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ORIGINAL PAPER

Associations Between Past Alcohol, Cannabis, and Cocaine Use and Current Schizotypy Among First-Degree Relatives of Patients With Schizophrenia and Non-Psychiatric Controls

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Abstract Associations between past use of alcohol, cannabis, and cocaine and various domains of schizotypy were examined in first-degree relatives of patients with schizophrenia and non-psychiatric controls. Substance use was operationalized in three ways: (1) having ever used the substance, (2) age at first use, and (3) past frequency/amount of use during three time periods in late adolescence/early adulthood. Schizotypy was assessed using the *Schizotypal Personality Questionnaire* (SPQ). Participants who had ever used cannabis had significantly higher *cognitive-perceptual*, *interpersonal*, and total schizotypy scores compared to those who had not. Younger age of alcohol use onset was associated with more schizotypy in adulthood, and younger age of first cannabis use was related to more *interpersonal* schizotypy. More frequent/heavier use of alcohol in the 25–29 age-range, and cannabis in early adulthood, were associated with more schizotypy. The use of addictive substances, particularly cannabis, is related to schizotypy in complex ways.

Keywords Alcohol · Cannabis · Cocaine · Psychosis-proneness · Schizotypy

Introduction

Schizotypy is a multidimensional construct encompassing a set of behavioral, perceptual, ideational, cognitive, and affective traits that exist along a continuum in the general population. Positive schizotypal traits include suspiciousness, ideas of reference, unusual perceptual experiences, odd beliefs and magical thinking, and odd or eccentric behavior.

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Negative schizotypal traits are exemplified by social isolation, lack of close friends, and excessive social anxiety. Disorganized schizotypal traits include allusive thinking and odd/eccentric thinking and speech. Schizotypy and schizotypal personality disorder (a categorical formal diagnosis that defines a clinical threshold of schizotypal traits) are thought to be genetically related to schizophrenia given that relatives of people with schizophrenia are more likely to exhibit schizotypal traits compared to individuals without a family history of the illness. Data from the Roscommon Family Study indicate that schizotypy—in the form of subpsychotic thought disorder, negative schizotypal signs, deficient occupational functioning, and social isolation/avoidance—significantly discriminates relatives of individuals with schizophrenia from relatives of controls [1], and that positive and negative symptoms in patients with schizophrenia predict corresponding positive and negative schizotypal traits in their relatives [2]. Like schizophrenia, both environmental and genetic factors are thought to underpin schizotypy [3, 4]. One environmental factor that has recently been associated with this personality dimension is substance use, though it should be noted that even "environmental factors" such as substance use may be at least partly genetically determined (in the case of substance use, by personality factors such as openness, impulsivity, and sensation-seeking, to name a few).

Substance misuse is known to be very common in persons with schizophrenia [5–7]. Despite the relatedness of schizophrenia and schizotypy, studies examining the association between substance use and schizotypy remain rather rare. Extant research on the relationship between misuse of particular substances, including alcohol, cannabis, and cocaine, and schizotypy are particularly limited.

The literature on the association between alcohol use and schizotypy is marked by mixed findings. Interviews with hospitalized alcohol-dependent patients evidenced that a specific type of alcoholism (termed clinical type B alcoholism) was associated with schizotypal personality disorder [8]. Craig and coworkers [9] also found an association between schizotypal personality style and alcohol addiction in participants from an inpatient rehabilitation treatment program. In a 10-year longitudinal study using a non-clinical sample of college students, Kwapil [10] found that higher positive schizotypal symptomatology scale scores—using the Perceptual Aberration Scale [11] and the Magical Ideation Scale [12]—corresponded to increased rates of alcohol use and abuse. However, a subsequent study by Nunn and colleagues [13], also using a non-clinical sample of undergraduate students, revealed that alcohol users did not show higher scores on scales related to positive schizotypal symptomatology, but did demonstrate significantly lower levels of negative symptomatology (introvertive anhedonia). In outpatients identified as having schizotypal personality disorder, levels of alcohol abuse were not found to be elevated when compared to other outpatient psychiatric controls; however, significant differences were reported for drug abuse [14].

