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RESEARCH ARTICLE

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Association between white matter microstructure and cognitive function in patients with methamphetamine use disorder

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Abstract

Methamphetamine use disorder (MUD) has been associated with broad neurocognitive impairments. While the cognitive impairments of MUD have been demonstrated, the neuropathological underpinnings remain inadequately understood. To date, the published human diffusion tensor imaging (DTI) studies involving the correlation between diffusion parameters and neurocognitive function in MUD are limited. Hence, the present study aimed to examine the association between cognitive performance and white matter microstructure in patients with MUD. Forty-five patients with MUD and 43 healthy controls (HCs) completed their demographic information collection, cognitive assessments, and DTI imaging. DTI images were preprocessed to extract fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD) of various fiber tracts. Univariate tests were used to examine group differences in cognitive assessments and DTI metrics. Linear regression was used to examine the relationship between these two metrics. The results revealed that patients with MUD had lower subset scores of the MATRICS Consensus Cognitive Battery (MCCB), which reflects five cognitive domains: processing speed, attention, verbal learning, visual learning, problem-solving. Patients with MUD also had significantly higher AD, MD, and RD values of the left superior longitudinal fasciculus than HCs. Furthermore, the RD value of the left superior longitudinal fasciculus was a significant predictor of processing speed and problem-solving ability, as shown by the digit-symbol coding test and NAB-Mazes scores, respectively. Findings extended our understanding of white matter microstructure that is related to neurocognitive deficits in MUD and provided potential targets for the prevention and treatment of this chronic disorder.

KEYWORDS

diffusion tensor imaging, methamphetamine use disorder, neurocognition, problem solving, processing speed, superior longitudinal fasciculus, white matter

1 | INTRODUCTION

Methamphetamine use disorder (MUD) has been associated with broad neurocognitive impairments (Dean et al., 2013; Harro, 2015; Teixeira-Gomes et al., 2015). In a recent meta-analysis, it was found that MUD was associated with moderate deficits in many cognitive domains, including attention, language/verbal fluency, memory, and executive functions (Potvin et al., 2018). In particular, many of these impairments persist after abstinence (Basterfield et al., 2019), which reduces daily functioning of patients (Kwon & Han, 2018) and contributes to poorer treatment outcomes (Downey & Loftis, 2014).

While the cognitive impairments of MUD have been demonstrated, the neuropathological underpinnings remain inadequately understood. Previous studies have provided evidence that compromised white matter (WM) tracts significantly impact cognitive function (Filley, 2010). Diffusion tensor imaging (DTI) is a powerful tool for detecting WM microstructure changes caused by myelin and axon injury or increased extracellular water accumulation (Le Bihan et al., 2001). Generally, there are four DTI measures: fractional anisotropy (FA) is generally regarded as a marker of fiber tract microstructure; mean diffusivity (MD) is sensitive to edema, cellularity, and necrosis; axial diffusion (AD) indicates damage to axon terminals; and radial diffusion (RD) indicates damage to myelin (Alexander et al., 2007). Recently, DTI has been widely applied to assess the effect of MA use on the directional organization and microstructure of WM tracts (Berman et al., 2008). Decreased FA and increased MD or RD were observed in individuals with MUD (Ottino-Gonzalez et al., 2022; Uhlmann et al., 2016; Zhuang et al., 2016). A meta-analysis of DTI studies revealed consistent WM compromise in individuals with stimulant use disorders, including MA (Beard et al., 2019). Another recent tract-based spatial statistics revealed higher MD, AD, and RD values in a wide range of WM tracts, including the superior longitudinal fasciculus (SLF) and corticospinal tract in individuals with MUD, as compared with normal controls (Huang, Yang, et al., 2020). These results have provided evidence that MUD is associated with altered WM microstructure.

Information obtained from DTI can be used along with cognitive performance to examine the relationship between changes in WM microstructure and behavior. To date, there have been limited human DTI studies on the correlation between diffusion parameters and neurocognitive function in MUD. Kim et al. found a significant negative correlation between the total error scores of Wisconsin Card Sorting Test (WCST) and FA values in the genu of the corpus callosum (Kim et al., 2009). The study conducted by Chung et al. revealed that the FA value of the right frontal WM was negatively correlated with the total and nonperseveration error scores of WCST in male MA abusers (Chung et al., 2007). A study by Fan et al. showed that the MD values of the right middle temporal gyrus were negatively correlated with the Digit Symbol Test score in MA addicts with long-term abstinence (Fan et al., 2019). Roos et al. also found that abnormal FA levels of children with MA exposure were significantly associated with poorer executive function, as shown by poorer scores in Kaufman Assessment Battery for Children-II Triangles, Hand movement, and story completion (Roos et al., 2015).

While the above findings demonstrated a connection between WM abnormalities and cognitive deficits, it should be noted that they are primarily focused on single performance domains instead of global cognitive function. Furthermore, the white matter alterations that may underlie these cognitive impairments in MUD remain largely unknown. Hence, the present study aims to fill this gap and examine the link between global cognitive performance measured by a standardized neurocognitive battery and WM microstructure in patients with MUD. To this end, we used DTI to measure WM changes and conducted multiple regressions to examine the associations between WM microstructure and cognitive functions. We hypothesized that MUD might be associated with broader WM microstructural changes, which might be associated with higher level of cognitive deficits.

2 | METHODS

2.1 | Participants

A total of 69 patients with MUD (the MUD group) and 47 healthy controls (the HC group) were included in the study. Patients with MUD were recruited between August 2019 and January 2020 from the Kangda Voluntary Drug Rehabilitation Centers in Changsha, Hunan Province, a controlled setting where access to illicit drugs or alcohol is prohibited through structural and regulatory efforts. Meanwhile, urine drug testing was performed regularly to verify drug abstinence. The participants in the center were typically provided with psychoeducation, physical exercise, group activities, and medically assisted detoxification treatment during abstinence. The inclusion criteria for MUD group were: (a) Han males aged between 18 and 45 years, (b) having completed at least 6 years of formal education, (c) with a current diagnosis of methamphetamine use disorder (MUD), as determined by at least two certified psychiatrists using the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), (d) with no other substance dependence except nicotine; and (e) with no other substance use except alcohol, nicotine, and betel nut for the past 6 months. HCs were recruited from local communities between September 2019 and March 2020 through a variety of social media, such as QQ, WeChat, and online flyers, with similar inclusion criteria applied for MUD except the history of illicit drug use. Participants with a history of major chronic medical illnesses, neurological disease, or psychiatric illness before MA use were excluded. Participants with contraindications to MRI scanning (e.g., claustrophobia, implants, metallic or electronic devices) were also excluded.

To ensure that the participants met all the inclusion criteria and none of the exclusion criteria, all the participants underwent a face-to-face structured clinical interview carried out by two certified psychiatrists. For the MA users, the interview was conducted when participants were not intoxicated or in withdrawal delirium (averagely 9.17 ± 5.29 days after the last MA use). After the on-site interview, 15 MA users were further excluded for not meeting DSM-5 criteria for MUD (9 of them used mainly ketamine, with occasional MA use, and 6 were diagnosed with MA abuse instead of dependence), as they were MA users without dependence. Then, the eligible participants

