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Incidence of concussion and recovery of neurocognitive dysfunction on ImPACT assessment among youth athletes with premorbid depression or anxiety taking antidepressants

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OBJECTIVE Concussions in youth sports comprise an estimated 1.6–3.8 million annual injuries in the US. Sex, age, and attention-deficit hyperactivity disorder (ADHD) have been identified as salient risk factors for concussion. This study seeks to evaluate the role of premorbid depression or anxiety (DA), with or without antidepressant use, on the incidence of concussion and the recovery of symptoms and neurocognitive dysfunction after concussion.

METHODS Immediate Postconcussion Assessment and Cognitive Testing (ImPACT) was administered to 7453 youth athletes at baseline. Throughout the season, concussions were examined by physicians and athletic trainers, followed by readministration of ImPACT postinjury (PI) and again at follow-up, a median of 7 days PI. Individuals were divided into three categories: 1) unmedicated athletes with DA (DA-only, n = 315), athletes taking antidepressants (DA-meds, n = 81), and those without DA or antidepressant use (non-DA, n = 7039). Concussion incidence was calculated as the total number of concussions per total number of patient-years. The recovery of neurocognitive measures PI was calculated as standardized deviations from baseline to PI and then follow-up in the 5 composite ImPACT scores: symptom score, verbal memory, visual memory, visual motor skills, and reaction time. Univariate results were confirmed with multivariate analysis.

RESULTS There was no difference in concussion incidence between the DA-only cohort and the non-DA group. However, the DA-meds group had a significantly greater incidence of concussion than both the DA-only group (OR 2.67, 95% CI 1.88–7.18, p = 0.0001) and the non-DA group (OR 2.19, 95% CI 1.16–4.12, p = 0.02). Deviation from baseline in PI symptom scores was greater among the DA-meds group as compared to the non-DA group (OR 1.14, 95% CI 1.01–1.28, p = 0.03). At follow-up, the deviation from baseline in symptom scores remained elevated among the DA-meds group as compared to the non-DA group (OR 1.62, 95% CI 1.20–2.20, p = 0.002) and the DA-only group (OR 1.87, 95% CI 1.12–3.10, p = 0.02). Deviation from baseline in follow-up verbal memory was also greater among the DA-meds group as compared to both the non-DA group (OR 1.57, 95% CI 1.08–2.27, p = 0.02) and the DA-only group (OR 1.66, 95% CI 1.03–2.69, p = 0.04).

CONCLUSIONS Premorbid DA itself does not seem to affect the incidence of concussion or the recovery of symptoms and neurocognitive dysfunction PI. However, antidepressant use for DA is associated with 1) increased concussion incidence and 2) elevated symptom scores and verbal memory scores up to 7 days after concussion, suggesting impaired symptomatic and neurocognitive recovery on ImPACT.

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KEYWORDS antidepressants; anxiety; concussion; depression; ImPACT; trauma

ABBREVIATIONS ADHD = attention-deficit hyperactivity disorder; DA = depression or anxiety; DLD = diagnosed learning disability; ImPACT = Immediate Postconcussion Assessment and Cognitive Testing; PCSS = Post-Concussion Symptom Scale; PI = postinjury.

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Concussions continue to be a concern among adolescent athletes in the US with an estimated 1.6–3.8 million annual injuries.[1] Despite concerns, participation in youth sports remains popular because of significant physical, cognitive, and lifestyle benefits.[2] As such, characterizing risk factors for concussion and minimizing their effects remains important. Sex, age, a significant history of past concussions, and psychiatric illness such as attention-deficit hyperactivity disorder (ADHD) have already been identified as salient risk factors for concussion by the Concussion in Sport Group.[3] However, the role of premorbid depression or anxiety (DA), with or without antidepressant use, in the incidence of concussion and the recovery of symptoms and neurocognitive dysfunction postinjury (PI) has not been as clearly identified.[4]

