

Involvement in Sports, Hippocampal Volume, and Depressive Symptoms in Children

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ABSTRACT

BACKGROUND: Recent studies have found that higher levels of exercise are associated with fewer symptoms of depression among young people. In addition, research suggests that exercise may modify hippocampal volume, a brain region that has been found to show reduced volume in depression. However, it is not clear whether this relationship emerges as early as preadolescence.

METHODS: We examined data from a nationwide sample of 4191 children 9 to 11 years of age from the Adolescent Brain and Cognitive Development Study. The parents of the children completed the Child Behavior Checklist, providing data about the child's depressive symptoms, and the Sports and Activities Questionnaire, which provided data about the child's participation in 23 sports. Children also took part in a structural magnetic resonance imaging scan, providing us with measures of bilateral hippocampal volume.

RESULTS: Sports involvement interacted with sex to predict depressive symptoms, with a negative relationship found in boys only ($t = -5.257$, $\beta = -.115$, $p < .001$). Sports involvement was positively correlated with hippocampal volume in both boys and girls ($t = 2.810$, $\beta = .035$, $p = .007$). Hippocampal volume also interacted with sex to predict depressive symptoms, with a negative relationship in boys ($t = -2.562$, $\beta = -.070$, $p = .010$), and served as a partial mediator for the relationship between involvement in sports and depressive symptoms in boys.

CONCLUSIONS: These findings help illuminate a potential neural mechanism for the impact of exercise on the developing brain, and the differential effects in boys versus girls mirror findings in the animal literature. More research is needed to understand the causal relationships between these constructs.

Keywords: Children, Depression, Exercise, Hippocampus, Neuroimaging, Structural

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Depression is associated with symptoms such as anhedonia, feelings of hopelessness, and suicidal ideation, and it can be debilitating in people of all ages (1). Unipolar depressive disorders are the third leading cause of the global burden of disease (2). Much of the research on depression has focused on adults. However, 3.1 million adolescents in the United States had at least one major depressive episode in 2016 alone (1). As such, it is imperative that more research be focused on understanding the development of depression in children and adolescents. Work that can identify early risk factors or pathways for prevention or early intervention in children and adolescents is particularly crucial. The goals of the current study are to examine the relationship between one potentially relevant factor, exercise, and depression in children, and to examine the neural mechanisms that might mediate such a relationship.

Exercise has been shown to have a positive relationship to mental health. For example, active lifestyles have been positively associated with reduced symptoms of depression and anxiety, improved self-concept, and more effective coping with stress (3). Additionally, a randomized controlled trial using older adults found that after 20 weeks, clinical depression had resolved in 73% of adults assigned to an exercise condition

but in only 36% of adults assigned to a control condition (4). Similarly, a meta-analysis found that resistance training significantly reduced depressive symptoms among adults (5). Fewer studies have examined the relationship between involvement in exercise and mental health in children. However, a review of reviews found that higher levels of exercise were significantly associated with fewer depression symptoms among young people 18 years of age and younger (6). Additionally, another study found that sports participation in high school was predictive of better school engagement, school performance, and self-esteem (7).

There are multiple aspects of exercise that may have beneficial effects on children and their mental health. One reason that exercise has a positive relationship to mental health may be because it often occurs through engagement in sports. Engagement in sports may be beneficial for mental health not just because of the exercise component but also potentially because of the social support that can arise from being a part of a team. One study found that being involved in at least one activity (sports, art, music, or another type of activity) was associated with higher life satisfaction, better self-rated health, and a lower frequency of feeling "low" (8). Interestingly, the strongest associations with healthy development

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indicators were found in adolescents engaged solely in sports and no other activities (8). This finding may suggest that there is something integral about sports that is causing their benefit over and above participation in organized activities in general.

Another mechanism by which exercise may relate to positive mental health is through its impact on the developing brain. Studies of rodents have found that aerobic exercise in the form of wheel running leads to increased neurogenesis and long-term potentiation in the dentate gyrus of the hippocampus (9). Furthermore, exercise promotes brain vascularization, changes in neuronal structure, neuronal resistance to injury, and increased levels of brain-derived neurotrophic factor in the hippocampus (10). Studies of humans show similar protective effects. In particular, aerobic exercise is associated with larger left and right hippocampi in elderly populations (11). In addition, a study of a 6-month aerobic exercise intervention in adults 60 to 79 years of age demonstrated increased regional gray matter volume in the frontal, parietal, and temporal lobes (12). Exercise also appears to have a beneficial effect on the brains of children. Greater aerobic fitness, measured through maximal oxygen uptake, is related to increased left middle prefrontal cortex volume and increased left precuneus and right occipital surface areas in male adolescents (13). Additionally, one study found that children who were more physically fit had greater bilateral hippocampal volumes, and that hippocampal volume mediated the relationship between fitness level and score on a relational memory task (14). Thus, it is important to understand the relationship between exercise and the hippocampus in preadolescent children.

The hippocampus has also been implicated in the development of depression (15–18). Hippocampal volume has been associated with depression symptom severity and illness duration (19) and the number of depressive episodes a person has experienced (20). Studies using younger populations have found similar associations between depression and hippocampal volume (21), with early-onset adolescent depression associated with a 17% reduction in left hippocampal volume (22). In addition, a meta-analysis found that patients with childhood-onset major depressive disorder had average reductions in hippocampal volume by 5.3% in the left hemisphere and 5.2% in the right hemisphere (23). The hippocampus is critical for the inhibition of the hypothalamic-pituitary-adrenal axis via the presence of glucocorticoid receptors that are part of a negative feedback loop (24). When cortisol levels are high, excitotoxic effects in the hippocampus may contribute to problems inhibiting the hypothalamic-pituitary-adrenal axis, resulting in even more cortisol and a problematic cascade (25). Depression has also been associated with the experience of life stress and altered stress reactivity, which may be at least part of the reason hippocampal volume may be reduced in patients with major depressive disorder (26,27).

