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ORIGINAL ARTICLE

White Matter Tract Integrity, Involvement in Sports, and Depressive Symptoms in Children

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Abstract

White matter tract integrity, measured via fractional anisotropy (FA), may serve as a mediating variable between exercise and depression. To study this, we examined data from 3973 children participating in the ABCD study. Parents of children completed the Sports and Activities questionnaire and the Child Behavior Checklist, and children completed a diffusion MRI scan, providing information about the FA of the parahippocampal cingulum and fornix. Results showed that involvement in sports was associated with reduced depression in boys. The number of activities and sports that a child was involved in was negatively related to FA of the left fornix but was unrelated to FA of other tracts. FA of these white matter tracts was also unrelated to depressive symptoms. This suggests that while white matter tract integrity is associated with exercise, it may not be part of a pathway linking exercise to depression levels in preadolescent boys.

Keywords Diffusion MRI · Exercise · Depression · Children · White matter tract integrity

Depression, which can be associated with anhedonia, disturbed energy and sleep, and thoughts of suicide, is a significant contributor to the global burden of disease [1, 2]. Childhood depression is particularly problematic because it is associated with dysfunctional interpersonal relationships, suicidal behavior, unemployment, and criminal behavior in the long term [3]. While most research on treatments for childhood depression focuses on therapy and medication, one potential alternative intervention is exercise. In fact, studies of children and adolescents have found higher levels of exercise to be associated with reduced depression [4, 5]. Moreover, exercise is associated with increased volume of certain brain regions in children, such as the hippocampus, dorsal striatum, and globus pallidus [5–7]. Therefore, more research is needed on the potential neuroprotective effects of exercise and how this relates to depression in childhood and adolescence. Thus, the goal of the present study is to examine the relationship between involvement in sports (a measure of exercise), white matter tract integrity, and depressive symptoms in a nationwide sample of nine- to eleven-year-old children.

Exercise is associated with better mental health of both adults and children, with some evidence for a causal relationship. For example, a study of adults across the United States and Canada found that having an active lifestyle was associated with reduced anxiety and depression, improved self-concept, and better coping with stress [8]. Additionally, a randomized controlled trial in elderly patients found exercise to be an effective antidepressant [9]. While fewer studies have examined exercise as a potential treatment for mental health related issues in children, one meta-analysis found that higher levels of exercise in adolescents was associated with reduced depressive symptoms [4]. However, because children and adolescents often partake in exercise through organized sports, it is unclear if it is the social support, structure, or cardiovascular benefits that provide anti-depressant effects. Together, these studies suggest that more research needs to be done to better understand the pathways by which exercise might relate to improved mental health in children and adolescents.

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Past research suggests that exercise's benefit to mental health may be related to its impact on the hippocampus, a structure of the brain critical for learning and memory. For example, one study found that kids who were more physically fit had greater bilateral hippocampal volumes [6]. Studies of animals also show that exercise can lead to increased neurogenesis and long-term potentiation in the hippocampus [10, 11]. Interestingly, reduced hippocampal volume has consistently been shown to be associated with depression [12], including being associated with a Major Depressive Disorder (MDD) diagnosis, depressive symptom severity, illness duration, and the number of depressive episodes that a person has had in their lifetime [13–17]. Likewise, antidepressants can increase the volume of the hippocampus in patients with depression [18]. Together, this literature suggests the hypothesis that part of the effect of exercise on mental health may be through its impact on the hippocampus.

In order to investigate the relationship between exercise, hippocampal volume, and depression in preadolescent children, past research by our group examined data from the Adolescent Brain and Cognitive Development (ABCD) study, a nationwide sample of about 4500 children. This study found that involvement in sports (a measure of exercise), but not non-sport activities was associated with reduced depression in boys [5]. In this study, we also broke sports into multiple categories, including team sports, individual sports and structured sports. Relationships to depression were strongest with team sports, suggesting that it is the combination of exercise and the social support that comes from being on a team that may be beneficial for mental health in boys. Further, this relationship in boys was partially mediated by hippocampal volume [5]. This finding was specific to depression and not anxiety symptoms. These results extended past literature to suggest that the hippocampus may be implicated in depression and exercise in children as young as nine years old, but more research using this sample of children is needed to better understand the full picture of these relationships, as it is quite possible that there are additional neural mechanisms that help explain the relationships of exercise to depression.

