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ORIGINAL PAPER

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Type 2 diabetes among persons with schizophrenia and other psychotic disorders in a general population survey

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Abstract Schizophrenia and other psychotic disorders are associated with increased risk of developing type 2 diabetes. However, previous studies are mainly based on clinical samples where the comorbidity may be stronger. We investigated in a general population survey the prevalence of type 2 diabetes in persons with psychotic disorders and in users of antipsychotic medication. The study was based on a nationally representative two-stage cluster sample of 8,028 persons aged 30 or over from Finland. Diagnostic assessment of psychotic disorders combined SCID-I interview and case note data. Prevalences of type 2 diabetes, adjusting for age and sex, were estimated by calculating predicted marginals. The prevalence estimate of type 2 diabetes was 22.0% among subjects with schizophrenia, 13.4% among subjects with other nonaffective psychosis and 6.1% in subjects without psychotic disorders. Only two subjects (3.4%) with affective psychosis had type 2 diabetes. Users of all types of antipsychotic medication had increased prevalence of type 2 diabetes. Our results suggest that type 2 diabetes is a major health concern among persons with schizophrenia and other nonaffective psychotic disorders and also in users of antipsychotic medication, but persons with affective psychosis in the general population may not have increased prevalence of type 2 diabetes.

Key words diabetes mellitus · type 2 · psychotic disorders · antipsychotic agents

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Introduction

Type 2 diabetes mellitus (T2DM) is a common chronic disease, with increasing incidence worldwide. The most severe consequences of T2DM relate to its complications: it accelerates atherosclerosis, and markedly increases the risk of myocardial infarction, stroke, amputation, and death [45].

Schizophrenia is associated with impaired glucose tolerance and increased incidence and prevalence of T2DM [7–11, 14, 19, 21, 25, 31, 38, 43, 46, 48]. Prevalence of T2DM across studies has varied between approximately 6 and 21%, being 2–3-fold higher among patients with schizophrenia than in the general popu-

lation [7–11, 14, 19, 21, 25, 31, 38, 46, 48]. Patients with schizoaffective and bipolar I disorder have also had high prevalence of T2DM in previous studies [6, 7, 40].

Impaired fasting glucose tolerance was found in one study already in first-episode, drug-naïve patients with schizophrenia, suggesting that defective glucose regulation may be partly associated with the disease process itself [43], although another study failed to replicate the finding [3]. Patients with schizophrenia have an unhealthy lifestyle [5] and increased prevalence of obesity [47], which further increase their risk of T2DM. However, recent studies have consistently shown that antipsychotic medication, particularly phenothiazines, clozapine and olanzapine, increase plasma glucose levels and other abnormalities of glucose metabolism [18, 22, 29, 35] and the risk of diabetes [17, 20, 28]. Part of the cause may be the weight gain induced by these medications [1], but glucose metabolism abnormalities have also been found in non-obese patients [18].

Our study is based on the Health 2000 study, a nationwide Finnish health examination survey [2]. We had three aims: (1) to compare the prevalence of T2DM in persons with psychotic disorders, in persons using antipsychotic medication, and in other members of the study population, (2) to investigate whether undiagnosed diabetes is more common in subjects with psychotic disorders and whether subjects with psychotic disorders receive medical treatment for T2DM as commonly as other participants of the survey, and (3) to investigate whether psychotic disorders and antipsychotic medication predict higher odds of having T2DM after controlling for its other risk factors.

Methods

Study population

The Health 2000 study is based on a nationally representative two-stage cluster sample of 8,028 persons aged 30 or over from 80 municipalities or groups of municipalities with joint primary care in Finland, including the 15 biggest towns. Subjects aged 80 years or over were oversampled by doubling their sampling fraction. The field work was carried out between September 2000 and June 2001, and consisted of a home interview and a health examination at the local health center, or a condensed interview and health examination of non-respondents at home. In addition, register information was gathered on the whole sample. From the total sample, 88% were interviewed, 80% attended a comprehensive health examination and 5% attended a condensed examination at home. The 7,112 subjects (88.6%) who attended at least one of these study phases and thus had the most essential information needed for diagnosing T2DM were used in the current analysis. The study was approved by the Ethics Committee of the Hospital District of Helsinki and Uusimaa. After complete description of the study to the subjects, written informed consent was obtained [2].

