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Cannabis abuse and risk for psychosis in a prodromal sample

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Abstract

The goal of the present study was to examine the rate of cannabis use among participants in the Cognitive Assessment and Risk Evaluation (CARE) Program, a longitudinal program for individuals who are “at risk” for developing a psychotic disorder. Cannabis abuse was assessed in 48 individuals identified as “at risk” for schizophrenia based on subsyndromal psychotic symptoms and/or family history. At 1 year follow-up, 6 of the 48 (12.5%) at risk subjects had made the transition to psychosis. Of the 6 subjects who converted to psychosis at follow-up, 83.3% met criteria for cannabis abuse or dependence in remission. Of the 42 who had not converted to psychosis at 1 year, 26.2% met criteria for cannabis abuse or dependence in remission. Nicotine use was also found to be significantly associated with later conversion. The significant associations between cannabis and nicotine abuse and conversion to psychosis in individuals at risk for schizophrenia suggest that early identification and intervention programs should screen for and provide education about the deleterious effects of these substances.

Keywords

Prodrome; Marijuana; Schizophrenia; Substance Use; At risk; Nicotine

1. Introduction

Epidemiological studies have shown an association between cannabis abuse and psychosis (Andreasson et al, 1987; Regier et al, 1990; Hambrecht and Hafner, 1996; Cantwell et al, 1999; Arseneault et al, 2002; Zammit et al, 2002). Recent literature reviews and meta-analyses (Arseneault et al, 2004; Sempé et al, 2005) suggest that cannabis “use” (not necessarily “abuse” or “misuse”) confers an overall two to three-fold increase in the relative risk for later schizophrenia. Additionally, the risk of developing schizophrenia increases with heavier (Smit et al, 2004) and earlier cannabis use (Arseneault et al, 2002).

Cannabis abuse may be responsible for 1–2 new cases of schizophrenia per 1000 people per year while the vast majority of cannabis abusers will not proceed to frank psychosis (Weiser et al, 2005). It is possible that cannabis use confers a greater risk for the later development of a psychotic illness in individuals who are already “at risk” for schizophrenia based on the presence of subsyndromal psychotic symptoms, a family history of schizophrenia and/or a recent deterioration in global functioning (Haroun et al, 2006).

The goal of the present study was to examine the rate of cannabis use among participants in the Cognitive Assessment and Risk Evaluation (CARE) Program, a longitudinal program for

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individuals who are “at risk” for developing a psychotic disorder. The primary aim of the CARE Program is to predict which individuals are at greatest risk for developing psychosis using a combination of clinical, familial and vulnerability marker risk assessment. Haroun et al. (2006) previously reported on a subset of the sample used in this report and showed that those individuals who developed psychosis had significantly higher clinical ratings at baseline (delusional-like experiences, suspiciousness and thought disorder). The converted group was more likely to have taken an antipsychotic agent and less likely to have a family history of psychosis in a first-degree relative. Additionally, the group who converted to psychosis was more likely to have a history of substance abuse or dependence.

The current report further explores the association of substance abuse to conversion to psychosis in this sample. We hypothesized that a history of cannabis use would increase the risk for psychosis because of the above-mentioned studies.

2. Methods

2.1 Participants

Participants included 48 (26M/22F) individuals between the ages of 12 and 30 (Mean Age=18.6 years, S.D.=4.2) who met CARE criteria (Seeber and Cadenhead, 2005) for being at risk for schizophrenia and had participated in the study a minimum of one year. All subjects were administered the Structured Interview for Prodromal Syndromes (SIPS) (Miller et al, 2003) and met at least one of 4 at risk states, as described in Table 1. The original sample recruited between 2000 and 2005 included 62 subjects but 13 were lost to follow-up prior to one year and one was missing cannabis use history.

