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Regular Article

Diabetes, physical activity participation and exercise capacity in patients with schizophrenia

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Aim: The aim of this study was to determine if in schizophrenia patients the presence of diabetes is associated with lower physical activity participation and lower exercise capacity compared to patients with pre-diabetes and to patients without (pre-) diabetes.

Methods: Schizophrenia patients without (pre-)diabetes ($n = 86$) were compared with pre-diabetic ($n = 10$) and diabetic patients ($n = 10$). Patients were assessed on physical activity participation using the Baecke physical activity questionnaire and on exercise capacity using a 6-min walk test (6MWT).

Results: The three groups were similar in age, sex, mean antipsychotic medication dose, negative and depressive symptoms and smoking behavior. Distance achieved on the 6MWT, however, was approximately 15% shorter ($P < 0.05$) in patients with diabetes than in patients without (pre-)diabetes (500.3 ± 76.9 m vs 590.7 ± 101.8 m). Patients with diabetes were also significantly less physically active ($P < 0.05$). No differences between diabetic and pre-diabetic patients were found. Pre-diabetic patients had a higher body mass index (BMI) than non-diabetic patients (30.0 ± 7.3 vs 24.3 ± 4.3, $P < 0.05$). An interaction effect with BMI for differences in Baecke ($F = 29.9$, $P < 0.001$) and 6MWT ($F = 13.0$, $P < 0.001$) scores was seen between diabetic and non-diabetic patients on univariate ANCOVA.

Conclusion: The additive burden of diabetes might place patients with schizophrenia at an even greater risk for functional limitations in daily life.

Key words: diabetes, exercise, physical activity, physical fitness, schizophrenia.

PATIENTS WITH SCHIZOPHRENIA are at a greater risk of type 2 diabetes, with prevalence rates reaching more than twofold those of the general population.[1,2] Although it has been reported that patients with schizophrenia may be genetically predisposed to type 2 diabetes,[3,4] antipsychotic treatment and an unhealthy lifestyle may equally contribute to the development of this severe metabolic disease.[5,6] Compared with first-generation antispsychotics, second-generation antipsychotics are associated with a slightly to moderately increased diabetes risk.[7] The risk of diabetes-related adverse events, however, differs between second-generation antipsychotics, with olanzapine and clozapine and, to a lesser extent, quetiapine and risperidone having the highest risks.[8,9] Therefore, switching antipsychotic medication to one with a lower metabolic liability as well as lifestyle changes, such as a healthy diet and physical activity, should be considered when managing pre-diabetes and type 2 diabetes in patients with schizophrenia.[10–16] Motivating patients with schizophrenia to have a more active lifestyle, however, is difficult.[17] For schizophrenia patients with metabolic

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abnormalities this can be even more challenging.[18] In the general population type 2 diabetes is associated with lower physical activity participation and reduced exercise capacity.[19,20] One of the putative mechanisms of this is the diminishment of peripheral circulation in the lower limbs by diabetes.[21] Poor peripheral circulation makes it difficult to participate in physical activities, creating a vicious circle of inactivity, worsening of metabolic parameters and progressive decline in function and deconditioning.[22,23] To date, it is not established whether, compared to schizophrenia patients with pre-diabetes or to those without (pre-)diabetes, physical activity participation and exercise capacity is lower in schizophrenia patients with diabetes.

The primary aim of this study was to investigate whether schizophrenia patients with diabetes were less involved in physical activity compared to patients with pre-diabetes and those without (pre-)diabetes. A secondary aim was to determine if the presence of diabetes also limits exercise performance in those patients with diabetes.