Diagnostic assessment of type 2 diabetes

T2DM was diagnosed by one of the authors (AR) according to the WHO 1999 criteria [50], combining information from several sources: self-reported diagnosis of T2DM which was further confirmed in the clinical examination, antidiabetic medication use—either self-reported or according to the National Prescription Register of the Social Insurance Institution, reimbursed antidiabetic medication because of T2DM according to the Medication Reimbursement Register of the Social Insurance Institution, fasting plasma glucose ≥7.0 mmol/l (126 mg/dl) or nonfasting glucose ≥11.1 mmol/l (200 mg/dl).

Diagnostic assessment of psychotic disorders

We screened subjects with possible psychotic disorder and interviewed them using the Research Version of the Structured Clinical Interview for DSM-IV-TR (SCID-I). Subjects were screened to participate in the SCID interview if they reported having been diagnosed with psychotic disorder, received a diagnosis of possible or definite psychotic disorder from the physician conducting the health examination, or had possible psychotic or manic symptoms in the CIDI interview conducted as a part of the health examination. A register-based screen was also used, including hospital treatment with a diagnosis of any psychotic disorder, free medication for psychotic or other severe mental disorder, disability pension because of psychotic or major depressive disorder, or mood-stabilizing medication use without a diagnosis of relevant somatic condition [37].

Of the screen-positive subjects, 64% participated in the SCID interview [37]. We diagnosed those who did not participate in the SCID interview by reviewing case notes from all lifetime hospital and outpatient treatments for mental health problems. Case notes for those who participated in the interview were also collected. Final DSM-IV-TR-based diagnoses were made by three experienced clinicians, JS, JP, and SIS, using all available information. Kappa values between the raters ranged from 0.74 to 0.97 for different psychotic disorders [37]. In this article, lifetime-ever diagnoses of psychotic disorders are classified into schizophrenia, other non-affective psychosis (ONAP) (schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, psychotic disorder not otherwise specified), and affective psychosis (major depressive disorder with psychotic features and bipolar I disorder).

Other measures

Fasting plasma glucose was taken at the beginning of the health examination or home health examination; serum insulin only in the health examination. Plasma glucose was measured with an Olympus AU600 analyser by a hexokinase method, with a between-series coefficient of variation (CV) of 2.3% [16]. Serum insulin concentrations were determined with an Abbott IMx 20238 analyzer by microparticle enzyme immunoassay (MEIA) [16]. We calculated the homeostasis model assessment of insulin resistance (HOMA-IR) index using the formula: fasting serum insulin concentration x fasting plasma glucose concentration/22.5.

Information on general education and on higher and vocational education was combined into a level of education variable (basic, secondary or higher) [2]. Antipsychotic medications were categorized as low-potency (thioridazine, chlorprotixene, levomepromazine, chlorpromazine, promazine, melperone, sulpiride), high-potency (fluphenazine, haloperidol, flupenthixol, zuclopenthixol, pericyazine, perphenazine), and atypical (clozapine, olanzapine, risperidone, quetiapine). Cardiovascular medication comprised beta-blockers, calcium channel blockers, diuretics, ACE inhibitors, angiotensin II antagonists, and statins. Healthiness of the diet was a summary variable based on standard, validated diet-related questions which assessed the habitual use of butter vs. vegetable oils, fat content in milk and cheese products, and daily use of raw vegetables [2]. Diet was coded as healthy (daily use of vegetables and infrequent use of dairy products with high saturated fat), average, and unhealthy (infrequent use of vegetables and frequent use of several dairy products with high saturated fat). Smoking status was categorized as current smoker, ex-smoker, and those who never

smoked regularly. Alcohol consumption in grams per week was calculated based on detailed quantitative questions on drinking habits [2]. Questions concerning alcohol consumption formed part of a questionnaire, while information on all the other variables was obtained in the interview.

Weight, height, waist circumference, and handgrip strength were measured in the health examination. Handgrip strength was used as a measure of physical condition; low handgrip strength has predicted insulin resistance in previous studies [26].

Statistical analyses

All analyses were conducted using SUDAAN Release 9.0 (Research Triangle Institute 2004), which is able to take account of two-stage cluster sampling design and calculates robust standard error estimates. Sampling design was taken into account in all statistical analyses. In addition, post-stratification weights estimated by Statistics Finland were applied to adjust for non-response and for the oversampling of individuals aged 80 years and over [2, 16].