TABLE 1 Demographic information and substance use status of participants

M (SD) or *n* (%)	HC ($N = 43$)	MUD ($N = 45$)	*t* or χ^2 value	*p* value
Age	26.05 (6.89)	31.33 (5.47)	$t(86) = 4.00$	<.001
Height	171.63 (5.47)	170.60 (6.41)	$t(86) = 0.81$	.42
Weight	68.67 (9.42)	72.58 (10.85)	$t(86) = 1.80$	.075
Education (year)	13.98 (3.23)	11.36 (3.14)	$t(86) = 3.86$	<.001
Marital status (%)				
Divorced	0 (0.00)	6 (13.33)	$\chi^2(2) = 21.77$	<.001
Married	10 (23.26)	26 (57.78)		
Single	33 (76.74)	13 (28.89)		
Employment (%)				
Employed	19 (44.19)	25 (55.56)	$\chi^2(3) = 35.36$	<.001
Freelance	3 (6.98)	11 (24.44)		
Student	21 (48.84)	0 (0.00)		
Unemployed	0 (0.0)	9 (20.00)		
Income (CNY, %)				
<2000	18 (41.86)	3 (6.67)	$\chi^2(3) = 16.18$	<.001
2000-5000	9 (20.93)	18 (40.00)		
5000–10,000	14 (32.56)	18 (40.00)		
>10,000	2 (4.65)	6 (13.33)		
Substance use				
Smoking (yes/no)	19/24 (44.19%)	43/2 (95.56%)	$\chi^2(1) = 25.46$	<.001
Duration of smoking (years)	3.31 (5.88)	12.13 (5.32)	$t(86) = 7.38$	<.001
Drinking (yes/no)	14/29 (32.56%)	23/22 (51.11%)	$\chi^2(1) = 2.39$	.12
Duration of drinking (years)	1.70 (3.30)	4.62 (5.29)	$t(86) = 3.09$	.0027
Betel use (yes/no)	17/26 (39.53%)	29/16 (64.44%)	$\chi^2(1) = 4.52$	.034
Duration of betel use (years)	1.47 (2.28)	5.56 (5.95)	$t(86) = 4.32$	<.001
Duration of MA use (years)	—	6.08 (3.16)	—	—
Duration of MA abstinence (days)	—	61.60 (40.30)	—	—

Abbreviations: HC, healthy control; MUD, methamphetamine use disorder.

(54 MA users and 50 HCs) entered cognitive assessments and the DTI scan. Among the eligible participants, 9 MA users and 7 HCs were removed from further analysis due to incomplete data or abnormal scan. A total of 24 MA users and 7 HCs were removed, resulting in a final sample size of 45 patients with MUD and 43 HCs.

All participants were fully informed about the study procedures, and their personal information was kept confidential. This study was approved by the Ethics Committee of the Kangda Voluntary Drug Rehabilitation Centers in Changsha, Hunan Province.

2.2 | Measures

2.2.1 | Demographics

Demographic information, including age, gender, ethnicity, height, weight, employment status, marital status, years of schooling completed, and average monthly income, were documented. Additionally, we kept a record of drug use measures (yes/no, duration) for nicotine, alcohol, and betel use. As the fourth most consumed psychoactive substance, betel nut is a recreational substance that is widely used in South and Southeast Asian countries and the Asia Pacific tropical regions (Tang & He, 2021); in China, there is also a large number of people chewing betel nut for recreation and refreshing. The durations of MA use (years) and abstinence (days) were also recorded for patients with MUD. See Table 1 for more details.

2.2.2 | Cognitive assessment

We used a set of standardized neurocognitive tests called MATRICS Consensus Cognitive Battery (MCCB) (Shi et al., 2015) to evaluate cognitive functions in patients with MUD and HCs. The MCCB provides 10 measures in 7 cognitive domains: speed of processing, attention/vigilance, working memory, verbal learning, visual learning, problem-solving, and social cognition. Speed of processing was examined with the digit-symbol coding test (DSCT), Category Fluency Test (CF), and Trail Making Test-Part A (TMT-A); attention was measured

using the Continuous Performance Test-Identical Pairs (CPT-IP); working memory was tested using the Visual Memory Spatial Span (SSP) and Letter–Number Span (LNSP); verbal learning was tested using the Hopkins Verbal Learning Test-Revised (HVLT-R); visual learning was tested using the Brief Visuospatial Memory Test-Revised (BVMT-R); planning and foresight, that is, problem solving, was assessed using the Neuropsychology Assessment Battery-Mazes (NAB-Mazes); and social cognition was assessed using the Mayer-Salovey-Caruso Emotional Intelligence Test: Managing Emotions (MSCEIT-ME).

2.3 | DTI data acquisition

The MRI scan was performed using a 3.0T Siemens Skyra MRI scanner (Siemens, Munich, Germany) equipped with a 16-channel head coil in Hunan Children's Hospital. For the scanning, the participants were placed in a supine position, with foam pads and earplugs to minimize head motion. A single-shot echo-planar imaging (EPI) sequence was applied for obtaining whole-brain diffusion tensor imaging data with the following parameters: TR = 9100 ms, TE = 84 ms, slice number = 75, orientation: transversal (axial), slice thickness = 2 mm, slice gap = 0 mm, slice order: interleaved, field of view = 224 × 224 mm, voxel size = 2 × 2 × 2 mm^3, phase partial Fourier factor = 6/8, and 3 *b*-values = 9 + 1, 64, and 1000 s/mm^2.

T1-weighted images for anatomical localization were acquired using a 3D magnetization preparing rapid acquisition gradient echo (MPRAGE) sequence with the following parameters: TR = 2530 ms, TE = 2.98 ms, flip angle = 7°, number of slices = 176, slice thickness = 1 mm, slice gap = 0 mm, field of view = 256 × 256 mm, and voxel size = 1 × 1 × 1 mm^3. All the images were reviewed by a senior radiologist to ensure that there was no structural abnormalities, ghosting artifacts, or excess subject motion.

2.4 | DTI data preprocessing and analysis

The DTI images were processed and analyzed through the following steps: (1) boundary-based registration between the b0 image (the first volume without diffusion weighting) and the T1 image was performed using FreeSurfer's bbregister (Greve & Fischl, 2009); (2) a whole brain mask was created using FSL's bet (Smith, 2002); (3) Eddy correction, motion correction and outlier replacement were performed using FSL's eddy_openmp (Andersson & Sotiropoulos, 2016); (4) diffusion tensor model was fitted at each voxel using FSL's dtifit; FA, MD, AD and RD measures were calculated based on the eigenvalues of diffusion tensor to represent the white matter microstructure; (5) T1 image was first registered into the MNI152 template using ANTs (Tustison et al., 2014), and the resultant T1-MNI152 transformation was combined with the b0-T1 registration result to transform the FA/MD/AD/RD maps into the MNI152 space; (6) mean FA/MD/AD/RD values were extracted based on the JHU white-matter tractography atlas supplied by FSL (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Atlases), consisting of 20 white matter structures (Hua et al., 2008); and (7) visual quality check of raw T1/DTI images, brain extraction and registration.

2.5 | Statistical analysis

Intergroup differences in demographic information and clinical characteristics were analyzed using independent-samples *t* tests or χ^2 test of independence as appropriate. We analyzed intergroup differences in cognitive performance and FA, MD, AD, and RD values, and select only significant variants for further regression analysis. Hence, analysis of covariances (ANCOVA), with age, years of education, smoking, drinking, and betel use as covariates, was used to investigate the inter-group differences on cognitive performance. The same ANCOVA was also used to investigate inter-group differences on FA, MD, AD, and RD values. Bonferroni correction was used to correct for multiple ANCOVA of cognitive performance ($k = 10$) and DTI metrics ($k = 80$ for 20 fibers and 4 metrics). Finally, significant variants were used in a multiple linear regression to predict cognitive scores using diffusion metrics. The same covariates, that is, age, years of education, smoking, drinking, and betel use, were used in a covariates-only model, followed by adding the significant diffusion metrics into the second model.

Assumptions for the ANCOVA and linear regression were checked before running the analysis. For ANCOVA, linearity, normality, and homogeneity of variance were checked. Multivariate normality, homoscedasticity, and multicollinearity for linear regressions were also checked using histograms, qq-plot, predicted values-standardized residual plot, and variance inflation factor (VIF).