METHODS

Participants and procedure

Over a 12-month period, all inpatients of the University Psychiatric Centre of Kortenberg in Belgium who were between 18 and 65 years old and who had a DSM-IV diagnosis of schizophrenia were invited to participate. Patients received a 2-h 75-g glucose load oral glucose tolerance test (OGTT) according to previously proposed guidelines.[24,25] This test was performed after an overnight fast. The presence of (pre)-diabetes was assessed, using the joint World Health Organization and International Diabetes Federation (IDF) criteria.[26] Accordingly, diabetes was defined as fasting blood glucose ≥7.0 mmol/L or treatment with anti-diabetic medication. Pre-diabetes was defined as fasting blood glucose 6.1–6.9 mmol/L. Bodyweight was measured in light clothing to the nearest 0.1 kg using a SECA beam balance scale (Medical Scales and Measuring Systems, Hamburg, Germany); height to the nearest 0.1 cm using a wall-mounted stadiometer. Patients were excluded if they had comorbid substance abuse according to DSM-IV criteria. Somatic exclusion criteria included evidence of acute and severe cardiovascular, neuromuscular and endocrine disorders which, according to the American Thoracic Society,[27] might prevent safe participation in sub-maximal walk tests. The study procedure was approved by the Scientific Committee of the University Psychiatric Centre of the Catholic University of Leuven, Belgium. All participants gave their written informed consent after the procedure was explained.

Physical activity participation: Baecke physical activity questionnaire

The 12-months recall Baecke physical activity questionnaire consists of 16 questions organized in three sections: physical activity at work (questions 1–8); sport during leisure time (questions 9–12); and physical activity during leisure excluding sport (questions 12–16).[28] Questions in each section are scored on a 5-point Likert scale, ranging from 'never' to 'always' or 'very often'. The two most frequently reported sports activities are explored in additional questions, assessing the number of months per year and hours per week of participation. We used only the total score as a measure of physical activity participation. Total scores range from 3 to 15, with higher scores indicating being more physically active. The Baecke questionnaire has been used previously in patients with schizophrenia.[29]

Exercise capacity: 6-min walk test

The 6-min walk test (6MWT) was performed according to the American Thoracic Society guidelines in an indoor corridor with a minimum of external stimuli.[27] Two cones, 25 m apart, indicated the length of the walkway. Participants were instructed to walk back and forth around the cones during 6 min, without running or jogging. Resting was allowed if necessary, but walking was to be resumed as soon as the participants were able to do so. The protocol stated that the testing was to be interrupted if threatening symptoms appeared. Standardized encouragements were provided at recommended intervals. The total distance walked in 6 min was recorded to the nearest decimeter. Supervision and measurement of the 6MWT was performed by one of four trained members (three physical therapists, one research nurse), not necessarily the same on both occasions. The 6MWT has been shown to be a reliable and feasible test to assess exercise capacity in patients with schizophrenia.[30]

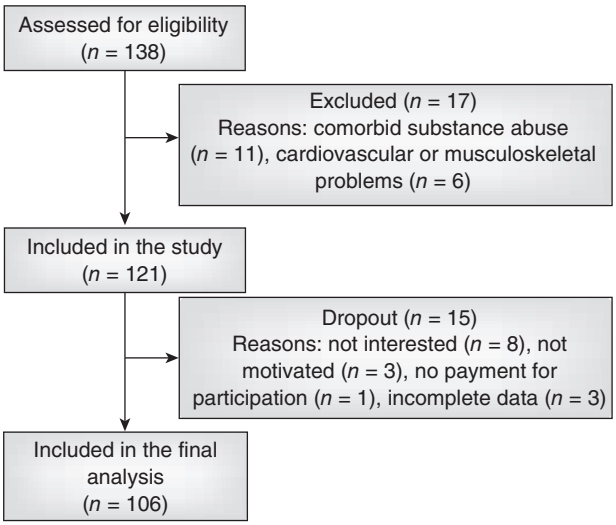

Figure 1. Flowchart of the eligible patients.