As reviewed, exercise may be positively related to mental health in children for a number of reasons, including the potential positive impact of social support through engagement in team sports and/or a positive impact on brain development. Here we focus on hippocampal volume, given the combined animal and human literature that converges on the relationship between exercise and hippocampal structure and because of the putative association between hippocampal integrity and

depression. To examine these hypotheses, we used data from 4191 children 9 to 11 years of age from across the United States who were participating in the Adolescent Brain and Cognitive Development (ABCD) study. We predicted that 1) greater involvement in sports, but not nonsport activities, would predict both fewer depressive symptoms and larger hippocampal volumes; 2) the relationship between sports, depression, and hippocampal volume would remain even if we controlled for involvement in activities not related to sports; 3) if at least part of this effect was due to the social support engendered by team sports, this effect would be largest in the case of participation in team sports over and above individual sports; 4) children with depressive symptoms would have smaller hippocampal volumes than their healthy peers would; and 5) hippocampal volume would serve as the mediating variable between sports participation and depressive symptoms.

METHODS AND MATERIALS

Participants

Participants took part in the ABCD study, a longitudinal study tracking >11,800 children 9 to 11 years of age from 21 different sites across the United States. The sampling strategy to approximate national norms is described elsewhere (28). All study procedures were approved either by the centralized institutional review board at the University of California San Diego or by an individual participating site's institutional review board. 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, 333 had to be removed for the current analyses because the brain data were unusable ($n = 328$) or they did not fall into the male/female binary ($n = 5$). Of those who did not define their gender as male or female, 1 person was transgender female, 1 person described their gender as "different," and 3 people did not report gender. Therefore, 4191 children's data were used in the analyses reported below. For a comparison of demographics of male and female participants, see Table 1. For information regarding demographics of the included versus excluded participants, please see Supplemental Table S1.

Measures

The ABCD study included a number of measures of mental health related constructs (29). The Child Behavior Checklist (CBCL), completed by the child's caregiver, provides information about mental health problems in the child. We examined the child's age-corrected T score for the depressive subscale. For analyses examining anxiety, we used the child's age-corrected T score for the anxiety subscale. The Child Behavior Checklist test-retest reliability over 8 days was $r = .84$ for the depressive score and $r = .80$ for the anxiety score (30).

The Sports and Activities Involvement Questionnaire measures lifetime involvement in sports, activities such as music and dance, and other hobbies (see Supplemental Table S2). It provides a parent report of 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

Table 1. Demographics as a Function of Sex

Characteristics	Male (n = 2197) ^a	Female (n = 1994) ^a	t Score	p Value
Age, Months	120.44 ± 7.350 [108–132]	120.27 ± 7.225 [108–132]	0.740	.459
Total Activities	3.70 ± 2.682 [0–18]	3.93 ± 2.839 [0–20]	–2.706	.007
Sports	2.76 ± 2.056 [0–14]	2.75 ± 2.134 [0–18]	0.065	.948
Nonsport Activities	0.94 ± 1.137 [0–6]	1.17 ± 1.212 [0–6]	–6.456	<.001
CBCL Depression T Score	53.79 ± 5.954 [50–89]	52.98 ± 5.124 [50–86]	4.745	<.001
Average Hippocampal Volume, mm ³	4208.69 ± 395.06 [2779.45–5675.40]	3938.24 ± 378.0 [2111.30–5486.60]	22.034	<.001
Family Income Level			0.005	.996
<\$25,000	11	9.9		
\$25,000–\$49,999	12.1	13.1		
\$50,000–\$99,999	27.8	27.9		
>\$100,000	41.2	41.6		
Parent Education			0.394	.693
High school/GED or less	13.9	13.5		
Some college or associate's degree	29.3	26.5		
Bachelor's degree	30.0	31.7		
Greater than bachelor's	26.5	28.5		
χ^2 Value				
Sport Participation				
Team sport (broad definition)	84.0	81.9	3.36	.070
Team sport (restrictive definition)	74.9	52.4	231.50	<.001
Individual sport	61.6	55.1	18.29	<.001
Structured sport	85.2	83.6	2.05	.159
Race/Ethnicity				
Caucasian	81.7	80.4	1.17	.286
African American	13.9	15.9	3.52	.062
Other	4.4	3.7		
Hispanic	20.4	19.5	0.53	.484

CBCL, Child Behavior Checklist; GED, general education diploma.

^aData are presented as mean ± SD [minimum–maximum] or %.

different sports (see [Supplemental Table S2](#) for list). 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 a sport at school or in an organized outside league. In the team sport (restrictive definition) category, the child engaged in a sport at school or in an organized outside league, and it had to be one of the following sports that 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 a sport on his or her own time or through private lessons. Finally, in the structured sport category, the child engaged in a sport at school, through an organized outside league, or through private lessons. These categories of sports were not mutually exclusive. For example, participation in baseball would count as both a team sport (broad definition) and a team sport (restrictive definition). The nonsport

Table 2. Relationship Between Involvement in Sports and Depressive Symptoms

Independent Variable	Overall		Sex Interaction FDR p Value	Male		Female	
	β	t Score		β	t Score	β	t Score
No. of Activities	–.072	–4.481 ^c	.023 ^a	–.097	–4.391 ^c	–.021	–0.850
No. of Sports	–.089	–5.590 ^c	.023 ^a	–.115	–5.257 ^c	–.041	–1.655
No. of Nonsport Activities	–.007	–0.428	.350	—	—	—	—
Team Sport (Broad)	–.093	–5.816 ^c	.0035 ^b	–.129	–5.888 ^c	–.031	–1.248
Team Sport (Restrictive)	–.112	–6.909 ^c	.0035 ^b	–.139	–6.401 ^c	–.059	–2.540
Individual Sport	–.076	–4.897 ^c	.023 ^a	–.103	–4.789 ^c	–.037	–1.601
Structured Sport	–.097	–6.092 ^c	.0047 ^b	–.133	–6.070 ^c	–.038	–1.525

All analyses use covariates of age (in months), race, ethnicity, parental education, and family income.

