Received: 16 July 2024 | Revised: 2 September 2024 | Accepted: 14 September 2024

DOI: 10.1002/pcn5.70018

PCN Reports
Psychiatry and Clinical Neurosciences
Open Access

ORIGINAL ARTICLE

White matter correlates of impulsive behavior in healthy individuals: A diffusion magnetic resonance imaging study

Fatemeh Rashidi MD[1] | Mohammadamin Parsaei MD[2] | Iman Kiani MBBS[1] | Arash Sadri PharmD[3,4] | Mohammad Hadi Aarabi PhD[5,6] | Seyed Reza Darijani MD[1] | Yune Sang Lee PhD[7,8] | Hossein Sanjari Moghaddam MD[9]

[1]School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

[2]Breastfeeding Research Center, Family Health Research Institute, Tehran University of Medical Sciences, Tehran, Iran

[3]Lyceum Scientific Charity, Tehran, Iran

[4]Interdisciplinary Neuroscience Research Program, Students' Scientific Research Center, Tehran University of Medical Sciences, Tehran, Iran

[5]Department of Neuroscience, University of Padova, Padova, Italy

[6]Padova Neuroscience Center, University of Padova, Padova, Italy

[7]School of Behavioral and Brain Sciences, The University of Texas at Dallas, Richardson, Texas, USA

[8]Department of Speech, Language, and Hearing, The University of Texas at Dallas, Richardson, Texas, USA

[9]Psychiatric Research Center, Roozbeh Hospital, Tehran University of Medical Sciences, Tehran, Iran

Correspondence

Dr. Hossein Sanjari Moghaddam, Psychiatric Research Center, Roozbeh Psychiatric Hospital, Tehran University of Medical Sciences, South Kargar Street, Tehran, Iran.
Email: g.h.sanjarimoghaddam@gmail.com

Funding information

None

Abstract

Aim: To explore white matter (WM) tracts linked to impulsivity using the diffusion magnetic resonance imaging (DMRI) connectometry method.

Methods: We analyzed 218 healthy participants from the Leipzig Study for Mind-Body-Emotion Interactions database. Impulsivity correlations with DMRI-derived WM changes were assessed using Urgency-Premeditation-Perseverance-Sensation (UPPS) Impulsive Behavior Scale subscales: lack of perseverance (PE), lack of premeditation (PM), sensation seeking (SS), and negative urgency. DMRI data were processed using connectometry, adjusting for sex and age, to examine WM tract integrity via quantitative anisotropy (QA). Also, two additional interaction analyses were conducted to separately examine the interaction effect between WM QA, and sex and age in predicting impulsive behavior scores. The significance level in our statistical analyses was set at a false discovery rate (FDR) below 0.05.

Results: QA in the bilateral cerebellum and middle cerebellar peduncle showed a negative association with PE and PM severity (FDR = 0.0004). QA in the middle cerebellar peduncle, corpus callosum body, and forceps major demonstrated a positive association with SS (FDR = 0.0001). Conversely, QA in forceps minor had a positive association with PM (FDR = 0.004), and QA in forceps minor and bilateral cingulum showed a positive association with SS (FDR = 0.0005). Age and sex had no significant effects on the association between WM QA and UPPS subscale scores.

Conclusion: Impulsivity is linked to distinct WM integrity changes in various tracts, including the corpus callosum, cerebellum, and cingulum, offering insights into the pathophysiology of impulsivity and guiding future research.

KEYWORDS

connectometry, diffusion magnetic resonance imaging, impulsive behavior, impulsivity

Fatemeh Rashidi and Mohammadamin Parsaei contributed equally to this paper.

INTRODUCTION

Impulsivity is a complex trait that is typically defined as the tendency to engage in immediate actions without adequate consideration of potential outcomes or consequences.[1] It is characterized by an array of deficits in areas such as delayed gratification, impulse and urge control, decision-making, and maladaptive behaviors.[2] Concordantly, it is associated with heightened propensities for risky decision-making, substance use disorders, eating disorders, and suicide attempts,[3–5] signifying an enhanced vulnerability and diminished quality of life among individuals exhibiting impulsive behaviors. Noteworthy, impulsivity has been marked by linguistic and conceptual ambiguities, making its characterization more challenging.

There also has been considerable research on the neural basis of impulsive behavior. Magnetic resonance imaging (MRI) sequences have revealed a discernible link between impulsivity and structural alterations in grey matter volume across diverse brain regions, encompassing the frontal, parietal, temporal, and occipital cortices.[6] Moreover, diffusion tensor imaging (DTI) sequences have uncovered alterations in white matter (WM) microstructure among individuals exhibiting impulsivity traits.[7–9] However, the observations on exactly how the WM microstructure alters in relation to impulsivity have been seemingly inconsistent and therefore controversies have ensued. Some studies have reported reduced WM integrity, as measured by fractional anisotropy (FA), within some WM tracts,[8] while others have reported increased integrity within some other WM tracts.[7] Collectively, there seems to be a substantive alteration in the WM tracts of impulsive individuals; however, the direction in which each tract gets altered is still unknown.

Diffusion MRI (DMRI) is an MRI method that enables the investigation of the brain microstructure by analyzing the diffusion of water within its tissues.[10] Connectometry is a DMRI analysis approach in which the water diffusion density is quantified within a voxel in various directions. This approach aims to find similarities in local connectivity patterns and map WM tracts.[11] Unlike traditional DTI, connectometry emphasizes water diffusion density over diffusivity or speed in specific directions.[11] This emphasis enhances spatial resolution, enabling the identification of WM fibers even in regions with intricate crossing or intersecting tracts, such as long associational WM fibers.[12] Utilizing a predefined atlas of diffusion density, the spin distribution function (SDF) is computed for each WM voxel in various directions.[11] SDF can be converted into quantitative anisotropy (QA), a density-based index, which can be used to extract fiber tracts, determine between-group differences, and establish correlations between diffusion density and variables of interest.[13–15]

The present study investigates the relationship between the microstructural integrity of WM tracts and impulsivity, as assessed by four items of the Urgency-Premeditation-Perseverance-Sensation (UPPS) scale, in healthy individuals. Moreover, taking into account previous research findings that have highlighted distinctions in impulsive behavior between males and females[16] and sex differences in brain structures among individuals exhibiting impulsivity,[17] we performed additional analyses to examine the relationships between WM connectometric measures and UPPS scores separately for males and females. Furthermore, additional interaction regression analyses were utilized to determine the precise effects of sex and age on the associations between the WM microstructure and impulsivity.