We compared mean fasting glucose and insulin, the proportion of subjects having impaired fasting glucose [41], and the mean or frequency of variables related to diabetes risk among subjects with psychotic disorders, subjects using antipsychotic medication, and the other participants. Differences were tested using the t test for continuous variables, and χ^2-test for categorical variables.

We estimated the prevalence of type 2 diabetes in subjects with psychotic disorders and users of antipsychotic medication as predicted marginals, using logistic regression and controlling for age and sex [27, 42]. Odds ratios, adjusting for age and sex, are also reported.

Using χ^2-test, we compared the proportion of subjects with psychotic disorders having T2DM diagnosed in the survey between the respective proportion in other participants, and the proportion of subjects using antidiabetic medication (insulin or oral antidiabetic medication (insulin sensitizers, sulfonylureas, repaglinide, nateglinide, and metformin)).

We explored factors that influence the odds of having T2DM by logistic regression. Besides psychiatric diagnosis and antipsychotic medication, we included the following explanatory variables: age, sex, education, abdominal obesity, healthiness of the diet, smoking, handgrip strength, alcohol consumption and use of cardiovascular medication. Abdominal obesity was defined according to the National Cholesterol Education Program—Adult Treatment Panel III criteria for metabolic syndrome [12] as waist circumference >102 cm in men and >88 cm in women. Use of cardiovascular medication was included as a covariate to adjust both for cardiovascular comorbidity and its treatment.

All statistical tests were two-tailed, with α level set at 0.05.

Results

Subjects with schizophrenia did not differ from the other participants in their mean age and proportion of males vs. females. They had significantly higher glucose and insulin levels, higher HOMA-IR index, weaker handgrip strength, higher waist circumference, and they drank less alcohol. Subjects with ONAP were significantly older, more often females, and had significantly higher BMI, waist circumference and weaker handgrip strength than the general population. Except for higher waist circumference, subjects with affective psychosis did not differ from other participants. As expected, current use of all classes of antipsychotic medication was significantly more common in subjects with different psychotic disorders compared with the other participants. Only one subject with schizophrenia and one with affective psychosis had no lifetime exposure to antipsychotic medication. In the ONAP group, 88% had lifetime exposure to antipsychotic medication (Table 1).

Users of antipsychotic medication were significantly older and had higher BMI, waist circumference, and blood glucose than the other participants. Of the 212 subjects who reported using antipsychotic medication, only 93 received a diagnosis of functional psychotic disorder (schizophrenia, ONAP, or affective psychosis). Most subjects (n = 82, 69%) who used antipsychotic medication and did not have functional psychotic disorder were 65 years or older, and many (n = 49, 40%) were living permanently in institutions (Table 2).

Prevalence of type 2 diabetes among subjects with psychotic disorders

The age- and sex-adjusted prevalence of T2DM was considerably increased among subjects with schizophrenia and ONAP (Table 3). Both females and males with schizophrenia, and males with ONAP had significantly higher prevalence of T2DM than the respective groups among the other participants. After adjusting for age and sex by logistic regression, the OR for having T2DM was 4.9 (95%CI 2.5–9.7) among subjects with schizophrenia and 3.5 (95%CI 1.2–10.8) among subjects with ONAP.

There were only two subjects with affective psychosis and T2DM (unadjusted prevalence 3.4%, 95%CI 0.8–13.5), of whom one was over 80 years old and had previously diagnosed, medication treated T2DM, and the other one was diagnosed in the survey. Of subjects with schizophrenia having T2DM, 30.3% received antidiabetic medication. The respective percentages were 53.5% for subjects with other nonaffective psychotic disorder and 51.6% in the other participants. The proportion of diabetic subjects having T2DM diagnosed in the survey was 30.7% among subjects with schizophrenia and 18.1% subjects with other nonaffective psychosis, compared with 26.4% in the total sample. None of these differences were statistically significant.

Prevalence of type 2 diabetes among subjects using antipsychotic medication

The prevalence of T2DM was higher among users of all categories of antipsychotic medication than among the other participants (Table 4). After adjusting for age and sex, the OR for having T2DM was 2.4 (95%CI 1.4–4.1), 2.5 (95%CI 1.3–4.6), and 3.1 (95%CI 1.2–7.9) among subjects using low-potency, high-potency, and atypical antipsychotic medication, respectively.