In fact, findings from animal studies suggest that the benefits of exercise may be further driven by changes in brain connections as well as changes in brain volume. For example, voluntary exercise increases levels of brain-derived neurotrophic factor (BDNF) and stimulates neurogenesis, or the production of new neurons [19]. Moreover, exercise increases long-term potentiation, or the strengthening of synapses, and angiogenesis, the development of new blood vessels [10, 20]. Together these studies point to the need for a better understanding of the broader changes that exercise has on the brain, such as its impact on the integrity of white matter tracts, or myelinated groups of axons that connect areas of the brain. In humans, hypotheses about changes in brain connections can be assessed using techniques such as diffusion MRI, which creates contrast images by tracking the diffusion of water molecules [21].

Two notable white matter tracts connected to the hippocampus include the fornix, which is a bundle of fibers that originates in the hippocampus, loops around the thalamus, and ends in the hypothalamus, and the parahippocampal cingulum, which courses longitudinally within the cingulate gyrus, goes around the corpus collosum, and ends in the parahippocampal gyrus. It is possible that the integrity of these tracts may be impacted by both depression and exercise, raising the possibility that their integrity might also mediate the relationship between exercise and improved mental health. Interestingly, multiple studies have linked depression with reduced white matter tract integrity of the fornix and parahippocampal cingulum. For example, diffusion tensor imaging (DTI) studies have demonstrated reduced fractional anisotropy (FA) (a measure of integrity) in the cingulum in patients with major depression [22, 23]. A similar finding has been demonstrated in people with treatment resistant depression [24], in people with a family history of major depressive disorder [25, 26], and in people with subclinical anhedonia [26]. Additionally, white matter tract integrity has also been linked to exercise. For example, one study found aerobic fitness to be positively correlated with white matter integrity of the cingulum [27]. Higher levels of fitness are also associated with increased global white matter volume [28]. Given the literature linking white matter tract integrity to both exercise and depression and the known changes in hippocampal volume in relation to both exercise and depression in the children in our sample, it is possible that white matter tracts connected to the hippocampus, such as the fornix and the parahippocampal cingulum, may also show variation related to sports involvement.

To summarize, prior literature raises the possibility that the effect of exercise on depression may be related to its impact on white matter tract integrity, in addition to hippocampal volume. However, it is unclear if the relationship between exercise and white matter tract integrity follows a dose response curve (i.e., more exercise, greater differences in white matter integrity), or if it is also related to the type of exercise (e.g., team sports versus individual sports, etc.) as we found in our work on hippocampal volume. It is also unclear if the relationships between white matter tract integrity, exercise, and mental health are different in preteen boys versus girls, as some literature suggests that white matter tracts may develop at different rates depending on sex. For example, white matter volume increases faster in adolescent boys than in adolescent girls, but girls have a greater rate of increase in fiber density compared with boys [29].Therefore, to examine the relationship between involvement in sports (a measure of exercise), depressive symptoms, and white matter tract integrity, we analyzed diffusion imaging (dMRI) and survey data from children participating in the Adolescent Brain and Cognitive Development (ABCD) study. We predicted that involvement in sports would be associated with increased integrity of the fornix and parahippocampal cingulum (i.e., greater FA), and that depression would be associated with reduced integrity of these white matter tracts. Moreover, we predicted that white matter tract integrity would partially mediate the relationship between exercise and depressive symptoms over and above hippocampal volume. For all of our predictions, we also examined interactions with sex. Finally, we predicted that these relationships would hold even when correcting for scanner type, socioeconomic status, parental education, race, ethnicity, and age, but that they would only be observed in boys, but not girls, given our prior findings.

Method

Participants

As described in [5], participants took part in the ABCD study, a longitudinal study tracking over 11,800 + children ages 9–11 years old from 21 different sites across the United States. Exclusionary criteria for the ABCD study included common MRI contraindications, inability to understand or speak English fluently, uncorrected vision, hearing or sensorimotor impairments, a history of major neurological disorders, gestational age of less than 28 weeks, birth weight of less than 1200 g, birth complications that resulted in hospitalization for more than one month, current diagnosis of schizophrenia, moderate or severe autism spectrum disorder, history of head injury, or an unwillingness to complete assessments. Therefore, the study population consisted of children both with and without mental health related symptoms. Additionally, the sample included 800+ sets of twins [30]. A more detailed explanation of this sampling strategy, including recruitment protocols, is described elsewhere [31]. All study procedures were approved either by the centralized IRB at the University of California San Diego or by an individual participating site's IRB. All parents signed informed consent and all children provided written assent prior to participation in the study. While there were 4524 children originally in the data set, 551 had to be removed for the current analyses because the brain data was unusable (N = 546, see imaging section) or they did not fall into the male or female binary (N = 5). Of those that did not define their gender as male or female, one person was trans female, one person described their gender as "different," and 3 people did not report gender. Therefore, 3973 children's data was used in the analyses reported below. For a comparison of demographics of male and female participants, please see Table 1. For information regarding demographics of the included versus excluded participants, please see Table 2.

