Altered White Matter Integrity in Adolescent Binge Drinkers

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Abstract

Background—White matter integrity has been found to be compromised in adult alcoholics, but it is unclear when in the course of alcohol exposure white matter abnormalities become apparent. This study assessed microstructural white matter integrity among adolescent binge drinkers with no history of an alcohol use disorder.

Methods—We used diffusion tensor imaging to examine fractional anisotropy (FA), a measure of directional coherence of white matter tracts, among teens with ($n = 14$) and without ($n = 14$) histories of binge drinking but no history of alcohol use disorder, matched on age, gender, and education.

Results—Binge drinkers had lower FA than controls in 18 white matter areas (clusters ≥ 27 contiguous voxels, each with $p < 0.01$) throughout the brain, including the corpus callosum, superior longitudinal fasciculus, corona radiata, internal and external capsules, and commissural, limbic, brainstem, and cortical projection fibers, while exhibiting no areas of higher FA. Among binge drinkers, lower FA in 6 of these regions was linked to significantly greater lifetime hangover symptoms and/or higher estimated peak blood alcohol concentrations.

Conclusions—Binge drinking adolescents demonstrated widespread reductions of FA in major white matter pathways. Although preliminary, these results could indicate that infrequent exposure to large doses of alcohol during youth may compromise white matter fiber coherence.

Keywords

Diffusion Tensor Imaging; Alcohol; Binge Drinking; Adolescence; Brain Imaging; Hangover

Heavy episodic or "binge" drinking is common among adolescents, with 55% of high school seniors reporting having gotten drunk, and 25% reporting consuming 5 or more drinks in a row in the past 2 weeks (Johnston et al., 2007). Despite the prevalence of heavy drinking during adolescence, it remains unclear how binge-pattern alcohol use may affect brain integrity and development.

Magnetic resonance imaging (MRI) studies report white matter degeneration in individuals with alcohol use disorders (AUD). Morphometric studies have demonstrated reductions in overall cerebral (Schottenbauer et al., 2007), gray matter (Chanraud et al., 2007; Makris et al., 2008; Pfefferbaum et al., 1997), white matter (Kril et al., 1997; Pfefferbaum et al., 1997), and corpus callosum (Estruch et al., 1997; Pfefferbaum et al., 1996) volumes among adult

alcoholics. Similarly, heavy drinking adolescents with (De Bellis et al., 2005) and without (Medina et al., 2008) comorbid psychiatric disorders exhibit smaller prefrontal white matter volumes. Alcohol-related white matter volume reductions may be due to axonal atrophy, cellular membrane breakdown, or myelin loss (Harper, 1998). While these changes are linked to very heavy drinking, less is known about the impact of monthly to weekly use of 4 to 10 drinks on adolescents' white matter integrity.

Heavy alcohol consumption may exert potent effects on the white matter environment resulting in alterations to fiber structure and orientation, observable with diffusion tensor imaging (DTI). DTI is an MRI technique sensitive to the random movement of water in cells of a target tissue, yielding measures of the magnitude and orientation of this movement (Pierpaoli et al., 1996). Fractional anisotropy (FA), a measure of the directional coherence of brain tissue, provides an estimate of white matter integrity. Higher FA values indicate greater hindrance to water diffusion, which is related to the presence of oriented structures. This index can be used to evaluate the influence of alcohol use on white matter quality (Rosenbloom et al., 2003). FA has been shown to be reduced in the corpus callosum (Pfefferbaum and Sullivan, 2005; Pfefferbaum et al., 2006a; Schulte et al., 2005), right frontal lobe (Harris et al., 2008), and global white matter (Pfefferbaum et al., 2006b) in adult alcoholics, suggesting potential disruption in white matter microstructure. Among adolescents, though, findings are more mixed. In a pilot study, we (Tapert et al., 2003) observed lower FA in the splenium of the corpus callosum among 8 teenagers with AUD and no comorbid Axis I diagnosis, as compared to 8 demographically similar controls. De Bellis and colleagues (2008) reported on 32 adolescents with AUD compared to 28 nondisordered controls, finding no FA decrements among callosal regions, rather increased FA in the rostral portion of the body, and in the isthmus. To date, no known studies have described the effects of binge-level drinking on FA among teenagers who do not meet alcohol abuse or dependence criteria.