3 | RESULTS

3.1 | Demographic information and clinical characteristics

The demographic information and clinical characteristics of the participants are presented in Table 1. Participants of the two groups did not differ in height, weight, drinking status (yes/no), and duration of drinking (years). However, the MUD group had higher age, lower education level, higher level of smoking (in terms of both amount and duration), and higher level of betel use (in terms of both amount and duration), as compared with those of HCs.

3.2 | Cognitive performance

Assumption checks revealed no violations for assumptions for all cognitive performance except BVMT-R ($F[1, 86] = 4.85$, $p = .030$). Checking of variances by groups showed that they were not far apart from each other ($SD_{HC} = 20.30$, $SD_{MUD} = 14.80$). Hence, we decided to continue with ANCOVA for BVMT-R instead of running nonparametric version of ANOVA, that is, Kruskal–Wallis test, which could

TABLE 2 Cognitive profile of participants

Estimated marginal means ± SD (95% CI)	HC ($N = 43$)	MUD ($N = 45$)	*F*-ratio	*p* value
DSCT	52.88 ± 2.24 [48.42, 57.33]	40.97 ± 2.79 [35.42, 46.53]	$F(1, 81) = 11.01$	.014
CF	50.13 ± 1.44 [47.26, 52.99]	44.42 ± 1.8 [40.85, 47.99]	$F(1, 81) = 6.11$	.16
TMT-A	57.79 ± 1.93 [53.95, 61.63]	55.95 ± 2.4 [51.17, 60.74]	$F(1, 81) = 0.35$	.99
CPT-IP	53.04 ± 2.14 [48.77, 57.31]	35.39 ± 2.67 [30.07, 40.72]	$F(1, 81) = 26.36$	<.001
SSP	47.13 ± 2.42 [42.31, 51.95]	38.43 ± 3.02 [32.41, 44.44]	$F(1, 81) = 5.03$	.28
HVLT-R	49.58 ± 2.1 [45.39, 53.76]	37.68 ± 2.62 [32.46, 42.89]	$F(1, 81) = 12.47$	.0069
LNSP	49.33 ± 1.66 [46.04, 52.63]	43.19 ± 2.07 [39.07, 47.3]	$F(1, 81) = 5.35$	.23
BVMT-R	43.63 ± 3.04 [37.58, 49.69]	31.45 ± 3.8 [23.89, 39]	$F(1, 81) = 6.24$	.15
NAB-Mazes	54.22 ± 1.71 [50.82, 57.61]	45.07 ± 2.13 [40.83, 49.3]	$F(1, 81) = 11.20$	.012
MSCEIT-ME	60.22 ± 2.49 [55.27, 65.18]	55.99 ± 3.11 [49.81, 62.17]	$F(1, 81) = 1.12$	.99

Note: The table shows the estimated marginal means of the neuropsychological tests after accounting for age, education, drinking status, smoking status, and betel use. *p* values have been corrected using Bonferroni correction. BVMT-R, Brief Visuospatial Memory Test-Revised; CF, category fluency; CPT-IP, continuous performance test-identical pairs; DSCT, digit-symbol coding task; HC, healthy control; HVLT-R, Hopkins Verbal Learning Test-Revised; LNSP, Letter-number span; MSCEIT, Mayer-Salovey-Caruso Emotional Intelligence Test: Managing Emotions; MUD, methamphetamine use disorder; NAB-Mazes, Neuropsychological Assessment Battery-Mazes; SSP, spatial span; TMT-A, trail-making test part A.

not account for covariates. After adjusting for age, education, drinking status, smoking status, and betel use, and after correction for multiple testing, there were group differences in DSCT ($F[1, 81] = 15.67$, $p = .0013$), CPT-IP ($F[1, 81] = 34.46$, $p < .001$), HVLT-R ($F[1, 81] = 12.47$, $p = .0069$), and NAB-Mazes ($F[1, 81] = 11.20$, $p = .012$). The estimated marginal means of the neuropsychological test results after accounting for the covariates are presented in Table 2.

In short, after controlling for the covariates, HC had (1) higher DSST scores ($M_{lsmeans}$ ± SE = 52.90 ± 2.24, 95% CI = [48.40, 57.30]) than MUDs ($M_{lsmeans}$ ± SE = 41.00 ± 2.79, 95% CI = [35.40, 46.50]), (2) higher CPT-IP scores ($M_{lsmeans}$ ± SE = 53.00 ± 2.14, 95% CI = [48.80, 57.30]) than MUDs ($M_{lsmeans}$ ± SE = 35.40 ± 2.67, 95% CI = [30.10, 40.70]), (3) higher HVLT-R scores ($M_{lsmeans}$ ± SE = 49.60 ± 2.10, 95% CI = [45.40, 53.80]) than MUDs ($M_{lsmeans}$ ± SE = 37.70 ± 2.62, 95% CI = [32.50, 42.90]), and (4) higher NAB-Mazes scores ($M_{lsmeans}$ ± SE = 54.20 ± 1.71, 95% CI = [50.80, 57.60]) than MUDs ($M_{lsmeans}$ ± SE = 45.10 ± 2.21, 95% CI = [40.80, 49.30]).

3.3 | Group differences in WM microstructure

Assumption checks revealed no violations for assumptions for all diffusion metrics. After correcting for $k = 80$ ANCOVA models, the ANCOVA showed significant group differences in AD ($F[1, 81] = 11.29$, $p = .024$), MD ($F[1, 81] = 17.44$, $p = .001$), and RD ($F[1, 81] = 15.05$, $p = .002$) of the left SLF, after adjusting for age, education, drinking status, smoking status, and betel use, and after correction for multiple testing (Figure 1). The other 77 ANCOVA models, including the FC of the left SLF, showed no significant results after Bonferroni correction. To complete the analysis of the left SLF, we also reported the ANCOVA model for the FA value of the left SLF. The ANCOVA found no significant group differences in the FA value ($F[1, 81] = 6.56$, $p = .246$) after Bonferroni correction.

Estimated marginal means showed that MUDs have (1) higher AD values ($M_{lsmeans}$ ± SE = 0.001082 ± 0.0000056, 95% CI = [0.001071, 0.001094]) than HC ($M_{lsmeans}$ ± SE = 0.001058 ± 0.0000045, 95% CI = [0.001049, 0.001067]), (2) higher MD values ($M_{lsmeans}$ ± SE = 0.0007337 ± 0.0000046, 95% CI = [0.0007244, 0.0007429]) than HC ($M_{lsmeans}$ ± SE = 0.0007087 ± 0.0000037, 95% CI = [0.0007013, 0.0007161]), and (3) higher RD values ($M_{lsmeans}$ ± SE = 0.0005595 ± 0.0000051, 95% CI = [0.0005494, 0.0005697]) than HC ($M_{lsmeans}$ ± SE = 0.000534 ± 0.0000041, 95% CI = [0.0005259, 0.0005422]).

3.4 | Association between left SLF and cognition

After checking for ordinary least-squares linear regression assumptions, we found high variance inflation factors (VIF) in AD (VIF = 771.44), MD (VIF = 4936.00), and RD (VIF = 2534.79) values of the left SLF. By examining the correlations, we found that the correlations between AD and MD values ($r = .81$, $p < .001$), between MD and RD values ($r = .95$, $p < .001$), and between AD and RD values ($r = .58$, $p < .001$) were significant. Therefore, we removed the MD values of the left SLF from the regression model and ran the linear regressions with age, education, drinking status, smoking status, and betel use as covariates, and AD and RD values of the left SLF as predictors (Figure 2).

For DSCT, the predictors from the covariates model accounted for a significant additional 8.76% of the variance in DCST [$\Delta F(2, 79) = 5.58$, $p = .0054$, $\Delta R^2 = 0.0876$], resulting in a total $R^2 = 0.38$ for the DCST regression model. The RD ($\beta = -.40$, $t = -3.48$, $p = .0013$) value of the left SLF was a significant predictor of DCST. The AD value of the left SLF, however, was not a significant predictor of DCST ($\beta = .22 = 1.82$, $p = .073$).