Negative and depressive symptoms: Psychosis Evaluation tool for Common use by Caregivers

Negative and depressive symptoms were assessed by independent and well trained nurses using the Psychosis Evaluation Tool for Common Use by Caregivers (PECC).[31] Negative and depressive symptoms were assessed, respectively, by two groups of four items (motor retardation, blunted affect, passive/apathetic withdrawal, poor rapport; and anxiety, depression, guilt feelings, somatic concern) on a 7-point scale with higher scores indicating more severe symptoms. The total negative and depressive symptoms scores range from 4 to 28. Validation results suggest that the PECC can be successfully used for the evaluation of these symptoms in schizophrenia.[32]

Antipsychotic medication dose

Antipsychotic medication was recorded for each patient and converted into a daily equivalent dosage of chlorpromazine.[33]

Statistical analysis

We used a one-way ANOVA with post-hoc Scheffe to assess whether differences in demographic and clinical characteristics existed between schizophrenia patients without (pre)diabetes versus patients with (pre)diabetes. For differences in Baecke physical activity and 6MWT scores between the different groups, univariate ANCOVA with body mass index (BMI) as covariate was calculated. Chi-squared test was used to test for differences in gender distribution. A priori, a two-sided level of significance was set at 0.05. Statistica 9 (Statsoft, Tulsa, OK, USA) was used for data analysis.

RESULTS

Participants

Out of 138 patients with schizophrenia, 106 met the inclusion criteria. Reasons for exclusion and dropout are presented in Figure 1.

An overview of the medication intake of the included participants is presented in Table 1. A total of 19% of the subjects had either diabetes (9.5%; $n = 10$) or pre-diabetes (also 9.5%; $n = 10$).

Differences between diabetes, pre-diabetes and non-diabetic patients with schizophrenia

There were no significant differences in age, gender, smoking behavior, antipsychotic medication dose,

Table 1. Medication use ($n = 106$)

Medication	No. patients (%)
No antipsychotic	1 (0.9)
Monotherapy antipsychotic	
Aripiprazole	7 (6.6)
Amisulpride	5 (4.7)
Clozapine	12 (11.3)
Quetiapine	7 (6.6)
Risperidone	22 (20.7)
Olanzapine	12 (11.3)
Combination of antipsychotics	
First-generation	2 (1.9)
Second-generation	24 (22.6)
First- and second-generation	14 (13.2)
Other medication	
Anticholinergic	12 (11.3)
Antidepressant	45 (42.4)
Benzodiazepine	33 (31.1)
Beta-blocking agent	5 (4.7)
Mood stabilizer	13 (12.3)
Somatic medication	26 (24.5)

Table 2. Schizophrenia subject characteristics vs presence of diabetes

Variables	Patients without (pre)diabetes ($n = 86$) Mean ± SD or n (%)	Pre-diabetic patients ($n = 10$) Mean ± SD or n (%)	Diabetic patients ($n = 10$) Mean ± SD or n (%)
Gender (M/F)	57/29	7/3	5/5
Age (years)	34.5 ± 10.5	38.0 ± 8.5	40.3 ± 10.9
BMI (kg/m^2)	24.3 ± 4.3[a,b]	30.0 ± 7.3[a]	30.1 ± 8.4[b]
Presence of a physical comorbidity[†]	18 (20.9)	2 (20.0)	3 (30.0)
Cigarettes (number/day)	13.5 ± 13.6	13.8 ± 15.9	11.0 ± 15.2
Antipsychotic dose (mg/day)	627.4 ± 386.3	572.9 ± 221.9	788.0 ± 599.0
Negative symptoms (PECC)	9.8 ± 4.7	9.9 ± 4.3	12.6 ± 5.9
Depressive symptoms (PECC)	9.8 ± 4.7	12.0 ± 6.4	11.6 ± 4.6
Baecke physical activity score	7.4 ± 1.6[b]	6.7 ± 1.6	5.9 ± 1.5[b]
6-min walk test score (m)	590.7 ± 101.8[b]	552.0 ± 131.9	500.3 ± 76.9[b]

[a,b]One-way ANOVA with post-hoc Sheffe test ($P < 0.05$): [a]without diabetes vs pre-diabetes, [b]without diabetes vs diabetes.
[†]Cardiovascular, neuromuscular or endocrine disorders (International Classification of Diseases-10 code). BMI, body mass index; PECC, Psychosis Evaluation tool for Common use by Caregivers.

presence of physical comorbidity, and negative and depressive symptoms between patients with diabetes compared to the two other subgroups (Table 2).