Because white matter maturation continues into late adolescence (Hasan et al., 2007; Nagel et al., 2006; Paus et al., 1999; Sowell et al., 2002), understanding the influence of heavy episodic drinking on neurodevelopmental processes is of great relevance. Therefore, the current study serves as an exploratory analysis of white matter integrity in major fiber tracts among typically developing youth (free from any history of psychiatric disorder) with histories of binge drinking, compared to control teens without any past binge episodes. Based on adult and limited adolescent literature, our preliminary hypothesis is that binge drinkers would show compromised white matter fiber coherence (i.e., lower FA). Additionally, greater alcohol involvement was expected to relate to poorer white matter integrity among drinkers.

Materials and Methods

Participants

Subjects were 28 adolescents ages 16 to 19 recruited from a larger study on brain functioning in adolescent substance users (Tapert et al., 2007). Binge drinkers were 14 teens who had consumed at least 5 or 4 alcoholic beverages (for males or females, respectively) in one sitting (NIAAA, 2004; Wechsler et al., 1994) during the 3 months prior to imaging. Controls were 14 teens without a history of a binge drinking episodes matched on age, gender, and level of education, and statistically similar on other demographic measures to the binge drinkers (see Table 1). Exclusionary criteria for this study were: histories of neurological concerns (e.g., learning disorder, head trauma with loss of consciousness >2 minutes, migraine) or psychiatric disorders; history of alcohol or other drug use disorder (abuse or dependence); left-handedness; prenatal exposure to alcohol or drugs; use of psychotropic medication; substance use in the past 72 hours; and MRI contraindications. Written assent and consent were obtained from adolescents and their parent/legal guardians in accordance with the University of California

San Diego Human Research Protections Program (18- to 19-year-olds provided their own consent).

Measures

Parents and youth completed screening interviews, including the Diagnostic Interview Schedule for Children Predictive Scales (Lucas et al., 2001), to rule out psychiatric disorders and other exclusions listed above. Parents provided socioeconomic status background information which was converted to a Hollingshead Index of Social Position score (Hollingshead, 1965), and completed the Child Behavior Checklist (Achenbach and Rescorla, 2001) yielding continuous indices of internalizing and externalizing psychopathological syndromes normalized by age and gender. Pubertal staging was assessed with the Pubertal Development Scale (Petersen et al., 1988), and calculated separately by gender. The Beck Depression Inventory (Beck, 1978) and Spielberger State Trait Anxiety Inventory (Spielberger et al., 1970) assessed mood state at the time of scanning. Premorbid intellectual functioning was estimated by the Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999) Vocabulary and Block Design subtests. Immediately preceding the scan session, subjects submitted samples for breathalyzer and urine toxicology analyses to ensure against recent intoxication, and were administered a 28-day Timeline Followback (Sobell and Sobell, 1992) to document patterns of recent substance use.

Detailed alcohol involvement history was assessed using the Customary Drinking and Drug Use Record (Brown et al., 1998) interview, administered to teens for lifetime and past 3-month information on alcohol, nicotine, and other drug use, DSM-IV abuse/dependence symptoms (APA, 1994), and hangover/withdrawal experiences. Peak and typical drinking amounts, consumption durations, and body mass index were used to estimate blood alcohol concentrations (BAC) (Fitzgerald, 1995; Widmark, 1922). To differentiate the impact of binge-type drinking versus other alcohol involvement on FA, bivariate analyses were conducted using peak BAC and total withdrawal experiences (indices of binge drinking), as well as years of alcohol use (duration) and total lifetime drinks.