MATERIALS AND METHODS

Study data

The data used in this research were obtained from the Leipzig Study for Mind-Body-Emotion Interactions (LEMON) dataset.[18] The LEMON dataset comprises two groups of young (20–35 years old) and old (59–77 years old) adults. The primary purpose of LEMON was to investigate the intricate interplay between mind, body, and emotions.[18] This dataset provides a comprehensive collection of information encompassing psychological evaluations, emotional and personality assessments (including the UPPS inventory), psychiatric evaluations, and physiological measurements (including DMRI data) from 227 healthy participants, collected from September 2013 to September 2015 in Leipzig, Germany.[18]

In the development of the LEMON dataset, individuals who fulfilled any of the following criteria were excluded: (1) diagnosis of hypertension without intake of antihypertensive medication, (2) diagnosis of any other cardiovascular disease, (3) history of any psychiatric disorder that required inpatient treatment for longer than 2 weeks within the last 10 years, (4) history of neurological disorders, (5) history of malignant diseases, (6) intake of any of centrally active medications, beta- and alpha-blockers, cortisol, any chemotherapeutic or psychopharmacological medications, (7) positive drug anamnesis (extensive alcohol, methylenedioxymethamphetamine, amphetamine, cocaine, opiates, benzodiazepine, and cannabis), (8) MRI exclusion criteria (metallic implants, braces, nonremovable piercings, tattoos, pregnancy, claustrophobia, tinnitus, and any surgical operation in the last 3 months), (9) previous participation in any scientific study within the last 10 years, and (10) previous or current enrollment in undergraduate, graduate, or postgraduate studies.

Participants

In total, 218 participants of the LEMON dataset were included in this study and their DMRI data and UPPS scores were extracted. The original study conducted for compiling the LEMON dataset was carried out according to the Declaration of Helsinki[19] and was approved by the Ethics Committee of the University of Leipzig (reference number 154/13-ff).

UPPS impulsive behavior scale

The self-reported questionnaire of UPPS was developed to assess impulsive behaviors, based on the five-factor model of personality

and consists of four subscales: (1) negative urgency (NU), which captures the propensity to engage in hasty actions as a response to intense negative emotions; (2) lack of premeditation (PM), entailing impulsive behaviors executed without prior consideration; (3) lack of perseverance (PE), indicative of a disposition to leave tasks incomplete; and (4) sensation seeking (SS), encompassing proclivities towards pursuing novel and stimulating experiences.[20] Each individual item within the assessment was evaluated using a four-point Likert scale, ranging from 1 (strongly agree) to 4 (strongly disagree), thereby indicating the participant's concurrence with the provided statements. Notably, every subscale consists of a range of 10 to 14 items, and a higher aggregate score within each subscale signifies an elevated degree of impulsivity.[20]

Diffusion MRI acquisition

Axial whole-brain high angular resolution DMRI images were acquired using a 3-Tesla Siemens MAGNETOM Verio device (Siemens Healthcare GmbH) equipped with a 32-channel head coil. The images were acquired with 60 diffusion directions, 1000 s/mm^2 b-value, 80 ms echo time, 7000 ms repetition time, 1502 Hz/pixel bandwidth, 0.78 ms echo spacing, 220 mm field of view, 1.7 mm isotropic voxel dimension, and 128 × 128 matrix. Additional details regarding the DMRI acquisition protocol can be found in the article by Babayan et al.[18]

Diffusion MRI processing and DMRI connectometry

The DMRI data were corrected for subject motion, eddy-current distortions, and susceptibility artifacts due to the magnetic field inhomogeneity using the ExploreDTI toolbox.[21] DMRI connectometry analyses were performed using the software DSI Studio (https://dsi-studio.labsolver.org). Using q-space diffeomorphic reconstruction (QSDR), DMRI data were reconstructed in the Montreal Neurological Institute (MNI) space (resolution = 2 mm) to obtain the SDF value, which is the peak distribution value for each voxel orientation. The angular threshold and step size were configured at 90° and 1.2 mm, respectively. Topology-informed pruning underwent six iterations. Anisotropy changes were determined with a minimum length of 20 mm and a differential tracking threshold of 0.2 for increased and decreased anisotropy, respectively. A 20% threshold was applied to identify significantly decreased QA. The SDF is subsequently transformed into QA, which is utilized to create a connectivity matrix of all the voxels within the region of interest.[22] The connectivity matrix derived from 1,000,000 seeds in the WM, based on the FreeSurferDKT cortical atlas. The QSDR algorithm is a model-free approach that generates a matrix of orientation functions at varying diffusing spins, which allows for the quantification of the density of water diffusion in different directions for each voxel.[23] This provides DMRI connectometry with greater spatial resolution and statistical power for fiber tracking than conventional DTI methods.[23]

Local connectomics, as delineated by Yeh et al., involves the utilization of QA computations to determine water diffusion density for a given fiber orientation.[24] This methodology subsequently facilitates the examination of WM tracts, enabling comparative analysis among different groups and the identification of associations between WM fibers and various variables. The present study employed the DSI Studio software in conjunction with the DMRI connectometry protocol to investigate associations between the QA values of WM tracts and the severity of impulsivity. Local connectomes were chosen to employ 1,000,000 seeds across the entire brain, utilizing a deterministic fiber tracking algorithm. This algorithm followed the core pathway of each fiber bundle, guided by default parameter values (e.g., anisotropy threshold and angular threshold). During this method, strings of adjacent voxels of a WM tract that have significant associations with the predictor are isolated. This method provides a more precise overview of the associations between the tract and our predictor (UPPS subscales).

Statistical analysis

The categorical data are presented as frequencies and percentages, while the continuous data are expressed as mean ± standard deviation. The comparison of baseline characteristics among study participants across different groups was conducted utilizing the Statistical Package for the Social Sciences (SPSS®, IBM®) version 25.0, using the chi-square test and independent *t*-test for the categorical and continuous data, respectively A significance level of P-value <0.05 was considered for statistical analysis.

