective domains. Cerebellar circuits are essential for sequence processing, irrespective of whether the material involved is sensory (Bower, 1997), motor (Thach et al., 1992), cognitive (Molinari et al., 2008), or behavioural (Leggio et al., 2008; Tedesco et al., 2011). This cerebellar functionality is illustrated in the "sequence detection theory" put forth by Leggio and colleagues (Leggio et al., 2011, 2008). According to this theory, the cerebellum possesses the capability to detect and encode patterns through its sequential processing abilities, subsequently constructing internal models of these perceived patterns. When an observed pattern of activity aligns with a memorized model, predictions consistent with the internally generated and stored

representation are activated. Thus, the cerebellum acts as a comparator (Ito et al., 2008), modulating cortical excitability across widespread regions in response to potential discrepancies between predicted and actual stimuli. The authors posit that the cerebellum's predictive capacity exerts a profound influence on overall brain function, priming specific neural systems – such as sensory, motor, autonomic, memory, attention, affective, speech, and language networks – to respond appropriately to stimuli across varying contexts (Leggio and Molinari, 2015). In a constantly evolving environment, the brain engages in continuous anticipation of future events to optimize behaviour. This anticipatory mechanism is crucial for the efficient processing of information across multiple domains, including perception, motor control, and cognitive regulation. In the specific context of cognitive functions, the cerebellum is thought to regulate the speed, capacity, and appropriateness of cognitive processes. Its involvement appears to be more pronounced for cognitive functions and experimental tasks that necessitate a higher predictive load (Siciliano et al., 2023). The results we obtained regarding cerebellar FA align with this theory of cerebellar functioning. However, FA is quite a complex measure and can be driven by a number of different features of the white matter. Indeed, FA is a local metric modulated by several factors such as intra-voxel orientational dispersion, the myelination, the packing density, membrane permeability, partial volume effects and, of course, the number of axons. Thus, a variation in FA most likely reflects some difference in one of the aspects of connectivity, although it is difficult to define which precise aspect and the direction of the change (Jones et al., 2013). Future studies, employing more complex models of diffusion (e.g., Palombo et al., 2020; Zhang et al., 2012) may provide further clarification.

Altogether, in this paper FA is considered as an index of microstructural organization and configuration, allowing us to assess the efficiency of communication between GM regions interconnected by WM tracts (Webb et al., 2020). Thus, communication between brain areas, and in our case, between the cerebellum and the brain, is mediated by the microstructure of WM tracts. In this context, the more organized the cerebellar microstructure, the better the cerebellum can properly modulate cortical areas during the execution of cognitive tasks, continuously updating internal models and intervening in the detection of discrepancies between the task's predictions and actual outcomes.

In light of the hypotheses proposed thus far regarding cerebellar involvement in cognitive functions, it becomes easier to explain the results obtained from the comparison between cerebellar GM and WM volumes and the various cognitive tests. Indeed, the presence of only one significant correlation suggests that changes in cerebellar GM and WM volumes, which are macrostructural measures, may not strongly correspond to variations in cognitive performance. This result can be explained based on the sample composition and the understanding of cerebellar functioning. Specifically, cerebellar modulation of cortical areas necessarily occurs through WM tracts, and it is likely that, at a macrostructural level, performance is only affected by greater levels of damage or individual differences between participants. Moreover, most of the participants were healthy, young students with intact, and in fact, above-average cognitive functions. The score discrepancies, with the exception of a few outliers, were small within the population, showing normal performance in almost all cases, with results similar to one another. Considering that GM and WM volumes are macrostructural measures, it is unlikely that substantial variations in these measures would be detectable within a sample of healthy subjects, particularly considering that factors such as age, education, and performance showed little variability. An additional explanation for the generally limited number of significant correlations between cerebellar macrostructure and cognitive performance may lie in the intrinsic sensitivity of the structural measures employed. Macrostructural measures such as GM and WM volumes offer a general overview of brain morphology, but they may overlook subtle neurobiological alterations that impact cognition. In contrast, microstructural indices like FA are more sensitive to the microarchitecture of neural pathways, including axonal density, myelination, and fiber coherence (Beaulieu, 2002). Several studies have demonstrated that microstructural degradation, even in the absence of gross volumetric loss, can significantly affect cognitive performance (Sasson et al., 2013; Bennett and Madden, 2014). White matter integrity within the cerebellar peduncles has been shown to correlate with executive function and processing speed, while corresponding volumetric data may fail to reveal such associations (Chang et al., 2022). This distinction becomes especially relevant in healthy, young adult samples, where interindividual variability in macrostructural features is minimal and insufficient to expose performance-linked structural differences. Microstructural measures, on the other hand, can capture more nuanced, functionally relevant differences that reflect the efficiency of cerebellar-cortical communication pathways, even among high-functioning individuals (Burzynska et al., 2010). Therefore, in studies aiming to elucidate cerebellar contributions to cognition, relying solely on macrostructural indicators may lead to an underestimation of the cerebellum's role, especially in healthy populations with subtle neurofunctional variations.