Procedures

Diffusion weighted data were collected on a 3.0-Tesla GE magnetic resonance scanner using whole brain echo planar imaging (repetition time = 12,000 ms; echo time = 93.4 ms; 36×3.0 mm thick axial slices; in plane voxel resolution 1.875×1.875). Diffusion gradients were applied in 15 directions with 4 averages and a b-value of 2,000 s/mm^2. Raw images were uniformly pre-processed by analyzers (TM and SB), blind to participant group status, to correct for: (1) eddy-current distortions using Functional Magnetic Resonance Imaging of the Brain's (FMRIB) Diffusion Toolbox (FDT; 2D with 6 degrees-of-freedom) (Smith et al., 2004); (2) head motion by registering the diffusion images to the b0 image as a reference, and (3) susceptibility distortions by applying field map unwarping (Smith et al., 2006). FA values were computed using a log-linear estimation procedure to fit each data point to a diffusion tensor model via FDT (Basser et al., 1994). FA maps from each participant were submitted to Tract-Based Spatial Statistics (TBSS) (Smith et al., 2006), which involved 3 steps: (1) all datasets were nonlinearly registered and aligned to a study-specific target, which was representative of the sample under investigation, and were resampled to 1 mm^3 in MNI-152 space (Evans et al., 2003); (2) a mean aligned FA image was created, from which a thresholded (FA > 0.3) skeletonized mean FA image was derived, representing white matter tracts common to all in the sample; and (3) each subject's FA values were projected onto the skeleton.

Data Analyses

Independent samples *t*-tests across the skeletonized FA map permitted voxel-wise comparison of mean differences between binge drinkers in controls (Cox, 1996). To control for type I error,

a combined *t* statistic magnitude ($p < 0.01$) and cluster volume thresholding method was utilized. Monte Carlo simulation revealed that 27 contiguous voxels exceeding the *t*-threshold were required to protect family-wise error at $p = 0.01$, assuming 4-mm FWHM intrinsic smoothing (Smith et al., 2006). No additional smoothing kernel was applied to the data. Areas representing group differences of FA on white matter tracts were identified using a DTI atlas (Wakana et al., 2004). To further explore the influence of alcohol use on white matter integrity, follow-up bivariate correlation analyses (using Pearson's *r*) related binge drinkers' alcohol involvement variables (lifetime hangover symptoms, estimated peak blood alcohol concentration, lifetime drinks, and duration of drinking) to mean FA in clusters that significantly differed between groups.

Results

Independent samples *t*-tests revealed that teen binge drinkers exhibited lower ($p < 0.01$) FA in 18 white matter areas (each ≥27 contiguous voxels) throughout the brain, relative to controls. Table 2 itemizes each area by cluster number while Fig. 1 depicts these regions, including the superior (Clusters 6, 15, 16, and 18) and inferior (Cluster 17) longitudinal fasciculi, corona radiata (Clusters 1, 7, and 14), internal (Cluster 8) and external (Clusters 9 and 10) capsules, corpus callosum (Clusters 2, 3, 4, and 5), cerebellum (Clusters 12 and 13), and limbic projection fibers (Cluster 11). No cluster showed higher FA in bingers than controls. All Hedge's *g* effect sizes exceeded 1.0 (very large range) for each cluster (see Table 2).

Exploratory bivariate correlations among binge drinkers, uncorrected for multiple comparisons, were run to determine if areas of group differences in FA were associated with alcohol involvement. More lifetime alcohol hangover/withdrawal experiences were related to lower FA in the corpus callosum (Cluster 2: $r = -0.65$, $p < 0.025$; Cluster 4: $r = -0.71$, $p < 0.025$; and Cluster 5: $r = -0.60$; $p < 0.025$; see Fig. 2), and trends were found in the left anterior corona radiata (Cluster 1: $r = -0.50$, $p = 0.06$) and left inferior cerebellar peduncle (Cluster 12: $r = -0.50$; $p = 0.06$). Peak estimated blood alcohol concentration in the 3 months prior to scanning was also inversely related to FA in the body of the corpus callosum (Cluster 5: $r = -0.54$, $p < 0.05$), left internal and right external capsules (Cluster 9: $r = -0.53$, $p < 0.05$; and Cluster 10: $r = -0.59$, $p < 0.025$), and left posterior corona radiata (Cluster 14: $r = -0.62$, $p < 0.025$). No relationships were observed between FA and lifetime drinks, and duration of drinking.

