THE JOURNAL OF
NERVOUS AND
MENTAL DISEASE

VOL. 183, NO. 9
September 1995
SERIAL NO. 1354

Alcohol, Cannabis, Nicotine, and Caffeine Use and Symptom Distress in Schizophrenia

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The high prevalence of substance use, *e.g.*, alcohol and illegal and nonprescribed drugs, in schizophrenia is widely recognized. One explanation for this high prevalence is that substance use may be a self-initiated method for managing symptoms. To test whether the intake of four substances—alcohol, cannabis, nicotine, and caffeine—would increase with increases in symptom distress, daily self-reports of symptom distress and substance intake over 12 weeks were analyzed with pooled time series analyses. Compliance with neuroleptic medication was added to the analyses to control for any changes in prescribed medication compliance while using nonprescribed drugs or alcohol. Of the four substances studied, only nicotine was significantly related to symptom distress. Higher distress with prodromal symptoms was related to decreases in nicotine use. Analysis of caffeine did not meet the criteria for significance but does provide direction for further research. Higher distress, with neurotic symptoms, was related to increases in caffeine use. Further research is needed to clarify the relationship between nicotine and symptoms.

—*J Nerv Ment Dis* 183:559–565, 1995

One explanation for the high prevalence of substance use in schizophrenia is that alcohol and drugs may be a self-initiated method for managing symptoms. Substance use in schizophrenia and its association with increases in psychosis, relapse, and rehospitalization is widely recognized (Carey et al., 1991; Cuffel, 1992; Kivlahan et al, 1991; Regier et al., 1990). If this high prevalence is an attempt to self-regulate symptoms, clinicians need to be able to identify this behavior and offer alternative means of alleviating symptom distress.

Studies supporting the use of alcohol and drugs to regulate internal experiences and symptoms are based on patient self-reports that relate symptom changes to substances used. Test and colleagues (1989) found subjects reported more positive than negative changes in symptoms after recent substance use regardless of the substance used. Other investigators have focused on specific substances and their relationship with symptoms. Some subjects with schizophrenia reported that alcohol improved tension and depression. A smaller number reported that alcohol either relieved or worsened psychotic symptoms (Alpert and Silvers, 1970; Bergman and Harris, 1985; Noordsy et al., 1991).

Differential effects for alcohol, cannabis, and cocaine on symptoms has been reported by patients with schizophrenia (Dixon et al., 1991). Both alcohol and cannabis decreased anxiety, whereas cocaine increased anxiety. Cocaine and cannabis increased energy more than alcohol, and cannabis increased suspiciousness more than alcohol. Castaneda and colleagues (1991) also reported differential symptom effects for the kind of substance used. Cocaine users reported more symptoms worsened than improved, while those who used alcohol reported a balance between symptom improvement and worsening.

Although believed to be more benign, caffeine and nicotine are drugs that individuals with schizophrenia can readily use to modulate symptoms. Individuals with schizophrenia are more likely to smoke than either individuals with other psychiatric disorders or the general public (Hughes et al., 1986; Lohr and Flynn, 1992). Some smokers with schizophrenia have reported smoking in response to auditory hallucinations and medication side effects (Glynn and Sussman, 1990). In a cross-sectional study of 78 outpatients with schizophrenia,

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This research was supported by grant RO3 MH46650 from NIMH, ADAMHA.

Goff and colleagues (1992) found smokers had fewer extrapyramidal symptoms than nonsmokers when gender, age, and caffeine consumption were controlled. This was despite the fact that smokers were prescribed twice the amount of neuroleptic medication. No differences were found between any other symptom and smoking status when using neuroleptic dose, caffeine, and age as covariates.

Caffeine consumption by individuals with schizophrenia is also high but tolerance appears to develop with chronic high intake. Koczapski and colleagues (1989) did not find changes in staff ratings on inpatients related to withdrawal or reintroduction of caffeine in inpatients. However, acute administration of caffeine has been found to produce significant changes in symptoms when preceded by a period of withdrawal from caffeine (Lucas et al., 1990). Psychotic and thought disorder symptoms worsened, while improvement was seen in mood, energy, and social involvement. These effects, however, appear to be short lived. The absorption of caffeine when taken concurrently with neuroleptic medication may lead to impairment in the absorption of both (Mikkelsen, 1978). Thus, individuals who consume large amounts of caffeine over long periods of time should experience fewer effects of both caffeine and neuroleptic medication.