In contrast, patients with diabetes had a higher BMI, a lower mean Baecke physical activity score and a lower mean distance on the 6MWT compared to patients without diabetes (Table 2).

Except for BMI, no significant differences could be found when comparing pre-diabetic patients with non-diabetic participants (Table 2). There were also no significant differences between pre-diabetic and diabetic participants in demographic and clinical variables and physical parameters (Table 2).

Univariate ANCOVA indicated an interaction effect with BMI for differences in Baecke ($F = 29.9$, $P < 0.001$) and 6MWT ($F = 13.0$, $P < 0.001$) scores between diabetes and non-diabetic patients.

DISCUSSION

To the authors' knowledge this is the first study to show that, in schizophrenia patients, the presence of diabetes is associated with a lower physical activity participation and exercise capacity as measured with 6MWT. No differences between diabetic and pre-diabetic patients and between pre-diabetic and non-diabetic patients were found. The present data are in accordance with that of Ingle *et al.*, who previously demonstrated in patients with heart failure that diabetic complications reduce the distance achieved on the 6MWT further by approximately 20%.[34] The dis tance achieved on the 6MWT in the present diabetic subgroup was approximately 15% less compared to those without (pre-)diabetes (500 m vs. 590 m).

We also found that BMI was significantly higher in diabetic patients, and an interaction effect of BMI between the presence of diabetes and lower physical activity and exercise capacity scores could not be excluded. Previous research in persons with type 2 diabetes without manifest mobility limitations already showed that a higher BMI and decreased muscle strength, but not neuropathy, are associated with a negative performance outcome on functional capacity tests.[35] Associations between metabolic abnormalities, BMI, bodyweight-related physical complaints, and physical activity participation and the distance achieved on the 6MWT, have been reported previously in patients with schizophrenia.[19,28]

Research comparing BMI-matched schizophrenia patients with and without diabetes is needed to clarify the relative contribution of diabetic complications on physical activity and exercise performance. This research should especially focus on the possible negative consequences of diabetes on ambulation and in particular on the peripheral circulation in the lower limbs. Impaired peripheral circulation could be assessed on calf blood flow during a 6MWT by using a mercury strain-gauge plethysmography or by measuring transcutaneous oxygen tension ($TcPO_2$) with a polarographic electrode and a $TcPO_2$ monitor.

Limitations

The present findings must be interpreted with caution because of some methodological limitations. Important limitations were the limited sample size, the inclusion of only inpatients and the reliance on self-reported physical activity, a method that is prone to both systematic and random errors.[36] Also, data on eating habits as a risk factor for diabetes were not assessed. Patients with schizophrenia on average consume a diet higher in fat, higher in refined sugar, lower in fiber and poor in fruits and in vegetables.[37,38] Last, the current study had a cross-sectional nature. Thus, the impact of diabetes and the effects of behavior modification could not be estimated directly.

Clinical relevance

This study adds to current knowledge that schizophrenia patients with diabetes are less physically active in daily life and have a lower exercise capacity than non-diabetic patients. Patients with diabetes may therefore be at greater risk for mobility loss. Multidisciplinary treatment protocols designed to reduce the risk factors of diabetes in patients with schizophrenia should target improvements in performing daily life activities such as walking. Current clinical guidelines state that physical activity is a cornerstone of diabetes management, along with dietary and pharmacological interventions. These guidelines recommend that patients with type 2 diabetes should perform at least 150 min per week of moderate-intensity physical activity (e.g. brisk walking) and should perform resistance exercise three times per week.[39,40] Health-care professionals should discuss the potential physical barriers that schizophrenia patients with diabetes are confronted with when complying with these guidelines.

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