Follow-up correlational analyses determined if age might account for FA differences in clusters that differed between groups ($n = 28$). Age was not linked to FA in any cluster, but advanced pubertal stage was marginally linked to higher FA in the body of the corpus callosum (Cluster 2: $r = 0.36$, $p = 0.06$; Cluster 5: $r = 0.34$, $p = 0.07$) and fornix/stria terminalis tracts (Cluster 11: $r = 0.31$, $p = 0.10$).

Discussion

This study compared white matter integrity between adolescents with binge alcohol consumption relative to controls matched on age, gender, verbal IQ, ethnicity, and socioeconomic status. Despite demographic similarities, widespread reductions in FA were observed in heavy episodic drinkers, suggesting the possibility of compromised white matter integrity in major fiber tract pathways in frontal (including the corpus callosum genu and body), cerebellar, temporal, and parietal regions. These findings extend previous reports of FA diminutions observed in adults both diffusely throughout white matter (Pfefferbaum et al., 2006b), and specifically in the corpus callosum (Harris et al., 2008; Pfefferbaum and Sullivan, 2005; Pfefferbaum et al., 2006a; Schulte et al., 2005) of individuals with alcohol use disorders,

yet this is the first report to describe reduced FA in drinkers as early as mid-adolescence and in youth who do not meet criteria for alcohol abuse or dependence.

Although we only observed FA decrements, De Bellis and colleagues (2008) found increased FA in the rostral body and isthmus of the corpus callosum among youth with an alcohol use disorder (AUD) in a region-specific study. Although the current study did not include adolescents with AUD, results here are consistent with our previous study of 8 teenagers with AUD (without concomitant psychiatric issues) compared to 8 control teens (Tapert et al., 2003). This pilot investigation showed reduced FA in the splenium [$F(1,16) = 4.39$, $p = 0.05$] and marginally in the body [$F(1,16) = 3.46$, $p = 0.08$] of the corpus callosum. Conflicting findings could stem from dissimilarities in samples. While, here, groups were matched by age and free from psychiatric conditions, De Bellis and colleagues studied youths with an AUD who were slightly older than their comparison group (16.9 years vs. 15.9 years, $p < 0.003$), and had comorbid Axis I disorders (75% cannabis use disorder, 72% lifetime major depressive episode, 69% attention deficit/hyperactivity disorder, and 63% conduct disorder) whereas such diagnoses were exclusionary for controls. These comorbid disorders have previously been linked to white matter abnormalities (Matochik et al., 2005; McAlonan et al., 2007; Medina et al., 2007a; Steingard et al., 2002). Thus, there is much difficulty extricating potential interactive effects of these conditions. However, both the present study and De Bellis and colleagues (2008) offer interesting contributions to understanding the relationships between adolescent alcohol involvement and white matter integrity. The present study examined sub-clinical drinking to better isolate alcohol effects on typically developing teenagers. Binge drinking teens are of particular interest, as it is estimated that more than 30% of minors who begin drinking before age 16 will develop alcohol dependence (Grant and Dawson, 1997). Indeed, studying nondisordered adolescent drinkers is of substantial import due to the increased risk for binge drinking teens to transition into an AUD by adulthood (Hawkins et al., 1992; Viner and Taylor, 2007). The sample in the De Bellis paper is representative of adolescents with an AUD, especially due to high rates of comorbid psychiatric disorders among such youth (Clark et al., 1997; Viner and Taylor, 2007).