Measures

As described in [5], the ABCD study included a number of measures of mental health related constructs [32]. The Child Behavior Check List (CBCL), completed by the child's caregiver, provides information about mental health problems in the child. We examined the child's Depressive age corrected T Score. The CBCL test-retest reliability over 8 days was $r = 0.84$ for the Depressive score [33]. Therefore, our analysis looked at a range of depressive symptoms rather than comparing children with and without a diagnosis of major depressive disorder.

The Sports and Activities Involvement Questionnaire measures lifetime involvement in sports, activities such as music and dance, and other hobbies. It assesses the frequency, duration, and type of activity, in addition to whether it is organized, private, individual, or structured. For the purposes of this study, we examined the child's involvement in 23 different sports, including dance, baseball, basketball, climbing, field hockey, football, gymnastics, ice hockey, horseback riding/polo, ice skating, martial arts, lacrosse, rugby, skateboarding, skiing/snowboarding, soccer, surfing, swimming/water polo, tennis, track/running/cross country, mixed martial arts, volleyball, and yoga. As we did in our prior work, in order to examine the effects of social support and structure that come with playing sports, we further divided the data into the categories of team sport (broad definition), team sport (restrictive definition), individual sport, and structured sport. In the team sport (broad definition) category, the child engaged in the sport at school or in an organized outside league. In the team sport (restrictive definition), the child engaged in the sport at school or in an organized outside league, but it needed to be one of the following sports where the sport was played as a team activity: baseball, basketball, field hockey, football, ice hockey, lacrosse, rugby, soccer, or volleyball. In the individual sport category, the child engaged in the sport on their own time or through private lessons. Finally, in the structured sport category, the child engaged in the sport at school, through an organized outside league, or through private lessons. The non-sport activities examined included music, art (drawing, painting, graphic art, photography, pottery, and sculpting), drama (theater, acting, film), crafts (like knitting or model cars), competitive games (like chess, darts, and cards), and hobbies (like collecting stamps or coins). The total number of activities (and more specifically sports and non-sport activities) was also used to examine "dose" relationships.

Table 1 Demographics as a function of sex

Characteristics	Male (N = 2060)				Female (N = 1913)				Statistic	p Value
	Mean	SD	Min	Max	Mean	SD	Min	Max	T Score	
Age (in months)	120.6	7.38	108	132	120.49	7.25	108	132	0.419	0.675
Number of total activities	3.73	2.66	0	18	3.91	2.82	0	20	− 2.089	0.037
Number of sports	2.79	2.05	0	14	2.74	2.13	0	18	0.768	0.443
Number of non-sports	0.94	1.14	0	6	1.18	1.2	0	6	− 6.258	0.000
CBCL depression T score	53.78	5.99	50	89	52.98	5.17	50	86	4.520	0.000
	%				%				T Score	p Value
Family income level									− 0.534	0.593
Under $25,000	10.3				9.4					
$25,000 to $49,999	12.7				13.0					
$50,000 to $99,999	27.9				28.2					
$100,000+	41.6				42.0					
Parent education									− 1.119	0.263
High school/GED or less	13.8				12.9					
Some college or associates degree	29.5				26.7					
Bachelor's degree	29.9				31.9					
Greater than bachelor's	26.6				28.4					
									X^2 Value	p Value
Team sport (broad definition)	84.9				82.2				5.184	0.023
Team sport (restrictive definition)	75.7				52.7				230.274	0.000
Individual sport	62.7				56.3				16.720	0.000
Structured sport	85.9				83.9				3.174	0.076
Race										
Caucasian	82.0				81.2				0.429	0.538
African-American	13.6				15.4				2.392	0.125
Other	4.4				3.4					
Hispanic	20.0				19.7				0.075	0.811

Diffusion Imaging Data Acquisition and Processing (dMRI)

