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Long-term risk factors for substance-induced and primary psychosis after release from prison. A longitudinal study of substance users

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ABSTRACT

Purpose: The purpose of this study was to determine long-term risk factors for substance-induced and primary psychosis after release from prison.
Material: We used a longitudinal register-based cohort study combining European version of Addiction Severity Index (Europ-ASI) interviews and the Swedish inpatient register. The study included 6217 individuals who were in the Swedish criminal justice system from 2001 to 2006.
Measurements: The outcomes were substance-induced and primary psychosis as defined by the International Classification of Disease — 10th version. All variables for estimating baseline risk were drawn from the Europ-ASI interview, and included information on substance use, demographics and health. The interview database and the inpatient register were coupled, and groups were compared by using tests of significance and logistic regression.
Results: Polydrug use was the strongest predictor for substance induced psychosis (OR = 9.55, 95% CI 3.42–26.67), but all substances imposed an increased risk. Previous psychiatric hospitalization and non-drug related hallucinations were significant, but weaker, risk factors. The only substance variable that predicted primary psychosis was cannabis (OR = 2.62, 95% CI 1.39–4.96), but previous psychiatric hospitalization (OR = 3.22, 95% CI 2.27–4.54) and non-drug related hallucinations (OR = 4.00, 95% CI 2.82–5.67) were even stronger predictors.
Conclusions: Cannabis use was a risk factor for primary psychosis, but other health related individual risk factors were even more important. Polydrug use was the strongest risk factor for substance-induced psychosis.

1. Introduction

Substance use can induce acute psychotic symptoms in the intoxication and withdrawal phase. Early clinical studies demonstrated that increasing doses of amphetamine administered to healthy voluntaries induced psychotic symptoms (Griffiths et al., 1968; Angrist et al., 1974). Recreational use of amphetamine (including methamphetamine) increases the risk of psychotic symptoms two to threefold (McKetin et al., 2010), and a dose–response relationship has been demonstrated (Chen et al., 2003; Ujike and Sato, 2004; McKetin et al., 2013). Risk factors such as childhood problems and genetic vulnerability affect how subjects respond to amphetamine (Chen et al., 2005; Salo et al., 2008; Kittirattanapaiboon et al., 2010; Ding et al., 2014). Cannabis can also induce transient psychotic conditions, supposedly distinguishable from acute schizophrenia (Nunez and Gurpegui, 2002). In a heroin user, the prevalence of delusions and hallucinations is relatively low (Maremmani et al., 2007), as is the case for alcohol-users (Soyka, 2008).

Substance use is also a risk factor for long-lasting psychotic conditions. A history of substance abuse is one of the five features that contributes uniquely to the prediction of schizophrenia in a clinical high-risk sample (Cannon et al., 2008). Numerous studies have documented that cannabis increases the risk of schizophrenia in a consistent dose-related manner (Arseneault et al., 2004; Semple et al., 2005; Moore et al., 2007; Radhakrishnan et al., 2014), with high consumers having a six fold risk compared to non-users (Andréasson et al., 1987). Daily use of high potency cannabis ("skunk"), compared with traditional cannabis, triggers earlier onset of psychosis (Di Forti et al., 2014) and also imposes a higher risk (Di Forti et al., 2015), though the latter study has been criticized for underestimating confounding and for unwarranted inferring causality (Coyne, 2015; Crow, 2015). The association may be moderated by age of exposure, family history of psychotic disorder, childhood trauma and genetic factors (Radhakrishnan et al., 2014). It remains uncertain whether cannabis triggers psychosis in individuals who would have remained healthy if unexposed. Some have argued that a steep increase in the use of cannabis over two decades with no

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corresponding increase in schizophrenia speaks against cannabis as a causal factor (Degenhardt et al., 2003). Others have disagreed (Hickman et al., 2007), as such a potential cannabis-related increase in the incidence of schizophrenia would be very modest and difficult to detect (Hall, 2015). When applying scientific criteria for disease causality, cannabis is considered to be neither a necessary nor a sufficient factor, but a component cause, interacting with other factors in producing schizophrenia (Arseneault et al., 2004). The methodological limitations of the cannabis-psychosis evidence have been described in detail in the works of D'Souza (D'Souza, 2007; D'Souza et al., 2009).

Amphetamine is mostly studied for its acute effects, but has also been shown to increase the risk of schizophrenia (Marshall and Werb, 2010; Grant et al., 2011). Asian research has long conceptualized psychotic conditions induced by amphetamine as persistent amphetamine-induced psychosis, even after years of abstinence (Ujike and Sato, 2004; Akiyama, 2006). A longitudinal study of substance-related hospitalizations found amphetamine and cannabis to impose higher risk for schizophrenia than alcohol and opioids, though all substances elevated the risk (Callaghan et al., 2012).