FDR, false discovery rate.

^ap < .05.

^bp < .01.

^cp < .001.

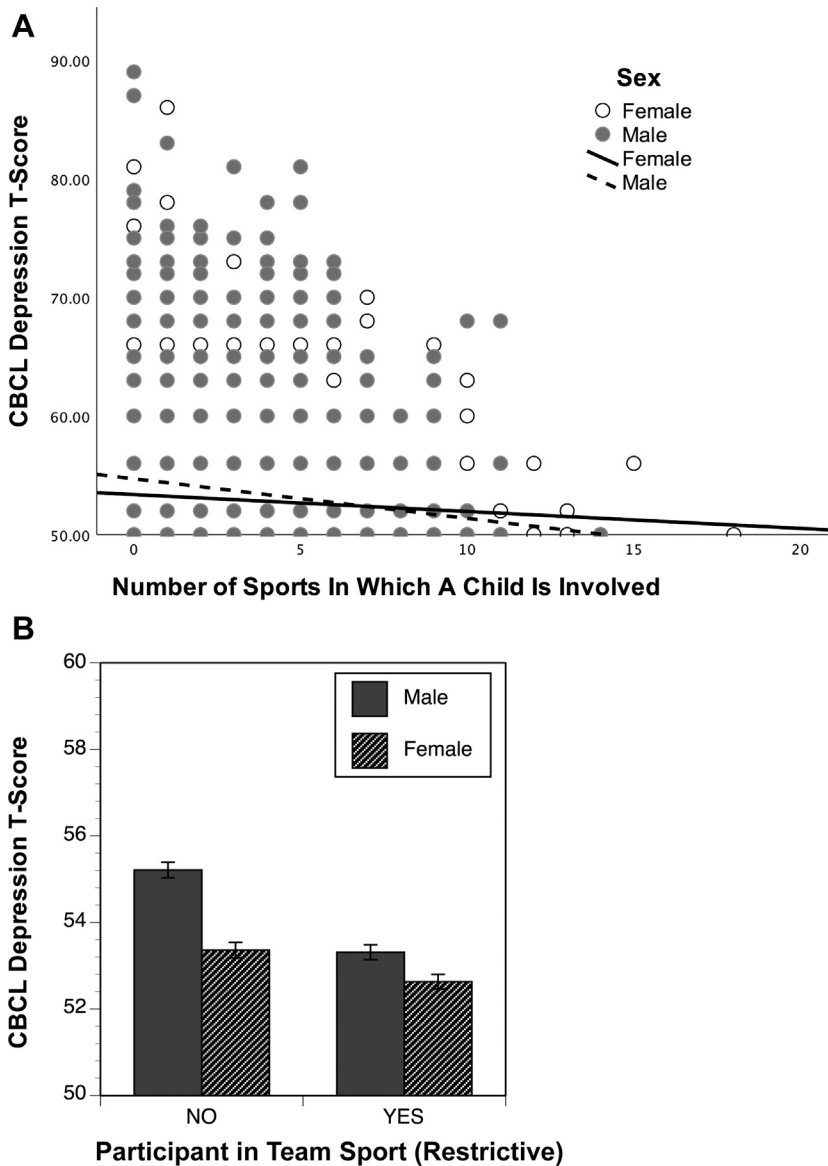


Figure 1. (A) Graph illustrating the relationship between depression symptom severity and the number of sports in which a child is involved. Regression lines are shown separately for girls and boys. Each dot represents >1 child. (B) Bar graph illustrating the relationship between participation in team sports (restrictive definition) and depression symptom severity, plotted separately for male children and female children. CBCL, Child Behavior Checklist.

activities that we examined are also listed in [Supplemental Table S2](#).

Magnetic Resonance Imaging Data

Brain data were collected across 21 sites on 3T scanners, specifically Siemens MAGNETOM Prisma scanners (Siemens Corp., Erlanger, Germany), GE Discovery MR750 scanners (GE Healthcare, Chicago, IL), and Philips Achieva scanners (Philips, Amsterdam, the Netherlands). The parameters for the T1 and T2 acquisitions for each of these platforms are listed in [Table 2](#) of the ABCD imaging article (31). The T1 and T2 images were corrected for gradient nonlinearity distortions, and the T2 images were registered to the T1 images using mutual information and atlas-based registration (32–34). Hippocampal and whole-brain volumes were computed from the preprocessed

T1 images using FreeSurfer version 5.3.0. Hippocampal and whole-brain volumes came from the “aseg” atlas. As we did not have hypotheses about the left versus right hippocampus, we combined them to form an average hippocampal volume variable, though analyses of left and right hippocampus separately provided similar results and are included in [Supplemental Table S7](#). The quality control of the T1 and T2 data is described in the ABCD image-processing article (35).