As described in detail in [34], the T1 weighted acquisition in the ABCD study is a 3D T1w inversion prepared RF-spoiled gradient echo scan that was 1 mm isotropic [35, 36]. The dMRI acquisition uses multiband echo planar imaging and was 1.7 mm isotropic [37, 38]. The dMRI acquisition uses a slice acceleration factor of 3. It has 96 diffusion directions, seven b = 0 frames, and four different b-values. The 96 directions included 6 directions with b = 500, 15 directions with b = 1000, 15 directions with b = 2000, and 60 directions with b = 3000. The processing of the dMRI data is also described in detail in [34]. Briefly, distortions due to eddy currents are corrected, outliers are removed from the data, head motion is corrected using rigid body registration, spatial and image intensity distortion from B0 field inhomogeneities are corrected, and the b = 0 images are registered to the T1 weighted images using mutual information. Then, the ABCD dMRI processing pipelines measure a number of different properties of white matter data, including FA, an index of the directionality of water diffusion within a voxel. Other properties include mean diffusivity (MD), a mean of the eigenvalues, longitudinal diffusivity (LD), the first eigenvalue, and transverse diffusivity (TD), the mean of the second and third eigenvalues [39]. These dMRI metrics were calculated for white matter fiber tracts using AtlasTrack, which is a method for segmenting white matter fiber tracts that uses a probabilistic atlas [40]. In this project, we focus on FA of the fornix and the parahippocampal cingulum in primary analyses. 546 children were excluded from analyses because their dMRI data was unusable.

Analyses

The analyses used linear regressions that allowed us to provide standardized beta weights as a measure of effect size. However, as described in [5], the sample included a number

Table 2 Demographics as a function of included versus excluded participants

Characteristics	Included (N = 3973)				Excluded (N = 551)				Statistic	p Value
	Mean	SD	Min	Max	Mean	SD	Min	Max	T Score	
Age (in months)	120.5	7.32	108	132	119.0	7.03	108	132	– 4.681	0.000
Number of total activities	3.82	2.74	0	20	3.71	2.90	0	16	– 0.836	0.403
Number of sports	2.76	2.08	0	18	2.66	2.2	0	12	– 1.040	0.298
Number of non-sports	1.05	1.173	0	6	1.05	1.2	0	6	– 0.105	0.916
CBCL depression T score	53.4	5.6	50	89	53.9	5.6	50	79	1.938	0.053
	%				%				T Score	p Value
Family income level									– 2.863	0.004
Under $25,000	9.9				14.4					
$25,000 to $49,999	12.8				11.5					
$50,000 to $99,999	28				27.2					
$100,000+	41.8				36.5					
Parent education									– 2.014	0.044
High school/GED or less	13.4				17.1					
Some college or associates degree	28.2				28.2					
Bachelor's degree	30.9				29.6					
Greater than bachelor's	27.5				25.2					
									X^2 Value	p Value
Team sport (broad definition)	83.6				78.6				8.677	0.004
Team sport (restrictive definition)	64.6				61.7				1.810	0.184
Individual sport	59.6				54.4				5.317	0.023
Structured sport	84.9				80.4				7.603	0.007
Race										
Caucasian	81.7				73.9				18.834	0.000
African-American	14.5				20.0				11.355	0.001
Other	3.8				6.1					
Hispanic	19.9				18.1				0.892	0.360

of sets of twins. Thus, to account for this in our analysis, we confirmed analyses using general linear models with participants nested within sites and families. Due to the large sample size, outliers were not excluded. However, participants whose data was missing and/or had a quality check (QC) score of 0 were excluded from the analyses.

We carried out analyses for each sports category predicting depression and FA of the fornix and parahippocampal cingulum, and for the relationships between FA of these tracts and depression. Therefore, we had a total of 39 generalized linear models [7 GLMs predicting depression from sports, 7 GLMs predicting FA of the left fornix from sports, 7 GLMs predicting FA of the right fornix from sports, 7 GLMs predicting FA of the left PHC from sports, 7 GLMs predicting FA of the right PHC from sports, and 4 GLMs predicting depression from FA of the 4 tracts (left and right fornix and PHC)]. In all analyses, we covaried for race, ethnicity, age, parental education, and family income and included both sex and the interactions between sex and independent variable of interest as predictors. Collinearity diagnostics confirmed that multicollinearity was not an issue for the predictors in the GLMs. Significant interactions with sex were followed up with regressions within each sex. Additionally, we used the False Discovery Rate (FDR) to correct for multiple comparisons [41, 42]. The mediation analysis used the process macro in SPSS.