White matter aberrancies were related to drinking in a dose-dependent manner. Higher estimations of peak blood alcohol concentrations were linked to poorer fiber tract quality in the corpus callosum, internal/external capsules, and posterior corona radiata. Further, teens reporting multiple hangover symptoms showed more compromised white matter in the body and genu of the corpus callosum, frontal lobe projection fibers (anterior corona radiata), and cerebellar tracts (inferior peduncle). This finding linking postdrinking effects to worse integrity is consistent with white matter deficits observed in adults with histories of alcohol withdrawal seizures (Sullivan et al., 1996). These relationships suggest that high-dose alcohol consumption, to the extent that hangover symptomatology arises, may index adverse influences on white matter caliber, particularly since associations were not observed for drinking frequency or duration. It is also possible that hangover may be more accurately recalled than other aspects of alcohol involvement.

The results of this study align interestingly with prior evidence for alcohol-related interruption of frontocerebellar circuitry (Sullivan and Pfefferbaum, 2005), involving network nodes pons and thalamus, which exhibit volumetric decrements among adult alcoholics (Sullivan et al., 2003). Although we did not examine the integrity of frontocerebellar white matter connectivity specifically, we did observe lower FA in the superior cerebellar peduncle, a fiber tract that connects the thalamus to deep cerebellar nuclei (Wakana et al., 2004). Thalamic projections also emanate from the posterior limb of the internal capsule, where reduced fiber coherence was detected. These observations of altered white matter microstructure, combined with results from other DTI, morphometric, fMRI, and neuropsychological studies, serve as converging lines of evidence pointing towards a deleterious influence of alcohol on frontocerebellar

circuitry (Sullivan and Pfefferbaum, 2005). Unlike the aforementioned studies with samples comprised of mature individuals with years of alcoholism, the sample of this exploratory analysis represents teenagers at the beginning stages of risky alcohol use, and related white matter abnormalities in these pathways detectable as early as 16 years of age.

The hippocampus is vulnerable to the effects of ethanol, particularly during adolescence (Medina et al., 2007b; Nagel et al., 2005). Running dorsally to the hippocampus are the fornix and stria terminalis, both compact limbic projections terminating at hippocampal and amygdala regions, respectively (Wakana et al., 2004). Since these fibers are tightly packed together, it is difficult to ascertain whether the decreased FA observed in this area indicates altered white matter integrity to the fibers making up the fornix, terminal stria, or both. As adolescents with alcohol use disorders have demonstrated impairments in learning and memory (Tapert et al., 2002), diminished FA in the fibers extending to the hippocampus may suggest changes in structural connectedness leading to functional aberrations in teenage drinkers. Multimodal neuroimaging studies will help solidify the nature of white matter connectivity between these regions (e.g., frontal lobe, thalamus, pons, cerebellum, insula, hippocampus, and amygdala), and elucidate the influence of heavy drinking on these networks.

Due to binge drinkers' relatively inchoate stages of alcohol use, results could alternatively highlight a premorbid white matter characteristic representing a vulnerability to risky drinking. However, the observed link between alcohol involvement (i.e., hangover) and reduced FA in this study lends support to a possible compromising influence of high-dose alcohol use on white matter quality. Several potential mechanisms could explain how FA might be reduced in heavy drinking teens. Years of alcoholism are linked to decreased *N*-acetylaspartate in white matter tissue, suggesting compounding axonal insult by chronic alcohol use (Meyerhoff et al., 2004; Schweinsburg et al., 2001). FA decrements could represent such a chemically induced axonal injury at a microstructural level. Animal models provide additional insights to rapid, alcohol-induced neural injury. Adult rats demonstrate neurodegeneration following once-daily ethanol exposure within as little as 5 days (Collins et al., 1998). Additionally, adolescent rats show differential sensitivity to brain damage compared to adults following 4 days of binge alcohol administration (Crews et al., 2000). Thus, human adolescents may be especially vulnerable to the deleterious effects of alcohol on neural tissues, including white matter. Another explanation of poor white matter integrity in binge drinking adolescents could relate to a disruption of neuromaturational processes. Developmental studies of white matter coherence have demonstrated increasing FA across adolescence (Giorgio et al., 2008; Hasan et al., 2007), reflected here by increased FA in the corpus callosum and fornix/stria terminalis with advancing pubertal stage. Low fiber tract coherence among drinkers could be due to an innate delay or an alcohol-related impediment in normal maturational processes. It is also possible that the observed changes may relate to axonal atrophy or membrane breakdown, important in the context of adolescent neuromaturation.

