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Psychological dysregulation, white matter disorganization and substance use disorders in adolescence

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Abstract

Aims—Adolescents with substance use disorders (SUD) have difficulties with cognitive, behavioral and affective regulation. White matter (WM) disorganization has been observed in adolescents with SUD and may be related to psychological dysregulation. This study compared adolescents with SUD and control adolescents to investigate relationships among psychological dysregulation, WM disorganization, and SUD symptoms.

Design—Cross-sectional observation.

Setting—Adolescents with SUD were recruited from SUD treatment programs. Controls were recruited from the community.

Participants—The 55 participants were ages 14–19; 35 with SUD, 20 controls without SUD.

Measurements—Psychological dysregulation was characterized by the Behavior Rating Inventory of Executive Function. WM disorganization was measured by diffusion tensor imaging, and fractional anisotropy, radial diffusivity and axial diffusivity were examined within cortical regions of interest.

Findings—Compared to controls, SUD adolescents showed significantly greater psychological dysregulation and prefrontal and parietal WM disorganization. WM disorganization was positively correlated with psychological dysregulation and cannabis-related symptoms. In multivariate mediation models, the results were consistent with both the Neurodevelopmental Immaturity model, in which WM disorganization leads to psychological dysregulation and cannabis-related symptoms, and with the Substance Effects Model, in which cannabis-related symptoms lead to WM disorganization and psychological dysregulation.

Conclusions—In adolescents, substance use disorder and psychological dysregulation appear to be associated with reduced frontoparietal network white matter maturation.

Keywords

adolescents; substance use disorders; neuroimaging

INTRODUCTION

Adolescents with substance use disorders (SUD) have difficulties with cognitive, behavior and affective regulation and evidence of neurodevelopmental immaturity [see 1 for review; 2,3]. Such difficulties may indicate pre-existing deficits that contribute to SUD or adverse substance use effects. Children and adolescents with psychopathology reflecting

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psychological dysregulation, such as disruptive behavior disorders (DBD: i.e., attention deficit hyperactivity disorder, oppositional defiant disorder, conduct disorder) have been found to have white matter (WM) disorganization [4,5,6]. WM disorganization may indicate neurodevelopmental immaturity contributing to both psychological dysregulation and SUD (i.e., Neurodevelopmental Immaturity Model). Alternatively, neurotoxic substance effects may lead to neurobiological deficits (i.e., Substance Effects Model). In this study, we examined relationships among adolescent SUD symptoms, psychological dysregulation, and WM disorganization to advance understanding of microstructural brain characteristics and SUD in adolescence.

Psychological dysregulation refers to deficiencies in cognitive functioning, behavioral inhibition, and emotional regulation that constitute a trait essentially synonymous with executive functioning, broadly defined, and neurobehavioral dysregulation [reviews:1,7]. Some mental disorders, including DBD and major depressive disorder (MDD), are thought to constitute clinical manifestations of psychological dysregulation [1]. DBD and MDD tend to cluster in adolescents with SUD [8, see 9 for review]. Dimensional constructs representing attentional, conduct and mood problems have been found to provide psychometrically valid representations of psychological dysregulation that predict adolescent SUD [10, 11]. Psychological dysregulation scales have been found to be elevated in adolescents with SUD compared to reference adolescents [12]. Prior studies have not examined psychological dysregulation in relation to WM disorganization and adolescent SUD.

According to the Neurodevelopmental Immaturity Model, the psychological dysregulation phenotype reflects delays or deficits in neuromaturation that precede and contribute to SUD. The prefrontal cortex (PFC) plays an important role in psychological regulation during adolescence, and its interaction with other functionally specialized brain regions via white matter tracts is critical for integrative brain functions [review:13]. WM tracts projecting to PFC continue to develop throughout adolescence [14,15,16]. The PFC is connected to the parietal cortex by the superior longitudinal fasciculus (SLF) to form the frontoparietal network [17]. Maturation of the frontoparietal network has been theorized to be critical for optimal psychological regulation [17, 18]. Frontoparietal network immaturity during adolescence may contribute to disinhibited, high risk behaviors including SUD.