An increasing body of research suggests a potential association between cannabis use and schizotypy. Correlations between cannabis use and scores on scales of positive schizotypal symptomatology have been reported in non-clinical samples of university students in numerous studies [13, 15–20]. Some studies suggest specificity of the association (i.e., that cannabis use specifically is associated with schizotypy in particular more than other personality/psychopathological variables). For example, Nunn and associates [13] found higher positive schizotypy scores among undergraduate students using cannabis, but not among those using alcohol, and associations were not found between cannabis use and anxiety or depression. Similarly, Williams and coworkers [21] found that cannabis use was more specifically related to schizotypal traits than to anxiety, and that the association between schizotypal traits and cannabis use remained significant even after

excluding participants who had used other drugs. In terms of a potential biologic gradient, one study found a significant positive correlation between total years of cannabis use and schizotypy scores [20]. Although most studies have found associations between cannabis use and positive schizotypal features only, among 60 undergraduates, Bailey and Swallow [15] found positive associations between cannabis use and positive, negative, and disorganized dimensions of schizotypy using a brief, self-report measure.

Cocaine is another commonly used substance among persons with schizophrenia [22, 23]; yet, there is a dearth of literature on the association between schizotypy and cocaine use. Survey research with veterans in a substance abuse treatment program revealed that cocaine users who experience transient paranoia while intoxicated exhibited more traits of psychosis-proneness than individuals who did not have transient cocaine-induced paranoid symptoms [24]. Another study with cocaine-dependent individuals reported that deficits in both sensory gating (the ability to filter out irrelevant stimuli) and attention may be associated with an elevated risk for developing psychotic symptoms, particularly in the subgroup of cocaine users vulnerable to cocaine-induced paranoia [25]. Using a self-report questionnaire, Kwapil [10] found a significant positive correlation between cocaine use and the trait of impulsive-nonconformity, a characteristic that contributes to the prediction of psychotic-like and schizotypal symptoms [26]. Additional research is needed to better characterize the relationship between cocaine use and schizotypy.

Considering the phenomenologic and likely genetic/etiologic similarities between schizophrenia and schizotypy, research exploring the relationship between substance use and schizotypy is warranted. This analysis sought to examine associations between past use of three specific substances—alcohol, cannabis, and cocaine—and current schizotypy in a sample of healthy first-degree relatives of patients with schizophrenia ($n = 28$) and non-psychiatric controls with no family history of psychosis ($n = 32$). Use of the three specific substances was operationalized in three ways: (1) history of having ever used the substance, (2) age at onset of use of the substance, and (3) past frequency/amount of use of the substance during three time periods (15–19 years, 20–24 years, and 25–29 years). Esterberg and colleagues [27] reported a positive association between cigarette smoking and level of schizotypy in the sample of relatives of patients with schizophrenia. This study aimed to extend these initial findings by assessing relationships between the use of other addictive substances and schizotypy.

Methods

Participants

This study was conducted at a large public-sector health system that serves a predominantly African American population. Exclusion criteria for all participants included: (1) inability to speak English, (2) a current substance dependence diagnosis not in early or sustained full remission, (3) any evidence of intoxication, (4) known or suspected mental retardation, and (5) history of neurological disease or clinically significant head injury. Exclusion criteria for first-degree relatives also included any personal history of psychotic or mood disorders. Controls were excluded if they endorsed any personal or family history (in first- or second-degree relatives) of psychotic or mood disorders. Personal history of these disorders was assessed using the *Structured Clinical Interview for DSM-IV Axis I Disorders* [28], and family history was assessed with the *Family Interview for Genetic*

Studies [29]. The research was approved by the university's institutional review board, and all participants provided written informed consent.

The sample for this analysis included 60 participants: 28 (46.7%) unrelated first-degree relatives of patients with schizophrenia or schizoaffective disorder and 32 (53.3%) non-psychiatric comparison subjects with no history of psychosis in first- or second-degree relatives. Of the first-degree relatives, 11 (39.3%) were mothers, nine (32.1%) were sisters, four (14.3%) were fathers, three (10.7%) were daughters, and one (3.6%) was a brother. Of the non-psychiatric controls, 17 (53.1%) were recruited from a food court in an indoor urban farmers' market, 10 (31.3%) came to the project by word of mouth from other controls, and five (15.6%) were drawn from an ambulatory medicine clinic waiting room.