There is still conflicting evidence about the relationship between the use of different substances and substance-induced and primary psychosis. As the outcome is rare, many studies include cases of psychosis and track risk factors retrospectively. Excluding cases that do not become psychotic represents a selection bias, but finding a large enough cohort is challenging. Register studies represent an intriguing solution to this power problem, but their weakness is in having little data at the individual level. Most studies investigate one substance, maybe overestimating the importance of that particular compound. Longitudinal studies complying with these challenges are warranted.

This study examines the long-term substance-related risk factors of substance-induced and primary psychosis after release from prison in a cohort of 6217 Swedish inmates. We compare users of alcohol, cannabis, amphetamine, heroin and polydrug with a group of low-frequency users. We also investigate the relevance of other known risk factors of psychosis related to demographic background, family morbidity, exposure to trauma and indicators of previous psychiatric problems.

2. Materials and method

2.1. Procedures

Information was taken from existing data sources. Baseline data came from a database of interviews administered by the Swedish Prison and Probation Service and outcome data on in-patient hospital treatment are from the Swedish National Patient Register (NPR).

When substance problems are suspected, subjects in the Swedish Prison and Probation Service have since 2001 been routinely interviewed with an extended version (Öberg et al., 2002) of the European version (Kokkevi and Hartgers, 1995) of the Addiction Severity Index (ASI) (McLellan et al., 1980). This is a semi-structured interview assessing substance use and substance-related problems. The information is used to guide interventions and to monitor problems and needs in the prison population. The interviews are gathered in a continuously growing database, to which researchers may apply for access. Only Swedish-speaking subjects are interviewed.

This study includes subjects who were interviewed between 2001 and 2006, and all information on background and substance use were drawn from the interview. The baseline data was coupled with follow-up data of cases of hospitalization due to psychosis from the NPR. This register contains information on all in-patient treatments in the country, including patient (personal identification number (PIN), gender, age), treatment (date of admission and discharge), and medical (main and secondary ICD−10 diagnoses) data. The two datasets were merged externally using the PIN, which subsequently was substituted by an arbitrary research-generated identification number for each subject. The follow-up time began at release for inmates and at interview time for subjects on probation or parole, and lasted until the end of 2010. Mean follow-up time was 5 years 4 months, and the total follow-up time was 28.540 person-years. The project has been approved by the Ethics Committee of Lund University.

Missing data were kept as missing with the exception of those parts of the ASI interview where it is natural to interpret blank fields as "not applicable" or "no". For the variable "born outside a Nordic country", missing data has been imputed as the most common response, which is being born in a Nordic country.

2.2. Subjects

This study included 6217 subjects who, in response to the ASI-question "Which substance is the major problem?" responded alcohol (N = 884), cannabis (N = 764), amphetamine (N = 1704), heroin (N = 509) or polydrug (N = 1282). The groups were mutually exclusive. Methadone, other opiates, pills (benzodiazepines and sedatives), cocaine, hallucinogens (LSD and mushrooms), inhalants and other (ecstasy, antidepressants and antipsychotics) were not included because of fewer than 200 subjects in each category. Some 1074 subjects responded that they did not have a substance use problem, and these individuals constitute the reference category in our substance variable. The subjects in this group reported little use of illicit drugs (0.3 versus 13.0 days as the mean in the other groups) during the 30 days before incarceration, and lifetime use was 88.5% (compared to 99.9% as the mean in the other groups). The reference group is thus not a substance-free group, but seems to consist of subjects with less severe and perhaps terminated substance use, evaluated as being less problematic.

Clients in the Swedish prison and probation service are unlikely to suffer from primary psychosis. According to the national penal code, an individual who is sentenced and who suffers from a severe mental illness as defined in the legislation, or who committed the offense under the influence of such a disorder, is to be referred to forensic psychiatric treatment instead of prison (Durbeej et al., 2010; Svennerlind et al., 2010). This includes primary psychosis.

2.3. Covariates and outcome measure

All covariates were taken from the ASI-interview. "Previous psychiatric hospitalization" includes those who confirmed inpatient admittance to a psychiatric hospital (not detoxification), regardless of cause. The hallucination variable is based on a question that instructs the interviewer to ensure that the hallucinations were not due to the influence of drugs. The two variables about relatives with problems are based on a matrix specifically mentioning all categories of first-degree relatives.

The outcome variable consists of all those who, according to the NPR, had been hospitalized for psychosis during follow-up. Primary psychosis was defined as all the F2 codes, and substance-related psychosis as all the F1x.5 codes. Subjects that during follow-up were hospitalized more than once and were registered with both substance-induced and primary psychosis were categorized as having a primary psychosis during follow-up. The routines and instruments for diagnostic evaluation may vary somewhat between the hospitals but were conducted by trained medical doctors or clinical psychologists.

2.4. Statistical analyses

The statistical analyses were performed using the IBM Statistical Package for Social Sciences (SPSS), version 22. We examined differences between groups using Person's chi square test and Fisher's exact test for categorical variables, and Mann–Whitney *U* tests for continuous variables. An alpha level of 0.05 was set for evaluating significance. In the unadjusted multivariate analyses we carried out a logistic regression with a 95% confidence interval for all dichotomous and continuous

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