Results

Table 1 describes the demographic characteristics of the children in the sample that we analyzed. 6.7% of children scored in the borderline or clinical range for depression. As shown in Table 3 and demonstrated in [5], greater participation in every category of sport, but not number of activities or number of non-sports activities, was associated with fewer depressive symptoms, even when correcting for socioeconomic status, maternal education, race, ethnicity, and age, with all

Table 3 Relationship between involvement in sports and depressive symptoms

IV	Overall						Sex interaction	Male				Female			
	t	B (SE)	− 95% CI	+95% CI	R	Adj. R^2	FDR *p*	t	B (SE)	− 95% CI	+95% CI	t	B (SE)	− 95% CI	+95% CI
# of activities	− 1.797	− .032 (.036)	− .136	.006	.157	.022	.104	− 2.126*	− .052 (.055)	− .224	− .009	− .324	− .009 (.047)	− .108	.078
# of sports	− 2.837*	− .050 (.047)	− .225	− 0.041	.162	.024	.070	− 3.031**	− .074 (.070)	− .351	− .075	− .893	− .023 (.062)	− .178	.066
# of non-sports	.943	.016 (.081)	− .082	.235	.153	.021	.706	–	–	–	–	–	–	–	–
Team sport (broad)	− 2.403*	− .042 (.270)	− 1.177	− .119	.163	.024	.0245*	− 3.272**	− .079 (.404)	− 2.114	− .530	0.076	.002 (.358)	− .674	.729
Team sport (restrictive)	− 3.625***	− .064 (.205)	− 1.144	− .341	.167	.025	.0257*	− 3.752 ***	− .088 (.325)	− 1.859	− .583	− 1.117	− .028 (.254)	− .781	.214
Individual sport	− 2.960*	− .049 (.188)	− .927	− .188	.163	.024	.0455*	− 3.355**	− .078 (.283)	− 1.503	− .394	− .692	− .017 (.248)	− .659	.315
Structured sport	− 2.466*	− .043 (.280)	− 1.239	− .141	.163	.024	.0245*	− 3.293**	− .079 (.416)	− 2.188	− .555	− .041	− .001 (.373)	− .748	.717

All analyses are using covariates of age (in months), sex, race, ethnicity, parental education, and family income

FDR p values: *p < .05. **p < .01. ***p < .001

Separate analyses in males and females for number of activities and number of sports were conducted due to the trend level of the sex interaction p values for these constructs relationships passing FDR correction. However, we also saw significant interactions with sex for many of the sports/activities predictors, with all but number of activities, number of sports, and number of non-sports activities passing FDR correction. Follow up analyses within sex indicated significant relationships between every type of activity/sport and depression in boys, but after FDR correction, no significant relationships in girls.

Next, we examined the relationships between sports and activities and FA of the parahippocampal cingulum and fornix. The coordinates and number of voxels in each of these tracts are displayed in another paper [34]. As shown in Table 4, involvement in sports was not associated with FA of either the left or the right parahippocampal cingulum. This result was the same for each of the types of sports and activities. Additionally, as shown in Table 5, involvement in sports and activities was unrelated to FA of the right fornix. However, as shown in Table 5 and demonstrated in Figs. 1 and 2, the number of activities and the number of sports in which a child was involved were each negatively related to FA of the left fornix. This relationship did not hold for involvement in non-sports, team sports (broad or restrictive definition), individual sports, or structured sports.

We next repeated the significant analyses controlling for average hippocampal volume and total brain volume to determine whether FA of the left fornix was related to sports involvement over and above hippocampal volume. Average hippocampal volume ($t=3.364$, $\beta=0.075$, $p=0.001$) predicted FA of the left fornix, but the number of activities also continued to predict FA of the left fornix even with hippocampal volume in the model ($t=-2.808$, $\beta=-0.052$, $p=0.005$). Similarly, both average hippocampal volume ($t=3.355$, $\beta=0.075$, $p=0.001$) and the number of sports ($t=-2.929$, $\beta=-0.053$, $p=0.003$) concurrently predicted FA of the left fornix. Thus, the relationships between the number of sports and activities and FA of the left fornix were independent of hippocampal volume. Once again, there were no significant interactions with sex.

We next examined the relationships between depressive symptoms and FA of the parahippocampal cingulum and the fornix. As shown in Table 6, neither the average FA of the left and right parahippocampal cingulum nor the average FA of the left and right fornix were related to depressive symptoms. Because of this lack of significant results, we did not test whether FA of the left fornix was a mediator of the relationships between involvement in sports and depressive symptoms in children.