These studies are all based on subjects' recall of subjective experiences. Differences in findings may reflect the length of time between actual use and recall of use as well as whether subjects were asked to recall immediate versus delayed symptomatic effects of the substance used. A common problem in all the studies is that subjects are directed to link substance intake with symptoms. These post hoc attributions may obscure the true natural relationship between symptoms and substance use, since they are susceptible to self-perception biases. The purpose of the present time series study is to examine the daily relationship between symptom distress and substance intake. In addition, the role of compliance with neuroleptic medication in the relationship between symptoms and substance use is considered. The hypothesis tested in this study is that the intake of four substances—alcohol, cannabis, nicotine, and caffeine—will increase as symptom distress increases.

Methods

Subjects

Subjects were recruited from community support programs (CSP) of two community mental health centers serving adjacent counties. Both CSPs used assertive case management as their main modality of treatment and offered an array of services, such as medication management and vocational counseling. The CSPs differed in the socioeconomic status of the counties they served. Initially, subjects (N = 14) were recruited from the first CSP, which serves a county with a per capita income of $23,346 and a 6% minority population. Three additional subjects were recruited from a second CSP serving a county with a per capita income of $12,752 and a 37% minority population.

Clinical diagnosis of schizophrenia or schizoaffective disorder was confirmed by administering the Mood Syndromes and Psychotic and Associated Symptoms sections of the Structured Clinical Interview for DSM-III-R (SCID; (Spitzer et al., 1989). Fifteen (88.2%) subjects had a lifetime SCID diagnosis of schizophrenia. Two (11.8%) subjects had a lifetime SCID diagnosis of schizoaffective disorder.

A criterion for participating in the study, the self-report of alcohol and/or drugs at least weekly, was assessed by having subjects complete an investigator-developed health behavior inventory. Of the subjects who met the diagnostic and substance use frequency criteria, 14 of 20 (70%) from the first CSP agreed to participate and three of four subjects (75%) from the second CSP agreed to participate. After procedures were explained fully, written consent was obtained.

Four of the subjects did not complete the entire 84 days of the study. One subject who had an unstable living situation dropped out after 21 days, one subject experiencing symptom exacerbation dropped out after 28 days, one subject decided to drop out after 56 days, and one subject was hospitalized after completing 63 days of the study. Data from all 17 subjects were included in the analyses. Excluding the days after the four subjects dropped out, there was a total of 52 (4%) days with missing data.

The size of the sample (N = 17) was adequate to test the hypothesis because the investigators pooled the individual time series (17 Ss $\times$ 84 days) (Kessler and Greenberg, 1981). Assuming a small effect size, 537 data points (subjects $\times$ days) were needed to test the hypothesis (Cohen and Cohen, 1983). After adjustment for days lost (from subjects who dropped out before completing the study), power exceeded .90.

Measures

Three self-administered checklists were used in this study to measure symptom distress, substance use, and medication compliance. The Symptom Checklist is composed of 12 symptoms modified for self-administration from the expanded version of the Brief Psychiatric Rating Scale (Lukoff et al., 1986). Subjects rated the amount of distress with each symptom for the previous 24 hours by checking one of five choices ranging from "not distressing at all" to "it was extremely distressing." A sixth choice, "did not have symptom," was also given so subjects would have a place to check when symp-

toms were not present. This sixth choice was also scored as "not distressing at all." In addition to the 12 symptoms, subjects also rated their distress on as many as three idiosyncratic prodromal symptoms. These are symptoms each subject identified as personal indicators of relapse. Data supporting the validity and reliability of the Symptom Checklist were assessed in a pilot study (N = 29).[4] Subjects' self-administered ratings of symptom distress correlated .81 with an interviewer-administered Brief Psychiatric Rating Scale. The internal consistency of the Symptom Checklist using coefficient alpha was .78.