Analyses

The analyses used linear regressions that allowed us to provide standardized β weights as a measure of effect size. However, the sample included a number of sets of twins. Thus, to account for the twins in our analysis, we confirmed analyses using general linear models with participants nested within

sites and families. We carried out analyses for each sports category predicting depression and hippocampal volume and for the relationships between hippocampal volume and depression. We covaried for race, ethnicity, age, parental education, family income, and intracranial volume, and we included both sex and the interactions between sex and independent variable of interest as predictors. Significant interactions with sex were followed up with regressions within each sex.

We additionally carried out analyses examining the relationships between nonsport activities and depression and between sports and depression while controlling for involvement in nonsport activities. Likewise, we carried out analyses examining the relationship between nonsport activities and hippocampal volume. Finally, we examined the relationship between involvement in team sports and hippocampal volume while controlling for individual sports. To determine if our results were specific to depressive symptoms, we additionally examined the relationship between involvement in sports and activities and anxiety T score while controlling for depressive symptoms and vice versa. In all analyses, we used the false discovery rate (FDR) to correct for multiple comparisons (36,37). The mediation analysis used the process macro in SPSS, version 24 (IBM Corp., Armonk, NY). See the Supplement for additional analyses of sports “dose” relationships.

RESULTS

Table 1 describes the demographic characteristics of the children in the sample that we analyzed. We found that 3.8% of children scored in the borderline clinical range for depression and 2.8% scored in the clinical range. As shown in Table 2, greater participation in every category of sport, but not in nonsport activities, was associated with fewer depressive symptoms, even when we corrected for socioeconomic status, parental education, race, ethnicity, and age, with all relationships passing FDR correction. However, we also saw significant interactions with sex for all of the sports and/or activities predictors, with all but nonsport activities passing FDR correction. Follow-up analyses (Table 2) within sex indicated significant relationships between every type of activity and/or sport and depression in boys, but after FDR correction, no significant relationship was found in girls (Figure 1 and Supplemental Figure S1). Rerunning the analyses while controlling for involvement in nonsport activities did not affect any of the results. Moreover, as shown in Supplemental Table S3, no subcategory of nonsport activities (group, individual, or structured) had a significant relationship to depressive symptoms after FDR correction.

Interestingly, the relationship between sports involvement and mental health appeared to be specific to depression and not anxiety. When we tested the association between anxiety and each of the sport and activity categories (Supplemental Table S4) using depression as a covariate, the relationship was not significant for any activity. Further, as shown in Supplemental Table S5, when we used anxiety as a covariate and tested the relationships between sports and activities and depression, all results remained significant.

We next examined the relationships between the different types of sports and activities and hippocampal volume.

Greater participation in every category of sport and/or activity, except for individual sports and nonsport activities, was associated with larger hippocampal volume (Table 3). Involvement in team sports (both broad and restrictive) was associated with greater hippocampal volume, even when we controlled for involvement in individual sports. Interestingly, unlike the interactions we found with depressive symptoms, we found no significant interaction with sex for any of the activity and/or sport variables. Follow-up analyses split by sex indicated that all of the relationships were significant for boys, with a similar trend for girls (Figure 2). Rerunning the analyses while controlling for involvement in nonsport activities did not change the results. As shown in Supplemental Table S6, no subcategory of nonsport activity had a significant effect on average hippocampal volume. Finally, we tested the associations between involvement in sports and activities and left and right hippocampal volume separately. The relationships were similar in the left and right hippocampus (Supplemental Table S7), with the only difference being the relationships of number of activities and number of sports with right hippocampal volume, which were trend level.

The analyses predicting depressive symptoms from average hippocampal volume (see Figure 3) showed both a significant main effect ($t = -2.428$, $\beta = -.052$, $p = .015$) and a significant interaction with sex ($t = 2.101$, $\beta = .355$, $p = .036$). Follow-up analyses within sex indicated that hippocampal volume was negatively associated with depressive symptoms in male children ($t = -2.562$, $\beta = -.07$, $p = .010$) but not in female children ($t = -0.830$, $\beta = -.025$, $p = .41$). Furthermore, depressive symptoms in male children were predicted separately by both left hippocampal volume ($t = -2.572$, $\beta = -.067$, $p = .01$) and right hippocampal volume ($t = -2.122$, $\beta = -.058$, $p = .034$).

Finally, we used a mediation analysis to further test hypotheses about the relationship between sports and activities, hippocampal volume, and depressive symptoms in boys. As shown in Table 4, hippocampal volume partially

Table 3. Relationship Between Involvement in Sports and Average Hippocampal Volume

Independent Variable	Overall (Male and Female)			Sex Interaction FDR p Value
	β	t Score	FDR p Value	
No. of Activities	.035	2.806	.007 ^a	.803
No. of Sports	.035	2.810	.007 ^a	.803
No. of Nonsport Activities	.019	1.517	.129	.857
Participation in a Team Sport (Broad)	.042	3.429	.002 ^a	.803
Participation in a Team Sport (Restrictive)	.042	3.354	.002 ^a	.803
Participation in an Individual Sport	.020	1.630	.120	.803
Participation in a Structured Sport	.044	3.567	< .001 ^b	.803

All analyses use covariates of age (in months), race, ethnicity, parental education, family income, and intracranial volume.

^a $p < .01$.

^b $p < .001$.