To assess the association between impulsivity and calculated QA measures, a multiple regression analysis was employed using the DSI Studio software. First, the regression analysis encompassed the entire sample, investigating the interplay between QA values of WM tracts and four distinct UPPS subscales. In these analyses, the UPPS subscale scores were treated as the dependent variable, while QA values in brain tracts served as the independent variable and participants' age, sex, and overall UPPS scores were included as covariates. Subsequently, the analysis was separately conducted on males and females, with their age and total UPPS scores being controlled. Also, separate additional analyses were performed on the younger (20–35 years) and older (59–77 years) cohort. Based on the recommendations from the software developer, obtained P-values were subject to correction for multiple comparisons using the false discovery rate (FDR) method. The computation of the FDR involved the application of 2000 random permutations to the group labels. This process served to establish the null distribution of tract lengths, enabling the derivation of an accurate FDR estimate. The employment of permutation tests facilitated the control and correction of type-1 error inflation arising from multiple comparisons. Finally, an FDR threshold of less than 0.05 was adopted for tract selection. This criterion guided the reporting of tracts exhibiting statistically significant correlations.

Furthermore, we conducted two additional separate analyses to examine the interaction effect between WM QA and sex and age in associating with UPPS scores. For this reason, the age variable was

converted to a dichotomous variable (age <40 and age >40). Interaction analyses were performed using the statistical software R version 4.0.3. Prior to analysis, data were screened for outliers and multicollinearity. No outliers exceeding three standard deviations from the mean were identified, and variance inflation factors indicated acceptable levels of multicollinearity among predictor variables. A multiple linear regression model was formulated with UPPS scores as the dependent variable and WM QA, sex, age, and their interactions as independent variables. The model is represented by the equations of (impulsive_behavior ~ white_matter_QA × sex) and (impulsive_behavior ~ white_matter_QA × age). The statistical significance level was set at P-value <0.05 in all of our interaction analyses.

RESULTS

Participant characteristics

A total of 218 participants with a mean age of 39.15 ± 20.18 years and a male-to-female ratio of 140/78 were enrolled. There were no significant differences between male and female participants in the mean scores for the PE and PM subscales of the UPPS questionnaire (P-values = 0.175 and 0.770, respectively). However, the mean scores for the SS and NU subscales were significantly higher in the male cohort compared to females (P-values = 0.002 and <0.001, respectively). Table 1 illustrates the demographic characteristics of the sample and the mean scores of four UPPS subscales in the whole sample, males, and females.

Correlations between UPPS and DMRI connectometry

Entire cohort

Table 2 presents an overview of the observed associations between the QA values of the WM tracts and the UPPS subscales. In the entire sample, we observed a negative association between the QA values of the middle cerebellar peduncles (MCP) and the bilateral cerebellum and the deficiencies in PE and PM (FDR = 0.0004 for both) (Figure 1a,b).

TABLE 1 Demographic characteristics of study participants.[a]

	Entire cohort (*n* = 218)	Male (*n* = 140)	Female (*n* = 78)	*P* value
Age	39.15 ± 20.18	36.17 ± 18.81	44.48 ± 21.56	0.005[b]
Handedness				0.014[c]
Right	193 (88.5)	124 (88.6)	69 (88.5)	
Left	21 (9.6)	16 (11.4)	5 (6.4)	
Ambidextrous	4 (1.8)	0 (0)	4 (5.1)	
BMI	24.24 ± 3.65	24.38 ± 3.47	23.99 ± 3.98	0.460[b]
Education				0.604[c]
None	2 (0.9)	1 (0.7)	1 (1.3)	
Gymsium	169 (77.5)	105 (75)	64 (82.1)	
Hauptschule	7 (3.2)	5 (3.6)	2 (2.6)	
Realschule	40 (18.3)	29 (20.7)	11 (14.1)	
Smoking				0.349[c]
Nonsmoker	181 (83)	117 (83.6)	64 (82.1)	
Occasional smoker	21 (9.6)	11 (7.9)	10 (12.8)	
Smoker	16 (7.3)	12 (8.6)	4 (5.1)	
UPPS scores				
Lack of perseverance	25.74 ± 4.85	25.41 ± 4.75	26.34 ± 5.00	0.175[b]
Lack of premeditation	22.52 ± 3.92	22.58 ± 3.95	22.42 ± 3.90	0.770[b]
Sensation seeking	19.18 ± 4.67	19.92 ± 4.90	17.85 ± 3.91	0.002[b]
Urgency	32.41 ± 7.02	34.30 ± 6.59	29.02 ± 6.51	<0.001[b]

Abbreviations: BMI, body mass index; UPPS, urgency-premeditation-perseverance-sensation.

[a]The categorical data are presented as numbers (percentages) and continuous as mean (standard deviations).

[b]Indepndent *t*-test.

[c]Chi-square test.

TABLE 2 Results of the correlation analysis between UPPS subscales and the QA values in white matter tracts.

Analysis group	UPPS subscale	Positive correlations	Negative correlations
Entire cohort (n = 218)	Lack of perseverance	NS	MCP and bilateral cerebellum (FDR = 0.0004)
	Lack of premeditation	Forceps minor (FDR = 0.004)	MCP and bilateral cerebellum (FDR = 0.0004)
	Sensation seeking	Forceps minor and bilateral cingulum (FDR = 0.0005)	MCP, body of CC, and forceps major (FDR = 0.0001)
	Urgency	NS	NS
Male cohort (n = 140)	Lack of perseverance	NS	Forceps minor and MCP (FDR = 0.001)
	Lack of premeditation	Forceps minor and major (FDR = 0.002)	MCP and L cerebellum (FDR = 0.0001)
	Sensation seeking	Tapetum of CC (FDR = 0.005)	MCP and fornix (FDR = 0.003)
	Urgency	Bilateral cingulum (FDR = 0.0005)	Forceps major, tapetum of CC, R. cerebellum (FDR = 0.001)
Female cohort (n = 78)	Lack of perseverance	R medial lemniscus, R CST, tapetum of CC (FDR = 0.013)	L cerebellum and MCP (FDR = 0.0004)
	Lack of premeditation	Body and splenium of CC, and bilateral cingulum (FDR = 0.004)	L cerebellum (FDR = 0.005)
	Sensation seeking	NS	NS
	Urgency	NS	Forceps minor, R ATR, L cingulum (FDR = 0.005)

Abbreviations: ATR, anterior thalamic radiation; CC, corpus callosum; CST, corticospinal tract; FDR, false discovery rate; L, left; MCP, middle cerebellar peduncle; NS, nonsignificant; QA, quantitative anisotropy; R, right; UPPS, Urgency-Premeditation-Perseverance-Sensation.

