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Brief report: The impact of alcohol and cannabis misuse on cognition among individuals with schizophrenia

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Substance misuse and cognitive deficits both impede the treatment and recovery of persons with schizophrenia (Buckley et al., 2009; Green et al., 2004a). Studies show that cognitive performance is one to two standard deviations below average in schizophrenia (Dickinson et al., 2003; Gold, 2004) and that such deficits span neurocognitive and social–cognitive domains (Nuechterlein et al., 2004), lead to poor long-term outcomes (Green et al., 2004a), and may become worsened when those with the disorder misuse substances (Potvin et al., 2012). However, while alcohol and cannabis misuse has been associated with poorer cognitive outcomes among healthy adults (Courtney & Polich, 2009; D'Souza et al., 2004), these relations are much more complex in schizophrenia.

Studies of the cognitive impact of alcohol or cannabis misuse in schizophrenia have yielded mixed results (Potvin et al., 2012). Cannabis-misusing schizophrenia patients tend to demonstrate better cognitive performance than their non-cannabis-misusing counterparts (Coulston et al., 2007; DeRosse et al., 2010; Jockers-Scherübl et al., 2007; Løberg & Hughdahl, 2009; Rabin et al., 2011; Rodriguez-Sanchez et al., 2010; Sevy et al., 2001; Yücel et al., 2012), yet a few studies have reported no between-group differences (Bahorik et al., 2014; Mata et al., 2008; Scholes & Martin-Iverson, 2010). In contrast, alcohol-misusing schizophrenia patients exhibit worse cognitive performance than their non-alcohol-misusing counterparts (Allen & Remy, 2001; Bowie et al., 2005; Manning et al., 2009; Mohamed et al., 2006; Thoma et al., 2006), with a few studies reporting no between-group differences (Addington & Addington, 1997; Allen et al., 2000; Nixon et al., 1996).

Regarding the mixed findings reported between substance misusing and non-misusing schizophrenia patients on cognitive outcomes, several questions about the way in which the severity associated with alcohol, cannabis, or the concurrent use of these substances impacts cognition among those seeking treatment to improve these deficits remain. Variability in the degree of severity, which has been defined within the context of the problems that necessitate substance use treatment (McLellan et al., 1980), may reveal important cognitive differences within this subgroup. To date, however, the way in which such misuse impacts cognition in substance-misusing schizophrenia (SMS) has remained largely unexamined. The objectives of this study were to investigate cognitive performance differences between SMS, schizophrenia, and control participants, and examine whether alcohol or cannabis severity impacts cognition within the SMS sample.

Participants included 32 SMS, 28 schizophrenia, and 37 control participants partaking in studies of Cognitive Enhancement Therapy (CET [Hogarty and Greenwald, 2006]) at the University of Pittsburgh. Inclusion criteria for schizophrenia outpatients consisted of an IQ ≥ 80; age 18 to 60; antipsychotic medication adherent; and schizophrenia/schizoaffective disorder confirmed by the Structured Clinical Interview for DSM-IV (SCID [First et al., 2000]). Inclusion criteria for SMS outpatients consisted of these criteria, as well as Addiction Severity Index (ASI [McLellan et al., 1980]) severity ratings ≥ 4 for alcohol or cannabis, and significant cognitive and social disability confirmed by the Cognitive Styles and Social Cognition Eligibility Interview (Hogarty and Greenwald, 2006). Cognitive and social disability criteria were part of the inclusion criteria for SMS patients to ensure that such participants had sufficient disability to need treatment. Inclusion criteria for controls consisted of an age 18 to 50; free from psychiatric diagnosis per the SCID; no substance abuse within 3 months. Participants' characteristics are presented in Table 1.

The Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS [Green et al., 2004b]) Consensus Cognitive Battery assessed neurocognition. This battery assesses processing speed, verbal/non-verbal working memory, attention/vigilance, verbal/visual learning, and problem solving.