For CPT-IP, the predictors from the covariates model accounted for an additional 1.34% of the variance in CPT-IP [$\Delta F(2, 79) = 0.84$,

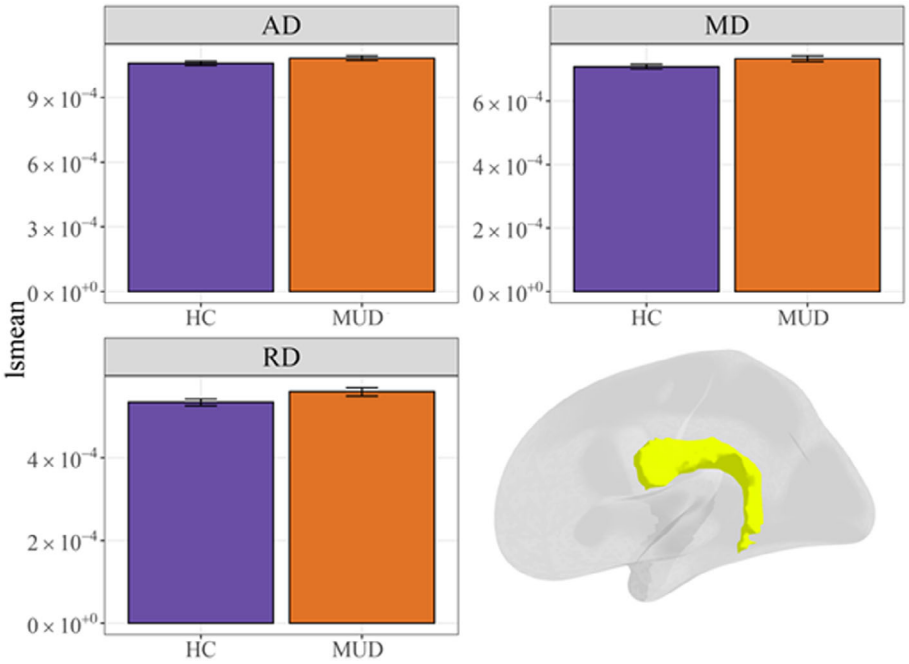

FIGURE 1 The figure displays the lsmean and standard error of the AD, MD, and RD values of the left SLF for the two groups. For all diffusivity values, the MUD group has higher AD, MD, and RD values of the left SLF than the HC group after controlling for age, level of education, drinking status, smoking status, and betel use, and after Bonferroni correction for multiple testing. The bottom right panel shows the left SLF. AD, axial diffusivity; HC, healthy control; MD, mean diffusivity; MUD, methamphetamine use disorder; RD, radial diffusivity; SLF, superior longitudinal fasciculus

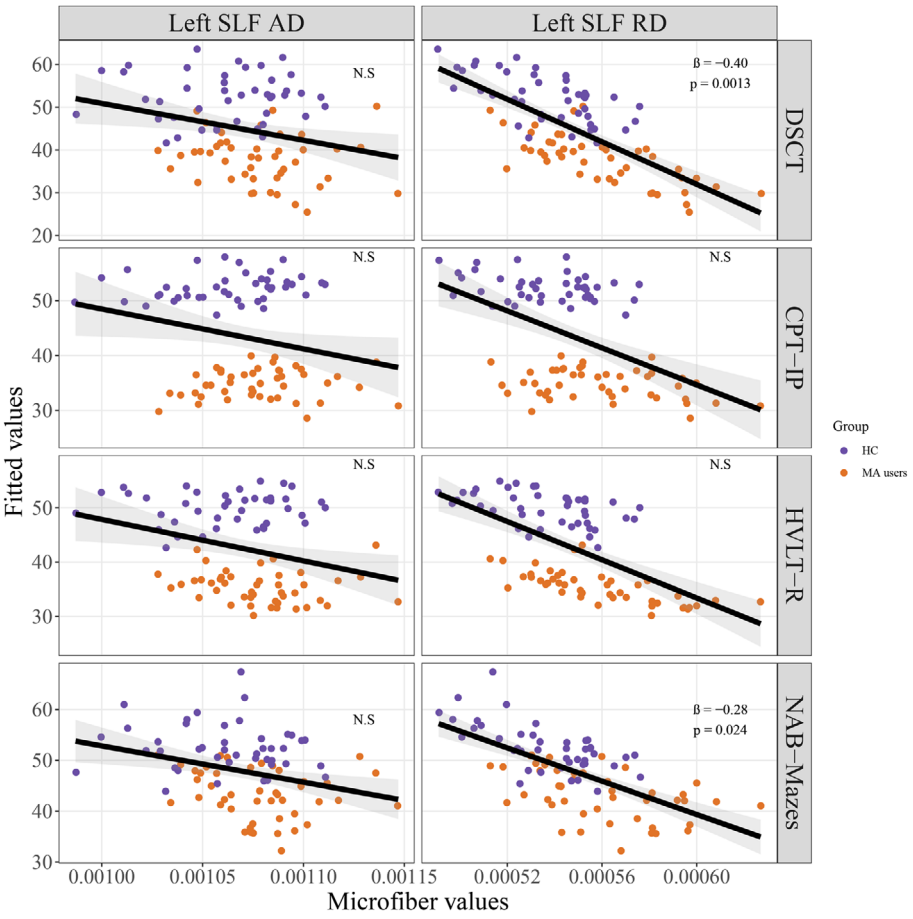

FIGURE 2 The figure shows the association between cognitive domains of the significant MCCB and the AD and RD values of the left SLF. Only RD value of the left SLF was predictive of DCST and MAB-mazes scores. AD, axial diffusivity; CPT-IP, continuous performance test-identical pairs; DSCT, digit-symbol coding task; HC, healthy control; HVLT-R, Hopkins verbal learning test-revised; MCCB, MATRICS consensus cognitive battery; MUD, methamphetamine use disorder; NAB-mazes, neuropsychological assessment battery-mazes; RD, radial diffusivity; SLF, superior longitudinal fasciculus

$p = .44$, $\Delta R^2 = 0.0134$], resulting in a total $R^2 = 0.37$ for the CPT-IP regression model. AD ($\beta = .15$, $t = 1.25$, $p = .22$) and RD ($\beta = -.11$, $t = -0.93$, $p = .36$) values of the left SLF were not significant predictors of CPT-IP.

For HVLT-R, the predictors from the covariates model account for an additional 2.30% of the variance in HVLT-R [$\Delta F(2, 79) = 1.32$, $p = .28$, $\Delta R^2 = 0.023$], resulting in a total $R^2 = 0.32$ for the HVLT-R regression model. AD ($\beta = .09$, $t = 0.72$, $p = .47$) and RD ($\beta = -.20$,

$t = -1.62$, $p = .11$) values of the left SLF were not significant predictors of HVLT-R.

Finally, for NAB-Mazes, the predictors from the covariates model accounted for an additional 5.28% of the variance in NAB-Mazes [ΔF (2, 79) = 3.17, $p = .047$, $\Delta R^2 = 0.0528$], resulting in a total $R^2 = 0.34$ for the NAB-Mazes regression model. The RD ($\beta = -.28$, $t = -2.30$, $p = .024$) value of the left SLF was a significant predictor of NAB-Mazes, while the AD value of the left SLF was not a significant predictor of NAB-Mazes ($\beta = .04$, $t = 0.31$, $p = .76$).

4 | DISCUSSION

The primary aim of this study was to investigate white matter tracts associated with cognitive deficits in patients with MUD. Our behavioral results indicated that patients with MUD had lower DSCT, CPT-IP, HVLT-R, and NAB-Mazes scores than HCs. Similarly, our neuroimaging results demonstrated higher AD, MD, and RD values of the left SLF in patients with MUD, as compared with HCs. Regression analyses revealed that the RD value of the left SLF was negatively associated with DCST and NAB-Mazes scores.