According to the Substance Effects Model, SUD disrupts WM. WM volume loss has been documented in SUD adults [19,20] and smaller PFC WM volumes have been reported in SUD adolescents [21]. However, regional cerebral volumes have not shown a consistent relationship with psychological dysregulation and substance use [22]. Compared to WM volumes, WM microstructure determined by diffusion tensor imaging (DTI) may be more sensitive in detecting SUD effects [23]. DTI quantifies water diffusion in WM, which reflects axonal organization as well as axonal caliber and myelin thickness [24]. Fractional anisotropy (FA) is a summary directional diffusion indicator calculated using variables that comprise more specific diffusion indices, including axial diffusivity (AD; diffusion along the axon) and radial diffusivity (RD; diffusion perpendicular to the axon) [25]. (For brevity, these DTI indicators will be interpreted as representing WM organization.) In adults, substance-related WM disorganization, more so than volume changes, have been found to correlate with cognitive performance [26]. Actively developing PFC WM in adolescents may be particularly vulnerable to SUD effects [1]. WM disorganization has been reported among adults with adolescent-onset cannabis use [27], a finding interpreted to indicate long-term cannabis effects [28]. Other studies have not observed cannabis effects [29].

A few studies have examined the relationship between DTI indicators and adolescent substance use or SUD. Bava and colleagues [2] compared adolescents with heavy marijuana

and alcohol use with controls using Tract Based Spatial Statistics (TBSS), and found that substance using adolescents exhibited lower FA in 10 brain regions, including the SLF. Ashtari and colleagues [30] found that adolescent heavy marijuana use was associated with reduced FA and increased RD in the arcuate fasciculus, which is relevant for frontotemporal integration. Alcohol-specific effects were suggested in a study by McQueeney and colleagues [31], in which adolescent binge drinkers, compared to non-binge drinking controls, had lower FA in 18 TBSS identified regions, including seven tracts projecting to the PFC (i.e., four corpus callosum regions, the left and right corona radiata, and the right SLF). In contrast, De Bellis and colleagues [32] compared adolescents with alcohol use disorder to control adolescents on corpus callosum FA and mean diffusivity (MD) and found no evidence for alcohol associated WM disorganization.

In a report on a subset of the subjects described here [3], we compared 24 SUD adolescents with 12 matched controls using TBSS, and found a large SLF cluster of significantly lower FA values in SUD adolescents, with similar group differences for AD and RD. A significant SUD group by gender interaction was observed for SLF, with the difference between SUD adolescents and control adolescents being greater among females than among males. In sum, TBSS-based research has most consistently indicated that SUD adolescents have WM disorganization in areas subserving the frontoparietal network (e.g., SLF). However, prior studies have not specifically tested theoretically derived hypotheses examining adolescent SUD characteristics and WM disorganization in specific regions of interest (ROI).

Statistical analyses with DTI variables use voxel-based or ROI approaches [33]. Voxel-based analyses, including TBSS, examine the entire brain in a model-free manner. The ROI approach used here, compared to TBSS, tests specific hypotheses involving ROIs with increased sensitivity. We used an automated segmentation method to distinguish grey and white matter and to identify cortical regions. By utilizing individual subject brain features to identify regions, this method avoids the distortion that may occur in TBSS with alignment to a common registration target [33].

The present study is the first examination of relationships among ROI WM disorganization, psychological dysregulation, and adolescent SUD. The hypotheses were: (1) psychological dysregulation will be elevated in SUD adolescents compared to controls; (2) PFC and parietal WM FA, indicating frontoparietal network WM maturity, will be lower in SUD adolescents; and (3) PFC and parietal FA will be inversely correlated with psychological dysregulation. While acknowledging the limitations of these cross-sectional data, the relationships among these variables were examined to explore the Neurodevelopmental Immaturity Model and the Substance Effects Model.

METHOD

Participants

Adolescents with SUD (n=35), ages 14–19, were recruited from SUD intensive out-patient treatment programs (see 34 for details). The controls (n=20) were adolescents without SUD recruited from the community. Control subjects were identified by random digit dialing and were screened for eligibility. Exclusion criteria for both groups included an inability to communicate in English, developmental disorders impairing participation, and a history of significant brain injury or concussion. Control subjects were excluded if they had any SUD history. This study was approved by the University of Pittsburgh Human Subjects Institutional Review Board and was conducted in accordance with the approved protocol. Written assent from the minor adolescent and written consent from a parent was obtained. Adolescents age ≥18 provided their own written informed consent.