The mean age of participants was 41.1 ± 13.3 years (range, 20–73 years). Thirty-seven participants were female (61.7%) and 23 were male (38.3%). The majority (53, 88.3%) were Black/African American, whereas seven (11.7%) were White/Caucasian. Thirty-six participants were single and had never been married (60.0%); 16 (26.7%) were separated, divorced, or widowed; and eight (13.3%) were married or living with a partner. The mean years of educational attainment was 12.6 ± 2.4. Nearly two-thirds of participants were currently unemployed (38, 63.3%).

Measures

The *Schizotypal Personality Questionnaire* [30] is a self-report, easy-to-administer, 74-item questionnaire used to screen for schizotypy or schizotypal personality disorder. Administration time is approximately 10 min. Each item presents a statement or question to the respondent, who simply circles "yes" or "no." All affirmatively-endorsed items count one point toward the total score (range, 0–74), with higher scores indicating higher levels of schizotypy. Examples of items include: "Have you ever had the sense that some person or force is around you, even though you cannot see anyone?" (from the *cognitive-perceptual* subscale, which measures positive schizotypy), "People sometimes find me aloof and distant." (from the *interpersonal* subscale, which assesses negative schizotypy), and "People sometimes find it hard to understand what I am saying." (from the *disorganized* subscale). Internal consistency reliability, test-retest reliability, and criterion validity of the SPQ are acceptable [30]. In a sample of 118 participants (relatives and controls) from this research group (many of whom are included in the current analysis), internal consistency of the SPQ subscales was found to be acceptable—0.89, 0.89, and 0.84, respectively—for the *cognitive-perceptual*, *interpersonal*, and *disorganized* subscales.

The *Adolescence and Young Adulthood Substance Use Questionnaire* (AYASUQ) was created by the research team to assess alcohol, cannabis, and cocaine use during adolescence and early adulthood due to a lack of measures that sufficiently quantify past use, especially during these critical developmental periods. The interviewer, a clinical psychologist who was blind to SPQ scores, asked participants questions about the age when they first began using a particular substance and how much/how often they used it. The interviewer recorded the age of first use, then selected the age period (10–14, 15–19, 20–24, 25–29) to begin querying about frequency and amount. The interviewer continued with subsequent age periods following the same procedure. For example, if a 35-year-old participant reported that he/she began smoking cannabis at age 16 years, the interviewer asked the participant to give an average frequency (per month) and the amount in joint equivalents (per usage) for ages 16–19 years, and then asked about average frequency and amount for the next two age periods (20–24, 25–29). Amounts were designated by units,

such that one unit of alcohol equaled one beer, glass of wine, liquor drink, or shot; one unit of cannabis equaled one joint; and one unit of crack cocaine equaled one rock. A frequency and an amount score was obtained for each age period for each substance, and then an overall use variable was calculated by multiplying these two scores (herein referred to as a frequency/amount score). For example, if a woman smoked an average of one cannabis joint two times per week during the age period 16–19 years, her overall use for that period would be eight (two times per week × four weeks per month × one joint each day she used).

Data Analysis

Descriptive statistics of SPQ scores were examined. Because SPQ total and subscale scores were not normally distributed, square root transformations were used for all analyses. Bivariate associations among study variables were examined using Pearson product-moment correlation coefficients, Spearman correlation coefficients, independent samples Student's *t*-tests, and chi-square tests of association. For the *t*-tests in the main analysis, Cohen's *d* was calculated as an effect size measure ($M_1 - M_2/\sigma_{\text{pooled}}$; where $\sigma_{\text{pooled}} = \sqrt{[(\sigma_1{}^2 + \sigma_2{}^2)/2]}$). The very high interdependence/multicollinearity between the various substances of abuse made multivariable analyses examining the independent effects of specific substances very difficult. Partial correlations were used to the extent possible to control for potential confounders.