DA, which presents as postconcussion sequelae in 30% of youth athletes, has been hypothesized to increase the risk for subsequent concussions by prolonging recovery of the initial injury.[4,5] However, symptoms of mood disorders overlap with those of concussion, making it difficult to differentiate the two and test the hypothesis. Analyzing premorbid DA diagnoses would separate overlap between mood disorders and postconcussion symptomology, allowing us to better understand how DA itself affects youth concussions.[4,5] To the best of our knowledge, no previous study has addressed whether patients with preexisting DA are at a higher baseline risk of being concussed.[4–7] Premorbid depression has, however, been associated with increased symptom scores, separately at both baseline and PI with Immediate Postconcussion Assessment and Cognitive Testing (ImPACT).[6,7] But such changes have not been longitudinally tracked, providing only a snapshot in the clinical course, either at baseline or PI. Additionally, it is unknown whether premorbid antidepressant use, currently used to treat postconcussion depression, affects the incidence of concussion or the recovery of symptoms and neurocognitive dysfunction PI.[8]

The present study examines concussion incidence and longitudinal neurocognitive testing among a large cohort of adolescent athletes with premorbid DA, differential antidepressant use, and ImPACT administered at baseline and twice PI. In doing so, this study seeks to improve our understanding of how DA and antidepressants affect concussions among youth athletes.

Methods

Data Collection and Subject Cohorts

Data were collected from 7453 subjects aged 12–22 years at baseline. Ninety percent of the athletes were of high school age (14–18 years old). Data included a questionnaire of demographic information and clinical history, a Post-Concussion Symptom Scale (PCSS) survey, and 39 separate ImPACT neurocognitive tests. The PCSS survey contributed to the "symptom score" composite, and the ImPACT neurocognitive tests contributed to the "verbal memory," "visual memory," "visual motor skills," and "reaction time" composites, for a total of 5 composite scores.[9]

Patients were divided into three categories: 1) those with DA and not taking antidepressants (DA-only, n = 315); 2) those taking antidepressants (DA-meds, n = 81); and 3) those without DA and not taking any antidepressants (non-DA, n = 7039). Antidepressants used by participants included fluoxetine, duloxetine, escitalopram, sertraline, and others. The IRB at the Icahn School of Medicine at Mount Sinai approved the study for human subject research. It was deemed exempt from informed consent as the data were de-identified prior to analysis.

Concussion Definition and Incidence

Student athletes were part of athletic organizations located in Westminster, Colorado; Durango, Colorado; Orlando, Florida; and Tallahassee, Florida. Throughout the season, sports-related head injuries were examined by physicians and athletic trainers. Concussions were defined as blunt trauma to the head or face causing a rapid alteration of the individual's mental status and/or the appearance of multiple symptoms not present before the injury, such as headaches, dizziness, nausea, vomiting, and blurred vision. Incidence of concussions was calculated as the total number of concussions per total number of patient-years in each of the three cohorts. Patient-years were calculated per Centers for Disease Control and Prevention guidelines.[10]

Longitudinal Neurocognitive Testing

After concussion, ImPACT was readministered at two sequential follow-up visits to track the recovery or persistence of symptoms and neurocognitive dysfunction over time.[11] The first visit was PI and the second was at follow-up, a median of 7 days after PI. Deviations from baseline to PI and then follow-up in the 5 composite ImPACT scores were used to track the recovery or persistence of symptoms and neurocognitive dysfunction postconcussion.[11] Deviations were standardized by S_{diff}.

Statistical Analysis

Statistical analysis was performed by GraphPad Prism (version 7.0, GraphPad Software) and RStudio (RStudio Software). Chi-square tests followed by Bonferroni's post hoc test and 1-way ANOVAs followed by Tukey's post hoc test were used in univariate analysis. Multivariate analysis accounted for demographic data and clinical history covariates including age, sex, football participation, ADHD diagnosis, ADHD stimulant use (amphetamine/dextroamphetamine, methylphenidate, or lisdexamfetamine), diagnosed learning disabilities (DLDs), epilepsy, dyslexia, autism, premorbid headaches, premorbid migraines, and a history of two or more concussions. A p value < 0.05 was considered significant for all tests.