Table 1 Demographic characteristics, mean blood glucose levels, and variables related to diabetes risk for subjects with and without psychotic disorders. 95% confidence intervals in parentheses

Characteristic	Total sample	Schizophrenia	ONAP	Affective psychosis
Age (years)	53.0 (52.6–53.4)	53.4 (50.8–56.0)	57.9 (54.5–61.3)**	53.4 (49.5–57.3)
Sex				
Males	3,175	26	26*	24
Females	3,937	35	53	21
Plasma glucose				
mmol/l	5.57 (5.54–5.61)	**6.11 (5.67–6.56)***	6.09 (5.45–6.73)	5.37 (5.15–5.60)
mg/dl	100.4 (99.8–101.1)	**110.1 (102.2–118.2)***	109.7 (98.2–121.3)	96.8 (92.8–100.9)
≥7.0 mmol/l (126 mg/dl)	5.1%	**19.6%**	10.6%	2.5%
6.1–<7.0 mmol/l (110-<126 mg/dl)	9.7%	**7.6%**	14.5%	15.2%
<6.1 mmol/l (<110 mg/dl)	85.3 %	**72.6%**	74.9%	82.3%
Serum insulin (mU/l)	9.65 (8.84–10.5)	**16.2 (10.9–21.4)***	12.2 (9.1–15.2)	9.8 (7.8–11.8)
HOMA-IR	2.52 (2.37–2.66)	**4.67 (2.81–6.53)***	4.27 (1.49–7.06)	2.36 (1.86–2.86)
BMI (kg/m^2)	26.9 (26.8–27.0)	28.2 (26.9–29.6)	**29.1 (27.9–30.4)*****	27.2 (26.0–28.4)
Waist circumference (cm)	92.9 (92.5–93.3)	**97.8 (93.6–101.9)***	**98.3 (94.5–102.1)****	**97.7 (93.6–101.8)***
Antipsychotic medication				
Low-potency	1.62%	**47.5%*****	**23.9%*****	**17.4%***
High-potency	1.16%	**40.1%*****	**27.2%*****	**12.1%***
Atypical	0.41%	**12.7%*****	**6.4%***	2.5%
Any	2.63%	**68.3%*****	**45.2%*****	**32.0%****
Antidiabetic medication				
No	96.4%	93.5%	91.6%	98.9%
Yes	3.6%	6.5%	8.4%	1.1%
Cardiovascular medication				
No	74.3%	70.7%	68.8%	82.1%
Yes	25.7%	29.3%	31.2%	17.9%
Smoking status				
Current	27.3%	43.7%	28.4%	29.4%
Previous	22.1%	17.0%	21.1%	29.5%
Never	50.6%	39.2%	50.5%	41.1%
Diet				
healthy	23.1%	13.6%	21.5%	22.5%
average	62.1%	72.8%	59.7%	55.9%
unhealthy	14.8%	13.6%	18.8%	21.6%
Handgrip strength (N)	372.7 (369.0–376.5)	**296.6 (266.2–327.0)*****	**331.1 (290.8–371.4)***	376.4 (338.2–414.6)
Alcohol consumption (grams/week)	76.9 (72.3–81.5)	**29.5 (7.8–51.2)*****	69.9 (39.4–100.3)	73.5 (41.4–105.7)

ONAP = other nonaffective psychotic disorder, HOMA-IR = homeostasis model assessment of insulin resistance, BMI = body mass index
* Contrast to other participants: $P < 0.05$
** Contrast to other participants: $P < 0.01$
*** Contrast to other participants: $P < 0.001$

Table 2 Prevalence of antipsychotic medication use, and characteristics of their users; 95% confidence intervals in parentheses

	Class of antipsychotic medication		
Characteristic	High-potency	Low-potency	Atypical
Number of users	89	131	33
Prevalence of antipsychotic medication use			
30–44 years	0.67% (0.39–1.13)	1.29% (0.91–1.83)	0.22% (0.09–0.54)
45–54 years	1.28% (0.85–1.92)	1.52% (1.03–2.25)	0.28% (0.12–0.66)
55–64 years	1.15% (0.70–1.89)	0.90% (0.51–1.60)	0.25% (0.08–0.76)
65 years and over	1.71% (1.23–2.36)	2.72% (2.12–3.48)	0.93% (0.59–1.46)
Total	1.16% (0.93–1.45)	1.62% (1.37–1.92)	0.41% (0.29–0.58)
Mean age (years)	**59.1 (56.3–61.9)*****	**58.9 (55.9–61.8)*****	**63.9 (58.3–69.5)*****
BMI	28.1 (26.8–29.4)	27.7 (26.6–28.8)	26.3 (24.4–28.3)
Waist circumference (cm)	**100.0 (96.4–103.7)*****	**97.5 (94.2–100.8)****	94.8 (88.4–101.1)
Mean blood glucose	107.2 (99.1–115.5)	**112.4 (103.8–121.1)****	109.5 (98.2–120.9)