Results

Demographic Correlates of Schizotypy Scores

First-degree relatives did not differ significantly from controls on *cognitive-perceptual*, *interpersonal*, *disorganized*, or total SPQ scores (relatives: 7.1 ± 6.7, 7.9 ± 6.4, 3.3 ± 3.6, 18.3 ± 15.0; controls: 6.5 ± 5.4, 7.5 ± 7.2, 2.5 ± 2.7, 16.3 ± 3.0). Given the absence of a meaningful difference in schizotypy scores between relatives and controls, subsequent analyses involved the entire sample in order to maximize power in light of the limited sample size. Before schizotypy was examined as a potential correlate of past alcohol, cannabis, and cocaine use, demographic correlates of schizotypy were examined. Age was significantly inversely correlated with the SPQ *disorganized* subscale score ($r = -0.26$, $P = 0.04$), but not with *cognitive-perceptual*, *interpersonal*, or total scores ($r = -0.21$, $P = 0.11$; $r = -0.23$, $P = 0.08$; $r = -0.15$, $P = 0.26$, respectively). It should be noted, however, that these non-significant correlation coefficients were of comparable magnitude to the significant inverse correlation between age and disorganized schizotypy. Neither gender nor race was significantly associated with the SPQ total score or any of the three subscales.

Demographic Correlates of Past Alcohol, Cannabis, and Cocaine Use

Among the 60 participants, 52 (86.7%) endorsed having ever used alcohol. Subgroup (first-degree relatives of patients with schizophrenia or schizoaffective disorder *versus* controls with no first- or second-degree family history) was not associated with past alcohol use ($\chi^2 = 2.98$, $df = 1$, Fisher's exact $P = 0.13$). Neither current age ($t = 0.58$, $df = 58$,

$P = 0.56$) nor gender ($\chi^2 = 0.69$, $df = 1$, Fisher's exact $P = 0.70$) was associated with history of alcohol use. Four out of seven White/Caucasian participants (57.1%) endorsed past alcohol use, compared to 48 of 53 (90.6%) Black/African American participants ($\chi^2 = 5.98$, $df = 1$, Fisher's exact $P = 0.04$).

Thirty-four of the 60 participants (57.6%) endorsed having ever used cannabis. Subgroup was not associated with past cannabis use ($\chi^2 = 1.83$, $df = 1$, $P = 0.18$), nor was current age ($t = 1.56$, $df = 57$, $P = 0.13$). Male participants were more likely to endorse past cannabis use (73.9%) than were female participants (47.2%; $\chi^2 = 4.09$, $df = 1$, $P = 0.04$). Race (White/Caucasian *versus* Black/African American) was not associated with past cannabis use ($\chi^2 = 2.75$, $df = 1$, Fisher's exact $P = 0.12$).

With regard to cocaine, 13 participants (21.7%) endorsed having ever used this drug. Controls were more likely to endorse past cocaine use (37.5%) than were relatives (3.6%; $\chi^2 = 10.13$, $df = 1$, $P = 0.001$). Current age was not associated with history of cocaine use ($t = 0.39$, $df = 58$, $P = 0.70$). Male participants were more likely to endorse past cocaine use (47.8%) than were female participants (5.4%; $\chi^2 = 15.04$, $df = 1$, Fisher's exact $P < 0.001$). Race was not associated with past cocaine use ($\chi^2 = 2.19$, $df = 1$, Fisher's exact $P = 0.33$).

Associations Between Uses of Various Substances

Not surprisingly, history of alcohol use and history of cocaine use both were associated with a history of past cannabis use ($\chi^2 = 12.59$, $df = 1$, Fisher's exact $P < 0.001$; $\chi^2 = 12.26$, $df = 1$, $P < 0.001$, respectively). However, history of alcohol use was not significantly associated with a history of past cocaine use ($\chi^2 = 2.55$, $df = 1$, Fisher's exact $P = 0.18$). Thirty-four (56.7%) participants endorsed current cigarette smoking. Participants who currently smoked cigarettes were more likely to have used alcohol/drugs than were participants who did not smoke cigarettes: alcohol, 100% compared to 69.2% ($\chi^2 = 12.07$, $df = 1$, Fisher's exact $P = 0.001$); cannabis, 85.3% compared to 20.0% ($\chi^2 = 25.15$, $df = 1$, $P < 0.001$); and cocaine, 38.2% compared to 0.0% ($\chi^2 = 12.69$, $df = 1$, $P < 0.001$).