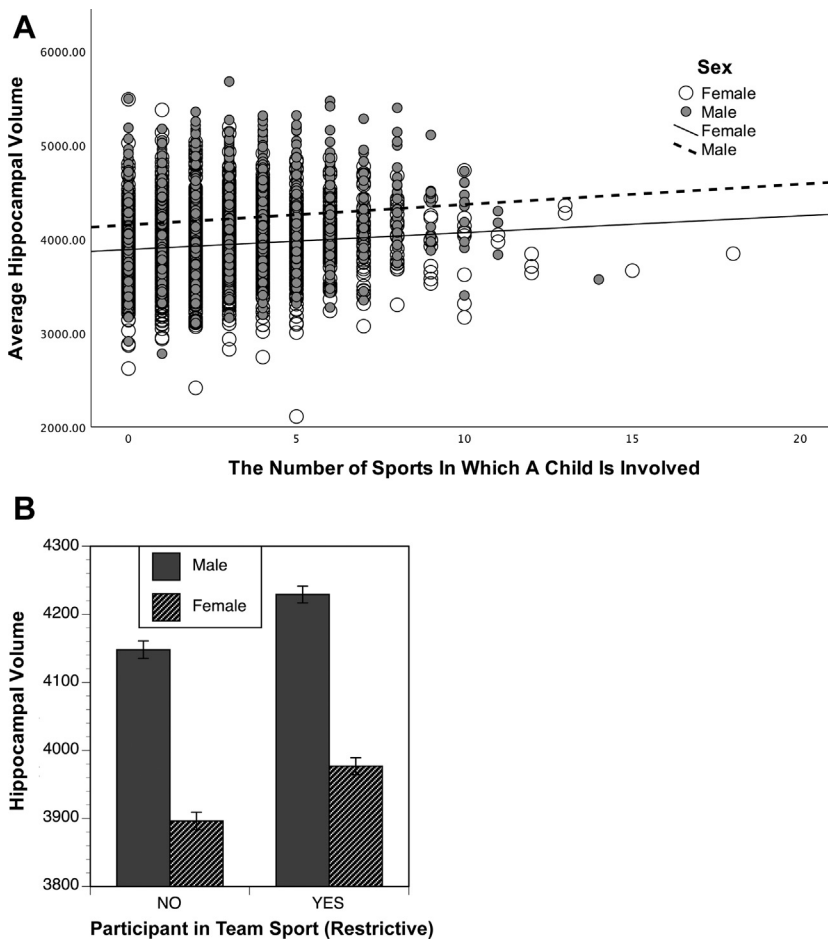


Figure 2. (A) Graph illustrating the relationship between hippocampal volume and the number of sports in which a child is involved. Regression lines are shown separately for girls and boys. Each dot represents >1 child. (B) Bar graph illustrating the relationship between participation in team sports (restrictive definition) and hippocampal volume, plotted separately for male children and female children.

mediated the relationship between depression and the number of activities, the number of sports, participation in both definitions of team sports, and participation in structured sports, though these predicted relationships would not survive FDR correction.

DISCUSSION

The goal of the current study was to better understand the relationship between sport and activity involvement and pre-adolescent children's brain development and mental health. Understanding the potential mechanisms of the relationship between participation in sports and depression is critical for developing informed public health guidelines about the importance of sources of exercise at a young age. We hypothesized that involvement in sports, but not nonsport activities, would predict fewer depressive symptoms, and this proved to be true across all subcategories of sports. However, surprisingly, these results held only among boys and not girls. Moreover, the beneficial effect of participation in sports was specific to depression and not anxiety symptoms. Additionally, we hypothesized that involvement in sports would be associated with larger hippocampal volume, and we found evidence for this relationship for all types of sports except individual

sports in both boys and girls. However, hippocampal volume was associated with depressive symptoms in male children only, and it partially mediated the relationships between involvement in multiple types of sports and depressive symptoms. Each of these results will be discussed in more detail below.

Our finding that greater sports involvement, but not nonsport activity involvement, was associated with less depression in boys suggests that exercise, a factor inherent to sports involvement, could be having antidepressant effects. This finding would be consistent with studies that found positive associations between active lifestyles and reduced depression, in addition to studies demonstrating exercise as an effective antidepressant (3–6). However, these earlier studies did not find sex differences. Our findings of sex specificity may relate to the age of our sample. Puberty tends to have an earlier onset in girls than in boys. Thus, during preadolescence, many boys may not yet be going through puberty, but girls may be starting to experience hormonal changes that may be having an impact on depression and might be obscuring the relationship between sports, hippocampal volume, and depression. Another contributor to this sex difference could be that young girls may be subject to cultural attitudes about sports that are very different from those boys are exposed to. If

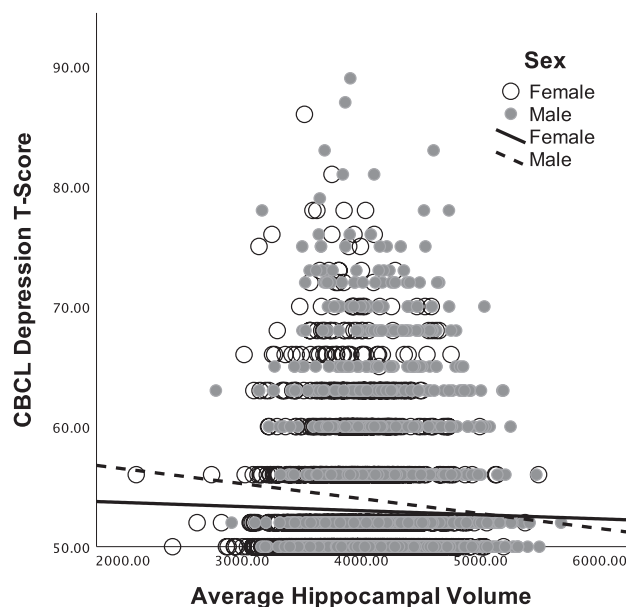


Figure 3. Graph illustrating the relationship between depression symptom severity and hippocampal volume. Regression lines are shown separately for girls and boys. Each dot represents >1 child. CBCL, Child Behavior Checklist.

a child is engaging in a sport for fun and it is not a stressful activity, it will have a very different effect than if it is played in a hypercompetitive environment. Moreover, if girls are engaging in sports in order to lose weight and fit society's thinness standards, the pressure may no longer make the sport a fun experience, taking away the antidepressant effects.