SUD adolescents were typically assessed within one month of initiating outpatient SUD treatment. The SUD and control groups (Table 1) were not significantly different on demographic characteristics. The average participating family was middle class according to the Hollingshead Two-factor Index [35]. The SUD (left-handed: n=2) and control (left-handed: n=2) were not significantly different on Edinburgh Handedness Inventory [36,37,38] score (χ^2=.3, d.f.=1, p=.6). Compared to the control group, the SUD group was significantly lower on IQ (Table 1). The most common current SUD was cannabis use disorders (n=31 or 89%), followed by alcohol use disorders (n=18 or 51%), and other drug use disorders (n=16 or 46%). Among 16 subjects with other drug disorders, the most common were opioid-related (n=12) and cocaine-related (n=9). The majority of SUD adolescents had diagnoses involving two or more substances (n=19), with the remaining involving only cannabis (n=11), alcohol (n=4) or opiates (n=1). SUD subjects were more likely than controls to have used substances in the 30 days prior to the imaging session (Table 1). The most frequently used substances were nicotine, followed by cannabis and alcohol. Other drugs were combined and included opioid use (6 subjects) and cocaine use (3 subjects). The average SUD onset age was 14.7 years old (s.d.:1.6; range 11 to 18). A lifetime history of mental disorders was significantly more common in the SUD group than in the Control group (Table 1), including conduct disorder (CD), attention deficit hyperactivity disorder (ADHD), and MDD. The groups were not significantly different on oppositional defiant disorders (ODD). (Other less common mental disorders were not examined.)

Clinical Measures

DSM-IV SUD diagnoses—A version of the Structured Clinical Interview for DSM-IV SUDs [SCID: 39] adapted for adolescents was used to determine SUD diagnoses and symptom counts. Adaptations included providing examples of adolescent-relevant symptoms (i.e., school grades dropping due to substance use) and developmentally specific probes. The adapted SCID demonstrated moderate to high inter-rater reliability for symptom ratings and acceptable concurrent validity in adolescents [39]. Substance use in the prior 30 days was determined by a structured interview using the Time Line Follow Back approach [40].

Mental disorders—The Schedule for Affective Disorders and Schizophrenia [K-SADS; 8,41] was used to assess lifetime occurrence of other DSM-IV Axis I psychopathology. Psychopathology Symptoms was the sum of DBD and MDD symptoms in the prior six months, considered indicative of psychological dysregulation. The K-SADS has demonstrated acceptable inter-rater reliability [8].

Psychological dysregulation—The Behavior Rating Inventory of Executive Function-Self-Report Version [BRIEF-SR; 42,43] is an 80-item self-report executive functioning rating scale. The items reference cognitive (e.g., “I forget instructions easily;” “I have a short attention span”), behavioral (i.e., “I have trouble sitting still;” “I talk at the wrong time”) and mood (i.e. “I get upset easily”) difficulties. The instrument yields a summary t-score, used here, and eight subscales. A higher score indicates more difficulties. As defined by scoring instructions [42], BRIEF t-scores over 2 standard deviations above the normative mean were classified as clinically relevant.

MRI Procedures

Image Acquisition—MRI images were acquired on a Siemens 3T Allegra Scanner (Siemens Medical Solutions, Erlangen, Germany). T1 weighted magnetization-prepared rapid gradient echo (MPRAGE) images were acquired for morphometric analyses (scan parameters: TR=1400ms; TE=2.48ms; FOV=256×256; 176 1mm slices × 2; matrix 256 ×

256). In addition to the structural scan, diffusion images were acquired using standard fast echo-planar imaging (TR=6500ms; TE=88ms; FOV=205×205; b=1000s/mm^2; 46 3mm slices × 12 directions in addition to b=0). To optimize signal to noise ratio, the sequence was collected twice.

Image Processing and Analysis

Volumetric and ROI analyses: Cortical reconstruction processing and volumetric segmentation were performed with Freesurfer [44–51]. Processing included motion correction and averaging of volumetric T1 weighted images, removal of non-brain tissue, automated Talairach transformation, tessellation of the gray/white matter boundary, automated topology correction, and surface deformation following intensity gradients to optimally place the gray/white and gray/cerebrospinal fluid borders. Freesurfer procedures have been validated against histological analysis and manual measurements [52,53].

DTI: DTI images were processed with Freesurfer. Diffusion data was motion and eddy current corrected. Tensors were calculated using DTI GLM Fit and registered to individual subject anatomical features using FLIRT [54] and to standard Talairach space. Since DTI is susceptible to motion artifacts, we evaluated images visually and by motion parameters. Rotational and translational motions were quantified using FSL [54]. On the resulting displacement index, SUD subjects (mean: 0.44, s.d.: 0.10) and control subjects (0.45; s.d.: 0.09) were not significantly different (t=−0.2, d.f.=53; p=.8).

