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ORIGINAL ARTICLE

A Signal Detection Analysis of Executive Control Performance Among Adolescent Inhalant and Cannabis Users

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***Background*: Inhalant users have multiple comorbid issues (e.g., polydrug use) that complicate identifying inhalant-specific cognitive deficits. *Objectives*: The aim of the present study was to use signal detection theory to identify inhalant-specific differences in executive control. *Methods*: We examined three well-matched groups: 19 inhalant users, 19 cannabis users, and 19 controls using Stroop and Go/No-Go tasks. *Results*: Inhalant users demonstrated significantly lower *d-prime* scores relative to controls, but not cannabis users, on both tasks, suggesting possible executive deficits relative to controls. *Conclusions/Importance*: The results of this study raise questions regarding inhalant toxicity and the vulnerability of the adolescent brain to drugs of abuse.**

Keywords cognitive control, inhalants, cannabis, signal detection, d-prime, Stroop, Go/No-Go

INTRODUCTION

Cognitive impairments are a consistent finding in studies of chronic inhalant users. Even when compared to other drug users, inhalant users frequently demonstrate deficits in a broad range of cognitive domains (e.g., attention, executive functioning; Rosenberg, Grigsby, Dreisbach, Busenbark, & Grigsby, 2002; Scott & Scott, 2013; Takagi, Lubman, & Yücel, 2011; Vilar-Lopez et al., 2013; Yücel, Takagi, Walterfang, & Lubman, 2008). However, many inhalant studies are criticized on methodological grounds (e.g., unmatched control groups, comorbid substance use) (Lubman, Hides, & Yücel, 2006; Takagi, Lubman, & Yücel, 2008), making it difficult to identify any inhalant-specific cognitive deficits. Takagi et al. (2011) attempted to control for several of the confounds frequently associated with inhalant users (e.g., comorbid substance use), by recruiting three groups of 19 young people (ages 14–24): an inhalant-using group, a drug-using control group, and a community control group. The inhalant and drug-using controls were statistically equivalent at the group level on demographic, clinical, and substance use measures, and all three groups were statistically equivalent on age, sex, and education. Takagi et al., (2011) utilized experimental variations of the Stroop and Go/No-Go tasks as these tests reliably probe attention and executive functioning, two domains commonly reported as deficient among inhalant users (Takagi, Lubman, & Yücel,, 2011).

By matching the two drug-using groups on several variables, Takagi et al., (2011) were able to more thoroughly investigate inhalant-specific effects on executive control, but found no significant differences between groups on any Stroop or Go/No-Go measure. This was surprising as inhalants are considered to be one of the most toxic drugs of abuse, and previous studies have identified differences in white matter integrity between similar drug-using groups (Yücel et al., 2010) and between inhalant users and controls (Takagi et al., 2013).

However, several cognitive results did approach significance (e.g., omission errors for the Go/No-Go and congruent errors for the Stroop), suggesting that the sample size may have been underpowered. In following this up, it is important to investigate other approaches to data analysis that allow a more sensitive examination of the issue.

Signal Detection Theory (SDT; Green & Swets, 1966; Swets, 1996) is one approach that allows for a more rigorous examination of Stroop and Go/No-Go data by

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more closely examining the decision-making process. SDT is a psychophysical model used for measuring performance (i.e., successfully discriminating between signal and noise; Macmillan & Creelman, 2004), and is widely used to more accurately measure differences in cognitive performance, including attention and executive functioning (Haatveit et al., 2010; Oades, 2000; See, Warm, Dember, & Howe, 1997; Tsoi et al., 2008).

SDT separates performance into two measures: sensitivity and bias. Sensitivity, measured as *d-prime*, identifies how well the participant is able to successfully discriminate between correct and incorrect stimuli. Response bias represents a participant's tendency to select one response or the other (i.e., an indication of a participant's bias toward responding "yes" or "no" based on their decision criteria, which is derived from the parameters of the experiment; Macmillan & Creelman, 2004). The aim of the present study was to examine whether inhalant users were less able to discriminate between correct and incorrect stimuli on the Stroop and Go/No-Go using SDT than cannabis and healthy controls. We hypothesized the inhalant users would have lower *d-prime* scores relative to the other groups, suggesting inhalant users were less able to successfully discriminate between correct and incorrect stimuli. We also hypothesized that lower *d-prime* scores would be significantly correlated with inhalant use parameters (e.g., lower *d-prime* scores would be negatively correlated with quantity of inhalant use).

METHOD

Participants

Three groups of young people (ages 13–24 years) were recruited for this study: a chronic inhalant-using group (daily or almost daily use for >12 months); a drug-using control group (daily or almost daily use for >12 months); and a community control group (no prior history of regular substance use [>weekly use]). Participants were requested to abstain from using any substance for at least 24 hours prior to testing and all groups were equivalent on age, sex, and education; the drug-using groups were statistically equivalent on substance use measures, IQ, and clinical measures [See Table 1, reproduced from Takagi et al. (2011)]. The clinical measures used to match the drug-using participants were the Youth Self Report from the Child Behaviour Checklist (Achenbach, 1997) and the Positive and Negative Affect Schedule (Watson, Clark, & Tellegen, 1988). All three groups were recruited from the western suburbs of Melbourne, Australia. The community controls were largely recruited from advertisements placed in local community centers, and the cannabis and inhalant groups were sourced through the Victorian Department of Human Services (DHS). See Takagi et al., (2011) for more detailed participant information.