Associations Between Having Ever Used Alcohol, Cannabis, and Cocaine and Current Schizotypy Scores

Using the square-root transformed SPQ scores, independent samples Student's *t*-tests were conducted to compare mean schizotypy scores in participants who had never used each of the three drugs of interest *versus* those who had ever used the respective drug. As shown in Table 1, participants who had used cannabis had significantly higher *cognitive-perceptual*, *interpersonal*, and total schizotypy scores compared to those who had never used cannabis. Effect sizes were in the medium range (0.57–0.66). Having ever used alcohol and having ever used cocaine were not significantly associated with schizotypy scores. However, in every comparison, those having used either drug had numerically higher schizotypy scores compared to those who had never used the drug. Though sample sizes were insufficient to achieve statistical significance, effect sizes were consistently in the small to medium range (0.27–0.57).

Although further multivariable techniques were desired (e.g., multivariate analysis of covariance examining the three SPQ subscale scores as dependent variables; past alcohol, past cannabis, past cocaine, and current nicotine use as factors; and age as a covariate), the very high interdependence/multicollinearity between the various substances of abuse

Table 1 Mean ± SD of schizotypy subscale and total scores by substance use history[a]

Alcohol	Never used ($n = 8$)	Ever used ($n = 52$)	t	df	p	d
Cognitive-perceptual	4.50 ± 5.04	7.14 ± 6.12	1.64	57	0.11	0.57
Interpersonal	6.00 ± 5.40	7.98 ± 6.37	0.80	57	0.42	0.30
Disorganized	2.25 ± 3.37	2.92 ± 3.14	0.72	58	0.48	0.27
Total	12.75 ± 10.87	18.02 ± 14.30	1.08	56	0.28	0.40
Cannabis	Never used ($n = 25$)	Ever used ($n = 34$)	t	df	p	d
Cognitive-perceptual	4.92 ± 4.40	8.24 ± 6.79	2.51	56	0.02	0.66
Interpersonal	5.88 ± 5.52	9.06 ± 6.57	2.15	56	0.04	0.57
Disorganized	2.16 ± 2.69	3.21 ± 3.38	1.29	56	0.20	0.37
Total	12.96 ± 10.51	20.56 ± 15.62	2.25	55	0.03	0.60
Cocaine	Never used ($n = 47$)	Ever used ($n = 13$)	t	df	p	d
Cognitive-perceptual	6.60 ± 6.14	7.50 ± 5.68	0.93	57	0.36	0.33
Interpersonal	7.20 ± 6.34	9.54 ± 5.72	1.60	57	0.12	0.55
Disorganized	2.70 ± 3.22	3.31 ± 2.95	0.95	58	0.35	0.31
Total	16.59 ± 14.00	20.00 ± 13.86	1.11	56	0.27	0.39

[a] Although mean ± SD scores are presented in terms of the actual SPQ scale scoring for ease of interpretation, t-tests were conducted using the square-root transformed variables

precluded multivariable analyses in which the independent effects of specific substances could be examined. For example, 29 participants who had used cannabis were current smokers and 20 who had never used cannabis and were not current smokers, whereas only five who had used cannabis were not current smokers, and five who had never used cannabis were current smokers. Similarly, multiple linear regressions examining the independent effects of past alcohol, past cannabis, past cocaine, current nicotine, and age on total SPQ subscale scores were overly influenced by multicollinearity when using the "enter" method in which all variables specified are entered in a single step. Using the backward elimination method yielded models in which: (1) past cannabis use was a significant predictor of *cognitive-perceptual* subscale scores, (2) current nicotine use was a significant remaining predictor of *interpersonal* subscale scores, and (3) age and current nicotine use were significant predictors of *disorganized* subscale scores.