The Substance Use Checklist consisted of 33 substances, including caffeine, cigarettes, alcohol, illegal drugs, over-the-counter drugs, solvents, and inhalants. Subjects checked the substances they used and entered the amount of intake in the previous 24 hours.

The validity of the subjects' self-report of substance use was assessed by urine drug screening. Urine specimens were collected from each subject during two randomly chosen weeks within the 12-week study. Urine was screened for amphetamines, cannabinoids (THC), alcohol, cocaine, barbiturates, opiates, and benzodiazepines using an enzyme immunoassay (SYVA Emit™). Drug screening was performed by a laboratory certified by the National Institute for Drug Abuse. The urine screenings showed only one discrepancy between self-report and use. One subject did not report using cocaine that did show up in the urine screening. Analyses were computed both with and without this subject's data. The results were not significantly changed, so this subject's data were retained.

The subjects' medications were listed on the Medication Checklist. Subjects were instructed to check one of four responses (took as prescribed, took some but not all prescribed, did not take at all, and took more than prescribed) to indicate how they took each of their medications in the previous 24 hours. For data analyses, neuroleptic medication was used as a covariate for those subjects who took oral neuroleptic medications. To be added as a covariate, compliance had to be a dichotomous variable. Based on the understanding that some subjects were advised to adjust their daily dosages as needed, compliance was described as any of the following: "took as prescribed," "took some but not all," or "took more than prescribed." Noncompliance was: "did not take at all."

Procedures

Prior to the study, the potential subject pool was assessed at the first CSP for data collection by interviewing case managers. Case managers identified 40 individuals, or 23% of their caseload, with clinical diagnoses of schizophrenia or schizoaffective disorders who were using drugs or alcohol. Of the 40 potential subjects, case managers believed 21 used drugs and alcohol at least once or twice a week, a criterion for participation in this study. The potential subject pool was not assessed at the second CSP because the program was in the midst of relocating and enlarging.

Subjects were recruited for the study by two methods. Case managers identified subjects thought to be eligible, *i.e.*, those who had a clinical diagnosis of schizophrenia or schizoaffective disorder and were believed to be using either alcohol and/or drugs. Subjects also were recruited directly by posting sign-up sheets at the CSP. Individuals who indicated interest in participating were contacted by members of the research team to clarify eligibility.

Subjects were given the checklists in notebooks with dividers separating each day of the week. The order of the checklists was always consistent. Symptom distress was listed first, medication compliance was second, and substance use was third. Subjects were taught how to complete each of the checklists. A place to keep the notebook where they lived was identified and a consistent time each day to complete the checklists was specified. To help subjects remember to fill out the checklists daily, the time to complete them was linked to a habitual activity. Twice weekly, subjects met with a nurse who reviewed the completed checklists, clarified responses, and replenished the notebooks. Subjects completed the forms daily for 84 days. They were paid a total of $165 on a scheduled basis for their participation.

Data Analysis

Daily ratings for the 84 days of symptom distress and amount of alcohol and drug intake from the 17 subjects were entered into a pooled time series. Daily compliance ratings of neuroleptic medication were used as a covariate. The pooled time series design, using the software selected for this study (Guass-TSCS 2.1, Aptech Systems, Inc., Kent, Washington), analyzes data with unequal time series per subject. Normally, repeated-measures designs require that each subject contribute data at each collection wave.

The use of pooled time series data presents problems with nonindependence of data points over time (days in the present study). This nonindependence raises the possibility of correlated error. A Durwin-H was calculated for each equation to determine the presence of correlated error. Significant correlations were found in each equation. To adjust for this correlated error, generalized least squares regression (GLS), rather than

[4] Hamera E, Schneider JK, Potocky M, Casebeer MA. Validity of self-administered symptom scales in clients with schizophrenia and schizoaffective disorders. Manuscript submitted for publication.

ordinary least squares regression, was used (Sayrs, 1989).

While the main focus of this study is on the structural parts of the equations that examine the relationship between symptoms and substance intake, the univariate ARIMA models were computed separately on the substance intake and symptoms for each subject as well. First-order autocorrelations indicated that ratings for consecutive days were correlated.