Regions of interest analyses: ROIs were created by adding bilateral Freesurfer regions. These regions were constructed so as to define areas functionally relevant for psychological regulation (e.g., prefrontal and parietal) while sufficiently inclusive so that mean FA values were anatomically meaningful. The WM ROIs were as follows: PFC: frontal pole, frontal superior, frontal caudalmiddle, frontal rostralmiddle, parsopercularis and parstriangularis; Parietal: parietal inferior and parietal superior; Orbitofrontal: frontal lateral orbital, frontal medial orbital, parsorbitalis; Temporal: temporal inferior, temporal middle, temporal pole, temporal superior, temporal transverse; Cingulate: cingulate caudal-anterior, cingulate rostral-anterior, isthmus and posterior. FA ROI analyses were done by resampling FA data into each individual subject's anatomical space and then extracting mean FA values for WM ROIs.

Statistical analyses and models

The SUD and control groups were compared on psychological dysregulation indicators and regional WM FA. These group comparisons included demographic covariates (i.e., age and race) and group-by-gender interactions. For hypothesized relationships, specifically those involving PFC and parietal ROIs, tests where $p<.05$ were considered statistically significant. For exploratory ROI analyses, interpretations including multiple comparison corrections with adjusted p values (i.e., .05/3) have been included. Variables showing significant group differences were further explored in correlational models. Using multivariate regression models with covariates, selected regional white matter FA variables were correlated with psychological dysregulation characteristics, SUD symptoms involving specific substance classes (i.e., alcohol, cannabis, or other illicit drugs), and recent substance use (i.e., the number of days of alcohol, cannabis, nicotine or other drug use in the past 30 days). The selection of variables for subsequent model testing was informed by these correlations. Finally, two multivariate mediation models using step-wise multiple regression were used to examine relationships among psychological dysregulation, WM disorganization and SUD symptoms. In addition to examining FA, these models included AD and RD. A mediation model was considered supported where the previously significant relationship between the

independent and dependent variables was no longer significant in the adjusted model [see 55–57 for reviews].

RESULTS

Psychological Dysregulation

On the BRIEF score, the groups were significantly different (Table 2; partial Eta^2 =.99), and the demographic covariates and group-by-gender interaction did not account for significant variance. Categorizing subjects with BRIEF t-scores ≥70 as clinically relevant, 29% (n=10) of the SUD group and none (0%) of the Control group had clinically relevant scores (χ^2=7.2, d.f.=1, p=.007). The SUD and Control groups were also significantly different on Psychopathology Symptoms (partial Eta^2=.98), and the covariates and group-by-gender interaction did not account for significant variance. BRIEF scores were significantly correlated with Psychopathology Symptoms (r=.67, d.f.=54, p<.001).

White Matter Volumes and FA

The comparisons of SUD and Control group on WM ROI volumes are presented in Table 2. The statistical tests included demographic covariates and group-by-gender interactions. None of these group comparisons were statistically significant, and the group-by-gender interactions did not account for significant variance.

In the PFC WM ROI, the SUD group compared to the control group showed significantly lower mean FA (Table 2; partial Eta^2=.83). Similarly, in the parietal WM ROI, the SUD group showed significantly lower mean FA (partial Eta^2=.90). For orbitofrontal, cingulate and temporal ROIs, the groups did not significantly differ. For all these group comparisons, the main effects of demographic variables examined as covariates (i.e., age, gender and race) and the SUD group by gender interaction did not account for significant variance. Excluding left hand dominant subjects (n=4), the results were essentially unchanged. The significant group differences for PFC and parietal FA supported their inclusion in subsequent analyses.

Psychological dysregulation, SUD symptoms and WM disorganization relationships

BRIEF score accounted for significant variance in PFC and parietal FA (Table 3), BRIEF score and IQ were significant correlated (r=−41, p=.003) and IQ did not account for significant additional variance in PFC FA (r=0.14, p=0.3) or parietal FA (r=0.19, p=0.2). PFC and parietal FA were significantly correlated with the cannabis-related symptom count (i.e., Cannabis Symptoms), and were not significantly correlated with other substance-related symptoms or substance use frequencies. Consequently, multivariate mediational models utilized Cannabis Symptoms in subsequent analyses.