We also found that involvement in all types of sports except for individual sports and nonsport activities was related to hippocampal volume in both boys and girls. As involvement in sports usually implies exercise, this finding is consistent with numerous studies linking exercise to greater hippocampal volumes in both humans and animals (9–12,14). However, the fact that involvement in individual sports did not predict hippocampal volume suggests that there may be a beneficial component of being on a team or being part of a structured program over and above the benefit from exercise for children. This idea is further supported by the fact that when we examined the relationship between team sports (both broad

and restrictive definitions) and hippocampal volume controlling for involvement in individual sports, involvement in team sports was still a significant predictor of hippocampal volume. Research specifically looking at the effects of team sports over solitary exercise on hippocampal volume will be necessary to fully understand how these relationships manifest in children.

Finally, we found that hippocampal volume was associated with depression in boys only, which was partially consistent with past research. Numerous studies have found an association between greater depressive symptoms and reduced hippocampal volume (15–17). Hippocampal volume has also been shown to be associated with depressive symptom severity and illness duration (19) and number of depressive episodes (20). However, to our knowledge, this sex difference has not been previously reported in a preadolescent sample. On the other hand, at least two studies have found that male participants with depression showed smaller left hippocampal volume than that of male control participants, but this relationship did not hold in female participants (38,39). While most studies of adolescents did not report sex differences (21), one study did find a stronger reduction in hippocampal volume in depressed male adolescents, but the reduction was still present in female adolescents (22). One potential reason for the differences in findings may be sample size. Most studies of hippocampal volume in adolescents with depression, with sample sizes of less than 100, are not very well powered to detect sex differences (21,22). However, the ABCD data set, with over 4000 children, has the statistical power to detect sex differences that a smaller data set might not allow.

Our finding that hippocampal volume was more strongly related to depression in boys than girls is at least indirectly consistent with some of the animal literature related to depression. Animal models often use interventions such as maternal deprivation or limited bedding and nesting to induce depressive-like states in the rodents. A number of these studies have found poorer behavioral and structural and/or neurological outcomes in male rodents, with female rodents relatively spared (40–42). This sex difference may be related to hormone levels, as studies in both rats and humans have demonstrated neuroprotective effects of estrogen (43–45). Moreover, testosterone has been shown to increase vulnerability to neurotoxic processes in rats (46). Thus, more research must be done in humans to better understand how the brain develops differently in male and female humans, how environment and other activities might differentially influence brain development across sexes, and how this relates to mental health.

Table 4. Mediation Analysis of Hippocampal Volume With Sports and Depression in Boys

Independent Variable	Indirect Effect	Lower Confidence Interval	Upper Confidence Interval
No. of Activities	–0.0065	–0.0153	–0.0002
No. of Sports	–0.0082	–0.0199	–0.0004
Team Sport (Broad)	–0.0545	–0.1245	–0.0048
Team Sport (Restrictive)	–0.0391	–0.0946	–0.0026
Structured Sport	–0.0597	–0.1367	–0.0033

All analyses use covariates of age (in months), race, ethnicity, parental education, family income, and intracranial volume.

Limitations

The way in which the data were collected allowed us to determine the number of sports in which children had been involved across their lifetimes, but it was difficult to examine how many activities were occurring at the same time for each child. (See the Supplement for analyses of “dose” relationships during the most intense period of sports engagement.) In addition, it would have been useful to have other measures of physical fitness, such as maximal oxygen uptake. We did not ask the children about the level of competitiveness of their sport, and this factor could have influenced the degree to

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which they experienced positive support from the activity. In addition, the current analyses were based on cross-sectional data and thus cannot address causality. However, the ABCD study is longitudinal, and it will be important to examine how these relationships change over time, as this will give us further information about the potential causal relationships between involvement in sports, hippocampal development, and mental health outcomes. Lastly, while we found significant relationships that would be predicted by the prior work in adults and animals, the magnitude of the effect sizes were small, with significance achieved in part through the very large sample sizes. Nonetheless, the presence of these predicted relationships in a large population sample is intriguing and provides motivation for future studies that can better address questions of causality.

Future Directions

All of our results are associations, meaning that we cannot infer causality. However, the ABCD study is longitudinal, and future work can utilize this longitudinal data to tease out causality in the relationships between involvement in sports, hippocampal volume, and depressive symptoms. For example, it is unclear whether smaller hippocampal volume is a risk factor for depression or a consequence of onset of the disorder. A study of patients with varying numbers of past episodes of depression suggests that hippocampal volume decreases as a result of illness onset, but future analyses with the ABCD data set will help determine the direction of this relationship in children (47). Furthermore, while involvement in sports and/or social activities may help reduce depressive symptoms, it is also possible that being depressed makes someone less likely to participate in activities, and this could further lead to hippocampal changes. Monitoring these relationships as the ABCD children progress through adolescence will be critical for determining the temporal dimension of these relationships. The majority of the children in this baseline ABCD sample were in prepuberty or early puberty. It is possible that the relationships examined here will change as a function of puberty status, and in future analysis, it will be important to examine puberty levels in order to explore our sex difference finding.