Furthermore, the QA values within the MCP, as well as the body and forceps major of the corpus callosum (CC) display significant negative associations with SS (FDR = 0.0001) (Figure 1a,b). Conversely, the QA values associated with the WM in the forceps minor exhibit a positive association with PM (FDR = 0.004), while the QA values within both the forceps minor and the bilateral cingulum manifest positive associations with SS (FDR = 0.0005) (Figure 1c,d).

Subgroup analysis based on the sex

In the male cohort, we observed statistically significant negative associations between the following: PE and the QA values within the forceps minor and the MCP (FDR = 0.001); PM and the QA values in the MCP and the left cerebellum (FDR = 0.0001); SS and the QA values of the MCP and the fornix (FDR = 0.003); and NU and the QA values in the forceps major, the tapetum of CC, and the right cerebellum (FDR = 0.001). On the other hand, we observed positive associations between PM and the QA values in the forceps minor and major (FDR = 0.002), and between SS and NU and the QA values in the tapetum of CC and the cingulum, respectively (FDR = 0.005 for both) (Table 2).

In the female cohort, we observed statistically significant negative associations between the following: PE and the QA values of the left cerebellum and the MCP (FDR = 0.0004); PM and the QA values of the left cerebellum (FDR = 0.005); and NU and the QA values within the forceps minor, the right anterior thalamic radiation (ATR), and the left cingulum (FDR = 0.005). On the other hand, we observed a positive association between the QA value of the right medial lemniscus, the right corticospinal tract (CST), and the tapetum of the CC and PE (FDR = 0.013). Similarly, there was a positive association between PE and the QA values of the body and the splenium of the CC, as well as the bilateral cingulum (FDR = 0.004) (Table 2).

Subgroup analysis based on the age

Given that our study population consisted of two distinct cohorts based on age—one younger cohort (20–35 years) and one older cohort (59–77 years)—we conducted a subgroup analysis to examine the association between WM microstructure and impulsivity within each group separately.

In the younger cohort (n = 146), we observed a positive association between PM and the QA values of the forceps minor (FDR = 0.001) and a negative association with QA in the MCP (FDR = 0.006). Furthermore, SS demonstrated a positive association with QA values in the bilateral cingulum (FDR = 0.0003) and showed a significant negative association with QA values in the left cerebellum and MCP (FDR = 0.007). However, no significant associations were identified for PE or NU with any of the QA values of brain WM tracts (Table 3).

In the older cohort (n = 72), there was a positive association between PE and the QA values of WM tracts in the body of the CC (FDR = 0.001). Additionally, PE showed a positive association with QA values of the splenium of the CC (FDR = 0.004) and had a negative association with QA values of the fornix (FDR = 0.004). However, no significant associations were found between SS or NU and any QA values of WM tracts (Table 3).

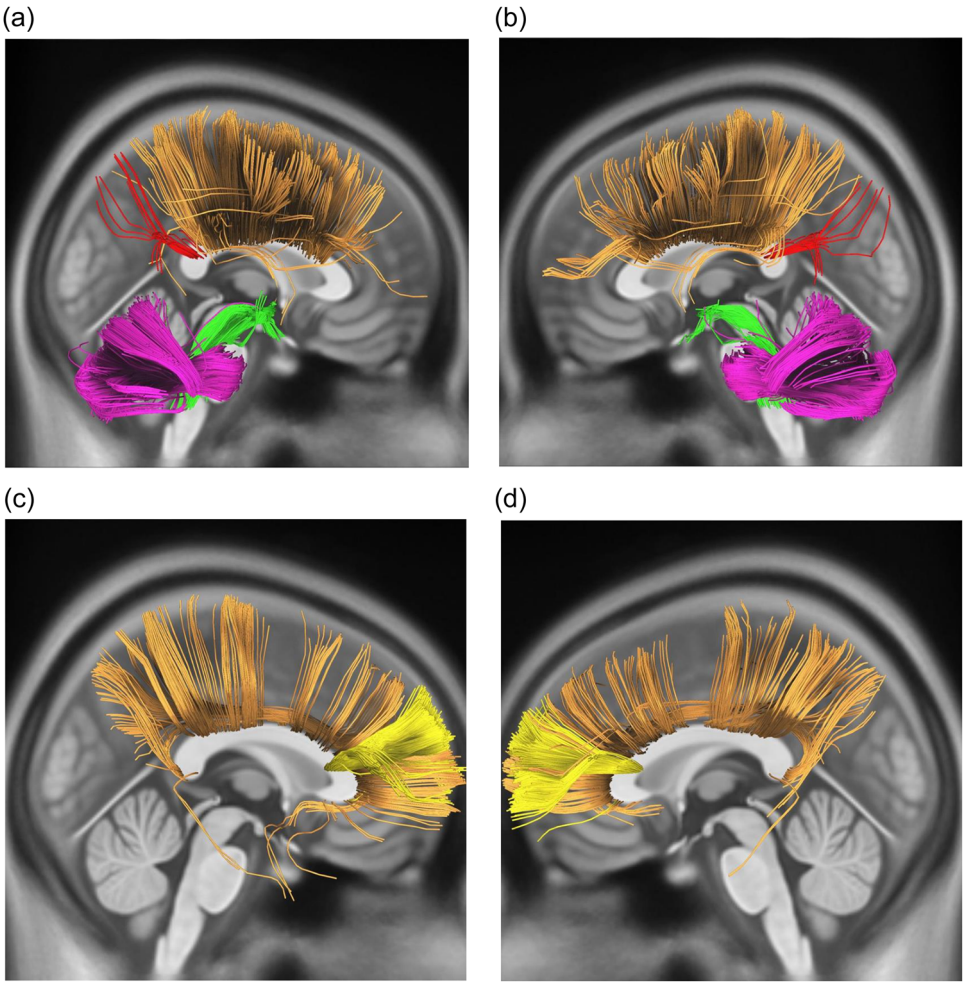

FIGURE 1 White matter tracts associated with Urgency-Premeditation-Perseverance-Sensation subscales in the entire cohort. (a, b) Middle cerebellar peduncle (green), bilateral cerebellum (pink), body of corpus callosum (orange), and forceps major (red). (c, d) Bilateral cingulum (orange) and forceps minor (yellow).