** Contrast to other participants: $P < 0.01$
*** Contrast to other participants: $P < 0.001$

Logistic regression of variables associated with increased odds of having type 2 diabetes

In the logistic regression model with T2DM as the dependent variable, schizophrenia (OR 3.91) and atypical antipsychotic medication (OR 5.20) remained associated with significantly increased odds of having T2DM. Other variables that were associated with significantly increased odds of having T2DM were advanced age, male sex, abdominal

Table 3 Adjusted prevalence and 95% confidence intervals of type 2 diabetes in subjects with nonaffective psychotic disorders and the total population

	Subjects without psychotic disorder	Schizophrenia	Other nonaffective psychotic disorder
Total[a]	6.1% (5.5–6.7)	**22.0% (13.6–33.5)*** **	**13.4% (7.7–22.3)** **
Sex[b]			
Males	6.7% (5.8–7.6)	**19.0% (8.0–38.8)***	**17.7% (8.4–33.5)** **
Females	5.5% (4.8–6.3)	**24.3% (13.2–40.3)*** **	10.7% (4.5–23.5)
Age[c]			
30–54 years	2.5% (2.1–3.1)	**11.5% (4.3–27.1)** **	**12.9% (5.0–29.2)** **
55- years	11.2% (10.0–12.5)	**35.2% (20.0–54.1)*** **	18.8% (9.3–34.5)

ONAP = other nonaffective psychotic disorder
[a] adjusted for age and sex
[b] adjusted of age
[c] adjusted for sex
* Contrast to other participants: $P < 0.05$
** Contrast to other participants: $P < 0.01$
*** Contrast to other participants: $P < 0.001$

obesity, having cardiovascular medication, lower education, weaker handgrip, and higher alcohol consumption. Healthier diet was associated with higher odds for T2DM, because subjects who had previously diagnosed T2DM had healthier diet than the total sample: 27.3% had healthy diet, and only 10.2% had unhealthy diet. Of subjects who were diagnosed as having T2DM in the survey, 15.5% had healthy and 15.9% unhealthy diet. Affective psychoses could not be included in the model because there were only two subjects with both T2DM and affective psychosis (Table 5).

Discussion

This study is a population-based survey of the prevalence of type 2 diabetes among subjects with psychotic disorder. The study population is representative of the adult Finnish population, and subjects were assessed in detail. Both psychotic disorders and T2DM were diagnosed by combining information from several sources. According to our study, T2DM is a common comorbid condition among subjects with schizophrenia and ONAP, but not among subjects with affective psychosis.

Almost one quarter of subjects with schizophrenia had T2DM. This figure is comparable to the lifetime morbid risk of T2DM among persons with a first-degree relative with T2DM [39]. We found a higher prevalence of T2DM than previous studies in the age group 55 and over (35.2%), while the prevalence in the younger patients aged 30–54 years (11.5%) was comparable to previous studies [7, 9, 19, 25, 31, 46]. As in previous studies [7, 11, 14, 25, 31, 38, 49], females with schizophrenia had higher prevalence of T2DM than males. This contrasts with findings from the other participants, among whom the prevalence of T2DM was higher in males. Consistently with high T2DM prevalence, subjects with schizophrenia also had significantly higher serum insulin and insulin resistance index. Our study was cross-sectional, which hampers interpretations of causal associations. However, after adjusting for covariates associated with T2DM, the OR dropped only from 4.9 to 3.9 and diagnosis of schizophrenia remained significantly associated with T2DM. The result would support the hypothesis that the disease process itself may somehow increase the risk of T2DM [14], or that there are shared risk factors [4, 15].