The Mayer–Salovey–Caruso Emotional Intelligence Test (MSCEIT [Mayer et al., 2003]) and the Penn Emotion Recognition Test (Kohler et al., 2000) assessed social cognition. The MSCEIT consists of 141-items, is scored using consensus norms with a mean (*SD*) of 100 (15), and has been validated in normative (Mayer et al., 2003) and psychiatric samples (Eack et al., 2010). The Penn Emotion Recognition Test (Kohler et al., 2000) assessed facial emotion perception.

The 35-item substance use scale of the ASI (McLellan et al., 1980) assessed substance misuse and severity. SMS patients were asked about current (total days within 30 days) and lifetime (total years) alcohol and cannabis use. Severity was rated on a 0 to 10 point scale and

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Table 1
Demographic and clinical characteristics of healthy individuals, and participants with schizophrenia-spectrum disorders with and without substance misuse problems (N = 97).

Variable	HC (n = 37)		SMS (n = 32)		SZ (n = 28)		Analysis[a]	
	M	*SD*	*M*	*SD*	*M*	*SD*	*p*	Direction
Age	25.81	5.66	39.25	12.91	27.39	6.67	<.001	HC < SZ < SMS
IQ	104.19	9.27	99.72	11.13	104.25	14.24	.199	
	N	%	*N*	%	*N*	%	*p*	Direction
Male	27	73.0%	22	68.8%	21	75.0%	.856	
White	31	83.8%	15	46.9%	12	42.9%	<.001	HC < SMS, SZ
Diagnosis[b]								
Schizoaffective disorder	–	–	16	50.0%	12	42.9%		
Schizophrenia	–	–	15	46.9%	16	57.1%		
Addiction Severity[c]								
High Alcohol	–	–	8	8.2%	–	–		
Moderate Alcohol	–	–	24	24.7%	–	–		
High Cannabis	–	–	10	10.3%	–	–		
Moderate Cannabis	–	–	22	68.7%	–	–		
Current Use[d]								
Alcohol	–	–	15	46.9%	–	–		
Cannabis	–	–	17	53.1%	–	–		

Note. HC = Healthy controls; SMS = substance misusing schizophrenia patients; SZ = patients with schizophrenia.
[a] χ^2 test or analysis of variance test, two tailed, for significant differences between healthy control, schizophrenia, and SMS participants.
[b] Diagnosis = schizophrenia or schizoaffective disorder as confirmed by the SCID.
[c] Addiction Severity = ASI addiction severity ratings were used to assess the degree of severity associated with SMS patients current use of alcohol or cannabis, their lifetime use of these substances, and treatment history. Severity was rated on a 0 to 10 point scale with regard to these criteria, and patients with severity ≥ 4 were enrolled in this study. ASI severity score cut-points were used to distinguish clinically meaningful subgroups of SMS patients with moderate (severity 4–5) and high (severity 6–9) severity.
[d] Current Use = Number of days in the past 30 days SMS patients used alcohol or cannabis as identified by the ASI. Patients who disclosed use were coded "yes = 1"; patients who did not disclose use were coded "no = 0".

consisted of the rater's impression of the patient's problem use and the patient's impression of their treatment need; higher scores signaled both greater severity and treatment need. ASI cut-points (McLellan et al., 1980) were used to distinguish clinically meaningful subgroups of SMS patients with moderate (scores, 4–5) or high (scores, 6–9) severity for post-hoc analyses.

Participants were recruited from the Pittsburgh area. Diagnostic interviews were carried out by staff using the SCID supervised by diagnosticians. Staff using the ASI carried out severity assessments; SMS patients with ratings ≥ 4 were enrolled. After determining eligibility, testers administered cognitive measures to participants. Pre-treatment data were analyzed for patients partaking in CET studies. This research was approved and reviewed annually by the University of Pittsburgh Institutional Review Board. Participants provided written informed consent.