Associations Between Age at Onset of Alcohol, Cannabis, and Cocaine Use and Current Schizotypy Scores

Among those having ever used alcohol ($n = 52$), age at onset of alcohol use was reported to range from 5 to 30 years (17.5 ± 4.3 years). Age at onset of alcohol use was inversely correlated with the *cognitive-perceptual*, *interpersonal*, *disorganized*, and total SPQ score (Table 2). Among those having ever used cannabis ($n = 34$), age at onset of cannabis use was reported to range from 10 to 30 years (17.5 ± 3.7 years). As shown in Table 2, age at onset of cannabis use was inversely correlated with the SPQ *interpersonal* score ($\rho = -0.40$, $P = 0.02$), though the inverse correlations did not reach statistical significance for the *cognitive-perceptual* ($\rho = -0.23$, $P = 0.20$), *disorganized* ($\rho = -0.30$, $P = 0.09$), or total SPQ score ($\rho = -0.31$, $P = 0.09$). Among those having ever used cocaine ($n = 13$),

Table 2 Correlations between age at onset of substance use and schizotypy subscale and total scores[a]

	Age at onset of alcohol use ($n = 52$)	Age at onset of cannabis use ($n = 34$)	Age at onset of cocaine use ($n = 13$)
Cognitive-perceptual	−0.28*	−0.23	−0.13
Interpersonal	−0.37*	−0.40*	−0.28
Disorganized	−0.37*	−0.30	−0.39
Total	−0.34*	−0.31	−0.15

[a] Spearman correlation coefficients

* $P < 0.05$

age at onset of cannabis use was reported to range from 15 to 30 years (21.3 ± 4.8 years). Age at onset of cocaine was not significantly correlated with SPQ score, though the limited sample size precludes a definite determination, and it should be noted that all correlations were in the expected (negative) direction. Controlling for current age and current nicotine use diminished the magnitude of all of these correlation coefficients only minimally.

Associations Between Frequency/Amount of Past Alcohol and Cannabis Use and Current Schizotypy Scores

Among the 52 participants having ever used alcohol, frequency/amount scores for the three time periods of interest (15–19 years, 20–24 years, and 25–29 years) were 41.9 ± 54.8 ($n = 37$), 40.7 ± 60.2 ($n = 43$), and 47.2 ± 68.3 ($n = 37$), respectively. Correlations among these frequency/amount scores were relatively high ($\rho = 0.61$–0.74). As shown in Table 3, frequency/amount of alcohol use in the 25 to 29-year age range was directly correlated with current SPQ *cognitive-perceptual*, *interpersonal*, and total scores ($\rho = 0.34$, $P = 0.04$; $\rho = 0.40$, $P = 0.02$; $\rho = 0.38$, $P = 0.02$, respectively).

Among the 34 participants having ever used cannabis, frequency/amount scores for the three time periods (15–19 years, 20–24 years, and 25–29 years) were 43.9 ± 54.3 ($n = 22$), 42.4 ± 107.2 ($n = 27$), and 22.5 ± 25.5 ($n = 19$), respectively. Correlations among these frequency/amount scores were moderate to high ($\rho = 0.43$–0.87). As shown in Table 3, frequency/amount of cannabis use in the 20 to 24-year age range was directly correlated with the SPQ *interpersonal* score ($\rho = 0.52$, $P = 0.006$). Furthermore, all four

Table 3 Correlations between frequency/amount of alcohol and cannabis use and schizotypy subscale and total scores[a]

	Alcohol			Cannabis		
	15–19 years ($n = 37$)	20–24 years ($n = 43$)	25–29 years ($n = 37$)	15–19 years ($n = 22$)	20–24 years ($n = 27$)	25–29 years ($n = 19$)
Cognitive-perceptual	0.20	0.10	0.34*	0.14	0.20	0.74*
Interpersonal	0.30	0.24	0.40*	0.24	0.52*	0.84*
Disorganized	0.23	0.22	0.23	0.22	0.07	0.65*
Total	0.29	0.17	0.38*	0.20	0.37	0.86*

[a] Spearman correlation coefficients

* $P < 0.05$

SPQ scores were significantly and strongly directly associated with frequency/amount of cannabis use in the 25 to 29-year age range ($\rho = 0.65$ to $\rho = 0.86$, all $P \leq 0.01$). Again, controlling for current age and current nicotine use minimally diminished the magnitude of these correlation coefficients, though frequency/amount of cannabis use in the 25 to 29-year age-range remained strongly correlated with SPQ total and subscale scores, in the range of 0.58–0.74. Frequency/amount of cocaine use in the three age ranges could not be examined due to small sample sizes.