This study is the first we are aware of to characterize white matter integrity in major fiber tracts throughout the cerebrum and cerebellum between subdiagnostic binge drinking teens and nondrinkers. The study is limited by its cross-sectional design and modest sample size, and serves as a preliminary characterization of white matter integrity in adolescent binge drinkers. Due to the exploratory nature of this study, the data require replication. If replicated, these results carry important public health implications as interventions targeting binge drinking behaviors could lessen the risk for developing an alcohol use disorder. Longitudinal investigations, currently underway, will also help ascertain the degree to which heavy drinking and postdrinking effects might influence the developing adolescent brain. Studies with larger sample sizes will examine gender differences, factors predating alcohol use (e.g., family history of alcoholism, personality, conduct disorder), and neuropsychological correlates of white matter abnormalities.

In sum, this study shows differences in white matter quality in adolescents with histories of heavy episodic drinking, revealing widespread areas of compromised white matter in projections to networks underlying complex cognitive abilities of learning, memory, and executive functions. Although preliminary, these results bolster the importance of elucidating the neural sequelae of heavy episodic drinking during adolescence.

Acknowledgments

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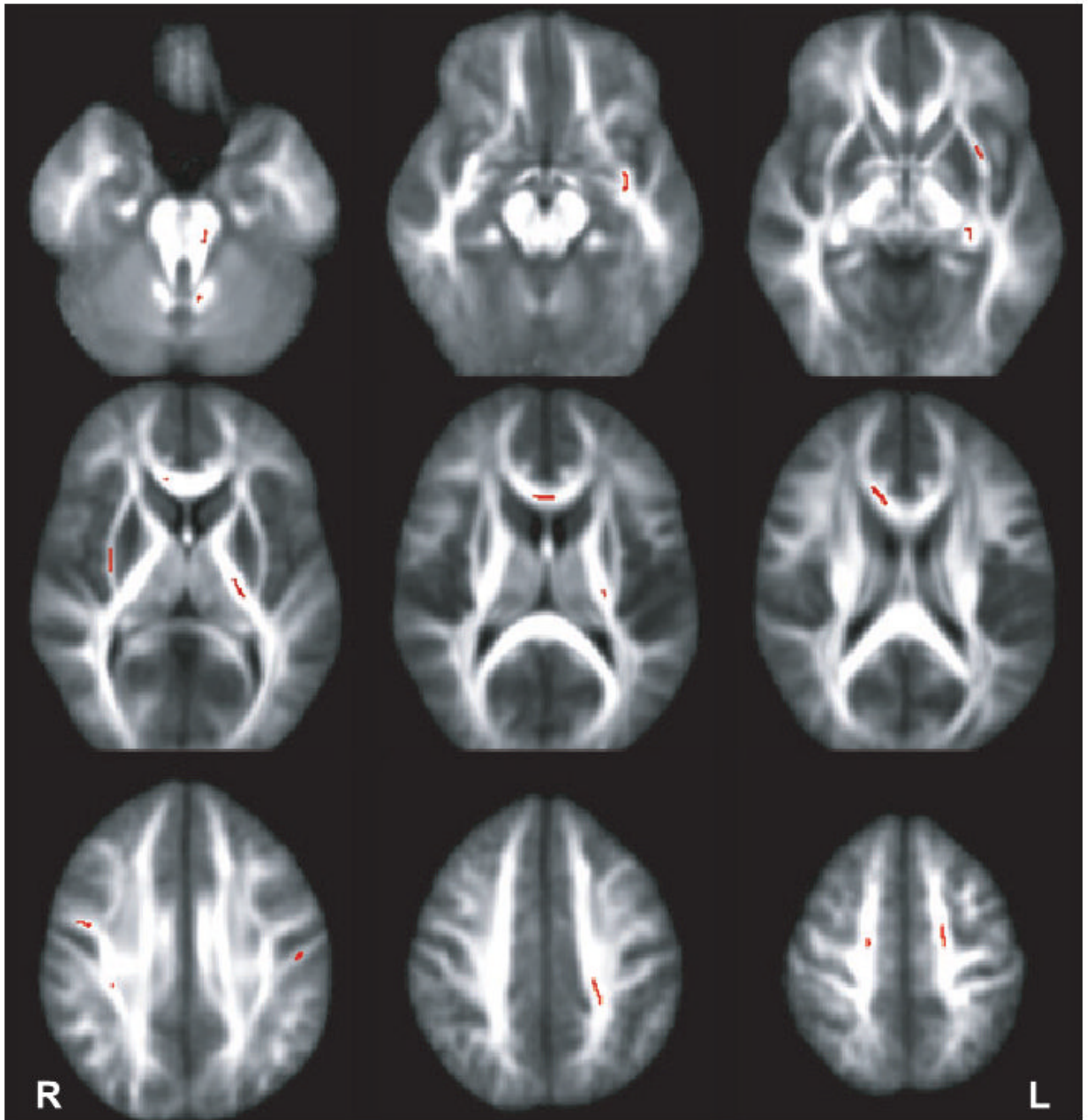
Fig. 1.
Clusters (darkened areas) overlaid on average fractional anisotropy mask highlight where binge drinking adolescents had lower fractional anisotropy than controls (clusters ≥27 contiguous voxels each at $p < 0.01$). In no cluster did drinkers have higher fractional anisotropy than controls.

