The Risk of Diabetes in Deficit Schizophrenia

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Introduction

There are several reasons to suspect that the risk of developing diabetes might be different between deficit (i.e., those with primary, enduring negative symptoms) and nondeficit schizophrenia. Increased rates of diabetes and insulin resistance in people with schizophrenia predate antipsychotics (1, 2). This indicates some innate biological predisposition to impaired glucose utilization and, since deficit schizophrenia may have a unique pathophysiology (3-5), people with deficit schizophrenia may show a different risk for diabetes when separated out from schizophrenia as a whole. Negative symptoms such as decreased activity, goals, and an absence of important relationships may also impair the ability of someone with deficit schizophrenia to implement the diet and exercise changes recommended for prediabetes (fasting blood sugar between 100–125 mg/dL) (6), leading to higher rates of progression to diabetes in this group.

Kirkpatrick et al. (7, 8) compared newly diagnosed, antipsychotic-naive deficit and nondeficit groups to healthy controls using an oral glucose tolerance test. There were significant differences among all three groups (controls 85.0±21.6 mg/dL, nondeficit 123.7±42.2 mg/dL, deficit 100.2±23.1 mg/dL). A second study by these authors replicated the finding that newly diagnosed deficit participants had lower blood sugar after glucose challenge compared to nondeficit participants (9). This difference between deficit and nondeficit participants supports the notion of differing biological risk.

We conducted a chart review to determine whether there is a differential risk of diabetes between deficit and nondeficit groups with chronic schizophrenia. Differential prevalence rates of diabetes would extend the work of Kirkpatrick and colleagues and further support differential biological mechanisms behind deficit and nondeficit schizophrenia. Differential prevalence rates between the groups might also support the utility of the deficit/nondeficit categorization in order to target scarce clinical resources toward one or the other group to produce the greatest impact on metabolic health in schizophrenia.

Methods

Data were abstracted from all current outpatient charts and from charts closed within the year from the Maryland Psychiatric Research Center (MPRC) Outpatient Research Program clinic. The deficit group was supplemented with data from discharged patients since 1988 and deficit patients from another MPRC clinic (the Schizophrenia Related Disorders Program). Patients were diagnosed with schizophrenia/schizoaffective disorder via best estimate approach (structured clinical interviews, examination of records, caregiver informants). Patients were categorized as deficit or nondeficit using the Schedule for the Deficit Syndrome (SDS) (10). Categorization was made by the SDS developers or people directly trained by them.

For all charts, the most recently documented laboratory work and medical information was collected: demographics (including antipsychotic), diabetes status (presence or absence and type 1 or 2), fasting plasma glucose level, hemoglobin A1c (HgA1c) percent, total cholesterol, weight, height, and blood pressure. If there was no diagnosis of diabetes, but fasting blood sugar (>125 mg/dL) or HgA1c (>6.5%) results were diagnostic for diabetes, then the patient was recorded as having type 2 diabetes. Records were

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connected via unique identifiers to a database containing deficit/nondeficit status. Type 1 diabetes was excluded from analysis as the etiopathophysiology is markedly different from type 2 diabetes.

This study was reviewed and approved by the University of Maryland Institutional Review Board.

Statistical analysis included chi-square and t-test comparisons as appropriate, and logistic regression using age, body mass index (BMI), sex, and deficit diagnosis.

Results

One hundred and seventy-six charts were reviewed. Seven new patients were excluded for lack of SDS, leaving 72 deficit and 97 nondeficit patients. There were no group differences in age, sex, ethnicity, or antipsychotic (see Table 1). However, there was a numerically higher proportion of males in the deficit group. There were no group differences in prevalence of diabetes, fasting blood sugar, weight/BMI, cholesterol, or blood pressure. Including only type 2 diabetes patients, there were no differences in fasting blood sugar or HgA1c between deficit and nondeficit groups.

Logistic regression was calculated to determine whether diabetes diagnosis was predicted by age, BMI, sex, and deficit diagnosis. The equation correctly classified 73% of cases, model $X^2(4)=9.61$, $p<0.05$. BMI was the only significant predictor of diabetes (B=-0.06; OR 0.95; 95% CI, 0.90–1.00, $p<0.04$); deficit diagnosis (B=-0.35; OR 0.71; 95% CI, 0.33–1.53), age (B=-0.03; OR 0.98; 95% CI, 0.95–1.01), and sex (B=0.23; OR 0.95; 95% CI, 0.55–2.87) were not predictors.