Subjects with a history of a DSM-IV psychotic disorder (psychotic mood disorder or schizophrenia), a neurological disorder or a serious head injury were excluded. Subjects who met DSM-IV criteria for drug or alcohol dependence at the time of initial evaluation were excluded because of the risk of affecting psychophysiological and neuropsychological test measures. Sixteen subjects reported a lifetime history of cannabis abuse (n=15) or dependence in remission (n=1). Of those who had a cannabis abuse or dependence history, five also met criteria for alcohol abuse and two for alcohol dependence in remission. Two of these subjects (who had misused both cannabis and alcohol) also had a history of amphetamine abuse or dependence. One subject who did not meet cannabis abuse or dependence met DSM-IV criteria for alcohol dependence in remission. Eight of the 48 subjects smoked cigarettes (amount of nicotine smoked ranged from 0.125 to 1.5 packs per day). Subjects who used illicit drugs (with the exception of cannabis) within 30 days of the initial assessment were excluded. Seven subjects reported having used cannabis in the month prior to the initial assessment and all denied intoxication at time of evaluation.

Subjects were recruited through health services, public schools and colleges in the community of San Diego and were seen in the CARE Program, which is located within the Outpatient Psychiatry Clinic at UCSD. All subjects signed written informed consent (UCSD IRB#050650) to participate in a 2 year longitudinal study after the procedures were fully explained.

2.2 Procedure

All potential subjects were given a preliminary screen in which presenting symptoms were assessed and/or entry criteria were reviewed. Demographic information including age, education, family history of psychiatric illness, medical history, psychiatric history and medication history was also obtained. Subjects who met the preliminary entry criteria received a more extensive intake diagnostic interview. The SIPS was used to assess prodromal symptoms. The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) (First et

al, 1995) or the Schedule for Affective Disorders and Schizophrenia for School Aged Children, Present and Lifetime Version (K-SADS-PL) (if under 18) (Kaufman et al, 1996) was used to assess Axis I disorders, including substance use disorders. To determine family psychiatric history, the Family History RDC (Andreasen et al, 1977) was used.

Study participants received clinical assessment interviews on a monthly basis to determine whether they were beginning to show signs of psychosis or other symptoms, including substance use. Participation in this study did not preclude individuals from receiving psychotropic or antipsychotic treatment. If study participants showed symptoms that caused significant distress and/or affected current functioning (e.g. school, work, family, peer relations), they were referred for additional services (e.g. individual or group psychotherapy, medication consultation with a psychiatrist) (Haroun et al, 2006).

The 48 subjects were divided into 2 groups based on lifetime cannabis use: 1) those with no cannabis use or minimal use without impairment ($n = 32$) or 2) those who met criteria for abuse or dependence in remission, per DSM-IV criteria ($n = 16$). During subsequent monthly clinical assessment interviews, subjects were asked about any drug use since the last contact. All subjects received a urine toxicology screen at initial testing and at 6-month testing intervals. Six subjects tested positive for cannabis during the course of the study and all of those were in Group 2.

2.3 Statistical Analysis

Statistical analyses were performed using SPSS 10.0 for Windows. Non-parametric statistics were used to assess the relationship of cannabis abuse to risk for developing psychosis within 1 year. Demographic data were compared by *t*-tests. Discrete variables were analyzed using Fisher's Exact Test. Results were considered statistically significant when the corresponding *P*-value was 0.05 or less by two-tailed analysis.

3. Results

Groups 1 and 2 did not differ significantly in education, baseline SIPS ratings, family history of psychosis in a first-degree relative, abuse of other drugs or use of antipsychotic medication at baseline. Males were significantly more likely than females to abuse cannabis (Fisher's Exact Test $P = 0.013$). Those who abused cannabis were significantly older than those who had little or no cannabis use (mean age = 20.6 (SD = 3.0) versus mean age = 17.6 (SD = 4.4), respectively, $t [46] = -2.409$, $P = 0.02$).