The results related to FA may also have been influenced by the limited variability within the sample. Indeed, FA tends to decrease with age, and this has been correlated with poorer cognitive performance in healthy older adults (Sheriff et al., 2024; Webb et al., 2020). This factor represents the primary limitation of this study. As a comparison study, the variability of the analysed measures is crucial for highlighting correlation patterns between cerebellar macro- and microstructure and cognitive performance. Furthermore, the gender distribution in the GM, WM and FA analyses was imbalanced, with a predominance of females. Although sex was included as a covariate in the analyses, it is possible that this imbalance contributed to the low variability in the sample, especially considering the known gender differences in GM, WM and FA (Kanaan et al., 2012; Parsaei et al., 2023). Another factor that may have influenced the results could be related to the type of cognitive tests used. It is well known that, even in the presence of cerebellar damage, cognitive alterations are often only detectable by targeted tests that consider the cerebellar operational mode (Hoche et al., 2018). It is possible that the tests employed here were not sensitive enough to detect subtle cerebellar structural differences in healthy participants, preventing any discrepancies in performance from emerging, and, consequently, limiting the ability to detect cerebellar influences on performance.

In conclusion, this study provides valuable insights into the relationship between cerebellar macrostructure and microstructure and their influence on cognitive performance in healthy individuals. The significant correlations found between cerebellar FA and various cognitive functions, particularly in language-related executive functions, long-term memory, abstract reasoning, and processing speed, highlight the cerebellum's essential role in modulating cognitive processes. However, aside from a single significant correlation, the general lack of associations between cerebellar GM and WM volumes and cognitive performance suggests that macrostructural changes alone may not sufficiently explain cognitive variability, particularly in a sample with limited variability. The findings also emphasize the importance of considering sample characteristics, the complexity of cognitive tasks, and the predictive nature of cerebellar functioning in future research. Further investigations with diverse samples and more targeted cognitive tests are needed to better understand the cerebellum's involvement in higher-order cognitive functions.

CRediT authorship contribution statement

Nicole Urbini: Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization. **Carolyn B. McNabb:** Writing – review & editing, Supervision, Software, Formal analysis, Data curation. **Derek K. Jones:** Writing – review & editing, Project administration, Methodology, Funding acquisition, Conceptualization. **Craig Hedge:** Writing – review & editing, Resources, Methodology, Formal analysis,

Data curation. **Eirini Messaritaki:** Writing – review & editing, Software, Investigation, Formal analysis, Data curation. **Pedro Luque Laguna:** Writing – review & editing, Formal analysis, Data curation. **Mara Cercignani:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Derek K. Jones reports financial support was provided by Wellcome Trust. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2025.121356.

Data availability

Data are available from https://gin.g-node.org/CUBRIC/WAND (McNabb et al., 2025).

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