Discussion

There was no indication that prevalence rates of diabetes differed between chronic deficit and nondeficit schizophrenia patients, nor was there a group difference in glycemic

Table 1 Demographics, Diabetes Diagnoses, and Metabolic Indices in Deficit and Nondeficit Groups

	Deficit		Nondeficit			
	N	Measure	N	Measure	Statistic (df)	P-Value
Total Sample						
Age, years, mean (SD)	72	45 (12.5)	97	43 (12.7)	t(164)=0.57	0.57
Male	53	74%	63	65%	$X^2(1)=1.44$	0.25
Race						
White	38	53%	56	58%	$X^2(3)=5.59$	0.13
African American	28	39%	38	39%		
Asian	2	3%	3	3%		
Other	4	6%	0	0		
Antipsychotic Treatment*						
First Generation	14	22%	14	16%	$X^2(2)=5.34$	0.07
Second Generation†	31	47%	30	34%		
Clozapine	20	31%	43	49%		
Diabetes, prevalence (%)	72	19 (26.4%)	97	24 (24.7%)	$X^2(1)=0.06$	0.81
Fasting Blood Sugar, mg/dL, mean (SD)	68	107 (34.7)	96	104 (34.4)	**t(162)=0.49**	**0.63**
HgA1c %, mean (SD)	37	6.0% (0.68)	95	6.0% (0.76)	**t(130)=0.31**	**0.76**
Weight, kg, mean (SD)	65	90.7 (24.4)	94	95.3 (21.9)	**t(157)=-1.17**	**0.25**
BMI, mean (SD)	56	30.4 (8.0)	93	31.2 (7.8)	**t(146)=-0.84**	**0.40**
Total Cholesterol, mg/dL, mean (SD)	65	181 (40.9)	95	178 (35.6)	**t(158)=0.53**	**0.60**
Blood Pressure, Systolic/Diastolic, mmHg, mean (SD)	65	126/79 (23.5/13.0)	94	126/77 (15.2/10.8)	**t(101)=0.26/ t(157)=0.96**	**0.80/ 0.33**
Sub-sample with Diabetes						
Fasting Blood Sugar, mg/dL, mean (SD)	19	127 (57.4)	24	130 (59.1)	t(41)=-0.20	0.84
HgA1c %, mean (SD)	15	6.34% (0.89)	24	6.68% (1.12)	t(37)=-0.99	0.33

*The proportion of deficit ($X^2=0.93$, $p=1.0$) and nondeficit patients ($X^2=0.44$, $p=0.63$) diagnosed with diabetes did not differ as a function of clozapine status. Deficit: clozapine with diabetes=30.0%; clozapine without diabetes=70.0%; non-clozapine with diabetes=28.9%; non-cloazpine without diabetes=71.1%. Nondeficit: clozapine with diabetes=23.3%; clozapine without diabetes=76.7%; non-clozapine with diabetes=29.5%; non-cloazpine without diabetes=70.5%. †Non-clozapine second-generation antipsychotics. BMI=Body Mass Index; df=degrees freedom; HgA1c=hemoglobin A1c; mmHg=millimeters of mercury; SD=standard deviation.

control. This indicates either there are no differences in the biological mechanism behind the development of diabetes in the two groups, or that different biological mechanisms in the two groups still lead to the same overall prevalence of diabetes. It also indicates the symptom constellation of deficit schizophrenia is not more likely to lead to poorer glycemic control compared to nondeficit schizophrenia.

This finding does not rule out differences in the biological mechanisms behind the occurrence of diabetes in the groups, but does argue against the utility of making the deficit/nondeficit categorization in a non-research setting in order to target resources aimed at enhancing metabolic health.

This study had a number of limitations. First, data quality was based on the accuracy of the medical record. Because only the most recent lab results were abstracted, cases of diabetes could have been missed (no formal chart diagnosis, recent labs were normal). However, diabetes rates observed in this study are consistent with those expected in a population with schizophrenia (11, 12), so it is likely few cases were missed. Another limitation is that we were unable to compare the groups on longitudinal risk for diabetes. Without knowing exactly when diabetes was diagnosed or, in many cases, the precise onset of schizophrenia, we do not know if there is a differential risk of diabetes in the groups over time (i.e., we measured prevalence, not incidence).

In summary, we found no difference in prevalence rates of type 2 diabetes between deficit and nondeficit schizophrenia. There were no differences in glycemic control between deficit and nondeficit schizophrenia groups, or between the subset of the groups with diabetes. This finding does not rule out differences in the biological mechanisms behind the occurrence of diabetes in the groups, but does argue against the utility of making the deficit/nondeficit categorization in a non-research setting in order to target resources aimed at enhancing metabolic health.

Conflicts of Interest

None of the authors report any conflicts of interest. Drs. Strauss and Fischer report past funding from the United States National Institutes of Health and the Department of Veterans Affairs. Dr. Fischer has also been funded by the Brain and Behavior Research Foundation (formerly NARSAD).

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