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Glucose abnormalities in the siblings of people with schizophrenia

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Abstract

Background: Some studies suggest that schizophrenia may be associated with an increased risk of diabetes, independently of antipsychotic medications and other confounding factors. Previous studies have also suggested that there is an increased prevalence of diabetes in the relatives of schizophrenia probands.
Method: First-degree siblings of schizophrenia probands ($N=6$) and control subjects ($N=12$) were administered a glucose tolerance test. Subjects were matched for gender, age, body mass index, neighborhood of residence, socio-economic status and smoking habits.
Results: The siblings of schizophrenia probands had a significantly increased two-hour mean glucose concentration compared to the control subjects (respective means [SD] were 100.5 mg/dL [27.7] vs. 78.0 [12.3]; $p<0.03$). Baseline glucose concentrations did not differ.
Conclusions: Although confirmation with larger samples is needed, these results and other studies suggest that diabetes may share familial risk factors with schizophrenia.

Keywords: Schizophrenia; Glucose metabolism; Diabetes; Psychosis; Siblings; Drug-naïve

1. Introduction

Several reports (Ryan et al., 2003;Spelman et al., 2007;Cohn et al., 2006;Venkatasubramanian et al., 2007), although not all (Arranz et al., 2004), suggest that schizophrenia is associated with abnormal glucose metabolism independently of antipsychotic use. A few studies have investigated that diabetes has an increased prevalence in the families of schizophrenia probands. Mukherjee et al. (1989) described an increased prevalence of type 2 diabetes mellitus (T2DM) among first-degree relatives of schizophrenia patients. We have recently replicated this finding (Fernandez-Egea et al., 2008). One study (Spelman et al., 2007) found an increased prevalence of impaired glucose tolerance in an oral glucose tolerance test (GTT) in newly diagnosed, antipsychotic-naïve patients with schizophrenia (10.8%) and their first-degree relatives (18%) compared to healthy controls (0%). However, the relatives and healthy controls were not well matched for age, body mass index (BMI), and smoking habit, which are known risk factors for developing diabetes.

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We tested the hypothesis that the first-degree siblings of patients with schizophrenia have abnormal glucose measures on a GTT, compared to matched control subjects.

2. Materials and methods

2.1. Subjects

The relative group consisted of first-degree siblings of patients from a psychiatric service in a general academic hospital (Hospital Clinic of Barcelona). The control subjects come from a sample of 62 healthy volunteers recruited for a study of glucose metabolism in newly diagnosed, antipsychotic-naïve patients with nonaffective psychosis.

Additional inclusion and exclusion criteria for all subjects were: 1) age 18 to 45, 2) no personal history of a major psychiatric disorder, and no psychotic symptoms, 3) no history of diabetes or other serious medical or neurological condition associated with glucose intolerance or insulin resistance (e.g. Cushing's disease), 4) not taking a medication associated with insulin resistance (hydrochlorothiazide, furosemide, ethacrynic acid, metolazone, chlorthalidone, beta blockers, glucocorticoids, phenytoin, nicotinic acid, cyclosporine, pentamidine, or narcotics), and 5) no history of cocaine use in the previous 30 days. All subjects gave informed consent for participation in the study, which was conducted under the supervision of the institutional review boards of the Hospital Clinic of Barcelona, the University of Maryland Baltimore and/or the Medical College of Georgia.

2.2. Matching strategy

This study was part of a larger ongoing study of diabetes in patients with nonaffective psychosis and matched control subjects. For each relative included, 2 control subjects were selected, blind to glucose measures, from the healthy control subjects in that study. The control subjects were recruited during the same time as the sibling group. The control subjects were selected so that they were matched to the siblings with regard to gender, age, BMI, smoking habit (average number of cigarettes per day), and residence in the middle class/upper middle class catchment area (yes/no) of the Hospital Clinic. All of the subjects were Caucasian residents of Spain.

2.3. Metabolic and psychiatric assessment

A two-hour 75 g oral glucose tolerance test began between 8 and 9 AM after an overnight fast. Cortisol blood levels were also recorded at baseline. Body mass index (BMI) was calculated using the formula [weight (kg)/height (m)^2]. All subjects were interviewed using the Spanish translation of the Structured Clinical Interview for DSM-IV Axis I Disorders, clinician version (SCID-I). They were also administered the Dartmouth Assessment of Lifestyle Inventory (Rosenberg et al., 1998), which quantifies substance abuse. Socio-economic status (SES) was assessed with the Hollishead–Redlich scale (Hollinshead and Rendlich, 1958).

2.4. Statistical analysis

The principal outcome variable was two-hour glucose concentration, as previous studies (Spelman et al., 2007; Cohn et al., 2006), including ours (Fernandez-Egea et al., submitted), have found patient/control differences in that measure but not in fasting glucose. The two groups were compared using the non-paired Student's *t*-test, or the χ^2 test for comparisons of proportions. Statistical tests were performed using version 12.0 for Windows of SPSS (Statistical Package for Social Sciences).

3. Results

The final study sample was composed of 6 siblings (2 women and 4 men) and 12 controls (4 women and 8 men). The two groups were well matched on the variables listed above and residence in the hospital's catchment area in central Barcelona vs. residence outside of that neighborhood (Table 1).

Baseline glucose concentrations were similar (mean [SD]): 86.7 mg/dL (6.6) for the siblings and 80.7 (7.9) for the comparison subjects ($p=0.13$). The values for HbA1c were 4.6% (0.42) vs. 4.4% (0.25; $p=0.243$). However, two hour glucose (2HG) differed significantly between the two groups: the sibling group had a mean concentration of 100.5 (27.7) mg/dL while the control subjects had a mean

Table 1
Characteristics of the relative group and control subjects

	Relatives ($N=6$)	Control ($N=12$)	Significance p
Mean age [SD]	30.6 [3.6]	31.2 [5.5]	0.811
Male/female	4/2	8/4	0.694
Mean body mass index [SD]	25.2 [2.5]	24.5 [2.5]	0.615
Mean number cigarettes per day [SD]	7.5 [8.8]	6.8 [9.9]	0.892
Cortisol blood levels (mg/dL) [SD]	20.0 [4.7]	20.7 [5.6]	0.807
Catchment area (yes/no)	4/2	10/2	0.407
Socio-economic status (mean and [SD])	35.0 [13.9]	47.8 [17.8]	0.164