4.1 | Differences in cognitive profiles

Our behavioral results revealed significant group differences in many aspects of cognition, including processing speed, sustained attention, verbal leaning, and problem solving after adjusting for education, drinking status, smoking status, and betel use, and after correction for multiple testing. We added these covariates, specifically drinking, smoking, and betel use due to their associations with cognitive profiles and WM microstructure (Hampton et al., 2019). For example, consistent research has documented the association between alcohol use (Spindler et al., 2022), smoking (Gray et al., 2020), betel use (Yuan et al., 2017), and WM microstructure. Patients with MUD had lower DSCT scores, indicating that they had lower processing speed. This is consistent with a recent meta-analysis demonstrating poorer processing speed in individuals with MUD, as compared to HCs (Potvin et al., 2018). This marked difference might be related to poorer functions in other cognitive domains, such as attention and working memory. Recent advancements in DCST have also suggested that the DSCT is associated with and is sensitive to other cognitive functions, including attention, visuospatial attention, and executive functions (Jaeger, 2018). However, despite its high sensitivity, the low specificity of the DCST obscures the impairments in specific cognitive domains (Jaeger, 2018), and whether poorer functions in processing speed and attention are interrelated in the context of MUD is still unclear. Currently, our findings could only demonstrate that patient with MUD had poorer processing speed.

Our study also demonstrated that patients with MUD had lower CPT-IP scores than HCs, indicating poorer sustained attention in MUD. Attention is crucial as it affects other cognitive functions such as language, memory, and problem-solving; it also reflects the complex interplay of multiple independent systems in the brain (Burgoyne & Engle, 2020; Fan et al., 2005; Pessoa et al., 2003). Reduced sustained attention (London et al., 2005; Pocuca et al., 2020; Rubenis et al., 2018) has been reported in previous studies, suggesting that MUD might be associated with sustained attentional deficits. Poor sustained attention is also indicative of limited improvement in motivation during early rehabilitation programs, suggesting its importance in the prediction of treatment outcome (Rubenis et al., 2018). Therefore, improving sustained attention in rehabilitation may be beneficial for patients with MUD.

Patients with MUD also exhibited poorer verbal learning, as shown by lower HVLT-R scores. A previous review reported that MUD often performed equally poor on verbal learning (Janke van Holst & Schilt, 2011) and memory (Potvin et al., 2018), suggesting that these deficits did not come from poor consolidation. Some other studies suggested that these deficits came from poor learning strategies (Woods et al., 2005) or compromised dopaminergic transmission and hippocampal microstructure, which led to poor verbal learning (Shukla & Vincent, 2021). Yet, the mechanisms underlying poor verbal learning is still unclear.

Finally, patients with MUD also exhibited poorer NAB-Mazes scores than HCs. NAB-Mazes require patients to plan and organize steps through a maze and is sensitive to frontal lobe dysfunction (Shi et al., 2015). A study conducted in rats found that methamphetamine caused apoptosis, resulting in atrophy of the prefrontal cortex (Tehrani et al., 2019). Humans with severe MUD also had lower prefrontal cortical volume, and this was associated with higher impulsivity ، which is an indicator of poor planning and foresight, that is, problem solving (Huang, Dai, et al., 2020). Repetitive transcranial magnetic stimulation (rTMS) to the left prefrontal cortex was shown to improve the score of the Groton maze learning task (a task assessing problem solving abilities, similar to the NAB-Mazes) (Su et al., 2020). This change was also associated with changes in γ-aminobutyric acid (GABA) levels in patients who underwent rTMS, but not in those who underwent sham-rTMS, suggesting a direct neurochemical association between methamphetamine, prefrontal cortex, and problem solving.

Generally, our findings are consistent with those of previous studies, suggesting that MUD is associated with a broad range of cognitive deficits. However, further research on the mechanisms of these deficits is required, as they are still debatable.

4.2 | Importance of the SLF in processing speed and problem solving in MUD

The SLF is a major intra-hemispheric fiber tract that connects the parietal, temporal, and frontal lobes. Damage to the SLF could lead to dysfunction in attention, visuospatial abilities, and processing speed (Makris et al., 2005). Recently, it has been found that the SLF was associated with visuospatial cognitive function and working memory performance (Koshiyama et al., 2020). However, very few studies have investigated or found significant associations between the SLF and cognitive functions in MUD. According to Huang et al., the FA,

AD, RD, and MD values were altered in bilateral SLF, but these values were not associated with any dimensions of cognition, including attention (Huang, Yang, et al., 2020).

The present study revealed higher AD, MD, and RD values of the left SLF in patients with MUD, as compared with HCs. Similarly, a recent study found that MA addicts had significantly higher AD, RD, and MD values in the bilateral SLF compared with controls (Huang, Yang, et al., 2020). Changes in AD, RD and FA were also found in many brain regions in children prenatally exposed to MA, especially in the SLF (Chang et al., 2012). In addition, findings from the ENIGMA-Addiction working group revealed that MUDs had higher RD in several WM tracts, including the SLF (Ottino-Gonzalez et al., 2022). RD is indicative of perpendicular diffusion and is often used as a proxy of myelin density, and thus higher RD values might suggest low myelin content (Song et al., 2002; Song et al., 2005); MD indicates the mean amount of water that is diffused, and might be suggestive of increased cellularity in the brain (Fellgiebel et al., 2004). This often occurs with edema or necrosis. On the other hand, AD indicates the mean diffusion coefficient of water molecules diffusing parallel to the tract, reflecting parallel diffusion. Lower AD values typically imply axonal damage, that is, cellular debris and injured structures of the axon barricade the diffusion of water making diffusion less coherent. Higher AD values are indicative of greater fiber alignment or density, and could have an underlying pathological cause when FA is low and RD and MD values are high as it may indicate neurofibrillary damage. We did not find any significant group differences in FA values, and thus cannot assume any white matter damage in any of the microstructure (Jones et al., 2013). At most, we could only suggest greater permeability and lower myelin in MUD compared to HC. Thus, more systematic studies are required to examine changes in white matter microstructure in MUD.

More importantly, our findings further suggested that the left SLF might be an important substrate of cognitive deficits in MUD, which was shown by significant associations between the RD value and processing speed as well as problem solving. The processing speed, as assessed by the DSCT, was closely related to the microstructure of WM tracts associated with the frontal, parietal, and temporal cortices. The SLF is the main tract subserving fronto-parietal integration, contributing significantly to the processing speed (Turken et al., 2008). Several previous studies have examined the relationship between the SLF and processing speed. One study reported that the SLF was a significant predictor of processing speed in inter-episode bipolar patients (McKenna et al., 2015). Investigation of SLF fiber complexity in recent-onset psychosis revealed its significant effects on processing speed (Szeszko et al., 2018). In the current study, we found that the RD value of the left SLF was a significant predictor of processing speed, as shown by DSCT. In accordance with those of the above previous studies, the findings may be used as additional evidence for the association between the SLF and processing speed.

The NAB-Mazes test examines problem solving, where those with typical frontal-lobe syndromes are likely to fail. Prolonged MA use causes abnormalities in the frontal lobes (Wu et al., 2018) and could have caused damage to the short-range fibers along the prefrontal cortex. As shown by our results, this change could have led to deficits in problem solving. Considering the influence of polysubstance use on white matter microstructure (Kaag et al., 2017), including frontal lobe functions (Pando-Naude et al., 2021), as shown in previous studies, we accounted for the use of other drugs as covariates. Even with the above measure, we still found significant association between the left SLF and NAB-Mazes scores, indicating the importance of the SLF in problem solving.