Testing the Neurodevelopmental Immaturity Model in multivariate mediation models, after accounting for demographic covariates, PFC and parietal WM disorganization indices (i.e., FA, AD and RD) accounted for significant additional variance in Cannabis Symptoms (R^2 change=.33, F change=3.8, d.f.=6,45, p=.004). After including BRIEF as a mediating variable, PFC and parietal WM disorganization indices did not account for significant additional variance in Cannabis Symptoms (R^2 change=.06, F change=1.3, d.f.=3,46, p=.3). The results indicated, consistent with the Neurodevelopmental Immaturity Model, that BRIEF mediated the relationship between WM disorganization (independent variable) and Cannabis Symptoms (dependent variable).

Testing the Substance Effects Model, after accounting for the effects of demographic covariates, Cannabis Symptoms accounted for significant additional variance in BRIEF (R^2 change=.24, F change=16.0, d.f.=1,49, p<.001). After including PFC and parietal WM

disorganization indices as a mediating variable, Cannabis Symptoms did not account for additional variance in BRIEF scores (R^2 change=.05, F change =3.8, d.f.=1,43, p=.06). These results indicated that, consistent with the Substance Effects Model, WM disorganization mediated the relationship between Cannabis Symptoms (independent variable) and BRIEF (dependent variable).

DISCUSSION

Prior studies have not examined relationships among SUD severity, WM disorganization and psychological dysregulation in adolescents. Consistent with prior research [12], adolescents with SUD showed elevated psychological dysregulation indicated by BRIEF and psychopathology symptoms. Adolescents with SUD, compared to control adolescents, showed PFC and parietal WM disorganization, with large effect size estimates. Since the SUD and control groups were not significantly different on WM ROI volumes, these positive findings are consistent with prior research suggesting that DTI indices provide more sensitive indicators of SUD effects. While the anatomical location of WM disorganization in SUD adolescents using the TBSS approach [3] and this ROI method differed, the common involvement of the SLF in both results points to a unifying neuroanatomical interpretation. In contrast to the TBSS study [3], however, the present analyses did not find significant SUD group by gender interactions on regional FA. Since both these studies involved relatively small samples, clarification of differential relationships by gender will require further research. Having established these group differences, subsequent analyses were conducted to provide additional explanatory information.

Consistent with the Neurodevelopmental Immaturity Model, the multivariate mediation models could be interpreted to indicate that immature PFC and parietal WM predicted psychological dysregulation which, in turn, predicted cannabis-related symptoms. A small effect size was noted. These findings support the hypothesis that the frontoparietal network, with the SLF as an important constituent, provides a neurobiological foundation for psychological regulation [17]. The SLF, the largest of the long association fibers, is the tract that contributes most to the PFC and parietal WM ROIs [58,59]. It is important to emphasize, however, that this cross-sectional study could not provide critical temporal information implied by this interpretation.

The findings were also consistent with the Substance Effects Model. That is, the alternative multivariate mediation analyses could be interpreted to indicate that cannabis-related symptoms predicted WM disorganization, and WM disorganization predicted psychological dysregulation. Here too, a small effect size was noted. These correlations are consistent with prior studies examining cannabis effects on component skills required for psychological regulation, such as working memory [60,61,62]. The PFC has been noted to have a relatively high density of cannabinoid receptors and may be particularly susceptible to cannabis effects [28].

The examination of specific substance-related variables in relationship to PFC and parietal FA indicated a particularly strong association with cannabis-related symptoms, and not with alcohol-related symptoms. This finding contrasts with prior research showing a relationship between alcohol use and WM disorganization [31]. The effects of cannabis and alcohol use on regional cerebral activation and responses on neuropsychological testing have also been studied [63,64,65]. The relative effects of alcohol and cannabis on adolescent functioning and neuromaturation remain unclear. We caution against over-interpretation of the differential correlations noted on substance-related variables. As in other similar studies, the SUD subjects in this study may have had idiosyncratic features. The generalizability of these findings will need to be tested in larger studies with refined methods. More importantly,

these cross-sectional studies have not been designed to distinguish the Neurodevelopmental Immaturity Model from the Substance Effects Model.

In addition to the cross-sectional design, this study had additional limitations. Although comparable to prior studies, optimal sample sizes would be considerably larger than those available here. The relatively small samples limited the extent to which exploratory analyses could be reasonably supported while taking into consideration correction for multiple comparisons. The examination of psychopathology dimensions distinct from the psychological dysregulation construct, for example, may be of interest in future studies. Laboratory alcohol and drug testing for recent use was not conducted and would have refined this methodology [66]. The examination of objective psychological regulation indicators by neuropsychological testing may have provided information distinct from the self-report BRIEF scale [67]. Prenatal substance exposure may influence brain development [see 68 for review] and was not examined here.