Results

Cohort Demographics

The average age of all three cohorts was 15.4 years old (Table 1). The two DA cohorts (DA-only and DA-meds) were more than 50% female, whereas the non-DA cohort was 33% female. Approximately 30% of both DA cohorts participated in football, whereas 40% of the non-DA cohort played football. Other sports included soccer (12% overall prevalence), basketball (9%), volleyball (6%), la-

TABLE 1. Cohort demographics

Variable	DA-Only (n = 315)	DA-Meds (n = 81)	Non-DA (n = 7039)	p Value		
				DA-Only vs DA-Meds	DA-Only vs Non-DA	DA-Meds vs Non-DA
Mean age (SD), yrs	15.5 (1.4)	15.3 (1.6)	15.4 (1.6)	0.64	0.48	0.87
Female	67.2%	54.9%	33.2%	0.09	**<0.0001**	**<0.0001**
Football	27.8%	26.2%	39.9%	0.88	**<0.0001**	**0.04**
ADHD	11.5%	18.8%	5.0%	0.21	**<0.0001**	**0.03**
DLD	8.2%	8.0%	2.6%	>0.99	**<0.0001**	**0.02**
Headaches	12.6%	13.1%	10.8%	>0.99	**0.04**	0.53
Migraines	6.4%	4.9%	7.7%	>0.99	0.44	0.63
Hx of concussion (>2)	14.2%	9.8%	8.2%	0.43	**0.0001**	0.64

Hx = history.
Boldface type indicates statistical significance.

crosse (6%), baseball or softball (6%), cheerleading (4%), and wrestling (4%). From the entire cohort, 7% had DA, 21% of whom were taking medications for DA. The prevalence of ADHD and DLD was greater in both DA cohorts compared with the non-DA group. The DA-only cohort also had a significantly greater incidence of premorbid headaches and clinical history of more than two concussions than the non-DA group.

Of those patients who reported medication use at the first follow-up, 85% indicated continued use of antidepressants from the preseason baseline. For ADHD stimulants, a classic set of long-term chronic pharmaceuticals, the analogous rate of medication continuation from baseline to the first follow-up was 89%.

Concussion Incidence

The DA-only group had an incidence of 50.2 concussions per 100 patient-years (Table 2). There was no difference in concussion incidence between the DA-only cohort and the non-DA group, which had a concussion incidence of 52.6 concussions per 100 patient-years ($p = 0.40$). However, the DA-meds group had an incidence of 89.7 concussions per 100 patient-years. This was greater than both the DA-only group ($p < 0.0001$) and the non-DA group ($p < 0.0001$). Differences in concussion incidence between the DA-meds cohort and the other two cohorts remained significant after multivariate analysis accounting for age, sex, football players, ADHD, DLD, chronic headaches, chronic migraines, and concussion history. The DA-meds group was twice as likely to get a concussion than the non-DA group (OR 2.19, 95% CI 1.16–4.12, $p = 0.02$), and almost three times as likely to suffer a concussion as compared to the DA-only cohort (OR 2.67, 95% CI 1.88–7.18, $p = 0.0001$; Table 3).

ImPACT PI

Deviations from preseason ImPACT to PI in 4 of the 5 composite scores—verbal memory, visual memory, visual motor skills, and reaction time—were elevated to a similar extent across the three cohorts. However, the DA-meds group had a greater deviation from baseline in PI symptom scores than the non-DA group (DA-meds 1.8, non-DA 1.1, $p = 0.03$). This difference in symptom score between the DA-meds and non-DA groups stemmed from all 4 symptom clusters: migraine (DA-meds 6.5, non-DA 2.5, $p < 0.0001$), cognitive (DA-meds 4.8, non-DA 1.9, $p < 0.0001$), sleep (DA-meds 1.3, non-DA 0.5, $p = 0.002$), and neuropsychiatric (DA-meds 1.8 non-DA 0.6, $p = 0.001$; Table 4). Although the DA-only group did not have a greater deviation from baseline in PI symptom scores than the non-DA

TABLE 2. Incidence and severity of concussions

Concussion Variable	DA-Only	DA-Meds	Non-AD	Test	p Value		
					DA-Only vs DA-Meds	DA-Only vs Non-DA	DA-Meds vs Non-DA
Incidence							
No./patient-yrs	50.2/100	89.7/100	52.6/100	Chi-square	**<0.0001**	0.3957	**<0.0001**
Severity, mean ± SD change from baseline							
Symptom score	1.40 ± 0.13	1.79 ± 0.33	1.12 ± 0.03	ANOVA	0.3636	0.0587	**0.0283**
Verbal memory	0.79 ± 1.48	0.71 ± 0.20	0.68 ± 0.02	ANOVA	0.9261	0.4298	0.9834
Visual memory	0.39 ± 0.06	0.36 ± 0.10	0.40 ± 0.01	ANOVA	0.9643	0.9776	0.9246
Visual motor skills	0.46 ± 0.07	0.44 ± 0.15	0.36 ± 0.01	ANOVA	0.9839	0.2231	0.8251
Reaction time	1.13 ± 0.77	1.09 ± 2.48	0.96 ± 0.3	ANOVA	0.9944	0.4656	0.8970

Boldface type indicates statistical significance.