TABLE 3 Results of the subgroup analyses on the correlation of UPPS subscales with QA values in white matter tracts across the two cohorts of younger (20–35 years) and older (59–77 years) individuals.

Analysis group	UPPS subscale	Positive correlations	Negative correlations
Younger cohort (n = 146)	Lack of perseverance	NS	NS
	Lack of premeditation	Forceps minor (FDR = 0.001)	MCP (FDR = 0.006)
	Sensation seeking	Bilateral cingulum (FDR = 0.0003)	L cerebellum and MCP (FDR = 0.007)
	Urgency	NS	NS
Older cohort (n = 72)	Lack of perseverance	Body of CC (FDR = 0.001)	NS
	Lack of premeditation	Splenium of CC (FDR = 0.004)	Fornix (FDR = 0.004)
	Sensation seeking	NS	NS
	Urgency	NS	NS

Abbreviations: CC, corpus callosum; FDR, false discovery rate; L, left; MCP, middle cerebellar peduncle; NS, nonsignificant; QA, quantitative anisotropy; UPPS, Urgency-Premeditation-Perseverance-Sensation.

Interaction analysis

Our further interaction analyses yielded no significant interaction effects between WM QA values and either the age or sex of the participants in predicting four UPPS subscales (P-values > 0.05).

DISCUSSION

In the present study, we investigated the association between the microstructural integrity of brain circuits and impulsive behavior, evaluated by the UPPS subscales, in a sample of healthy adults. Based on our findings, greater PE and PM scores appear to be negatively associated with lower integrity of the MCP and the bilateral cerebellum. Also, PE showed a positive association with the QA values in the forceps minor. Furthermore, SS seems to be positively associated with the QA values in the forceps minor and the bilateral cingulum, and negatively associated with the QA values in the MCP, the body of CC, and the forceps minor. Additionally, no significant effects were found for the age and sex of participants on the association between their WM integrity and impulsivity. To our knowledge, this is the first study using DMRI connectometry to explore the brain WM alterations associated with impulsive behaviors.

Our most consistent observation was the negative association between the QA values in the cerebellar regions (cerebellum and MCP) and the degree of impulsiveness This is in line with previous research that has reported decreased WM integrity within the anterior lobe of the left cerebellum in schizophrenic patients.[25] Also, patients with cerebellar ataxia demonstrate a higher prevalence of impulsive behaviors.[26,27] Moreover, altered frontocerebellar functional connectivity has been observed in patients with higher impulsivity.[28,29] These findings are in line with the observations and hypothesis that the cerebellum has a modulatory role in preventing immediate and unplanned behaviors by inhibiting the prefrontal cortex.[30] Based on this hypothesis, the cerebellum regulates ongoing behaviors in the face of changing environmental conditions by modifying the prefrontal reaction to the incoming external and internal stimuli.[30] Overall, our findings supported earlier research on the critical role of cerebellar regions in maintaining balance in individuals' behavioral activities, which explains its lower integrity in persons with higher impulsive tendencies.

Our findings reveal a notable link between WM integrity within the CC tract and impulsivity. Within the entire cohort, the degree of sensation seeking has a negative correlation with the QA values in the body and the forceps major of the CC. This concurs with the prior investigations that have highlighted an inverse relationship between impulsivity and WM integrity, as measured by FA, in the genu and the body of the CC among individuals with borderline personality disorder and alcohol dependence.[31,32] CC is a neural bridge that connects the cerebral hemispheres and facilitates the transmission of visual, auditory, and somatosensory information to the regions accountable for higher-order cognitive functions.[33] Comprising four components—forceps major (splenium), body, genu, and forceps minor (rostrum)—the CC plays a pivotal role in interhemispheric communication.[33] The fibers of the genu traverse and give rise to the forceps minor and connect the frontal cortices. Those of the splenium extend posteriorly to form the forceps major, linking the occipital lobes.[33] Transversely traversing the cerebral cortex, the body fibers give rise to the corona radiata and other substantial WM pathways.[33] Lastly, rostral fibers connect the orbital regions of the frontal lobes.[33] Given the vital role of CC in transferring emotion-related data, it is reasonable to expect that individuals exhibiting impulsive behaviors might manifest altered CC structures.[34]

The existing literature has predominantly indicated that the WM integrity decreases within the CC of individuals showing impulsive behaviors; however, conflicting observations have also been reported. For instance, Treit et al., Alfano et al., and Stansberry et al. have reported that individuals with higher FA values in the corpus callosum tend to exhibit greater impulsivity.[35–37] These observations are in line with our results, which have revealed a positive correlation between the integrity of the forceps minor and the degree of SS and PM.

Another important finding of our investigations was the positive correlation between the QA values in the bilateral cingulum and PM. The cingulum bundle, located above the corpus callosum, links the frontal, parietal, and temporal lobes[38] and plays a critical role in facilitating the cognitive control and the executive function governed by the frontal cortex.[39] While prior reports predominantly indicate an inverse relationship between the WM integrity in the cingulum tract and impulsivity in patients with attention deficit hyperactivity disorder (ADHD) and bipolar disorder,[40–42] our study demonstrates a positive correlation in healthy individuals. A plausible explanation for this discrepancy is the mediating function of the cingulum tract on the activities of the frontal lobe. According to this conjecture, decreased cingulum integrity could potentially lead to diminished control over the frontal cortex, thereby elevating the risk of impulsive behaviors. However, we primarily observed a positive correlation between cingulum integrity and impulsivity in healthy individuals, possibly stemming from a compensatory mechanism aimed at repressing escalated frontal cortex function. Noteably, our study exclusively encompassed healthy individuals, in contrast to the cited investigations, which focused on psychiatric patients, particularly ADHD. This emphasizes the need for further research aimed at elucidating the intricate role of the cingulum tract in the manifestation of impulsive behaviors.