At 1 year follow-up, 6 of the 48 (12.5%) at risk subjects had made the transition to psychosis. Of those who became psychotic, 3 met criteria for schizophrenia, 2 for schizoaffective disorder, and 1 for bipolar mania with psychotic features (Haroun et al, 2006). Of the 32 subjects who had no use or minimal cannabis use (Group 1) one subject (3.1%) converted to psychosis. Of the 16 subjects who met criteria for cannabis abuse/dependence (Group 2), five (31.3%) converted to psychosis. The results show a significant association between cannabis abuse and conversion to psychosis in this sample (Fisher's Exact Test $P = 0.012$). Three of the 6 subjects who tested positive for cannabis during the course of the study converted to psychosis.

Further analyses show that abuse/dependence of alcohol or cocaine was not associated with conversion to psychosis (amphetamine was not analyzed since only 2 subjects used it and neither of those 2 converted). Nicotine use (amount smoked per day ranged from 0.125 to 1.5 packs per day) was found to be significantly associated with later conversion to psychosis (Fisher's Exact Test $P = 0.005$). Eight of 48 subjects smoked cigarettes. Seven of the 8 cigarette smokers also used cannabis. Four of the 6 subjects who converted to psychosis smoked both cigarettes and cannabis.

4. Discussion

Individuals at high risk for psychosis, based on empirically derived criteria for the schizophrenia prodrome, were more likely to develop psychosis within one year if they had also abused cannabis and nicotine. In a similar sample of “ultra high risk” subjects, Yung et al (2004) did not find this association between conversion to psychosis and cannabis abuse but their sample had a relatively low base rate of cannabis use that may explain the negative finding.

Research findings are mixed with regard to the role of nicotine and conversion to psychosis. Cannabis use is more common in cigarette smokers (Lewinsohn et al, 1999). In a historical-prospective cohort study of Israeli military recruits, Weiser et al (2004) found that the risk for schizophrenia was higher in adolescents who smoked at least one cigarette a day. There was also a significant association between the number of cigarettes smoked and the risk of schizophrenia, with heavier smoking being associated with greater risk for schizophrenia. However, in their investigation of a cohort of Swedish conscripts, Zammit et al (2003) found a lower risk of schizophrenia in cigarette smokers. Due to our small sample size, it is not possible to know whether nicotine or cannabis use or some other variables like sex or age accounted for the conversion to psychosis.

The present findings are limited due to the small sample size and reliance on self-report measures of cannabis use. Future studies with larger sample sizes, specific information about age of first drug use and more frequent drug-testing may help to further elucidate the observed association between cannabis use and risk of psychosis. Additionally, a larger sample size will allow us to explore the association of other risk factors such as smoking to cannabis abuse and future psychosis.

Based on the current findings, however, we recommend vigorously screening and monitoring for potential cannabis use in at risk subjects. Psychoeducation regarding the deleterious effects of cannabis use in vulnerable individuals could discourage use, and perhaps improve outcome.

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Table 1

Criteria for At Risk States in the Cognitive Assessment and Risk Evaluation (CARE) Program.

At risk Groups

Brief Psychosis Group

- Severity Scale Score of 6 on one item P1–P5* or D1–D4** from SIPS
- Frequency <1 hour and <3–6X/week or >1 hour and ≤2X/week
- Each episode of symptoms is present for less than one week and symptoms spontaneously remit on every occasion.
- Symptoms began or worsened in the last year

Subsyndromal Group

- Severity Scale Score of 3–5 on one item P1–P5 or D1–D4 from SIPS
- Frequency at least 1X in the past month
- Symptoms began or worsened in the last year

Genetic Risk and Deterioration Group

- Family history of psychosis in first degree relative OR Schizotypal Personality Disorder in identified subject
- Deterioration in functioning and/or mood, anxiety or deficit symptoms
- Symptoms began or worsened in the last year

* P1–P5 – Psychosis Items 1 through 5 from the Structured Interview for Prodromal Symptoms (SIPS)

** D1–D5 – Disorganized Items 1 through 5 from the SIPS