Conclusions

This study was one of the first, to our knowledge, to show that involvement in sports is associated with the mental health and brain development of children as young as 9 to 11 years of age. Involvement in sports was associated with fewer depressive symptoms in boys, and this relationship was partially mediated by hippocampal volume. These associations highlight potential causal mechanisms that can be investigated using longitudinal data. This finding is critical for public policy, because if involvement in sports does change children's brain development through the impact on the hippocampus and related networks, there is a strong incentive to encourage children as young as 9 to 11 years of age to participate in sports regularly.

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LSG and DMB had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

LSG, DMB, JH, and TJ were responsible for the concept and design of analyses; acquisition, analysis, or interpretation of data; critical revision of the manuscript for important intellectual content; and administrative, technical, or material support. LSG and DMB were responsible for the drafting of the manuscript and for statistical analysis. TJ and DMB obtained funding. DMB supervised.

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All authors report no biomedical financial interests or potential conflicts of interest.

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REFERENCES

1. National Institute of Mental Health (2017): Major depression. Available at: <https://www.nimh.nih.gov/health/statistics/major-depression.shtml>. Accessed June 11, 2018.
2. World Health Organization (2004): Part 4: Burden of disease: DALYs. In: Mathers C, Boerma T, editors. *Fat DM. The Global Burden of Disease: 2004 Update*. Geneva, Switzerland: WHO Press, 39–52.
3. Stephens T (1988): Physical activity and mental health in the United States and Canada: Evidence from four population surveys. *Prev Med* 17:35–47.
4. Singh NA, Clements KM, Singh MA (2001): The efficacy of exercise as a long-term antidepressant in elderly subjects: A randomized, controlled trial. *J Gerontol A Biol Sci Med Sci* 56:M497–M504.
5. Gordon BR, McDowell CP, Hallgren M, Meyer JD, Lyons M, Herring MP (2018): Association of efficacy of resistance exercise training with depressive symptoms: Meta-analysis and meta-regression analysis of randomized clinical trials. *JAMA Psychiatry* 75:566–576.
6. Biddle SJ, Asare M (2011): Physical activity and mental health in children and adolescents: A review of reviews. *Br J Sports Med* 45:886–895.
7. Bohnert AM, Aikins JW, Arola NT (2013): Regrouping: Organized activity involvement and social adjustment across the transition to high school. *New Dir Child Adolesc Dev* 2013:57–75.
8. Badura P, Geckova AM, Sigmundova D, van Dijk JP, Reijneveld SA (2015): When children play, they feel better: Organized activity participation and health in adolescents. *BMC Public Health* 15:1090.
9. van Praag H, Christie BR, Sejnowski TJ, Gage FH (1999): Running enhances neurogenesis, learning, and long-term potentiation in mice. *Proc Natl Acad Sci U S A* 96:13427–13431.
10. Cotman CW, Berchtold NC (2002): Exercise: A behavioral intervention to enhance brain health and plasticity. *Trends Neurosci* 25:295–301.
11. Erickson KI, Prakash RS, Voss MW, Chaddock L, Hu L, Morris KS, et al. (2009): Aerobic fitness is associated with hippocampal volume in elderly humans. *Hippocampus* 19:1030–1039.