TABLE 3. Multivariate analysis of concussion incidence and severity

Comparison	OR	95% CI	p Value
DA-meds (1) vs non-DA (0)*			
Concussion incidence	2.19	1.16–4.12	**0.0158**
Concussion symptom score (per point)	1.14	1.01–1.28	**0.0292**
Migraine cluster (per point)	1.06	1.03–1.09	**<0.0001**
Cognitive cluster (per point)	1.08	1.04–1.12	**0.0002**
Sleep cluster (per point)	1.17	1.05–1.30	**0.0047**
Neuropsychiatric cluster (per point)	1.11	1.04–1.19	**0.0021**
DA-meds (1) vs DA-only (0)			
Concussion incidence	2.67	1.88–7.18	**0.0001**

Boldface type indicates statistical significance. Covariates included age, sex, football, DLDs, premorbid headaches, premorbid migraines, and history of concussion (> 2).
* (1) represents the dependent variable for which the logistic regression was run, as compared to (0), which is the variable that was compared.

group, it still had greater deviation in 3 of the 4 symptom clusters: migraine, cognitive, and neuropsychiatric. After multivariate analysis, the DA-meds group still had greater deviations from baseline in PI symptom scores than the non-DA group (OR per point 1.14, 95% CI 1.01–1.28, p = 0.03). This difference was driven by all 4 symptom clusters: migraine (OR per point 1.06, 95% CI 1.03–1.09, p < 0.0001), cognitive (OR per point 1.08, 95% CI 1.04–1.12,

TABLE 4. Change in individual symptom scores between baseline and PI

	Mean Change From Baseline (± SD)			p Value		
Symptom Clusters	DA-Only	DA-Meds	Non-DA	DA-Only vs DA-Meds	DA-Only vs Non-DA	DA-Meds vs Non-DA
Migraine	4.446 (± 0.469)	6.500 (± 1.169)	2.475 (± 0.083)	0.06	**<0.0001**	**<0.0001**
Headache	0.942 (± 0.101)	1.440 (± 0.236)	0.649 (± 0.019)	**0.04**	**0.003**	**<0.0001**
Vomiting	0.038 (± 0.017)	0.060 (± 0.044)	0.031 (± 0.004)	0.86	0.093	0.73
Nausea	0.483 (± 0.070)	0.820 (± 0.203)	0.212 (± 0.011)	**0.01**	**<0.0001**	**<0.0001**
Balance	0.525 (± 0.075)	0.840 (± 0.190)	0.273 (± 0.012)	**0.04**	**<0.0001**	**<0.0001**
Dizziness	0.758 (± 0.093)	0.800 (± 0.200)	0.359 (± 0.014)	0.96	**<0.0001**	**0.005**
Sensitivity to light	0.738 (± 0.090)	1.140 (± 0.221)	0.446 (± 0.016)	0.06	**0.0003**	**<0.0001**
Sensitivity to noise	0.717 (± 0.085)	0.920 (± 0.191)	0.390 (± 0.015)	0.43	**<0.0001**	**0.001**
Numbness	0.217 (± 0.053)	0.180 (± 0.093)	0.074 (± 0.006)	0.87	**<0.0001**	0.25
Visual	0.375 (± 0.068)	0.620 (± 0.145)	0.204 (± 0.010)	0.09	**0.001**	**0.0003**
Cognitive	3.408 (± 0.411)	4.760 (± 1.062)	1.901 (± 0.066)	0.16	**<0.0001**	**<0.0001**
Fatigue	0.654 (± 0.087)	0.940 (± 0.218)	0.315 (± 0.014)	0.14	**<0.0001**	**<0.0001**
Drowsiness	0.554 (± 0.078)	0.800 (± 0.206)	0.365 (± 0.014)	0.26	**0.01**	**0.007**
Slowed down	0.642 (± 0.088)	1.020 (± 0.224)	0.307 (± 0.013)	**0.02**	**<0.0001**	**<0.0001**
Fogginess	0.633 (± 0.082)	1.06 (± 0.218)	0.338 (± 0.014)	**0.02**	**<0.0001**	**<0.0001**
Concentration	0.708 (± 0.086)	0.820 (± 0.191)	0.446 (± 0.016)	0.80	**0.001**	**0.049**
Memory	0.492 (± 0.076)	0.680 (± 0.170)	0.257 (± 0.012)	0.33	**<0.0001**	**0.001**
Sleep	0.754 (± 0.130)	1.280 (± 0.344)	0.506 (± 0.022)	0.09	0.05	**0.002**
Falling asleep	0.342 (± 0.059)	0.520 (± 0.170)	0.239 (± 0.012)	0.37	0.16	0.05
Sleeping more	0.363 (± 0.077)	0.640 (± 0.215)	0.189 (± 0.011)	0.06	**0.003**	**0.0002**
Sleeping less	0.242 (± 0.058)	0.400 (± 0.167)	0.154 (± 0.009)	0.28	0.11	**0.03**
Neuropsychiatric	1.400 (± 0.228)	1.840 (± 0.544)	0.648 (± 0.032)	0.45	**<0.0001**	**0.001**
Irritability	0.504 (± 0.073)	0.760 (± 0.180)	0.256 (± 0.012)	0.12	**<0.0001**	**<0.0001**
Nervousness	0.313 (± 0.063)	0.420 (± 0.137)	0.139 (± 0.009)	0.51	**<0.0001**	**0.005**
Sadness	0.363 (± 0.065)	0.540 (± 0.162)	0.137 (± 0.009)	0.19	**<0.0001**	**<0.0001**
More emotional	0.396 (± 0.065)	0.560 (± 0.157)	0.187 (± 0.010)	0.34	**<0.0001**	**0.001**