Results

Demographic and Treatment Characteristics

Thirteen (76.5%) of the 17 subjects were male; four (23.5%) were female. Age ranged from 21 to 54 years (mean age = 34.2 ± 8.5 years). Three subjects were black, one was a Pacific Islander, and the rest were white. One subject had less than a high school education, seven had a high school education or equivalent, eight had some college, and one had a bachelor's degree. Eight subjects were competitively employed, five were employed by the mental health center, and one was not employed. Most subjects lived independently (N = 12), three lived with relatives, and two had other living arrangements. The subjects' average monthly income ranged from $379 to $2200 (mean = $597.3 ± 425.8). All of the subjects received case management services.

With the exception of one subject, all had one or more lifetime alcohol and/or drug abuse or dependency disorders. Fourteen subjects had a lifetime diagnosis of alcohol abuse or dependency. Twelve subjects had a lifetime diagnosis of cannabis abuse or dependency. A smaller number of subjects had lifetime diagnoses for stimulants, cocaine, opioid, hallucinogens, sedatives, and polydrug abuse or dependency.

Symptom Distress

Items from the Symptom Checklist that intercorrelated .6 or higher were parceled into subsets of items. This reduces multicollinearity, which is especially problematic in GLS. One item measuring confusion correlated highly with more than one symptom parcel and therefore was deleted from the analyses.

Parcel I-Ideas of Reference included two items: a) feeling that something on the television or radio was about the subject or was sending special messages to the subject, and b) feeling that the subject caused special or unusual things to happen. The daily mean for these two items was 2.96 ± 1.55 (possible and observed ranges = 2–10). Parcel II-Neurotic Symptoms included items that related to feeling depressed, guilty, nervous, restless, irritable, and isolating self. Daily mean score for these six items was 10.55 ± 4.77 (possible and observed ranges = 6–30). Parcel III-Hallucinations was a single item dealing with hearing voices or sounds or seeing, smelling, or tasting things that others did not. Parcel III had a daily mean of 1.55 ± 1.00 (possible and observed ranges = 1–5). Parcel IV-Talk or Move Slow dealt with feeling that you were talking or moving slower than usual. This item had a daily mean of 1.51 ± .92 (possible and observed ranges = 1–5). The single item of Parcel V-Paranoid Symptoms dealt with feeling paranoid or suspicious and had a daily mean of 1.69 ± .98 (possible and observed ranges = 1–5). Only subjects' first idiosyncratic prodromal sign or symptom was used to form Parcel VI-Prodromal Symptom because some subjects did not identify more than one prodromal symptom. The mean rating for subjects' prodromal symptom was 1.75 ± .98 (possible and observed ranges = 1–5). Two subjects reported psychotic symptoms as their first idiosyncratic prodromal sign, while the rest reported a variety of nonpsychotic signs and symptoms. Although the full range of symptom distress ratings was observed from the sample, the mean symptom ratings were slightly positively skewed, indicating mild distress. Pooled time series analysis is robust enough to handle this restriction in variability.

Type and Amount of Substance Use

All subjects used caffeine, 16 (94.1%) smoked cigarettes, and 16 (94.1%) drank alcohol. Nine (52.9%) subjects used cannabis, four (23.5%) subjects reported taking ephedrine, two (11.8%) reported taking caffeine pills, two (11.8%) subjects reported cocaine use, one (5.9%) used amphetamine, and one (5.9%) used benzodiazepines. Table 1 depicts the mean and range of percentage of days of substance use for subjects who used alcohol, cannabis, nicotine, and caffeine. It also includes the mean and range of daily use for those days of reported use. Subjects' alcohol entries were converted to number of drinks based on alcoholic content.

Correlations among the amount of alcohol, cannabis, caffeine, and nicotine over the 84 days of the study were computed using the Pearson product-moment correlation coefficient. Two pairs of substances were significantly correlated. Nicotine was moderately correlated with caffeine (r = .30, $p \leq .001$) and alcohol was weakly correlated with cannabis (r = −.07, $p \leq .01$).

Medication Use

All subjects were on a neuroleptic medication. Five (29.4%) received an injectable neuroleptic only. Nine (52.9%) took an oral neuroleptic medication only. Three (17.6%) of the subjects received both injections and oral neuroleptic medications. A review of clinical records showed that the subjects received scheduled injections during the study.