Furthermore, our subgroup analysis has unveiled additional WM tracts whose integrity seems to be correlated with impulsivity in healthy individuals. For instance, we observed a positive correlation between the QA values in the right medial lemniscus and the severity of PE in the female cohort. This discovery is consistent with the findings of Alfano et al., who observed that healthy individuals exhibiting impulsivity tend to exhibit elevated FA values in the medial lemniscus tract.[37] The medial lemniscus is a pivotal conduit for conveying sensory spinothalamic information to the primary somatosensory cortex.[43] Thus, the positive correlation between impulsivity and the WM integrity within this tract can be justified by the

hypothesis that the heightened integrity may facilitate an augmented flow of somatosensory information to the somatosensory cortex, potentially resulting in exaggerated responses to external environmental stimuli. Analogous to the medial lemniscus tract, the ATR constitutes a WM pathway responsible for transmitting sensory and motor information to the cerebral cortex.[44] On the other hand, we observed a negative correlation between the QA values in the right ATR and the severity of NU in the female cohort. Based on this observation, it might be hypothesized that the ATR conveys a different set of information to the cerebral cortex, predominantly engendering inhibition of impulsive behaviors rather than their induction.

Moreover, we found a positive correlation between the QA values in the right CST and the PE in the female cohort. This was in line with previous reports of the increased integrity within the CST of healthy individuals showing an increased tendency for impulsive behaviors.[37] CST is a WM tract that controls primary motor functions and is involved in voluntary movements.[45] Consequently, individuals with heightened CST integrity and function may exhibit a heightened susceptibility to motor impulsive behaviors. However, a deeper exploration is imperative to ascertain the precise role of the CST in impulsive behavior.

Concomitantly, an inverse relationship emerged between the WM integrity of the fornix and the severity of sensation seeking in the male cohort. The fornix, an integral component of the limbic system situated beneath the corpus callosum, constitutes a C-shaped WM tract along the medial aspects of the cerebral hemispheres, facilitating connectivity between the medial temporal lobes and the hypothalamus.[46] Crucially, the fornix functions as the primary afferent and efferent pathway of the hippocampus, exerting a pivotal influence on cognitive processes.[46] Given its role, the presence of altered fornix integrity in individuals with impulsivity is not unexpected; however, sufficient evidence on this matter is lacking. For instance, Onnink et al. observed distinct diffusivity patterns in the fornix of ADHD patients compared to their healthy counterparts.[47] Nevertheless, there is a paucity of research focusing explicitly on WM alterations in individuals exhibiting impulsive traits and this underscores the necessity for further investigations to untangle the precise involvement of the fornix in impulsivity.

Nonetheless, our interaction analyses yielded no significant effects of sex on the relationship of WM alterations and impulsivity in healthy individuals. Accordingly, a considerable body of research on the sex differences in the severity of impulsive behaviors did not identify significant effects of sex on the occurrence of impulsive behaviors.[48,49] However, some previous studies also reported that sex tends to significantly affect the severity and frequency of impulsive behaviors.[50] Also, some studies identified significant effects of sex on WM structure and impulsivity.[51] These divergent findings suggest the need for further research to determine the precise effects of sex on the brain structure.

Our study possesses several strengths. Notably, it employs an imaging analysis technique, namely DMRI connectometry, to elucidate the intricate associations between WM microstructure and impulsivity. Furthermore, the study undertakes a comprehensive examination of the potential age and sex-based disparities inherent in these associations.

On the other hand, our study has several limitations. Foremost among these is the relatively modest sample size, which may curtail the generalizability of our findings. Additionally, impulsivity was assessed using a self-reported questionnaire (UPPS), which may introduce significant bias into the reliability of our findings, despite the application of rigorous statistical analysis methods. Moreover, the cross-sectional nature of the study design necessitates prudence in drawing causal inferences. While our investigation offers valuable insights, further research endeavors employing longitudinal approaches could potentially provide a more robust understanding of these dynamics.

In conclusion, there are notable associations between impulsivity and alterations in the WM integrity across diverse tracts, encompassing the forceps minor and major, corpus callosum, cerebellar pathways, and cingulum. While our study contributes valuable insights by unveiling considerable associations between microstructural modifications in WM and impulsive behaviors of healthy individuals, further research is imperative to better understand these dynamics.

AUTHOR CONTRIBUTIONS

Fatemeh Rashidi: Writing—original draft. **Mohammadamin Parsaei:** Investigation; validation; project administration; writing—original draft. **Iman Kiani:** Writing—original draft. **Arash Sadri:** Writing—review and editing. **Mohammad Hadi Aarabi:** Supervision; writing—review and editing. **Seyed Reza Darijani:** Writing—review and editing. **Yune Sang Lee:** Supervision; writing—review and editing. **Hossein Sanjari Moghaddam:** Conceptualization; data curation; formal analysis; visualization. All of the authors have read and approved the final draft.

ACKNOWLEDGMENTS

The authors have nothing to report.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS APPROVAL STATEMENT

The original study conducted for compiling the LEMON dataset was carried out according to the Declaration of Helsinki and was approved by the Ethics Committee of the University of Leipzig (reference number 154/13-ff).

PATIENT CONSENT STATEMENT

N/A.

CLINICAL TRIAL REGISTRATION

N/A.