Table 4 Relationship between involvement in sports and fractional anisotropy of parahippocampal cingulum

IV	Left						Right					
	t	B (SE)	− 95% CI	+ 95% CI	R	Adj. R^2	*t*	B (SE)	− 95% CI	+ 95% CI	R	Adj. R^2
# of activities	− 1.171	− .019 (.000)	− .001	.000	.498	.246	− 1.774	− .028 (.000)	− .001	.000	.506	.254
# of sports	− .856	− .013 (.000)	− .001	.000	.498	.246	− 1.803	− .028 (.000)	− .002	.000	.506	.254
# of non-sports	− 1.180	− .018 (.001)	− .002	.001	.499	.246	− .898	− .014 (.001)	− .002	.001	.506	.254
Team sport (broad)	− 1.266	− .020 (.002)	− .008	.002	.498	.246	.334	.005 (.002)	− .004	.006	.505	.253
Team sport (restrictive)	.251	.004 (.002)	− .003	.004	.498	.245	1.447	.023 (.002)	− .001	.006	.506	.253
Individual sport	− .844	− .013 (.002)	− .005	.002	.498	.246	.022	.000 (.002)	− .003	.003	.505	.253
Structured sport	− 1.386	− .022 (.003)	− .009	.001	.498	.246	− .205	− .003 (.003)	− .006	.004	.505	.253

All analyses are using covariates of scanner type, sex, age (in months), race, ethnicity, parental education, family income, and a sex interaction

FDR p values: *$p<.05$. **$p<.01$. ***$p<.001$

Table 5 Relationship between involvement in sports and fractional anisotropy of fornix

IV	Left						Right					
	t	B (SE)	− 95% CI	+95% CI	R	Adj. R^2	*t*	B (SE)	− 95% CI	+95% CI	R	Adj. R^2
# of activities	− 2.490*	−.044 (.000)	−.001	.000	.244	.057	− 1.072	−.018 (.000)	−.001	.000	.380	.141
# of sports	− 2.688*	−.047 (.000)	−.001	.000	.244	.057	−.718	−.012 (.000)	−.001	.000	.379	.141
# of non-sports	−.935	−.016 (.000)	−.001	.000	.241	.055	− 1.198	−.019 (.000)	−.001	.000	.380	.142
Team sport (broad)	1.874	.033 (.001)	.000	.005	.243	.056	1.681	.028 (.000)	.000	.005	.380	.141
Team sport (restrictive)	.865	.015 (.001)	−.001	.003	.241	.055	.456	.008 (.001)	−.002	.003	.379	.141
Individual sport	− 2.216	−.037 (.001)	−.004	.000	.243	.056	−.918	−.015 (.001)	−.003	.001	.379	.141
Structured sport	1.518	.027 (.001)	−.001	.005	.242	.056	1.070	.018 (.001)	−.001	.005	.379	.141

All analyses are using covariates of scanner type, age (in months), sex, race, ethnicity, parental education, family income, and a sex interaction

FDR p values: *p < .05. **p < .01. ***p < .001

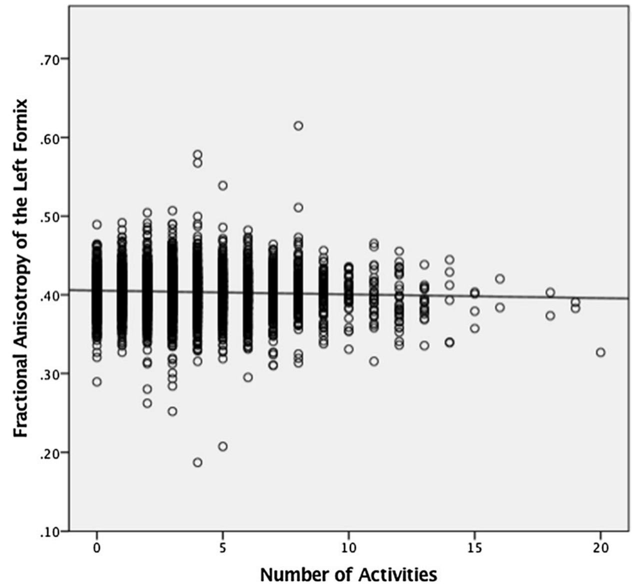

Fig. 1 Graph illustrating the relationship between the number of activities in which a child is involved and fractional anisotropy of the left fornix

Discussion

The goal of the current study was to extend research on the relationship between involvement in sports and depressive symptoms in children and determine if the relationship was mediated by FA of two white matter tracts, the parahippocampal cingulum and the fornix. We hypothesized that involvement in multiple types of sports would be associated with reduced depression, and this was true in boys, but not girls, which was consistent with our previous results with this sample [5]. We further hypothesized that involvement in sports would be positively associated with FA of both the parahippocampal cingulum and fornix, but we did not find support for such a relationship. FA of the left fornix was negatively related to the number of activities and number of sports in which a child was involved but was unrelated to any other type of sport or activity. FA of the parahippocampal cingulum was unrelated to involvement in sports. Finally, we hypothesized that FA of these two tracts would be negatively related to depressive symptoms, but also did not find support for such a relationship.