Boldface type indicates statistical significance.

p = 0.0002), sleep (OR per point 1.17, 95% CI 1.05–1.30, p = 0.005), and neuropsychiatric (OR per point 1.11, 95% CI 1.04–1.19, p = 0.002; Table 3).

ImPACT at Follow-Up

A majority of athletes across all three groups came in for follow-up testing (DA-meds 72%, DA-only 73%, non-DA 70%, p > 0.99). Follow-up tests were administered at a median of 8 days (IQR 5–12 days) PI for the DA-only cohort, and 7 days (IQR 5–13 days) for the other two cohorts (p = 0.90). Multivariate analysis accounting for PI ImPACT scores, loss to follow-up, and latency to follow-up, in addition to demographic data and clinical history, showed that the DA-meds cohorts had greater deviation from baseline in follow-up verbal memory scores (OR per point 1.57, 95% CI 1.08–2.27, p = 0.02) and symptom scores (OR per point 1.62, 95% CI 1.20–2.20, p = 0.002) than the non-DA cohort (Table 5). The DA-meds cohort also had significantly greater deviation from baseline in follow-up verbal memory scores (OR per point 1.66, 95% CI 1.03–2.69, p = 0.04) and symptom scores (OR per point 1.87, 95% CI 1.12–3.10, p = 0.02) than the DA-only cohort. Lastly, there was no deviation from baseline in follow-up symptom scores (OR per point 0.97, 95% CI 0.72–1.32, p = 0.85) or verbal memory scores (OR per point 0.91, 95% CI 0.67–1.24, p = 0.55) between the DA-only and non-DA groups.

TABLE 5. Recovery from concussions at follow-up

Comparison	OR	95% CI	p Value
DA-meds (1) vs non-DA (0)			
Follow-up verbal memory	1.57	1.08–2.27	**0.0174**
Follow-up symptom score	1.62	1.20–2.20	**0.0017**
DA-meds (1) vs DA-only (0)			
Follow-up verbal memory	1.66	1.03–2.69	**0.0389**
Follow-up symptom score	1.87	1.12–3.10	**0.0160**
DA-only (1) vs non-DA (0)			
Follow-up verbal memory	0.91	0.67–1.24	0.5537
Follow-up symptom score	0.97	0.72–1.32	0.8470

Boldface type indicates statistical significance. Covariates included PI neurocognitive and symptom ImPACT scores, loss to follow-up, and latency to follow-up (days), in addition to demographic data and clinical history.