In summary, this study found significant relationships among WM disorganization, psychological dysregulation, and SUD in adolescents. The PFC actively develops during adolescence and the integration of the PFC with other brain areas through WM tracts is thought to be critical in cognitive, behavioral and affective regulation. With cannabis use common in adolescence and cannabis use disorders occurring in a substantial portion of adolescents and young adults, the possibility that cannabis involvement may lead to WM disorganization and psychological dysregulation is worrisome. A larger, systematically recruited sample assessed in early adolescence prior to the initiation of substance use and followed over several years would constitute an approach that may advance understanding of the relationships studied here.

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Table 1

Demographic and clinical characteristics for adolescents with SUD and control groups.

	SUD (n=35)		Control (n=20)			
	n	**%**	**n**	**%**	**χ^2**	**p**
Gender						
Male	19	46	9	55	.4	.5
Female	16	54	11	45		
Ethnic group						
White	33	94	17	85	2.2	.3
African American	2	6	2	10		
Other	0	0	1	5		
	mean	s.d.	mean	s.d.	t	p
Age in years	16.8	1.2	16.2	1.0	1.8	.07
SES	41.7	12.6	47.7	15.3	−1.6	.1
IQ	98	15	110	12	−3.2	.002
Substance (# days/30)						
Alcohol	1.8	2.9	0.3	0.7	3.0	.005
Cannabis	6.6	11.1	0.0	0.0	3.5	.001
Other drugs	1.5	3.3	0.0	0.0	2.6	.01
Nicotine	21.0	13.5	1.8	6.5	7.1	.001
Mental Disorders	n	%	n	%	χ^2	p
Conduct Disorder	11	31	0	0	7.9	.005
Oppositional Defiant	2	6	0	0	1.2	.3
ADHD	14	40	1	5	7.9	.005
Major Depression	12	34	1	5	6.0	.01

Table 2

Psychological dysregulation and white matter variables for adolescents with substance use disorders (SUD) and control adolescents.

	SUD (n=35)			Control (n=20)			Main effects	
	mean	**s.d.**	**range**	**mean**	**s.d.**	**range**	**F**	**p**
Psychological Dysregulation								
BRIEF	61.4	14.4	34–91	42.6	9.8	30–69	218.1	.001
Psychopatholgy Symptoms	7.8	6.6	0–22	1.6	4.5	0–20	310.2	<.001
White Matter Volumes								
Prefrontal	5.6	.4	5.0–6.3	5.9	.5	4.8–7.0	2.8	.3
Orbitofrontal	1.4	.1	1.2–1.6	1.4	.1	1.2–1.7	.7	.7
Cingulate	1.6	.1	1.4–1.8	1.6	.1	1.4–1.8	.6	.6
Parietal	3.1	.2	2.6–3.5	3.0	.2	2.7–3.4	3.7	.3
Temporal	2.6	.2	2.4–2.9	2.7	.2	2.3–3.4	0.8	.5
White Matter FA								
Prefrontal	.348	.021	.29–.39	.353	.013	.33–.39	23.4	.005
Parietal	.364	.035	.28–.42	.378	.028	.32–.43	21.6	.03
Orbitofrontal	.326	.026	.27–.39	.323	.018	.29–.36	0.1	.7
Cingulate	.484	.033	.41–.55	.483	.028	.43–.56	1.1	.5
Temporal	.312	.023	.26–.36	.319	.015	.29–.35	13.1	.03

Footnote: Abbreviations: DBD: disruptive behavior disorders; FA: fractional anisotropy

Table 3

Correlations for PFC and parietal regional fractional anisotropy with BRIEF score, substance use disorder symptoms, and recent substance use frequency.

	PFC FA		Parietal FA	
	r	p	r	p
BRIEF	−.304	.03	−.357	.01
Cannabis symptom count	−.310	.03	−.375	.006
Alcohol symptom count	−.135	.3	−.041	.8
Other drug symptom count	−.171	.2	.047	.7
Alcohol use days	.072	.6	.086	.5
Cannabis use days	.065	.6	−.069	.6
Other drug use days	−.161	.2	−.030	.8
Nicotine use days	.001	.9	−.172	.2

Abbreviations: BRIEF: Behavior Rating Inventory of Executive Function; FA: fractional anistropy; PFC: prefrontal cortex; n = 55