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Prevalence of metabolic syndrome in female and male patients at risk of psychosis

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ABSTRACT

Metabolic Syndrome (MetS) is one of the most common factors underlying the high rate of mortality observed in patients with schizophrenia. Recent research on this topic revealed that many of the patients studied were, in fact, in a medicated state. As such, it is unclear whether MetS is causally associated with the disorder itself or the medication used to treat it. In this study, patients with a clinically high risk of expressing first episode psychosis (CHR) were examined regarding the prevalence of MetS. $N = 144$ unmedicated and antipsychotic-naïve CHR patients, aged between 18 and 42 years and suffering from unmanifested prodromal symptoms, were compared with a cohort of $N = 3995$ individuals from the "German Metabolic and Cardiovascular Risk Study" (GEMCAS). A slightly higher prevalence of individual MetS criteria was observed in the CHR group compared to the GEMCAS sample; specifically, the following were noted: a higher blood pressure (35.0% vs. 28.0%), increased waist circumference (17.6% vs. 15.1%), and increased fasting blood glucose (9.4% vs. 4.0%) in CHR patients. Additionally, the rate of reduced HDL cholesterol concentrations was lower in the control group (20.2% vs. 13.3%).

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1. Introduction

Patients with schizophrenia have a risk of mortality that is 2–3 times higher than that of the general population (Brown, 1997; Rössler et al., 2005; Ösby et al., 2000; Casadebaig and Philippe, 1998). This mortality differential has increased in recent decades and has resulted in a reduced life expectancy of between 13 and 30 years for patients with schizophrenia (Saha et al., 2007; Capasso et al., 2008; Wahlbeck et al., 2011). This higher risk of mortality can be attributed to unnatural causes, in particular suicides, as well as natural deaths, which are

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usually related to cardiovascular disorders (Healy et al., 2012). According to a recent long-term observational study on a sample of $N = 335$ schizophrenia patients, Healy and colleagues found that after 10 years, 16 of 33 deaths were from suicide, while 8 of 33 deaths resulted from cardiovascular disorders (Healy et al., 2012).

The screening and monitoring of cardiovascular risk factors are therefore important for allowing clinicians to focus on the CVD risks of patients with schizophrenia (De Hert et al., 2009).

Every second schizophrenia patient aged over 45 years is afflicted with Metabolic Syndrome (MetS), with an incidence that continues to increase linearly with the age of the patient (De Hert et al., 2006). Metabolic syndrome also increases the risk of cardiovascular morbidity and mortality (Isomaa et al., 2001). According to the "National Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults" (NCEP-ATP-III, 2001), MetS is diagnosed when at least three of the following five criteria are fulfilled: 1. Waist circumference of >102 cm for men and >88 cm for women; 2. Serum triglycerides ≥150 mg/dl; 3. Reduced HDL cholesterol (< 40 mg/dl in males and <50 mg/dl in females); 4. Increased blood pressure (systolic ≥130 mm Hg or diastolic ≥85 mm Hg); and 5. Increased fasting serum glucose levels (>110 mg/dl or the existence of diabetes mellitus type 2) (Eckel et al., 2005; Grundy et al., 2004). It remains controversial, however, whether the higher prevalence of MetS and CVD in schizophrenia result from poor lifestyle factors or the antipsychotic treatment or are associated with schizophrenia itself. Several studies have reported higher prevalence rates of MetS in schizophrenia patients treated with antipsychotics, with figures ranging from 32 to 68%, whereas in untreated patients, MetS rates of between 3.3% and 26% have been found (Chadda et al., 2013). Verma et al. (2009) reported that in an untreated sample who had suffered their first episode between the ages of 18 and 40 years, there was a significantly higher incidence of diabetes. It could be assumed from this finding that the overweightness and dyslipidemia were due largely to the antipsychotic treatment; however, counter to this notion, there may also be an association between the risk of diabetes and schizophrenia due to the influence of behavioural and lifestyle factors.

Medicated patients seem to show the highest rate of metabolic syndrome (Mitchell et al., 2013; Mitchell et al., 2012). Ryan et al. (2003) reported that drug-naive, first-episode patients with schizophrenia had a lower fasting glucose tolerance and higher levels of plasma glucose, insulin and cortisol than non-affected controls. They assumed that schizophrenia may be associated with metabolic syndrome independent of medical treatment or the course of the disease (Ryan et al., 2003).