The findings that the RD value of the left SLF was associated with poorer problem solving connect to a broader memory and learning deficit in MUD. A previous study found that verbal memory impairments in individuals with MUD were related to poor strategic control (Woods et al., 2005), as these individuals failed in planning their learning strategies during verbal encoding or retrieving. However, we did not find any associations between verbal memory (HVLT-R) and white matter microstructure of the left SLF. Notably, the structural connectivity of the SLF is distributed among subregions and white matter tracts, that is, SLF-I, SLF-II, SLF-III, and the arcuate fascicle (Nakajima et al., 2020). In our analysis, we did not divide the SLF into several parts to examine the association between the parts of SLF and cognitive performance, which may have led to null findings for HVLT-R. A second reason could be that there were no real associations between WM microstructure of the left SLF and CPT-IP and HVLTT-R even though there were significant group differences in both WM microstructure of the left SLF and CPT-IP and HVLT-R. Furthermore, polysubstance use may add complexity to the analysis (Hampton et al., 2019). Even after adjusting for alcohol, smoking, and betel use, we still found negligible associations between the AD and RD of the left SLF and CPT-IP AND HVLT-R. In future studies, the SLF in MUD can be explored in greater detail to provide more precise markers of cognitive dysfunctions in MUD.

4.3 | Limitations

Several limitations should be noted. First, we only selected tracts from our initial univariate analysis to reduce the number of regression models. Thus, only the left SLF was included in our regression models. Second, as the demographic information and clinical profiles differed between patients in compulsory and voluntary drug rehabilitation centers in China (Huang et al., 2021), the results of this study may not be representative enough. Third, we opted for an exploratory analysis using Bonferroni correction due to the limited literature. Hence, there could be associations between different white matter tracts and cognitive profiles even though no significant inter-group differences had been found regarding these measures. Thus, more studies are needed to build a better foundation on the association between white matter microstructure and cognitive changes in MUD. Finally, future works on the impact of gender and longitudinal studies should be considered, and studies are also needed to determine whether there is any association between DTI metrics and MA use, in order to better understand the characteristics of MUD.

4.4 | Conclusion

In conclusion, the present study demonstrated that MUD was associated with a variety of cognitive deficits. Patients with MUD often have compromised left SLF microfibers, specifically in AD, MD, and RD. This study also revealed that only the RD value was negatively associated with processing speed and problem solving, as shown by the DCST and NAB-Mazes scores, respectively. Our findings may provide further evidence for the important role of the left SLF in processing speed and problem solving. Further functional imaging studies on the SLF in MUD may extend our understanding of how this tract breaks down in MUD and how it impacts the cognitive function of patients.

AUTHOR CONTRIBUTIONS

The study was designed and supervised by Tieqiao Liu and Yanan Zhou. Data were collected by Yanan Zhou, Yuzhu Hao, Manyun Li, and Yunfei Wang. Data were processed by Yang Hu and Zhi Yang and interpreted by Yanan Zhou, Jinguang Li, Shubao Chen, and Winson Fu Zun Yang. The manuscript was drafted by Yanan Zhou and was revised by Qianjin Wang, Winson Fu Zun Yang, Yuejiao Ma, Qiuxia Wu, Dong Yang, and Tieqiao Liu. All co-authors revised and approved the final version to be published.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article.

ETHICS STATEMENT

This study was approved by the Ethics Committee of the Second Xiangya Hospital, Central South University (No. S095, 2013).

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REFERENCES

Alexander, A. L., Lee, J. E., Lazar, M., & Field, A. S. (2007). Diffusion tensor imaging of the brain. *Neurotherapeutics*, *4*(3), 316–329.

Andersson, J. L. R., & Sotiropoulos, S. N. (2016). An integrated approach to correction for off-resonance effects and subject movement in diffusion MR imaging. *NeuroImage*, *125*, 1063–1078. https://doi.org/10.1016/j.neuroimage.2015.10.019

Basterfield, C., Hester, R., & Bowden, S. C. (2019). A meta-analysis of the relationship between abstinence and neuropsychological functioning in methamphetamine use disorder. *Neuropsychology*, *33*(5), 739–753. https://doi.org/10.1037/neu0000552

Beard, C. L., Schmitz, J. M., Soder, H. E., Suchting, R., Yoon, J. H., Hasan, K. M., Narayana, P. A., Moeller, F. G., & Lane, S. D. (2019). Regional differences in white matter integrity in stimulant use disorders: A meta-analysis of diffusion tensor imaging studies. *Drug and Alcohol Dependence*, *201*, 29–37. https://doi.org/10.1016/j.drugalcdep.2019.03.023

Berman, S., O'Neill, J., Fears, S., Bartzokis, G., & London, E. D. (2008). Abuse of amphetamines and structural abnormalities in the brain. *Annals of the New York Academy of Sciences*, *1141*, 195–220. https://doi.org/10.1196/annals.1441.031

Burgoyne, A. P., & Engle, R. W. (2020). Attention control: A cornerstone of higher-order cognition. *Current Directions in Psychological Science*, *29*(6), 624–630. https://doi.org/10.1177/0963721420969371

Chang, L., Cloak, C., Buchthal, S., Wright, T., Jiang, C., Oishi, K., Skranes, J., Fujimoto, L., Mori, S., & Ernst, T. (2012). Brain imaging in children prenatally exposed to methamphetamine. *Neurotoxicology and Teratology*, *3*(34), 376.

Chung, A., Lyoo, I. K., Kim, S. J., Hwang, J., Bae, S. C., Sung, Y. H., Sim, M. E., Song, I. C., Kim, J., Chang, K. H., & Renshaw, P. F. (2007). Decreased frontal white-matter integrity in abstinent methamphetamine abusers. *The International Journal of Neuropsychopharmacology*, *10*(6), 765–775. https://doi.org/10.1017/s1461145706007395

Dean, A. C., Groman, S. M., Morales, A. M., & London, E. D. (2013). An evaluation of the evidence that methamphetamine abuse causes cognitive decline in humans. *Neuropsychopharmacology*, *38*(2), 259–274. https://doi.org/10.1038/npp.2012.179

Downey, L. A., & Loftis, J. M. (2014). Altered energy production, lowered antioxidant potential, and inflammatory processes mediate CNS damage associated with abuse of the psychostimulants MDMA and methamphetamine. *European Journal of Pharmacology*, *727*, 125–129. https://doi.org/10.1016/j.ejphar.2014.01.032

Fan, J., McCandliss, B. D., Fossella, J., Flombaum, J. I., & Posner, M. I. (2005). The activation of attentional networks. *NeuroImage*, *26*(2), 471–479. https://doi.org/10.1016/j.neuroimage.2005.02.004

Fan, L., Zhang, Q., Liang, S., Li, H., He, Z., Sun, J., Situ, W., Zhang, Z., Wu, D., Zhang, Z., Kou, Z., Zhang, J., & Liu, J. (2019). Imaging changes in brain microstructural in long-term abstinent from methamphetamine-dependence. *Zhong Nan Da Xue Xue Bao. Yi Xue Ban*, *44*(5), 491–500. https://doi.org/10.11817/j.issn.1672-7347.2019.05.004

Fellgiebel, A., Wille, P., Muller, M. J., Winterer, G., Scheurich, A., Vucurevic, G., Schmidt, L. G., & Stoeter, P. (2004). Ultrastructural hippocampal and white matter alterations in mild cognitive impairment: A diffusion tensor imaging study. *Dementia and Geriatric Cognitive Disorders*, *18*(1), 101–108. https://doi.org/10.1159/000077817

Filley, C. M. (2010). White matter: Organization and functional relevance. *Neuropsychology Review*, *20*(2), 158–173. https://doi.org/10.1007/s11065-010-9127-9

