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Substance use, medication adherence and outcome one year following a first episode of psychosis

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ABSTRACT

Both substance use and poor medication adherence are associated with poor outcome in psychosis. To clarify the contributions of substance use and poor medication adherence to poor outcome in the year following a first episode of psychosis, 205 patients were evaluated for use of tobacco, alcohol, cannabis and stimulants at their psychosis onset, and in a 1-year follow-up. Data on medication adherence and symptom remission were also collected. Patients had high rates of overall substance use before (37–65%) and after psychosis onset (45–66%). 44% showed poor medication adherence and 55% did not reach remission from psychosis. Nicotine dependence and cannabis use after psychosis onset significantly predicted both poor medication adherence and non-remission, and poor medication adherence mediated the effects of these substances on non-remission. In conclusion, medication adherence lies on the causal pathway between nicotine dependence and cannabis on the one hand and non-remission on the other.

1. Introduction

A number of studies have evaluated the impact that poor adherence to antipsychotic medication has on quality of life and hospitalizations in patients with psychosis (Gray et al., 2002; King et al., 2014; Park et al., 2014). Thus, poor medication adherence in patients following the first episode of psychosis (FEP) is associated with more frequent readmissions (Caseiro et al., 2012; Verdoux et al., 2000), and a greater risk of relapse (Kahn et al., 2008; Malla et al., 2006; Novak-Grubic and Tavcar, 2002).

Rates of poor adherence in FEP studies have been reported to range up to 71% (Hill et al., 2010; Levy et al., 2012; Miller et al., 2011). Use of substances, including cannabis and alcohol, has been found in several studies to be associated with poor medication adherence (Faridi et al., 2012; Hill et al., 2010; Lambert et al., 2010; Miller et al., 2009), as have a number of other demographic and clinical factors (Hill et al., 2010; Lambert et al., 2010). Furthermore, comorbid substance use has emerged as one of the greatest obstacles to the effective treatment of persons with psychosis; substance use is a risk factor for both poor medication adherence and dropout from treatment. Moreover, some studies suggest a dose–response relationship between severity of substance use and medication adherence rates (Dixon, 1999; Miller et al., 2009; Wade et al., 2007).

Two major limitations of the published data on substance use disorder and poor medication adherence are the small sample size of most studies and the narrow focus, usually on use of only one substance. In addition, the relation of poor adherence to tobacco smoking has not to date been investigated. This is important given that tobacco smoking is highly prevalent among psychotic patients, and there have been recent suggestions that tobacco smoking may be a risk factor for both onset (Gurillo et al., 2015) and outcome (Krishnadas et al., 2012) of psychosis.

In a one year follow-up of first episode psychosis patients, we obtained detailed information on the most commonly used substances among psychiatric patients, including tobacco, alcohol, cannabis and stimulants (such as amphetamines) both at baseline and during their subsequent clinical contact. Therefore the strength of our study is the ability to address the following hypotheses: 1. substance use following illness onset (tobacco, alcohol, cannabis and other stimulants) impairs medication adherence; 2. Substance use is associated with poor

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outcome at 1 year follow-up, and poor medication adherence mediates this effect.

2. Materials and methods

2.1. Study design and sample

Participants were recruited as part of the Biomedical Research Centre (BRC) Genetics and Psychosis (GAP) and the Physical Health and Substance Use Measures (PUMP) studies carried out at the Institute of Psychiatry, Psychology and Neuroscience, London (Di Forti et al., 2009). All patients presenting to the Adult Psychiatric services (18 years < age < 65 years) of the South London and Maudsley NHS Foundation Trust between December 2005 and October 2010 with their first episode of psychosis (FEP) who gave consent, were recruited into the study. Eligibility was determined through examination of the clinical notes of new admissions and consultation with clinical teams, and then validated by the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) interview (World Health Organization, 1992). Inclusion criteria required that patients had 7 or more consecutive days of psychotic symptom(s) and were presenting to the psychiatric services for the first time with psychosis. Patients with an IQ < 70, poor English fluency, and with a known or suspected organic cause for psychosis were excluded.

The data presented here are based on the subset of the whole GAP/PUMP sample (N = 205/461, 44%) on whom we were able to complete follow-up assessments for the year after the first contact with psychiatric services for psychotic disorder, and obtain satisfactory data on substance use and medication adherence. The most common reasons for attrition during the follow-up period were disengagement from clinical team after first hospitalization/contact with mental health services (N = 62, 13.4%) or insufficient/unavailable clinical information on the entire follow-up period because of disengagement from mental health services at some point during the one year follow-up period (N = 137, 29.7%). Other reasons for drop out included: a) left the UK (N = 16, 3.5%) or transferred to other mental health services within the UK (N = 10, 2.2%); b) death (non-suicide) (N = 11, 2.4%) or suicide (N = 3, 0.7%). Moreover, a small proportion of patients (N = 17, 3.7%) were excluded from the study because they were found to have already been treated with antipsychotics before enrolment in the study.