Discussion

This analysis assessed associations between past use of alcohol, cannabis, and cocaine and current self-reported schizotypy in a sample of healthy, first-degree relatives of patients with schizophrenia and schizoaffective disorder and non-psychiatric controls. Use of these three substances was operationalized in three ways: (1) history of having ever used the substance, (2) age at onset of use of the substance, and (3) past frequency/amount of use of the substance during three time periods in late adolescence and early adulthood. Several findings related to each of these approaches were very interesting. First, participants who had ever used cannabis had significantly higher *cognitive-perceptual*, *interpersonal*, and total schizotypy scores compared to those who had never used cannabis. Second, age at onset of alcohol use was inversely correlated with the *cognitive-perceptual*, *interpersonal*, *disorganized*, and total SPQ score, and age at onset of cannabis use was inversely correlated with the SPQ *interpersonal* score. Third, frequency/amount of alcohol use in the 25 to 29-year age range was directly correlated with current SPQ *cognitive-perceptual*, *interpersonal*, and total scores, frequency/amount of cannabis use in the 20 to 24-year age range was directly correlated with the SPQ *interpersonal* score, and all four SPQ scores were significantly and strongly directly associated with frequency/amount of cannabis use in the 25 to 29-year age range.

These results suggest that the use of addictive substances, particularly cannabis (but also nicotine, based on previous findings reported by Esterberg and associates [27]), is related to schizotypy in complex ways. Greater elucidation of these associations, ideally using longitudinal research designs, could provide crucial information not only on the connection between substance use and schizotypy, but between substance use and schizophrenia. This could be very beneficial given the well-established, very high comorbidity between schizophrenia and cigarette smoking [5, 31], alcohol misuse [32, 33], cannabis abuse and dependence [34, 35], and the use of psychostimulants such as cocaine [23, 33].

This study relied on data from both first-degree relatives of individuals with schizophrenia or schizoaffective disorder and non-psychiatric controls without a first- or second-degree family history of psychosis because it was presumed that, based on prior research [36–38], relatives would have higher schizotypy scores. One report discussed potential explanations for the lack of difference in levels of schizotypy between relatives and controls [39], including the possibility of a biased group of relatives with fewer schizotypal traits, as well as the greater likelihood of defensive reporting in relatives [40, 41].

Dumas and coworkers [16] commented that the association between cannabis use and schizotypy could be explained by: (1) direct pharmacological effects of cannabis that lead to schizotypal traits, (2) a pathway in which schizotypal traits lead to cannabis use consistent with a "self-medication" model, or (3) a common etiopathological factor that leads to both cannabis use and schizotypy. Although the current findings provide more evidence of an association between schizotypy and the use of addictive substances, directionality/

causality of the association cannot be determined, even though *past* substance use and *current* schizotypy were measured. There is virtually no research available to clarify causality. In a sample of 189 undergraduate college students, Schiffman and colleagues [18] found, by amending the items of the SPQ-B with the question "If yes, how old were you when you first noticed this?" to each endorsed item, that schizotypal symptoms generally preceded the onset of cannabis use. That is, among the recent cannabis users, self-reported average age of onset of schizotypal symptoms (across all three SPQ-B subscales, as well as the total score) significantly preceded age of initiation of cannabis use. Further research should similarly attempt to elucidate temporality, and longitudinal research, especially with adolescents, is needed. Causality could not be determined in the present study, and it should be noted that some SPQ items could be endorsed due to the immediate psychoactive properties of some substances (e.g., "People sometimes find it hard to understand what I am saying" in the context of alcohol intoxication or "Do everyday things seem unusually large or small?" in the case of cannabis use).

Aside from the inherent limitations of a cross-sectional approach in terms of not being able to test causality, another limitation of the current study was the relatively small sample size. This, in combination with the high level of multicollinearity between measures of use of various substances, precluded multivariable statistical techniques that could examine specificity of associations between schizotypy and each substance. Furthermore, the limited sample sizes were deemed inappropriate for further analyses in the two subgroups (relatives and controls) separately.

In general, these findings support an association between schizotypal features and substance misuse. Future research should examine these associations in general population samples, as well as in those with elevated genetic risk for schizophrenia (e.g., first-degree relatives). Additionally, extended family (and twin) studies would benefit from using multivariate behavior genetic modeling to estimate the correlations between substance-use propensities (e.g., openness, impulsivity, sensation-seeking) and schizotypal features.

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