Gray, J. C., Thompson, M., Bachman, C., Owens, M. M., Murphy, M., & Palmer, R. (2020). Associations of cigarette smoking with gray and white matter in the UKbiobank. *Neuropsychopharmacology*, *45*(7), 1215–1222. https://doi.org/10.1038/s41386-020-0630-2

Greve, D. N., & Fischl, B. (2009). Accurate and robust brain image alignment using boundary-based registration. *NeuroImage*, *48*(1), 63–72. https://doi.org/10.1016/j.neuroimage.2009.06.060

Hampton, W. H., Hanik, I. M., & Olson, I. R. (2019). Substance abuse and white matter: Findings, limitations, and future of diffusion tensor imaging research. *Drug and Alcohol Dependence*, *197*, 288–298. https://doi.org/10.1016/j.drugalcdep.2019.02.005

Harro, J. (2015). Neuropsychiatric adverse effects of amphetamine and methamphetamine. *International Review of Neurobiology*, *120*, 179–204. https://doi.org/10.1016/bs.irn.2015.02.004

Hua, K., Zhang, J., Wakana, S., Jiang, H., Li, X., Reich, D. S., Calabresi, P. A., Pekar, J. J., van Zijl, P. C., & Mori, S. (2008). Tract probability maps in stereotaxic spaces: Analyses of white matter anatomy and tract-specific quantification. *NeuroImage*, *39*(1), 336–347. https://doi.org/10.1016/j.neuroimage.2007.07.053

Huang, K., Yu, C., Chen, X., Hao, Y., Ding, Y., Wu, Z., & Wang, X. (2021). A quasi-experimental study on the effectiveness of compulsory and voluntary treatment settings for 1,299 drug abusers in Hunan, China. *Frontiers in Psychiatry*, *12*, 613665. https://doi.org/10.3389/fpsyt.2021.613665

Huang, S., Dai, Y., Zhang, C., Yang, C., Huang, Q., Hao, W., & Shen, H. (2020). Higher impulsivity and lower grey matter volume in the bilateral prefrontal cortex in long-term abstinent individuals with severe methamphetamine use disorder. *Drug and Alcohol Dependence*, *212*, 108040. https://doi.org/10.1016/j.drugalcdep.2020.108040

Huang, S., Yang, W., Luo, J., Yan, C., & Liu, J. (2020). White matter abnormalities based on TBSS and its correlation with impulsivity behavior of methamphetamine addicts. *Frontiers in Psychiatry*, *11*, 452. https://doi.org/10.3389/fpsyt.2020.00452

Jaeger, J. (2018). Digit symbol substitution test: The case for sensitivity over specificity in neuropsychological testing. *Journal of Clinical Psychopharmacology*, *38*(5), 513–519. https://doi.org/10.1097/JCP.0000000000000941

Janke van Holst, R., & Schilt, T. (2011). Drug-related decrease in neuropsychological functions of abstinent drug users. *Current Drug Abuse Reviews*, *4*(1), 42–56.

Jones, D. K., Knosche, T. R., & Turner, R. (2013). White matter integrity, fiber count, and other fallacies: The do's and don'ts of diffusion MRI. *NeuroImage*, *73*, 239–254. https://doi.org/10.1016/j.neuroimage.2012.06.081

Kaag, A. M., van Wingen, G. A., Caan, M. W. A., Homberg, J. R., van den Brink, W., & Reneman, L. (2017). White matter alterations in cocaine users are negatively related to the number of additionally (ab)used substances. *Addiction Biology*, *22*(4), 1048–1056. https://doi.org/10.1111/adb.12375

Kim, I. S., Kim, Y. T., Song, H. J., Lee, J. J., Kwon, D. H., Lee, H. J., Kim, M. N., Yoo, D. S., & Chang, Y. (2009). Reduced corpus callosum white matter microstructural integrity revealed by diffusion tensor eigenvalues in abstinent methamphetamine addicts. *Neurotoxicology*, *30*(2), 209–213. https://doi.org/10.1016/j.neuro.2008.12.002

Koshiyama, D., Fukunaga, M., Okada, N., Morita, K., Nemoto, K., Yamashita, F., Yamamori, H., Yasuda, Y., Matsumoto, J., Fujimoto, M., Kudo, N., Azechi, H., Watanabe, Y., Kasai, K., & Hashimoto, R. (2020). Association between the superior longitudinal fasciculus and perceptual organization and working memory: A diffusion tensor imaging study. *Neuroscience Letters*, *738*, 135349. https://doi.org/10.1016/j.neulet.2020.135349

Kwon, N. J., & Han, E. (2018). A commentary on the effects of methamphetamine and the status of methamphetamine abuse among youths in South Korea, Japan, and China. *Forensic Science International*, *286*, 81–85. https://doi.org/10.1016/j.forsciint.2018.02.022

Le Bihan, D., Mangin, J. F., Poupon, C., Clark, C. A., Pappata, S., Molko, N., & Chabriat, H. (2001). Diffusion tensor imaging: Concepts and applications. *Journal of Magnetic Resonance Imaging: An Official Journal of the International Society for Magnetic Resonance in Medicine*, *13*(4), 534–546.

London, E. D., Berman, S. M., Voytek, B., Simon, S. L., Mandelkern, M. A., Monterosso, J., Thompson, P. M., Brody, A. L., Geaga, J. A., Hong, M. S., Hayashi, K. M., Rawson, R. A., & Ling, W. (2005). Cerebral metabolic dysfunction and impaired vigilance in recently abstinent methamphetamine abusers. *Biological Psychiatry*, *58*(10), 770–778. https://doi.org/10.1016/j.biopsych.2005.04.039

Makris, N., Kennedy, D. N., McInerney, S., Sorensen, A. G., Wang, R., Caviness, V. S., Jr., & Pandya, D. N. (2005). Segmentation of subcomponents within the superior longitudinal fascicle in humans: A quantitative, in vivo, DT-MRI study. *Cerebral Cortex*, *15*(6), 854–869. https://doi.org/10.1093/cercor/bhh186

McKenna, B. S., Theilmann, R. J., Sutherland, A. N., & Eyler, L. T. (2015). Fusing functional MRI and diffusion tensor imaging measures of brain function and structure to predict working memory and processing speed performance among inter-episode bipolar patients. *Journal of the International Neuropsychological Society*, *21*(5), 330–341. https://doi.org/10.1017/S1355617715000314

Nakajima, R., Kinoshita, M., Shinohara, H., & Nakada, M. (2020). The superior longitudinal fascicle: Reconsidering the fronto-parietal neural network based on anatomy and function. *Brain Imaging and Behavior*, *14*(6), 2817–2830. https://doi.org/10.1007/s11682-019-00187-4

Ottino-Gonzalez, J., Uhlmann, A., Hahn, S., Cao, Z., Cupertino, R. B., Schwab, N., Allgaier, N., Alia-Klein, N., Ekhtiari, H., Fouche, J. P., Goldstein, R. Z., Li, C. R., Lochner, C., London, E. D., Luijten, M., Masjoodi, S., Momenan, R., Oghabian, M. A., Roos, A., … Garavan, H. (2022). White matter microstructure differences in individuals with dependence on cocaine, methamphetamine, and nicotine: Findings from the enigma-addiction working group. *Drug and Alcohol Dependence*, *230*, 109185. https://doi.org/10.1016/j.drugalcdep.2021.109185

Pando-Naude, V., Toxto, S., Fernandez-Lozano, S., Parsons, C. E., Alcauter, S., & Garza-Villarreal, E. A. (2021). Gray and white matter morphology in substance use disorders: A neuroimaging systematic review and meta-analysis. *Translational Psychiatry*, *11*(1), 29. https://doi.org/10.1038/s41398-020-01128-2

Pessoa, L., Kastner, S., & Ungerleider, L. G. (2003). Neuroimaging studies of attention: From modulation of sensory processing to top-down control. *The Journal of Neuroscience*, *23*(10), 3990–3998. https://doi.org/10.1523/jneurosci.23-10-03990.2003