Discussion

This study examines concussion trends among a large cohort of youth athletes with premorbid DA and differential antidepressant use as compared to their peers. There was no difference in concussion incidence between the DA-only cohort and the non-DA group. However, the DA-meds group had a twofold greater incidence of concussions than both the DA-only group and the non-DA group. Deviation from preseason ImPACT to PI in symptom scores was greater among the DA-meds group compared with the non-DA group. These differences were driven by all 4 symptom clusters: migraine, cognitive, sleep, and neuropsychiatric. Deviation in symptom scores and verbal memory from baseline ImPACT remained two times greater at follow-up among the DA-meds cohort as compared to the non-DA and DA-only groups, even when PI ImPACT scores were accounted for in multivariate analysis, suggesting impaired symptomatic and neurocognitive recovery on ImPACT.

Concussion in Unmedicated DA

Although we had initially hypothesized that premorbid DA would increase the baseline risk for concussions,[4,5] multivariate analysis accounting for sex, learning disorders, and a history of past concussions showed that the DA-only group had a similar concussion incidence as the non-DA group. Multiple hypotheses can explain this unexpected finding. Physicians evaluate postconcussive symptoms in light of individual patient history. More severe posttraumatic symptomology, including increased sadness, nervousness, irritability, and emotionality, is evaluated relative to preinjury levels. More intense PI neuropsychiatric symptoms, but with comparable differences from baseline to PI in the DA-only group as compared to the non-DA group, would therefore correlate with comparable rather than elevated concussion rates. Although physicians were not privy to ImPACT scores when examining head injuries, ImPACT symptom scores did not significantly deviate from baseline to PI between the DA-only and non-DA cohorts, providing corollary evidence for this hypothesis. Additionally, coaches are often aware of their athletes' mood disorders and choose to sideline individuals when they are experiencing the worst of their symptomology.[12] This phenomenon is widespread, with a reported 70% of coaches demonstrating concern about mental health issues among their athletes. This intervention would normalize or even reduce the risk for concussion among those with mood disorders. Unfortunately, we were unable to control for such a covariate in the multivariate analysis.

The DA-only group had similar deviation from baseline to PI in symptom and neurocognitive scores as the non-DA group. Weber et al. found that those with a history of mental illness reported higher symptom severity on baseline concussion assessment tests than controls.[6] We similarly found elevated baseline symptom scores (Supplementary Tables 1 and 2). Lariviere et al. found that PI symptom severity among those with premorbid DA was greater than that of control patients.[7] Both studies examined a snapshot in the clinical history, either at baseline or PI. The longitudinal nature of our study allowed us to examine the relationship between baseline, PI, and follow-up tests to derive a normalized marker of symptomatic and neurocognitive change. When analyzing standardized deviation from preseason ImPACT to PI, we found symptom scores did not significantly deviate between the DA-only and non-DA cohorts. If both baseline and PI symptom scores were consistently higher than the controls in our study and the aforementioned literature, it may explain why we did not find a difference in normalized PI symptom scores between the DA-only and non-DA groups. When normalizing with preseason or baseline ImPACT, those with mood disorders do not seem to experience greater concussion symptoms or neurocognitive burden than their peers.

Concussion Among Antidepressant Users

The DA-meds group had a twofold greater incidence of concussion than either the DA-only or non-DA groups after accounting for sex, learning disorders, and a history of past concussions in multivariate analyses. Individuals who take antidepressants tend to have the more severe symptoms before therapy.[13,14] As such, they tend to require pharmaceutical control in addition to psychotherapy for symptom control. Even a relatively mild impact on the head can upset the balance achieved by a carefully planned prescription regimen, triggering the disinhibition of pharmaceutically masked symptomatology.[15] Such "disinhibition" of symptomology would increase the likelihood of concussion, which requires the appearance of four or more symptoms not present before the injury, including headaches, dizziness, nausea, vomiting, and blurred vision. Indeed, those taking medications had greater deviation from baseline in PI symptom scores (OR per point 1.14), even after multivariate analysis accounting for confounding covariates. Although these odds may seem small at first, deviation of symptom scores from baseline to PI among the DA-meds cohort averages 1.79, with a few scores exceeding 5.00. For a student with a deviation of 5.00, the likelihood of taking antidepressants for DA is 70% greater. Yengo-Kahn et al. found that those medicated for depression had faster ImPACT reaction time scores compared to controls at baseline.[16] As with aforementioned studies analyzing baseline ImPACT scores among unmedicated DA, the study examined a snapshot in the patients' clinical history rather than tracking scores longitudinally over the course of an injury, at baseline, PI, and follow-up.