12. Colcombe SJ, Erickson KI, Scaff PE, Kim JS, Prakash R, McAuley E, *et al.* (2006): Aerobic exercise training increases brain volume in aging humans. *J Gerontol A Biol Sci Med Sci* 61:1166–1170.
13. Herting MM, Keenan MF (2017): Exercise and the developing brain in children and adolescents. In: Watson RR, editor. *Physical Activity and the Aging Brain: Effects of Exercise on Neurological Function*. Cambridge, MA: Academic Press, 13–19.
14. Chaddock L, Erickson KI, Prakash RS, Kim JS, Voss MW, Vanpatter M, *et al.* (2010): A neuroimaging investigation of the association between aerobic fitness, hippocampal volume, and memory performance in preadolescent children. *Brain Res* 1358:172–183.
15. Cole J, Costafreda SG, McGuffin P, Fu CH (2011): Hippocampal atrophy in first episode depression: A meta-analysis of magnetic resonance imaging studies. *J Affect Disord* 134:483–487.
16. Norbury R, Godlewska B, Cowen PJ (2014): When less is more: A functional magnetic resonance imaging study of verbal working memory in remitted depressed patients. *Psychol Med* 44:1197–1203.
17. Suzuki H, Botteron KN, Luby JL, Belden AC, Gaffrey MS, Babb CM, *et al.* (2013): Structural-functional correlations between hippocampal volume and cortico-limbic emotional responses in depressed children. *Cogn Affect Behav Neurosci* 13:135–151.
18. Malykhin NV, Carter R, Seres P, Coupland NJ (2010): Structural changes in the hippocampus in major depressive disorder: Contributions of disease and treatment. *J Psychiatry Neurosci* 35:337–343.
19. Cheng YQ, Xu J, Chai P, Li HJ, Luo CR, Yang T, *et al.* (2010): Brain volume alteration and the correlations with the clinical characteristics in drug-naïve first-episode MDD patients: A voxel-based morphometry study. *Neurosci Lett* 480:30–34.
20. Videbech P, Ravnkilde B (2004): Hippocampal volume and depression: A meta-analysis of MRI studies. *Am J Psychiatry* 161:1957–1966.
21. Rao U, Chen LA, Bidesi AS, Shad MU, Thomas MA, Hammen CL (2010): Hippocampal changes associated with early-life adversity and vulnerability to depression. *Biol Psychiatry* 67:357–364.
22. MacMaster FP, Kusumakar V (2004): Hippocampal volume in early onset depression. *BMC Med* 2:2.
23. McKinnon MC, Yucel K, Nazarov A, MacQueen GM (2009): A meta-analysis examining clinical predictors of hippocampal volume in patients with major depressive disorder. *J Psychiatry Neurosci* 34: 41–54.
24. Frodl T, O'Keane V (2013): How does the brain deal with cumulative stress? A review with focus on developmental stress, HPA axis function and hippocampal structure in humans. *Neurobiol Dis* 52: 24–37.
25. Sapolsky RM, Krey LC, McEwen BS (1986): The neuroendocrinology of stress and aging: The glucocorticoid cascade hypothesis. *Endocr Rev* 7:284–301.
26. Burke HM, Davis MC, Otte C, Mohr DC (2005): Depression and cortisol responses to psychological stress: A meta-analysis. *Psychoneuroendocrinology* 30:846–856.
27. Kessler RC (1997): The effects of stressful life events on depression. *Annu Rev Psychol* 48:191–214.
28. Garavan H, Bartsch H, Conway K, Decastro A, Goldstein RZ, Heeringa S, *et al.* (2018): Recruiting the ABCD sample: Design considerations and procedures. *Dev Cogn Neurosci* 32:16–22.
29. Barch DM, Albaugh MD, Avenevoli S, Chang L, Clark DB, Glantz MD, *et al.* (2018): Demographic, physical and mental health assessments in the adolescent brain and cognitive development study: Rationale and description. *Dev Cogn Neurosci* 32:55–66.
30. Achenbach TM, Rescorla LA (2007): *Manual for the ASEBA School-Age Forms and Profiles*. Burlington, VT: University of Vermont, Research Center for Children, Youth and Families.
31. Casey BJ, Cannonier T, Conley MI, Cohen AO, Barch DM, Heitzeg MM, *et al.* (2018): The Adolescent Brain Cognitive Development (ABCD) study: Imaging acquisition across 21 sites. *Dev Cogn Neurosci* 32:43–54.
32. Dale AM, Fischl B, Sereno MI (1999): Cortical surface-based analysis. I. Segmentation and surface reconstruction. *Neuroimage* 9:179–194.
33. Fischl B, Salat DH, Busa E, Albert M, Dieterich M, Haselgrove C, *et al.* (2002): Whole brain segmentation: Automated labeling of neuroanatomical structures in the human brain. *Neuron* 33:341–355.
34. Fischl B, Sereno MI, Dale AM (1999): Cortical surface-based analysis. II: Inflation, flattening, and a surface-based coordinate system. *Neuroimage* 9:195–207.
35. Hagler DJ, Hatton SN, Makowski C, Cornejo MD, Fair DA, Dick AS, *et al.* (2018): Image processing and analysis methods for the Adolescent Brain Cognitive Development Study [published online ahead of print Nov 4]. *bioRxiv*.
36. Benjamini Y, Hochberg H (1995): Controlling the false discovery rate: A practical and powerful approach to multiple testing. *J R Stat Soc Series B Stat Methodol* 57:289–300.
37. Benjamini Y, Yekutieli D (2001): The control of the false discovery rate: A practical and powerful approach to multiple testing. *Ann Stat* 29:1165–1188.
38. Kronmüller KT, Schröder J, Kohler S, Gotz B, Victor D, Unger J, *et al.* (2009): Hippocampal volume in first episode and recurrent depression. *Psychiatry Res* 174:62–66.
39. Frodl T, Meisenzahl EM, Zetsche T, Born C, Groll C, Jäger M, *et al.* (2002): Hippocampal changes in patients with a first episode of major depression. *Am J Psychiatry* 159:1112–1118.
40. Loi M, Mossink JC, Meerhoff GF, Den Blaauwen JL, Lucassen PJ, Joels M (2017): Effects of early-life stress on cognitive function and hippocampal structure in female rodents. *Neuroscience* 342:101–119.
41. Oomen CA, Girardi CE, Cahyadi R, Verbeek EC, Krugers H, Joels M, *et al.* (2009): Opposite effects of early maternal deprivation on neurogenesis in male versus female rats. *PLoS One* 4:e3675.
42. Walker CD, Bath KG, Joels M, Korosi A, Larauche M, Lucassen PJ, *et al.* (2017): Chronic early life stress induced by limited bedding and nesting (LBN) material in rodents: Critical considerations of methodology, outcomes and translational potential. *Stress* 20:421–448.
43. Alkayed NJ, Harukuni I, Kimes AS, London ED, Traystman RJ, Hum PD (1998): Gender-linked brain injury in experimental stroke. *Stroke* 29:159–165; discussion 166.
44. Miller DB, Ali SF, O'Callaghan JP, Laws SC (1998): The impact of gender and estrogen on striatal dopaminergic neurotoxicity. *Ann N Y Acad Sci* 844:153–165.
45. Singer CA, Rogers KL, Dorsa DM (1998): Modulation of Bcl-2 expression: A potential component of estrogen protection in NT2 neurons. *Neuroreport* 9:2565–2568.
46. Nishino H, Nakajima K, Kumazaki M, Fukuda A, Muramatsu K, Deshpande SB, *et al.* (1998): Estrogen protects against while testosterone exacerbates vulnerability of the lateral striatal artery to chemical hypoxia by 3-nitropropionic acid. *Neurosci Res* 30:303–312.
47. MacQueen GM, Campbell S, McEwen BS, Macdonald K, Amano S, Joffe RT, *et al.* (2003): Course of illness, hippocampal function, and hippocampal volume in major depression. *Proc Natl Acad Sci U S A* 100:1387–1392.