2.2. Baseline assessments

2.2.1. Clinical and socio-demographic measures

Baseline information about age, gender, self-reported ethnicity, relationship status, employment status and level of education was collected using the Medical Research Council Social Scale (MRCSS; Mallett et al., 2002). Diagnosis was made according to DSM-IV/ICD-10 criteria using the Operational Criteria OPCRIT (McGuffin et al., 1991) based on both the clinical notes and the data collected with the SCAN (World Health Organization, 1992) in the month following the first contact with psychiatric services for psychosis. All diagnoses were made by qualified psychiatrists and clinical researchers, who attended training and OPCRIT intra-class correlation assessment ($0.70 \leq$ Cronbach's $\alpha \leq 1$). Diagnoses were combined in two main categorical groups: 1. non-affective psychosis (ICD10 codes: F20-F29; World Health Organization, 1992) and 2. affective psychosis (ICD 10 codes: F30-F33; World Health Organization, 1992).

2.2.2. Substance use evaluation

Subjects who reported tobacco use were interviewed using the Fagerström Test for Nicotine Dependence (FTND; Heatherton et al., 1991). This questionnaire is a standard instrument for assessing the intensity of physical addiction to nicotine in the general population and provides an ordinal measure of nicotine dependence related to cigarette smoking. It contains six items that evaluate the quantity of cigarette consumption, the compulsion to use, and dependence. In the FTND, yes/no items are scored from 0 to 1 and multiple-choice items are scored from 0 to 3. The items are summed to yield a total score of 0–10. The higher the total Fagerström score, the more intense is the patient's physical dependence on nicotine. Subjects with FTND scores ≥5 were classified as nicotine-dependent.

Similarly, participants who reported alcohol use were interviewed using the Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 1989). This questionnaire is a reliable and simple screening tool which is sensitive to early detection of risky and high risk (or hazardous and harmful) drinking. It has ten questions on alcohol consumption (1 to 3), dependence (4 to 6), and the consequences or problems related to drinking (7 to 10). Questions 1 to 8 are scored on a five-point scale from 0, 1, 2, 3, and 4. Questions 9 and 10 are scored on a three-point scale from 0, 2 and 4. The maximum total score is 40. Evidence from studies determining the validity and reliability of the AUDIT for detecting problem drinking in a population of FEP indicate that the AUDIT functions best with a cut-off score of 10 (sensitivity, 85%; specificity, 91%; Cassidy et al., 2008). Subjects with AUDIT scores ≥10 were classified as problem drinkers in this study.

FEP patients were administered the Cannabis Experience Questionnaire modified version (CEQ_{MV}; Colizzi et al., 2015a; Colizzi et al., 2015b; Di Forti et al., 2012) at baseline. This questionnaire provides information on lifetime use of cannabis, tobacco, stimulants and other drugs at enrollment. The CEQmv allows detailed assessment of patterns of cannabis and as well as use of other illicit drugs including stimulants, including age at first use, frequency and duration of use, and the specific type of cannabis used.

2.3. Case-tracing procedure

The one-year follow-up period was taken as the date of first contact with mental health services of the South London and Maudsley Mental Health NHS Foundation Trust (SLAM) for psychosis to the date exactly one year later using the clinical records held on the SLAM electronic Patient Journey System (ePJS). All of the following measures were completed by a researcher retrospectively from the electronic mental health records system (ePJS of SLAM).

2.4. Follow-up assessments

Clinical, socio-demographic and substance use data were collected with the Follow-up Psychiatric and Personal History Schedule (FU-PPHS). The PPHS is a schedule to record information about mental state, general behavior, substance use, events and personal history of the patient during a follow-up period; information can be obtained from patients, informants, case notes and other records (Janca and Chandrashekar, 1995). Researchers involved in rating the PPHS at follow-up achieved an excellent intra-class correlation (>0.90) on all PPHS items when duplicate ratings were compared.

2.4.1. Clinical assessment: medication adherence and remission

Information on medication adherence and remission during the one year follow-up was extracted from the PPHS (Janca and Chandrashekar, 1995). In the PPHS, poor adherence is defined as: 1 = lapses of 3 or more days more than once; 2 = not taking any prescribed medication. Remission is operationally defined as: absence of positive, negative or disorganized symptoms for at least 30 days.

2.4.2. Substance use evaluation

Substance use over the one year follow-up was scored using FTND (Heatherton et al., 1991), AUDIT (Babor et al., 1989), and CEQ_{MV} (Colizzi et al., 2015a; Colizzi et al., 2015b; Di Forti et al., 2012), in the same manner as for baseline.

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