While we predicted that sports involvement would be associated with greater FA of both the left and right fornix and parahippocampal cingulum, we only found one of these relationships to be significant. More importantly, this was in the opposite direction of what we predicted—namely, involvement in sports and activities was associated with *reduced* FA of the left fornix rather than increased FA. One potential reason why our results contrasted with our predictions could be that our sample was much younger than that

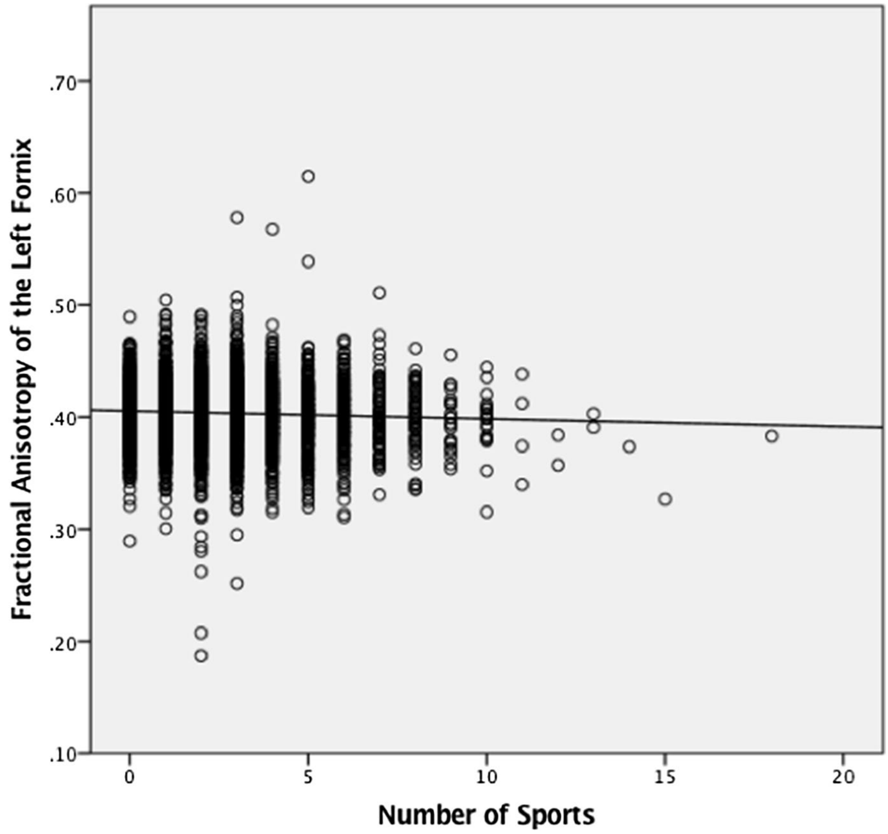

Fig. 2 Graph illustrating the relationship between the number of sports in which a child is involved and fractional anisotropy of the left fornix

Table 6 Relationship between fractional anisotropy of PHC and fornix and depressive symptoms

IV	Left						Right					
	t	B (SE)	− 95% CI	+ 95% CI	R	Adj. R^2	*t*	B (SE)	− 95% CI	+ 95% CI	R	Adj. R^2
Parahippocampal cingulum	1.436	.027 (1.840)	− .965	6.252	.163	.024	− .253	− .005 (1.868)	− 4.136	3.191	.161	.023
Fornix	− .273	− .005 (3.273)	− 7.311	5.523	.161	.023	1.270	.023 (3.198)	− 2.209	10.330	.163	.023

All analyses are using covariates of scanner type, age (in months), sex, race, ethnicity, parental education, family income, and a sex interaction