TABLE 1
Substances Used, Number and Range of Days Used, and Mean and Range of Daily Use

Substance	No. of Subjects Using Substance	For Subjects Who Used		For Subjects Who Used	
		Mean days used (%)	Range of days used (%)	Mean daily use	Range of daily use
Alcohol	16 (94.1)	43.7	4.8–100	6.16 drinks[a]	1–37
Cannabis	9 (52.9)	25.9	1.2–100	4.70 joints	1–9
Nicotine	16 (94.1)	96.2	85.7–100	31.32 cigarettes	1–98
Caffeine	17 (100)	91.1	61.9–100	9.44 cups	1–65

[a] One drink equals 1 oz. hard liquor or 1 can/bottle of beer or 5 oz. of wine.

Relationship of Symptom Distress and Substance Use

The relationships between the six symptom parcels and the amount of alcohol, cannabis, nicotine, and caffeine were analyzed by pooled time series analyses. Analyses were performed with and without the covariate of compliance with oral neuroleptic medication. Nonstandardized parameter estimates were reported rather than standardized parameter estimates because the covariate neuroleptic compliance was a dichotomous variable. Nonstandardized parameter estimates are also easier to interpret when using GLS and comparing parameter estimates from analyses of different samples (Pedhazur, 1982). Although not completely independent, the 12 subjects (768 cases) taking oral neuroleptic medications were analyzed as a group to examine the effect of medication compliance on each of the four substances in addition to analyses of the total 17 subjects (1189 cases). Four sets (with alcohol, caffeine, nicotine, and cannabis as dependent variables) of two regression equations (with and without the covariate neuroleptic compliance) were run for a total of eight analyses. The six symptom parcels were entered in each equation as predictor variables. Because this number of analyses increases family-wise error, an alpha level of .006 was used to identify significant findings (Keppel, 1991).

The results of the pooled time series on the same-day ratings of symptoms and reports of substance use are shown in Table 2. Significant parameter estimates were obtained with nicotine as the dependent variable, but not when alcohol and cannabis were used as dependent variables. The analyses with caffeine as the dependent variable yielded parameter estimates that were very near the accepted alpha level of .006.

For Symptom Parcel VI-Prodromal Symptom, parameter estimates were significant when the dependent variable was nicotine, measured by the number of cigarettes smoked. An inverse relationship was found with nicotine. The nicotine intake decreased with increased distress with prodromal symptoms (Symptom Parcel VI), both with and without the covariate of neuroleptic compliance.

Although not meeting the criterion for significance (.006), the relationship between caffeine and neurotic symptoms (Symptom Parcel II) reached an alpha level of .007. Caffeine intake increased as distress with neurotic symptoms increased. This was true with and without the neuroleptic compliance covariate.

Discussion

This study provides a rigorous test of the symptom self-regulation explanation for the high prevalence of substance use in individuals with schizophrenia. The type of analysis performed allowed us to examine the relationship between changes in symptom distress and changes in substance intake. Analysis and use of a pooled time series design make it difficult to compare the results with previous studies that have examined subjects' post hoc attributions about the relationship of symptoms to substance intake. Instead of asking subjects to link their symptoms with substance intake, in the present study we examined the natural relationship between daily ratings of symptom distress and daily substance intake over an 84-day period.

The absence of significant findings with alcohol and cannabis in the present study extends the findings of previous researchers (Alpert and Silvers, 1970; Bergman and Harris, 1985; Dixon et al., 1991; Noordsy et al., 1991) who reported that some, but not all, subjects make post hoc associations linking alcohol and cannabis use with a decrease in symptoms. The present findings cast doubt on the empirical bases of self-reports that alcohol and cannabis are used to regulate symptom distress. However, because investigators selected a population who were not too impaired to participate, the findings can be generalized only to individuals with schizophrenia who are similar to the sample studied.

The nicotine findings are new. Nicotine has not been studied as a method of self-regulating symptoms to the extent that alcohol and drugs have been. The significant inverse relationship between prodromal symptom distress and nicotine is contrary to the hypothesized direction that increases in symptom distress lead to increases in substance use. This observed inverse

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