ORCID

Fatemeh Rashidi http://orcid.org/0000-0002-2203-1305
Mohammadamin Parsaei http://orcid.org/0000-0002-7764-0319
Iman Kiani http://orcid.org/0000-0003-1556-1129
Arash Sadri http://orcid.org/0000-0002-3726-243X
Mohammad Hadi Aarabi http://orcid.org/0000-0002-5550-9782
Seyed Reza Darijani http://orcid.org/0000-0002-9956-9787
Yune Sang Lee http://orcid.org/0000-0001-8401-6007
Hossein Sanjari Moghaddam http://orcid.org/0000-0001-7461-541X

REFERENCES

1. Dalley JW, Robbins TW. Fractionating impulsivity: neuropsychiatric implications. Nat Rev Neurosci. 2017;18(3):158–71.
2. Robbins T, Curran H, de Wit H. Special issue on impulsivity and compulsivity. Psychopharmacology. 2012;219(2):251–2.
3. Dawe S, Loxton NJ. The role of impulsivity in the development of substance use and eating disorders. Neurosci Biobehav Rev. 2004;28(3):343–51.
4. Barati F, Pourshahbaz A, Nosratabadi M, Mohammadi Z. The role of impulsivity, attentional bias and decision-making styles in risky driving behaviors. Int J High Risk Behav Addic. 2020;9(2):e98001.
5. Parsaei M, Taghavizanjani F, Cattarinussi G, Moghaddam HS, Di Camillo F, Akhondzadeh S, et al. Classification of suicidality by training supervised machine learning models with brain MRI findings: a systematic review. J Affect Disord. 2023;340:766–91.
6. Chen Y, Ide JS, Li CS, Chaudhary S, Le TM, Wang W, et al. Gray matter volumetric correlates of dimensional impulsivity traits in children: sex differences and heritability. Hum Brain Mapp. 2022;43(8):2634–52.
7. Ikuta T, Del Arco A, Karlsgodt KH. White matter integrity in the fronto-striatal accumbofrontal tract predicts impulsivity. Brain Imaging Behav. 2018;12(5):1524–8.
8. Moeller FG, Hasan KM, Steinberg JL, Kramer LA, Dougherty DM, Santos RM, et al. Reduced anterior corpus callosum white matter integrity is related to increased impulsivity and reduced discriminability in cocaine-dependent subjects: diffusion tensor imaging. Neuropsychopharmacology. 2005;30(3):610–7.
9. Rashidi F, Khanmirzaei MH, Hosseinzadeh F, Kolahchi Z, Jafarimehrabady N, Moghisseh B, et al. Cingulum and uncinate fasciculus microstructural abnormalities in Parkinson's disease: a systematic review of diffusion tensor imaging studies. Biology. 2023;12(3):475.
10. Chilla GS, Tan CH, Xu C, Poh CL. Diffusion weighted magnetic resonance imaging and its recent trend-a survey. Quant Imaging Med Surg. 2015;5(3):407–22.
11. Yeh FC, Badre D, Verstynen T. Connectometry: a statistical approach harnessing the analytical potential of the local connectome. Neuroimage. 2016;125:162–71.
12. Huisman TAGM. Diffusion-weighted and diffusion tensor imaging of the brain, made easy. Cancer Imaging. 2010;10 (1A):S163–71.
13. Yeh FC, Tang PF, Tseng WYI. Diffusion MRI connectometry automatically reveals affected fiber pathways in individuals with chronic stroke. NeuroImage Clin. 2013;2:912–21.
14. Sobhani S, Rahmani F, Aarabi MH, Sadr AV. Exploring white matter microstructure and olfaction dysfunction in early parkinson disease: diffusion MRI reveals new insight. Brain Imaging Behav. 2019;13(1):210–9.
15. Moghaddam HS, Parsaei M, Taghavizanjani F, Cattarinussi G, Aarabi MH, Sambataro F. White matter alterations in affective and non-affective early psychosis: a diffusion MRI study. J Affect Disord. 2024;351:615–23.
16. Dretsch MN, Tipples J. Sex differences moderate decision making behaviour in high impulsive sensation seekers. Cogn Emot. 2011;25(1):149–55.
17. Kogachi S, Chang L, Alicata D, Cunningham E, Ernst T. Sex differences in impulsivity and brain morphometry in methamphetamine users. Brain Struct Funct. 2017;222(1):215–27.
18. Babayan A, Erbey M, Kumral D, Reinelt JD, Reiter AMF, Röbbig J, et al. A mind-brain-body dataset of MRI, EEG, cognition, emotion, and peripheral physiology in young and old adults. Sci Data. 2019;6:180308.
19. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191–4.
20. Whiteside SP, Lynam DR. The five factor model and impulsivity: using a structural model of personality to understand impulsivity. Pers Individ Dif. 2001;30(4):669–89.
21. Leemans A, Jeurissen B, Sijbers J, Jones DK. ExploreDTI: a graphical toolbox for processing, analyzing, and visualizing diffusion MR data. Proc 17th Annu Meet Intl Soc Mag Reson Med. 2009;17(1):3537.
22. Yeh FC, Verstynen TD, Wang Y, Fernández-Miranda JC, Tseng WYI. Deterministic diffusion fiber tracking improved by quantitative anisotropy. PLoS One. 2013;8(11):e80713.
23. Razek AAKA, El-Serougy L, Abdelsalam M, Gaballa G, Talaat M. Differentiation of residual/recurrent gliomas from postradiation necrosis with arterial spin labeling and diffusion tensor magnetic resonance imaging-derived metrics. Neuroradiology. 2018;60(2):169–77.
24. Yeh FC, Panesar S, Fernandes D, Meola A, Yoshino M, Fernandez-Miranda JC, et al. Population-averaged atlas of the macroscale human structural connectome and its network topology. Neuroimage. 2018;178:57–68.
25. Wei QL, Han ZL, Wu XL, Kang Z, Li LJ, Zheng LR, et al. [Comparison of white matter integrity of schizophrenic patients with and without impulsive behaviors by diffusion tensor magnetic resonance imaging]. Zhonghua Yi Xue Za Zhi. 2011;91(43):3030–3.
26. Lai RY, Desai NA, Amlang CJ, Lin CYR, Chen TX, Minyetty MJ, et al. Gambling associated risk-taking decision in cerebellar ataxia. Parkinsonism Rel Disord. 2023;107:105252.
27. Chen TX, Lin CYR, Aumann MA, Yan Y, Amokrane N, Desai NA, et al. Impulsivity trait profiles in patients with cerebellar ataxia and Parkinson disease. Neurology. 2022;99(2):e176–86.
28. Jung YC, Schulte T, Müller-Oehring EM, Namkoong K, Pfefferbaum A, Sullivan EV. Compromised frontocerebellar circuitry contributes to nonplanning impulsivity in recovering alcoholics. Psychopharmacology. 2014;231(23):4443–53.
29. Piccoli T, Maniaci G, Collura G, Gagliardo C, Brancato A, La Tona G, et al. Increased functional connectivity in gambling disorder correlates with behavioural and emotional dysregulation: evidence of a role for the cerebellum. Behav Brain Res. 2020;390:112668.
30. Miquel M, Nicola SM, Gil-Miravet I, Guarque-Chabrera J, Sanchez-Hernandez A. A working hypothesis for the role of the cerebellum in impulsivity and compulsivity. Front Behav Neurosci. 2019;13:99.
31. Sadek MN, Ismail ES, Kamel AI, Saleh AA, Youssef AA, Madbouly NM. Diffusion tensor imaging of corpus callosum in adolescent females with borderline personality disorder. J Psychiatr Res. 2021;138:272–9.
32. Liu IC, Chiu CH, Chen CJ, Kuo LW, Lo YC, Tseng WYI. The microstructural integrity of the corpus callosum and associated impulsivity in alcohol dependence: a tractography-based segmentation study using diffusion spectrum imaging. Psychiatry Res. 2010;184(2):128–34.
33. Goldstein A, Covington BP, Mahabadi N, Mesfin FB. Neuroanatomy, corpus callosum.In: StatPearls. Treasure Island (FL): StatPearls Publishing LLC; 2023.