Fig. 2.
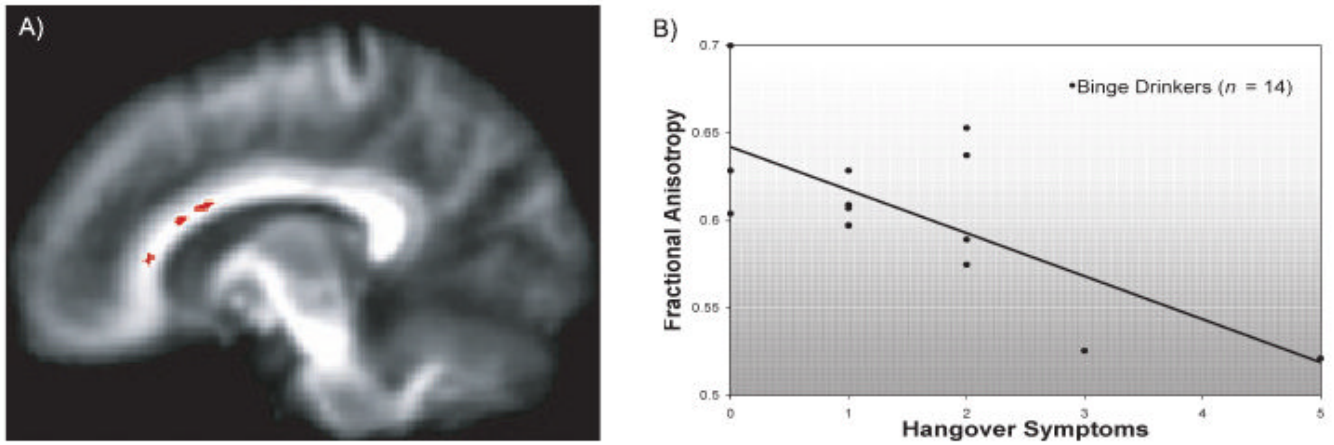(**A**) Clusters (darkened area along callosal fibers) and (**B**) bivariate scatterplot indicate where lower fractional anisotropy was significantly linked to more hangover symptoms in the body and genu of the corpus callosum ($r = -0.71$, $p < 0.005$).