Contrary to previous research, the prevalence of T2DM was not increased among subjects with affective psychosis. However, the subjects in previous studies have mostly been inpatients [6, 40], while our subjects had a lifetime diagnosis of major depressive disorder with psychotic features or bipolar I disorder. In both groups, there was one subject with T2DM. Although a previous study found that patients with mood disorder who use antipsychotic or other psychotropic medications had increased risk of developing T2DM [13], in our study the mean plasma glucose was nonsignificantly lower among subjects with affective psychosis who used antipsychotic, antidepressant, or mood-stabilizing medication compared with those that did not use these medications (data not shown). Consistently with Kupfer's suggestion that medical comorbidity may worsen during depressive episodes due to loss of dis-

Table 4 Prevalence and 95% confidence intervals of type 2 diabetes in subjects using antipsychotic medication

	Class of antipsychotic medication		
	High-potency	Low-potency	Atypical
Total[a]	**13.2% (7.9–21.2)** **	**12.8% (8.3–19.1)** **	**15.9% (7.5–30.6)***
Sex[b]			
Males	13.6% (5.6–29.5)	12.0% (5.5–24.2)	20.5% (5.5–53.5)
Females	**12.7% (6.4–23.8)***	**12.8% (7.3–21.5)** **	13.5% (5.4–29.9)
Age[c]			
30–54 years	**14.4% (6.6–28.6)*** **	**9.4% (3.4–23.4)***	10.1% (1.3–49.3)
55- years	19.5% (10.8–32.7)	**25.6% (17.6–35.8)*** **	**33.1% (16.3–55.7)** **

[a] adjusted for age and sex
[b] adjusted of age
[c] adjusted for sex
* Contrast to other participants: $P < 0.05$
** Contrast to other participants: $P < 0.01$
*** Contrast to other participants: $P < 0.001$

Table 5 Logistic regression result for variables associated with increased odds of having type 2 diabetes

Explanatory variable	OR (95% CI)	*P* value
Age		
30–44 (reference)	1	
45–54	1.35 (0.84–2.18)	0.022
55–64	**1.96 (1.20–3.20)**	**0.0074**
65–	**2.53 (1.51–4.27)**	**0.0005**
Sex		
Female (reference)	1	
Male	**3.55 (2.44–5.17)**	**<0.0001**
Education		
Basic (reference)	1	
Secondary	0.81 (0.62–1.06)	0.13
Higher	**0.65 (0.47–0.90)**	**0.010**
Schizophrenia		
No (reference)	1	
Yes	**3.91 (1.63–9.40)**	**0.0023**
Other nonaffective psychotic disorder		
No (reference)	1	
Yes	1.58 (0.70–3.60)	0.27
High-potency antipsychotic medication		
No (reference)	1	
Yes	1.45 (0.70–3.01)	0.32
Low-potency antipsychotic medication		
No (reference)	1	
Yes	0.71 (0.26–1.88)	0.49
Atypical antipsychotic medication		
No (reference)	1	
Yes	**5.20 (1.31–20.6)**	**0.019**
Cardiovascular medication		
No (reference)	1	
Yes	**3.13 (2.45–4.00)**	**<0.0001**
Diet		
Healthy (reference)	1	
Average	0.95 (0.71–1.29)	0.76
Unhealthy	**0.58 (0.40–0.85)**	**0.0045**
Smoking		
Never smoked (reference)	1	
Ex-smoker	1.11 (0.81–1.51)	0.51
Current smoker	1.19 (0.85–1.65)	0.31
Alcohol consumption (OR per 100 g/week increase)	**1.11 (1.02–1.20)**	**0.011**
Abdominal obesity		
No (reference)	**1**	
Yes	**3.31 (2.53–4.33)**	**<0.0001**
Handgrip (OR per 100 N increase)	**0.71 (0.61–0.83)**	**<0.0001**

All variables were entered into the model simultaneously

cipline and motivation in its treatment [24], it is possible that subjects who complied with treatment also took better care of themselves in other respects, which was reflected in their blood glucose values. Our results underline the importance of investigating medical comorbidity in psychotic disorders also in general population surveys. Subjects with affective psychosis in our study actually had lower odds of T2DM and lower mean blood glucose, although just below statistical significance. These results suggest that there might not be any association between T2DM and affective psychoses in the general population.

Subjects with ONAP had two-fold increased odds of having T2DM; 27% of them had schizoaffective disorder. As half of the patients with schizoaffective disorder in a previous study had T2DM [40], we checked whether the association between T2DM and ONAP was caused entirely by subjects with schizoaffective disorder. Indeed, the prevalence of T2DM among subjects with schizoaffective disorder was similar to the prevalence in subjects with schizophrenia, 23.7% (95% CI 9.7–47.1). However, in other subjects with ONAP, the prevalence of T2DM was still higher than in the remaining study population, 10.7% (95%CI 5.3–20.5). In the logistic regression model, ONAP was not an independent predictor of T2DM, suggesting that other variables, e.g. antipsychotic medication and obesity, possibly mediated the association between ONAP and T2DM.

