Body Mass Index and Future Schizophrenia in Israeli Male Adolescents

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Background: Compared with the general population, individuals suffering from schizo-phrenia are more likely to be overweight, a finding attributed to the effect of antipsychotic medications, poor nutrition, and sedentary life-style. As evidence accumulates indicating that some aspects of the illness manifest before the onset of psychosis and establishment of the diagnosis, it has been suggested that increased weight, like other metabolic dysfunctions, might precede active illness.

Method: Data on height and weight of 203,257 male adolescents assessed by the Israeli Draft Board, and followed for 2–6 years for later hospitalization for schizophrenia using the Israeli National Psychiatric Hospitalization Case Registry, were analyzed.

Results: From the entire cohort, 309 (0.15%) were later hospitalized for schizophrenia (ICD-10). After removing adolescents with evidence of illness before or within 1 year of the Draft Board assessment, 204 future schizophrenia patients were available for analysis. Compared with the rest of the cohort, future schizophrenia patients had lower body mass indexes $(21.24 \pm 3.3 \text{ kg/m}^2 \text{ vs. } 21.77 \pm 3.5 \text{ kg/m$ kg/m^2 ; F = 4.682, df = 1, p = .03) and weighed slightly but significantly less (64.2 ± 11.6 kg vs. 66.3 ± 12.0 kg; F = 6.615, df = 1, p = .01). The mean height of the future patients did not differ significantly from the mean height of the remaining cohort $(173.63 \pm 6.7 \text{ cm vs.} 174.40 \pm 6.9 \text{ cm};$ F = 2.520, df = 1, p = .112). When reanalyzing the data, controlling for physical activity and socioeconomic status, the differences between the groups remained significant.

Conclusion: Before the onset of illness, future schizophrenia patients are not heavier compared with their peers. This implies that the increased weight of patients with schizophrenia is related to illness effects, including the effects of antipsychotic medication.

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E vidence indicates that in comparison with the general population, individuals suffering from schizophrenia are more likely to be overweight or obese.^{1,2} Previous studies have indicated that compared with the general population, future schizophrenia patients exhibit more negative symptoms and report fewer physical and social activities prior to the onset of illness.^{3,4} Since physical inactivity is correlated with weight gain,^{5,6} one might hypothesize that the overweight exhibited by many schizophrenic patients may exist prior to the onset of illness. Furthermore, it has been suggested that individuals who will develop schizophrenia are predisposed to metabolic disorders such as diabetes⁷ and that treatment-naive patients in the first episode of psychosis have impaired glucose tolerance.⁸

In this study, we sought to examine the weight of future schizophrenia patients before the onset of illness and antipsychotic treatment. To this end, we utilized a historical-prospective design by analyzing data from a population-based cohort of Israeli male adolescents who had undergone measurements of weight and height as part of the assessment performed by the Israeli Draft Board before induction to the military. Later hospitalization for schizophrenia was ascertained using the Israeli National Psychiatric Hospitalization Case Registry, which records all psychiatric hospitalizations in the country.

METHOD

Draft Board Assessment

All Israeli adolescents aged 16 to 17 years are assessed by the Draft Board in order to determine their eligibility

Analysis	BMI				Weight				Height			
	kg/m ²	Effect Size	F (df = 1)	р	kg	Effect Size	F (df = 1)	р	cm	Effect Size	F (df = 1)	р
First analysis		-0.15	4.682	.03		-0.18	6.615	.01		-0.11	2.520	.112
Future schizophrenia patients, N = 204												
Mean	21.24				64.17				173.63			
SD	3.31				11.58				6.68			
Remaining population, N = 202,673												
Mean	21.77				66.33				174.40			
SD	3.53				12.03				6.90			
Reanalysis ^a		-0.19	4.228	.04		-0.19	4.137	.042		-0.06	0.173	.678
Future schizophrenia patients, N = 145												
Mean	20.96				63.52				173.97			
SD	3.18				10.93				7.01			
Remaining population, N = 143,458												
Mean	21.63				65.83				174.39			
SD	3.49				11.89				6.88			

and aptitude for military service. This assessment includes a medical evaluation, including measurements of weight and height, and an interview assessing behavior. As the behavioral assessment is not performed on females, we report on males only.

Behavioral and personality traits are assessed using an interview that is administered by college-aged individuals who participated in a 4-month-long training course on the administration of the interview. The behavioral assessment includes a number of subscales, including a measure of physical activity, which assesses involvement in extracurricular physical activities such as hiking and sports. Physical activity is rated on a scale ranging from 1 (poorest) to 5 (best); a score of 1 reflects very low levels of physical activity; a score of 3 reflects intermediate, common levels; and a score of 5 reflects high, abovenormal levels of physical activity. The test-retest reliability of the behavioral assessment for inductees interviewed after several days by different interviewers is above 0.8, and population-based norms are available.9,10

Israeli National Psychiatric Hospitalization Case Registry

The Israeli National Psychiatric Hospitalization Case Registry is a complete listing of all ICD-10 discharge diagnoses assigned by a board-certified psychiatrist at the facility. All psychiatric hospitals, day hospitals, and psychiatric units in general hospitals are required by law to report all admissions and discharges to the registry.

Study Population

We obtained data regarding height and weight in a cohort of 203,257 male adolescents who were assessed by the Israeli Draft Board. Data regarding physical activity and socioeconomic status (SES) were available for 163,765 members of this cohort. The members of the cohort were followed for later hospitalization for schizophrenia using the Israeli National Psychiatric Hospitalization Case Registry. The study protocol was approved by the local Institutional Review Board.