34. Lischke A, Domin M, Freyberger HJ, Grabe HJ, Mentel R, Bernheim D, et al. Structural alterations in the corpus callosum are associated with suicidal behavior in women with borderline personality disorder. Front Hum Neurosci. 2017;11:196.
35. Treit S, Chen Z, Rasmussen C, Beaulieu C. White matter correlates of cognitive inhibition during development: a diffusion tensor imaging study. Neuroscience. 2014;276:87–97.
36. Stansberry TE, Willliams AL, Ikuta T. The interhemispheric auditory white matter tract is associated with impulsivity. Behav Brain Res. 2022;429:113922.
37. Alfano V, Longarzo M, Aiello M, Soricelli A, Cavaliere C. Cerebral microstructural abnormalities in impulsivity: a magnetic resonance study. Brain Imaging Behav. 2021;15(1):346–54.
38. Wu Y, Sun D, Wang Y, Wang Y, Ou S. Segmentation of the cingulum bundle in the human brain: a new perspective based on DSI tractography and fiber dissection study. Front Neuroanat. 2016;10:84.
39. Bubb EJ, Metzler-Baddeley C, Aggleton JP. The cingulum bundle: anatomy, function, and dysfunction. Neurosci Biobehav Rev. 2018;92:104–27.
40. Chiang HL, Chen YJ, Lo YC, Tseng WYI, Gau SSF. Altered white matter tract property related to impaired focused attention, sustained attention, cognitive impulsivity and vigilance in attention-deficit/hyperactivity disorder. J Psychiatry Neurosci. 2015;40(5):325–35.
41. Scholz V, Houenou J, Kollmann B, Duclap D, Poupon C, Wessa M. Dysfunctional decision-making related to white matter alterations in bipolar I disorder. J Affect Disord. 2016;194:72–9.
42. Damatac CG, Chauvin RJM, Zwiers MP, van Rooij D, Akkermans SEA, Naaijen J, et al. White matter microstructure in attention-deficit/hyperactivity disorder: a systematic tractography Study in 654 individuals. Biol Psychiatry: Cogn Neurosci Neuroimaging. 2022;7(10):979–88.
43. Navarro-Orozco D, Bollu PC. Neuroanatomy, medial lemniscus (Reils band, Reils ribbon). In: StatPearls. Treasure Island (FL): StatPearls Publishing LLC; 2023.
44. George K, Das JM. Neuroanatomy, thalamocortical radiations. In: StatPearls. Treasure Island (FL): StatPearls Publishing LLC; 2023.
45. Van Wittenberghe IC, Peterson DC. Corticospinal tract lesion. In: StatPearls. Treasure Island (FL): StatPearls Publishing LLC; 2023.
46. Choi YJ, Lee EJ, Lee JE. The fornix: functional anatomy, normal neuroimaging, and various pathological conditions. Investig Magn Reson Imaging. 2021;25(2):59–75.
47. Onnink AMH, Zwiers MP, Hoogman M, Mostert JC, Dammers J, Kan CC, et al. Deviant white matter structure in adults with attention-deficit/hyperactivity disorder points to aberrant myelination and affects neuropsychological performance. Prog Neuropsychopharmacol Biol Psychiatry. 2015;63:14–22.
48. DeVito EE, Weinberger AH, Pang RD, Petersen N, Fagle T, Allen AM. Impulsivity across substance use categories: consideration of sex/gender. Curr Behav Neurosci Rep. 2020;7(3):109–27.
49. MacKinnon-Lee KA, Bahr M. Are you more impulsive with age? Examining age, marital status, and gender on cognitive ageing. Appl Neuropsychol Adult. 2022;31(1):1–13.
50. Adise S, Boutelle KN, Rezvan PH, Kan E, Rhee KE, Goran MI, et al. Sex-specific impulsivity, but not other facets of executive function, predicts fat and sugar intake two-years later amongst adolescents with a healthy weight: Findings from the ABCD study. Appetite. 2024;192:107081.
51. Silveri MM, Rohan ML, Pimentel PJ, Gruber SA, Rosso IM, Yurgelun-Todd DA. Sex differences in the relationship between white matter microstructure and impulsivity in adolescents. Magn Reson Imaging. 2006;24(7):833–41.

How to cite this article: Rashidi F, Parsaei M, Kiani I, Sadri A, Aarabi MH, Darijani SR, et al. White matter correlates of impulsive behavior in healthy individuals: a diffusion magnetic resonance imaging study. Psychiatry Clin Neurosci Rep. 2024;3:e70018. https://doi.org/10.1002/pcn5.70018