Symptoms and Neurocognitive Testing at Follow-Up

ImPACT at follow-up showed deviation from baseline in symptom scores, and verbal memory scores remained almost two times greater among the DA-meds cohort as compared to the non-DA and DA-only groups, even after controlling for PI ImPACT scores, loss to follow-up, and latency to follow-up, along with demographic data and clinical history in multivariate analyses. It appears symptom scores and verbal memory remain more impaired among those taking antidepressants for DA up to 7 days after concussion. To the best of our knowledge, no study has examined the persistence of postconcussion ImPACT scores or overall recovery from concussion between those medicated for DA and the general population. A few studies have analyzed recovery among those not medicated for DA and the general population. A prospective cohort study showed that females and those younger than 12 years of age with a history of psychiatric conditions such as DA took significantly longer to recover from concussion.[17] However, the study did not normalize postconcussion symptom scores with baseline values or account for it in a multivariate analysis, leaving the DA patients to overcome a greater gap to be considered "concussion free," defined as a standard symptom score of 3 or less for all patients. A seminal prospective cohort study by Zemek et al. found a univariate relationship between premorbid depression diagnosis and a tendency for persistent symptoms.[18] However, they did not include the variable as a covariate in multivariate analysis, nor did they separate out medicated individuals. In multivariate analysis accounting for demographic data, clinical history, loss to follow-up, and PI severity, we found that deviation from baseline in symptom scores and verbal memory remained twice as large among the DA-meds cohort at follow-up as compared to the other two cohorts.

Limitations of the Study

The retrospective nature of the study prevented us from gleaning information on the dosage of medication use among the students. Dosage of antidepressants plays a significant role in modulating symptoms and neurocognitive scores.[19] However, the literature shows that most adolescents are prescribed antidepressant doses within a narrow range, suggesting that although dosage has shown to modulate baseline symptom and neurocognitive scores, the variation among a cohort of youth athletes may be inconsequential.[20] Additionally, individuals with severe DA are more likely to be treated with antidepressants in addition to cognitive behavioral therapy.[20] This suggests that those taking medications likely had worse DA before antidepressant use than their nonmedicated counterparts, a potential limitation for this study. However, baseline ImPACT scores show that the symptom and neurocognitive scores of the DA-meds and DA-only cohorts were comparable (Supplementary Tables 1 and 2), suggesting equitable disease severity at the start of the study. Finally, studies show that more than 9% of American youth are diagnosed with DA and 20% of them take antidepressants chronically.[21,22] We found 7% of youth athletes had DA, with 21% of them taking medications. There could be a difference in mood disorder rates among the general population and athletes.[23] In addition, a larger overall sample size, maybe 10,000–20,000 individuals, may have yielded a more representative cohort.

Conclusions

Premorbid DA itself does not appear to affect concussion incidence, nor does it seem to affect the recovery or persistence of symptomatic and neurocognitive dysfunction PI. However, premorbid DA along with antidepressant use is associated with increased concussion incidence as well as elevated symptom scores and verbal memory scores up to 7 days after concussion, suggesting impaired symptomatic and neurocognitive recovery on ImPACT.

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Disclosures

Mark Lovell is a co-founder of ImPACT, although he no longer owns any rights in the company.

Author Contributions

Conception and design: Ali, Lovell, Choudhri. Acquisition of data: Lovell, Choudhri. Analysis and interpretation of data: Ali, Asghar, Li, Hannah, Lovell, Choudhri. Drafting the article: Ali, Asghar. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Ali. Statistical analysis: Ali, Asghar. Administrative/technical/material support: Lovell, Choudhri. Study supervision: Choudhri.

Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

Supplementary Tables 1 and 2. https://thejns.org/doi/suppl/10.3171/2020.11.PEDS20821.

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