Data Analysis

The comparison of body mass index (BMI), weight, and height between future cases and controls was performed using univariate analysis of variance (ANOVA). The ANOVA was first run without covariates, and was then re-run controlling for physical activity, SES, and the year of the draft board assessment (Table 1). The SES measure was based on Israeli National Bureau of Statistics data linking parental residential address to income.¹¹ Effect sizes were calculated according to Cohen¹² by subtracting the mean values of the remaining population from the mean values of the future schizophrenia patients and dividing by the standard deviation of the remaining population.

As described elsewhere,^{13–15} adolescents with BMIs of 18.4 kg/m² and below were defined as below normal, adolescents with BMIs of 18.5 through 25 kg/m² were defined as normal, and adolescents with BMIs of 25.1 kg/m² and above were defined as obese. Differences in the distributions of BMIs in these categories between future patients and the remaining population were calculated using the Pearson χ^2 test.

We assumed that adolescents who had already been hospitalized for schizophrenia before the Draft Board assessment had been treated with antipsychotics before the Board's assessment of weight and height, and therefore might be heavier than future schizophrenia patients who



had not yet been treated. We therefore compared height, weight, and BMI of adolescents who had already been hospitalized for schizophrenia before the Draft Board assessment with height, weight, and BMI of future schizophrenia patients who had not yet been treated, using independent-samples t tests. All analyses were done using SPSS 11 (SPSS Inc., Chicago, Ill.).

RESULTS

In the entire cohort (N = 203,257), 309 (0.15%) were later hospitalized for schizophrenia (ICD-10, F20.0-F20.9). This prevalence is affected by the relatively short (2-6 years) follow-up. In order to decrease the chance that some of the patients were already receiving antipsychotics at the time of the Draft Board assessment, we removed adolescents who had been hospitalized before or 1 year after the Board's assessment and adolescents who at the assessment were diagnosed as suffering from psychotic disorders or major affective disorders (some of whom might have had major affective disorder with psychotic features and had therefore received antipsychotic treatment). In addition, in order to enable comparisons between adolescents later hospitalized for schizophrenia and adolescents not later hospitalized, adolescents later hospitalized for disorders other than schizophrenia were also removed. The analysis was thus performed on 204 male adolescents later hospitalized for schizophrenia and 202,673 in the remaining population. Compared with male adolescents not later hospitalized, future schizophrenia patients had lower BMIs and weighed less, but did not differ in terms of height from the rest of the cohort (Table 1). This difference remained statistically significant after controlling for SES and physical activity.

Figure 1 shows the differences in distribution of BMIs between future schizophrenia patients and the unaffected population and shows a greater prevalence of future schizophrenia patients in the below-normal group compared with adolescents not later hospitalized. The differences in distribution were statistically significant (Pearson $\chi^2 = 14.806$, p = .022).

Adolescents (N = 26) who were hospitalized before the Draft Board assessment were nonsignificantly heavier (65.6 ± 11.2 kg vs. 64.2 ± 11.6 kg, t = 0.657, p = .525) and had nonsignificantly higher BMIs (22.1 ± 4.2 kg/m² vs. 21.2 ± 3.3 kg/m², t = 1.308, p = .192) compared with adolescents who were hospitalized 1 year or more after the Draft Board assessment (N = 204).

DISCUSSION

In a population-based cohort of male adolescents, we found that, as a group, future schizophrenia patients were lighter and had lower BMIs compared with the means of the remaining cohort. Other studies that looked at weight, height, and BMI before the onset of psychosis yielded mixed results. Wahlbeck et al.¹⁶ conducted a populationbased prospective study on a Finnish cohort and reported that future schizophrenia patients were thinner than control subjects between 7 and 15 years of age. Our findings replicate these results. A similar study,¹⁷ which was conducted on a cohort of recruits into the Swedish military, did not find significant differences between future schizophrenia patients and controls, but did show trends of increased risk for schizophrenia with decreasing BMIs, which are consistent with those of the Finnish cohort and ours. A study of U.S. army recruits,¹⁸ which also compared BMIs between future schizophrenia patients and controls, found no difference between future patients and controls.

The greater prevalence of future schizophrenia patients in the below-normal BMI group indicates that the finding of lower weight and BMI is not due to a subgroup of very thin future schizophrenia patients causing differences between group means.

Finding that adolescents hospitalized before the Draft Board assessment, who had presumably received antipsychotic treatment, were nonsignificantly heavier and had nonsignificantly higher BMIs supports our hypothesis that the increased BMI and weight seen in patients who are already ill are due to illness-related effects, possibly antipsychotic treatment.

Limitations

A relevant concern is that the case registry diagnoses are clinical, not research, diagnoses. However, in a study recently completed by our group, we found that, compared with research diagnoses established using a Schedule for Affective Disorders and Schizophrenia-Lifetime (SADS-L) interview, the registry diagnoses of schizophrenia have a sensitivity of 0.89.¹⁹ An additional limitation is that the prevalence of adolescent obesity in the United States (28.2% in 15-year-old boys) is significantly greater then the prevalence of adolescent obesity in Israeli 15-year-old boys (20.1%).²⁰ Thus, the generalizability of these findings might be limited to countries with a relatively low prevalence of adolescent obesity.

Conclusions

In male adolescents, we found that, compared with the means of the remaining cohort, future schizophrenia patients weighed significantly less and had lower BMIs. These findings imply that the increased weight seen in schizophrenia patients apparent after the onset of the illness is related to illness effects, possibly the administration of antipsychotic medications.

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