FDR p values: *p < .05. **p < .01. ***p < .001

of most dMRI studies, and developmental status may influence how FA can be interpreted. While one study of older adults with a genetic risk for Alzheimer's disease did find reduced FA of the left fornix in people who engaged in more physical activity (as compared to a group who engaged in less physical activity) [43], most studies of adults report that higher FA is associated with an increase in exercise and a reduction in depressive symptoms [22–28]. For example, one study of adult patients with schizophrenia found that a 6-month exercise intervention led to increases in FA of the left corticospinal tract, the left superior longitudinal fascicle, and the forceps major [44].Therefore, increased FA is generally interpreted as a positive feature in the adult literature. On the other hand, our results suggest that it is possible that high FA values in children reflect a different phenomenon. When a child has only a few fibers going in the same direction, water molecules are traveling in the same direction, resulting in an increased FA value. On the other hand, when a child has lots of fibers going in different directions, water molecules may be traveling in multiple different directions, resulting in a decreased FA value. Thus, rather than suggesting increased white matter connectivity, a high FA value in a child may instead indicate less branching or less crossing of other fibers (i.e., less complexity in fibers), which is important for development [45]. This hypothesis has also been used to help explain why increased FA of certain white matter tracts has been found in children with autism [46–48]. If this were true in our sample, reduced FA in the left fornix in children who participate in more sports may actually be an encouraging phenomenon, because it would suggest that exercise is associated with more branching and crossing of fibers in a manner characteristic of healthy development. Longitudinal research tracking white matter tract integrity from childhood through adulthood will be necessary in order to fully understand how to interpret FA results.

Additionally, we found that involvement in sports was associated with FA of the left, but not the right, fornix. The majority of the literature examining the relationships between FA and exercise show no clear differences between left and right hemispheres, but past work with this sample may help explain the finding. While involvement in sports was associated with both left and right hippocampal volume, the relationship was slightly stronger with the left hippocampus [5]. Therefore, this difference between the left and right fornix somewhat parallels the left and right hippocampal volume results. However, because we had no a priori reason to predict a stronger relationship between involvement in sports and the left fornix over the right fornix, further research replicating this analysis in other samples will be necessary to more definitively interpret this result.

Another key finding was that FA of the left fornix was associated with the number of sports and activities in which a child was involved, but not with participation in specific categories of sports. This result differed from the pattern seen with hippocampal volume, where the strongest relationships were seen with team sports (restrictive definition) [5]. This finding suggests that changes in FA are more related to overall sports engagement, more akin to a dose response curve. Additionally, because FA was unrelated to participation in team, individual, or structured sports, it may be more related to exercise than any social factors a child might be exposed to while participating in team sports. Thus, while hippocampal volume seems to be impacted by the combination of exercise, social support, and structure that comes from being on a team, FA may be mostly impacted by the amount of exercise garnered through sports.

We also found that FA of the fornix and the parahippocampal cingulum was not related to depressive symptoms. This contrasts with multiple studies linking reduced FA in the cingulum to depressive symptoms [22–26]. Once again, this difference between our current results and the previous literature may be because of the age of our sample. Three of the aforementioned studies were in adults [22, 24, 26], and a final study was in adolescents between the age of 12 and 20 [25]. All of these samples are using participants older than the children in our sample, who were between the ages of 9 to 11 years old. Additionally, it may be possible that differences in FA associated with depression do not appear until later in life, as these effects could be a result of cumulative or severe depression or could be related to treatment status or experience.

A major limitation of our study was that dMRI data was collected on multiple types of scanners at different sites. Scanner type was included as a covariate in all analyses and did account for a significant portion of the variability in our FA measures. It is possible that this confound may have masked certain effects, though we did see significant relationships for the left fornix. A second limitation is that our data is all from one developmental time point, so we cannot infer causality between our constructs or yet understand developmental changes. Additionally, although highly significant, our effect sizes were all quite small, making it hard to conclude any public health implications. Finally, we hypothesized that sports involvement would be associated with FA of the fornix and parahippocampal cingulum, but it is possible that other white matter tracts that we did not examine could be related to these constructs.

The Adolescent Brain and Cognitive Development study is longitudinal, and future work will need to examine how the relationship between FA of the left fornix changes in relation to involvement in sports and depression over time. Monitoring FA of both the fornix and parahippocampal cingulum across development will be critical in order to determine how FA changes as a function of age. It is quite possible that the directionality of the relationships between involvement in sports, FA, and depression will change as the children develop. Examining these relationships longitudinally will also help tease out causality, particularly between involvement in sports and FA of the left fornix.

Summary

This study expanded on previous work to conclude that involvement in sports and activities is negatively associated with FA of the left fornix in children. This relationship was independent from the relationship of involvement in sports to hippocampal volume. However, FA of the fornix and parahippocampal cingulum were unrelated to depressive symptoms. This suggests that while hippocampal volume partially mediates the relationship between involvement in sports and depression, FA of these structures is not part of this pathway in children ages 9–11 years old.

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