Our results concerning antipsychotic medication must be interpreted with caution, since they are based on cross-sectional data and almost all subjects with psychotic disorders had used antipsychotic medication at some point during their illness. However, the sample included a substantial number of individuals who used antipsychotic medication despite not having a psychotic disorder, and in this respect the results are interesting. We found that use of all types of antipsychotic medication was associated with increased odds of having T2DM, but the effect of low-potency and high-potency antipsychotics disappeared when other covariates were controlled for. Causal associations cannot be reliably assessed on the basis of cross-sectional data, but the results suggest that the association between low-potency and high-potency medication and T2DM may be mediated through obesity and lifestyle-related factors.

In contrast, atypical antipsychotics remained an independent predictor of T2DM. Most of the subjects having atypical antipsychotics were taking risperidone (26 out of 33). Only four subjects used clozapine, and three olanzapine; all of them had psychotic disorder and were under 55 years old. One clozapine user and none of the olanzapine users had T2DM. We repeated the analysis using all covariates but risperidone instead of all atypical antipsychotics, and the odds ratio of having T2DM associated with risperidone use was 5.64 (95% CI 1.67–19.0, $P = 0.0053$). Our findings contradict the results of many previous studies, which have found no difference between risperidone and conventional antipsychotic medication in the risk of T2DM [20, 28]. The mean age of risperidone users was 71.3 years, and only eight of them had functional psychotic disorder. An potential confounder related to the association between diabetes and risperidone use in the elderly is somatic comorbidity, T2DM being associated with increased risk of dementia [44]. However, it is also possible that elderly subjects are more vulnerable to the side effects of atypical antipsychotic drugs [23], one of them being T2DM.

T2DM was underdiagnosed and undertreated both in subjects with psychotic disorders and in the general population. There were no significant differences in the proportion of subjects with T2DM and with and without schizophrenia or ONAP receiving antidiabetic

medication, which is consistent with the study by Cohen et al. [7] but contrary to the findings from the CATIE study [32]. However, the number of subjects with comorbid T2DM and psychotic disorder was relatively small, which limited our statistical power to detect differences in their treatment.

Limitations

The study was cross-sectional, and causal associations between T2DM and psychotic disorder and antipsychotic medication cannot be drawn. Information on medication was self-reported, although usually based on prescriptions shown to the interviewer. Dosage was not recorded, neither was the duration of medication.

Use of atypical antipsychotic medication in Finland in 2000 was less frequent than currently. Based on defined daily dose per thousand inhabitants, the most frequently used antipsychotic medications in Finland presently are olanzapine, risperidone, and clozapine [33], whereas phenothiazines were the most frequently used antipsychotic medications in 2000 [34]. Unfortunately, this study could not provide general population-based information on the association between T2DM and olanzapine and clozapine use.

Diet and smoking were not associated with increased odds of having T2DM, although they have been risk factors for T2DM in previous studies [30, 36]. One explanation was that subjects who had been diagnosed with T2DM had improved dietary habits, but there may also be problems with the reliability of self-reported lifestyle data. Contrary to previous research [5], subjects with schizophrenia did not differ significantly from the general population in these lifestyle-related variables, which suggests that the use of self-report data may be particularly problematic in this group.

The prevalence of affective psychoses, particularly bipolar I disorder, was low [37]. Although this accords with previous Finnish studies, it is still possible that some persons with less severe form of bipolar I disorder or major depressive disorder with psychotic features remained undetected [37]. However, such ascertainment bias should actually increase the association between T2DM and affective psychoses, not decrease it.

Finally, it would have been interesting to model predictors of T2DM among subjects with schizophrenia only, but their number was too small for meaningful logistic regression analysis.

Conclusions

Almost one quarter of patients with schizophrenia have T2DM, and particularly females and elderly individuals with schizophrenia are at increased odds of having T2DM. Findings concerning other nonaffective psychotic disorders were similar but less striking. In contrast, subjects with affective psychosis did not differ from other survey participants. Antipsychotic medication increased the odds of having T2DM but did not explain the association between schizophrenia and T2DM. T2DM was underdiagnosed and undertreated both in subjects with psychotic disorders and in the general population. Regular monitoring of fasting blood glucose in subjects with psychotic disorders and users of antipsychotic medication is essential.

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