Pocuca, N., Young, J. W., MacQueen, D. A., Letendre, S., Heaton, R. K., Geyer, M. A., Perry, W., Grant, I., & Minassian, A. (2020). Sustained attention and vigilance deficits associated with HIV and a history of methamphetamine dependence. *Drug and Alcohol Dependence*, *215*, 108245. https://doi.org/10.1016/j.drugalcdep.2020.108245

Potvin, S., Pelletier, J., Grot, S., Hebert, C., Barr, A. M., & Lecomte, T. (2018). Cognitive deficits in individuals with methamphetamine use disorder: A meta-analysis. *Addictive Behaviors*, *80*, 154–160. https://doi.org/10.1016/j.addbeh.2018.01.021

Roos, A., Kwiatkowski, M. A., Fouche, J. P., Narr, K. L., Thomas, K. G., Stein, D. J., & Donald, K. A. (2015). White matter integrity and cognitive performance in children with prenatal methamphetamine exposure. *Behavioural Brain Research*, *279*, 62–67. https://doi.org/10.1016/j.bbr.2014.11.005

Rubenis, A. J., Fitzpatrick, R. E., Lubman, D. I., & Verdejo-Garcia, A. (2018). Sustained attention but not effort-based decision-making predicts treatment motivation change in people with methamphetamine dependence. *Journal of Substance Abuse Treatment*, *95*, 48–54. https://doi.org/10.1016/j.jsat.2018.09.007

Shi, C., Kang, L., Yao, S., Ma, Y., Li, T., Liang, Y., Cheng, Z., Xu, Y., Shi, J., Xu, X., Zhang, C., Franklin, D. R., Heaton, R. K., Jin, H., & Yu, X. (2015). The matrics consensus cognitive battery (MCCB): Co-norming and standardization in China. *Schizophrenia Research*, *169*(1–3), 109–115. https://doi.org/10.1016/j.schres.2015.09.003

Shukla, M., & Vincent, B. (2021). Methamphetamine abuse disturbs the dopaminergic system to impair hippocampal-based learning and memory: An overview of animal and human investigations. *Neuroscience*

and Biobehavioral Reviews, *131*, 541–559. https://doi.org/10.1016/j.neubiorev.2021.09.016

Smith, S. M. (2002). Fast robust automated brain extraction. *Human Brain Mapping*, *17*(3), 143–155. https://doi.org/10.1002/hbm.10062

Song, S. K., Sun, S. W., Ramsbottom, M. J., Chang, C., Russell, J., & Cross, A. H. (2002). Dysmyelination revealed through MRI as increased radial (but unchanged axial) diffusion of water. *NeuroImage*, *17*(3), 1429–1436. https://doi.org/10.1006/nimg.2002.1267

Song, S. K., Yoshino, J., Le, T. Q., Lin, S. J., Sun, S. W., Cross, A. H., & Armstrong, R. C. (2005). Demyelination increases radial diffusivity in corpus callosum of mouse brain. *NeuroImage*, *26*(1), 132–140. https://doi.org/10.1016/j.neuroimage.2005.01.028

Spindler, C., Mallien, L., Trautmann, S., Alexander, N., & Muehlhan, M. (2022). A coordinate-based meta-analysis of white matter alterations in patients with alcohol use disorder. *Translational Psychiatry*, *12*(1), 1–9. https://doi.org/10.1038/s41398-022-01809-0

Su, H., Chen, T., Zhong, N., Jiang, H., Du, J., Xiao, K., Xu, D., Wang, Z., & Zhao, M. (2020). Gamma-aminobutyric acid and glutamate/glutamine alterations of the left prefrontal cortex in individuals with methamphetamine use disorder: A combined transcranial magnetic stimulation-magnetic resonance spectroscopy study. *Annals of Translational Medicine*, *8*(6), 347. https://doi.org/10.21037/atm.2020.02.95

Szeszko, P. R., Tan, E. T., Ulug, A. M., Kingsley, P. B., Gallego, J. A., Rhindress, K., Malhotra, A. K., Robinson, D. G., & Marinelli, L. (2018). Investigation of superior longitudinal fasciculus fiber complexity in recent onset psychosis. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *81*, 114–121. https://doi.org/10.1016/j.pnpbp.2017.10.019

Tang, Q., & He, L. (2021). A discourse analysis on betel nut chewing in Hunan province, China. *Journal of Psychoactive Drugs*, *53*(1), 40–46. https://doi.org/10.1080/02791072.2020.1740362

Tehrani, A. M., Boroujeni, M. E., Aliaghaei, A., Feizi, M. A. H., & Safaralizadeh, R. (2019). Methamphetamine induces neurotoxicity-associated pathways and stereological changes in prefrontal cortex. *Neuroscience Letters*, *712*, 134478. https://doi.org/10.1016/j.neulet.2019.134478

Teixeira-Gomes, A., Costa, V. M., Feio-Azevedo, R., Bastos Mde, L., Carvalho, F., & Capela, J. P. (2015). The neurotoxicity of amphetamines during the adolescent period. *International Journal of Developmental Neuroscience*, *41*, 44–62. https://doi.org/10.1016/j.ijdevneu.2014.12.001

Turken, A., Whitfield-Gabrieli, S., Bammer, R., Baldo, J. V., Dronkers, N. F., & Gabrieli, J. D. (2008). Cognitive processing speed and the structure of white matter pathways: Convergent evidence from normal variation and lesion studies. *NeuroImage*, *42*(2), 1032–1044. https://doi.org/10.1016/j.neuroimage.2008.03.057

Tustison, N. J., Cook, P. A., Klein, A., Song, G., Das, S. R., Duda, J. T., Kandel, B. M., van Strien, N., Stone, J. R., Gee, J. C., & Avants, B. B. (2014). Large-scale evaluation of ants and freesurfer cortical thickness measurements. *NeuroImage*, *99*, 166–179. https://doi.org/10.1016/j.neuroimage.2014.05.044

Uhlmann, A., Fouche, J. P., Lederer, K., Meintjes, E. M., Wilson, D., & Stein, D. J. (2016). White matter microstructure and impulsivity in methamphetamine dependence with and without a history of psychosis. *Human Brain Mapping*, *37*(6), 2055–2067. https://doi.org/10.1002/hbm.23159

Woods, S. P., Rippeth, J. D., Conover, E., Gongvatana, A., Gonzalez, R., Carey, C. L., Cherner, M., Heaton, R. K., Grant, I., & Group, H. I. V. N. R. C. (2005). Deficient strategic control of verbal encoding and retrieval in individuals with methamphetamine dependence. *Neuropsychology*, *19*(1), 35–43. https://doi.org/10.1037/0894-4105.19.1.35

Wu, Q., Qi, C., Long, J., Liao, Y., Wang, X., Xie, A., Liu, J., Hao, W., Tang, Y., Yang, B., Liu, T., & Tang, J. (2018). Metabolites alterations in the medial prefrontal cortex of methamphetamine users in abstinence: A 1h MRS study. *Frontiers in Psychiatry*, *9*, 1–8. https://doi.org/10.3389/fpsyt.2018.00478

Yuan, F., Zhu, X., Kong, L., Shen, H., Liao, W., & Jiang, C. (2017). White matter integrity deficit associated with betel quid dependence. *Frontiers in Psychiatry*, *8*, 1–6. https://doi.org/10.3389/fpsyt.2017.00201

Zhuang, W., Tang, Y., Zhong, N., Jiang, H., Du, J., Wang, J., & Zhao, M. (2016). Persistent microstructural deficits of internal capsule in one-year abstinent male methamphetamine users: A longitudinal diffusion tensor imaging study. *Journal of Neuroimmune Pharmacology*, *11*(3), 523–530. https://doi.org/10.1007/s11481-016-9673-x

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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