Table 1

Participant Demographic and Substance Use Characteristics

	Binge drinkers (*n* = 14) M (SD) or %	Controls (*n* = 14) M (SD) or %
Age	18.09 (0.69)	17.95 (0.88)
% Female	14.3	14.3
% Caucasian	69.2	57.2
% Family history negative[a]	92.9	92.9
Parent annual salary ($ thousands)	131.83 (68.27)	104.92 (61.19)
Hollingshead socioeconomic index	31.14 (17.08)	33.93 (19.12)
Body mass index	23.98 (4.25)	22.73 (2.41)
Pubertal Development Scale total	3.53 (0.44)	3.50 (0.46)
Years of education	11.71 (0.99)	11.50 (0.76)
WASI Vocabulary *T*-score	61.43 (9.91)	57.57 (7.89)
WASI Block Design *T*-score	56.50 (9.05)	56.00 (6.69)
Beck Depression Inventory total	2.07 (2.09)	2.36 (2.92)
Spielberger State Anxiety *T*-score	35.35 (3.70)	40.42 (10.19)
Child Behavioral Checklist Externalizing *T*-score[b]	40.09 (9.35)	46.57 (10.29)
Child Behavioral Checklist Internalizing *T*-score[b]	45.36 (9.60)	45.64 (8.25)
Lifetime alcohol use episodes[***]	54.57 (48.80)	4.57 (6.21)
Drinks per month, past 3 months[***]	15.43 (7.82)	0.21 (0.80)
Peak drinks on an occasion, past 3 months[***]	8.21 (3.02)	0.07 (0.27)
Estimated peak BAC, past 3 months[***]	240 (0.070)	000 (0.010)
Number of hangover symptoms, past 3 months[**]	1.43 (1.74)	0.14 (0.53)
Days since last alcohol use[*]	30.29 (10.53)	513.29 (417.27)
Tobacco cigarettes per day	0.14 (0.53)	0.00 (0.00)
Lifetime marijuana use episodes	2.21 (3.09)	0.64 (1.39)
Lifetime other drug use episodes	0.29 (0.73)	0.00 (0.00)

BAC, blood alcohol concentration.

[a] No first or second degree biological relative with alcohol or drug abuse or dependence.

[b] Not available for 3 binge drinkers.

Binge drinkers significantly differ from controls (

[*] $p < 0.05$,

[**] $p < 0.01$,

[***] $p < 0.001$).

Table 2

Binge Drinkers Show Lower Fractional Anisotropy Than Controls (Clusters ≥27 Contiguous Voxels Each at $p < 0.01$) in 18 Regions Referred to by Cluster Number

Cluster number	Anatomic region	Number of voxels	MNI coordinates[a]			Effect size Hedge's g[b]
			x	y	z	
Frontal lobe						
1	Left anterior coronal radiata	90	18	12	55	1.69
2	Corpus callosum—body	44	−14	−21	21	1.58
3	Corpus callosum—genu	29	−14	−32	8	1.47
4	Corpus callosum—body & genu	29	−1	−20	14	1.57
5	Corpus callosum—body	29	−13	−15	24	1.47
6	Right superior longitudinal fasciculus	31	−49	3	36	1.42
7	Right anterior coronal radiata	27	−17	9	60	1.31
Subcortical areas						
8	Left posterior limb of internal capsule	179	25	23	5	1.57
9	Left external capsule	72	33	−9	−3	2.11
10	Right external capsule	40	−35	11	5	1.42
11	Left fornix/stria terminalis	32	28	27	−9	1.54
Cerebellum						
12	Inferior cerebellar peduncle	42	5	58	−32	1.58
13	Superior cerebellar peduncle	39	9	30	−25	1.52
Parietal lobe						
14	Left posterior coronal radiata	122	24	37	53	1.48
15	Right superior longitudinal fasciculus	33	−34	31	39	1.32
16	Left superior longitudinal fasciculus	28	51	18	39	1.54
Temporal lobe						
17	Left inferior longitudinal fasciculus	47	36	3	−17	1.72
18	Left superior longitudinal fasciculus	29	45	60	0	1.56

[a] Montreal Neurological Institute (MNI) coordinates point to maximum difference within cluster.

[b] Hedge's g calculated from t-value averaged across all voxels within the cluster.