Considering this background of conflicting data regarding MetS in patients with schizophrenia, we assessed the prevalence of MetS in unmedicated patients with a clinically high risk of first episode psychosis (CHR) who were participating in the PREVENT study, which is a randomised, double-blind, placebo-controlled trial evaluating different treatment approaches for the prevention of psychosis (Bechdolf et al., 2011). We expected that in the sample of CHR individuals, there would be a higher prevalence of metabolic syndrome than in a comparative unselected sample of patients recruited from everyday general practice.

2. Materials and methods

2.1. Sample

Our study sample consisted of a subsample of the PREVENT trial. Thus, $N = 144$ antipsychotic-naïve (31.9% women) CHR patients who had agreed to participate in the PREVENT trial (Bechdolf et al., 2011) were included. PREVENT is a randomised controlled trial of interventions in CHR patients comparing cognitive behavioural therapy, low-dose aripiprazole and placebo in the prevention of psychosis. The patients who were included in our analyses were not enrolled in the course of the main study. This is because they did not manifest any prodromal symptoms at the time of their participation and were consequently unmedicated. Of the female patients, 28.6% took antidepressants, 2.40% took sedatives, and 69.0% took no medications, whereas of the male patients, 17.6% took antidepressants, 2.0% took sedatives and 80.4% took no medications. Of all CHR patients, 20.8% took antidepressants, 2.10% took sedatives or hypnotics, and 77.1% took no medications.

Patients in the main sample were aged between 18 and 42 years and were assigned to one of the following groups: 1) those with attenuated positive symptoms; 2) those with brief, limited, intermittent psychotic symptoms; 3) those with predictive basic symptoms; and 4) those with a familial risk plus reduced functioning (for more details, see Bechdolf et al., 2011). The PREVENT sample was examined in nine specialised outpatient centres at the Departments of Psychiatry and Psychotherapy at the Universities of Cologne, Bonn, Aachen, Düsseldorf, Bochum, Hamburg, Göttingen, München and Berlin. Written informed consent was obtained in all cases.

The PREVENT sample was compared with a subsample ($N = 3995$) of the national cross-sectional "German Metabolic and Cardiovascular Risk Study" (GEMCAS) ($N = 35{,}869$; 61% female), which involved the participation of $N = 1511$ randomly selected primary care practices (Moebus et al., 2006). The GEMCAS study was designed to provide as robust as possible data within the confines of an epidemiological study. Based on the low level of missing data and the high data quality, the feasibility of this type of research setting (short evaluation period, practitioners as data assessment sites) was considered very good. According to Kohler and Ziese (2004), 91.8% of all adults in Germany consult a general practitioner during the course of a single year. Germany has a publicly funded health care system for physician services with almost no user fees (Moebus et al., 2006). We believe that the GEMCAS sample is appropriate for comparison with schizophrenia patients because it is the largest representative cross-sectional study to date on the assessment of MetS in the general population in Germany (Moebus et al., 2006; Moebus et al., 2007). Subsamples from GEMCAS have also been used in other studies to compare the frequency of MetS in major depressive disorder and borderline personality disorder with data from the German population (Kahl et al., 2012; Kahl et al., 2013).

The analysis was limited to those aged between 18 and 30 years, as there were only 19 participants (9 men, 10 women) aged between 31 and 42 who were included in the PREVENT sample. A subsample of the overall GEMCAS sample was chosen by adapting the selected age range. GEMCAS was originally designed for an age range of 18–99 years. By selecting patients who were between 18 and 30, only $N = 3995$ patients remained. The same demographic data were applied, and thus the samples were comparable regarding age and demographic data. The approach followed in this study can be found in Kahl et al. (2012 and 2013).

In one of our subgroup analyses, however, we included all participants in the PREVENT trial, and thus the GEMCAS sample was extended to include all ages between 18 and 42 inclusively. In the PREVENT trial, the mean age was 22.7 (±3.5) years, while in the GEMCAS subsample, it was 24.2 (±3.7) years. In Table 1, additional characteristics of the two subsamples from the GEMCAS and PREVENT studies are provided. Additional subject information regarding the main samples is provided in publications by Bechdolf et al. (2011) for the PREVENT trial and by Moebus et al. (2007) for the GEMCAS study.

2.2. Methods

To assess MetS in CHR patients, baseline data (2010) from the PREVENT trial were used. PREVENT represents a randomised, double-blind, placebo-controlled parallel study with 3 study conditions, including an antipsychotic intervention (aripiprazole and clinical management), cognitive behavioural therapy and a placebo (placebo and clinical management). The PREVENT study was registered with the identifier ISRCTN: 02,658,871. A more detailed description of the methods used in the PREVENT study is provided elsewhere (Bechdolf et al., 2011).

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