Comparisons of overall performance differences on domain measures of neurocognition and social cognition between control, SMS, and schizophrenia participants adjusting for sex, age, race, and IQ revealed significant differences in neurocognitive function across the domains measured (all $p < .027$), and in emotion accuracy, emotion understanding, and total emotional intelligence social–cognitive function (all $p < .013$). Planned follow-up pairwise comparisons showed that schizophrenia and SMS participants had marked impairment in these domains of cognitive function compared to controls. Few differences in neurocognitive performance were observed between schizophrenia and SMS participants, and no differences in social–cognitive performance were observed. Attention/vigilance was the only domain with SMS participants demonstrating superior cognitive performance compared to those with schizophrenia (Table 2).

Subsequent analyses were then conducted to examine overall performance differences on the domain measures of neurocognition and social cognition between SMS patients with high (score, 6–9) or moderate (score, 4–5) alcohol or cannabis severity. The proportion of patients comprising these severity groups is presented in Table 1. Results revealed moderate alcohol severity patients ($M = 33.88$; $SE = 5.35$) had better reasoning neurocognitive function than those ($M = 13.94$; $SE = 2.24$) with high alcohol severity ($p < .001$). However, high alcohol severity patients ($M = 35.48$; $SE = 1.08$) exhibited better emotion perception than those with ($M = 30.68$; $SE = 0.91$) moderate alcohol severity ($p < .001$). High alcohol severity ($M = 101.43$; $SE = 2.42$) patients also had better emotion management than those with moderate alcohol ($M = 84.85$; $SE = 1.91$) severity ($p < .001$). No between-group differences were observed among high or moderate cannabis severity patients (all $p > .231$) patients. Patient's not using cannabis within 30 days of enrollment had better emotion processing, attention/vigilance, and processing speed compared to non-cannabis users within 30 days (all $p < .039$). No differences were observed between alcohol users or non-users within 30 days of enrollment (all $p > .173$).

Prior studies examining the impact of substance misuse on cognition in schizophrenia have varied (Potvin et al., 2012). Since such studies have not adequately addressed the severity associated with misusing substances, a more extensive examination of these effects is warranted. We found few differences between SMS and schizophrenia patients, indicating similar degrees of cognitive impairment. Further, recent cannabis, but not alcohol use had a negative impact on various cognitive domains. Interestingly, moderate alcohol severity patients had worse emotion processing than high alcohol severity patients.

Limitations and implications of this research should be noted. Our modest sample limits generalizability, with additional limitations including a lack of statistical control for chronicity of substance misuse and schizophrenia, the absence of biomedical testing, and the lack of sample representativeness. Despite such limitations, our results have implications for future research. Prior research reports cognitive advantages for SMS (alcohol/cannabis) over schizophrenia patients in terms of processing speed (Herman, 2004; McCleery et al., 2006; Potvin et al., 2005; Thoma et al., 2007), but we observed that schizophrenia patients had better processing speed than SMS patients. Of the studies reporting improved processing speed in SMS patients, McCleery et al. (2006) studied first-episode patients, Herman (2004) studied inpatients, and both Potvin et al. (2005) and Thoma et al. (2007) included polysubstance misusers in their samples. We used an outpatient sample and did not focus on first-episode patients or substances other than alcohol/cannabis, which may account for differences in our findings. Aside from finding better attention/vigilance in SMS patients, no other between-group differences were observed, which is consistent with comparative studies (Barnes et al., 2006; Harrison et al., 2008; Pencer

Table 2
Neurocognitive and social–cognitive test performance of healthy individuals, and participants with schizophrenia-spectrum disorders with and without substance misuse problems (N = 97).

	HC		SMS		SZ					
	N = 37		*N* = 32		*N* = 28		Analysis			
Variable	*M*	*SE*	*M*	*SE*	*M*	*SE*	*F*	*df*	*p*	Direction[a]
Neurocognition Domain										
MCCB[b]										
Processing Speed	78.78	4.01	24.17	4.82	41.11	5.85	37.88	2	<.001	HC > SZ > SMS
Attention/Vigilance	53.46	4.99	31.13	5.23	16.00	3.47	20.80	2	<.001	HC > SMS > SZ
Working Memory	53.68	5.03	31.83	5.89	30.11	4.93	6.81	2	<.001	HC > SMS, SZ
Verbal Learning	53.25	4.89	19.76	4.54	32.87	6.20	11.85	2	<.001	HC > SMS, SZ
Reasoning/Problem Solving	56.22	4.78	38.00	4.99	40.55	6.35	3.76	2	.027	HC > SMS
Visual Learning	60.62	4.38	34.48	5.35	25.44	5.73	14.36	2	<.001	HC > SMS, SZ
Social Cognition Domain										
MSCEIT[c]										
Total Score	100.78	2.30	92.12	2.38	91.02	2.50	5.18	2	.007	HC > SMS, SZ
Emotion Perception	102.62	2.89	98.64	4.17	94.79	3.07	1.89	2	.156	–
Emotion Facilitation	102.37	2.27	97.33	3.49	97.05	2.78	1.15	2	.319	–
Emotion Understanding	102.42	1.85	89.24	2.02	89.00	2.29	15.35	2	<.001	HC > SMS, SZ
Emotion Management	95.19	1.96	90.61	2.28	91.78	1.86	1.32	2	.271	–
Penn Emotion Recognition Test										
Accuracy	34.52	0.53	32.27	0.87	32.06	0.78	4.56	2	.013	HC > SZ
Reaction Time (log)	7.57	0.34	7.71	0.06	7.66	0.04	2.22	2	.115	–

Note. HC = Healthy controls; SMS = substance misusing schizophrenia patients (alcohol or cannabis); SZ = patients with schizophrenia. Performance differences between study groups were investigated by using linear mixed-effects models, which were carried out utilizing R version 2.15.0. (R Development Core Team, 2014). The means account for age, sex, race, and IQ differences. Neurocognitive and social–cognitive domain scores were standardized by scaling test items to a common (*z*) metric. Higher scores indicate better neurocognitive or social cognitive functioning.

[a] The statistical significance of all pairwise comparisons are adjusted using Hochberg's (1988) correction.

[b] MCCB = MATRICS Consensus Cognitive Battery.

[c] MSCEIT = Mayer–Salovey–Caruso Emotional Intelligence Test.

& Addington, 2003; Thoma and Daum, 2008). Since SMS patients exhibit strong novelty seeking traits (Dervaux et al., 2001), it has been suggested that such patients have emotion processing deficits (Potvin et al., 2012). Within our SMS sample, moderate alcohol severity was associated with worse emotion processing, perhaps because such patients engaged in more novelty seeking behaviors than high alcohol severity patients. Compared to moderate alcohol severity patients, high alcohol severity patients may be better positioned to engage in emotional decision making because such persons no longer experience the intoxicating effects of the substance. While this explanation may account for our finding of better emotion processing in high alcohol severity patients, the exploratory and unexpected nature in which these results emerged signals a need for future studies to test these effects in larger SMS samples. Although our findings revealed few differences between SMS and schizophrenia patients overall, the deficits observed in SMS patients can create difficulties when forming social relationships, negotiating out of dangerous situations, and implementing strategies to abstain from substance misuse (Gearon & Bellack, 1999). All of these factors can interact with cognition; therefore interventions are needed that target the challenges that are worsened by substance misuse and the cognitive deficits affecting these major areas of role functioning. Such patients may benefit from the novel therapeutics of cognitive remediation (Eack et al., 2009), which could not only improve their cognitive function but also help address the problems that are linked with substance misuse in this population.

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Contributors

All authors contributed and have approved the final manuscript.

Conflict of interest

The authors report no conflicts of interest.

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