Although both drug-using groups used other drugs (e.g., alcohol), the drugs they abused most frequently were inhalants and cannabis, respectively. Thus, for the remainder of this paper, we will refer to them as the "inhalant group" and the "cannabis group". The inhalant group comprised 19 (7 males and 12 females, ages 14–20 years) participants who reported abusing inhalants (all abused spray paints) daily or almost daily for a minimum of 12 months. The majority of participants in the drug-using group were not included in traditional education streams for a variety of reasons (e.g., behavioral difficulties) and thus their level of education was not commensurate with their non-drug-using peers. Considering the strong impact education has on IQ performance (Matarazzo & Herman, 1984), participants with an IQ < 70 were included in the study.

The cannabis group comprised 19 (11 males and 8 females, ages 15–21 years) participants who regularly abused (continuous daily or almost daily use for a minimum of 12 months) other substances (primarily cannabis). The community control group comprised 19 participants (7 males and 12 females, ages 13–24 years) recruited from the general population who had no prior history of regular substance use. Participants who were diagnosed with a psychotic disorder, head injury, an unstable medical illness or were prescribed psychotropic medications were excluded from the study.

Cognitive Measures

The Go/No-Go task parameters analyzed in the present study are described elsewhere (Takagi et al., 2011). Individuals saw alternating left- and right-facing arrows and indicated the direction of the arrows. Arrows were usually green; however, occasionally, a red arrow was presented. In this case, individuals waited until the arrow disappeared and then continuing responding to the green arrows. Arrows were always alternating from left to right to further enhance predictability and induce errors in responding.

The Stroop task analyzed in the present study was modified by Carter et al. (2000). In this task, participants were presented with the color words BLUE, GREEN, RED, or YELLOW, written in either congruent (i.e., YELLOW presented in yellow) or incongruent (i.e., YELLOW presented in blue) conditions. The Stroop tasks were presented on a PC laptop and responses were made using the keyboard with colored stickers to identify the correct colors. Six blocks of 96 trials were presented. Three blocks had high expectancy for congruent trials [75% congruent trials (C/C) and 25% incongruent trials (C/I)]; the other three blocks comprised high expectancy for incongruent trials [75% incongruent (I/I) and 25% congruent (I/C)]. The purpose of this task is to probe executive control by manipulating the participant's expectancies for congruent/incongruent stimuli. For the 75% incongruent blocks, the participant's expectations for incongruent stimuli are high and they recruit more cognitive resources. Thus, the prepotent response of word reading is reduced, which leads to a reduced Stroop effect. In contrast, for the 75% congruent trials, expectations for congruent trials are high, which suggest less top-down cognitive resources being recruited given the relatively infrequent occurrence of the incongruent trials. Therefore, word reading more strongly interferes with color naming, leading to a larger Stroop effect (Carter et al., 2000). The results of the standard Stroop

TABLE 1. Basic demographic and substance use histories for the inhalant, cannabis, and community control groups

		Inhalant group $N = 19$	Cannabis group $N = 19$	Community controls $N = 19$	Test statistic	Test statistic value	df	p-value
Age	Mean (SD)	17.71 (1.8)	18.9 (2.0)	18.44 (3.5)	F	1.05	2, 54	.359
Years of education	Mean (SD)	9.37 (1.3)	9.63 (1.3)	10.11 (1.9)	F	1.15	2, 54	.325
Sex	% Male	36.8	57.9	36.8	χ^2	2.28	2	.320
FSIQ	Mean (SD)	80.37 (13.4)	88.1 (13.7)	103.2 (17.3)	F	11.58	2, 54	$< .001^*$
Lifetime substance use								
Alcohol	%	100	100	100	χ^2	N/A	N/A	N/A
Cannabis		94.7	94.7	26.3		29.4	2	$<.001^*$
Inhalants		100	47.4	0		11.0	1	$.001^*$
Regular substance use								
Alcohol	%	52.6	78.9	26.3	χ^2	10.56	2	$.005^*$
Cannabis		84.2	89.5	N/A		.000	1	1.0
Inhalants		100	15.8	N/A		24.3	1	$<.001^*$
Age of first use								
Alcohol	Mean	12.74 (3.0)	12.63 (2.7)	13.53 (2.8)	F	0.56	2, 54	.576
Cannabis	(SD)	13.22 (1.6)	13.94 (1.7)	15.8 (2.8)	F	4.13	2, 38	$.024^*$
Inhalants		14.84 (1.3)	14.56 (2.2)	N/A	t	.358	26	.728
Age of regular use								
Alcohol	Mean (SD)	15.9 (1.2)	14.47 (2.4)	17.4 (1.5)	F	4.7	2, 27	$.018^*$
Cannabis		14.81 (1.1)	15.18 (1.8)	N/A	t	$-.691$	31	.495
Inhalants		15.6 (1.5)	13.67 (1.5)	N/A	t	1.6	20	.126
Average daily use								
Alcohol (standard drinks)	Mdn.	0.45, 0.54 (0.3)	0.56, 1.9 (3.5)	0.3, 0.37 (0.3)	KW	3.7	2	.160
Cannabis (grams)	Mean	0.75, 1.2 (1.4)	1.0, 0.94 (0.9)	N/A	U	110.5	1	.950
Inhalants (cans)	(SD)	2, 2.4 (2.5)	N/A	N/A	N/A	N/A	N/A	N/A

$*$ = significant result, Mdn. = median, SD = standard deviation, KW = Kruskal–Wallis, U = Mann–Whitney U, FSIQ = full scale IQ, FSIQ *post hoc*: inhalant & cannabis: $p = .258$; inhalant & controls: $p < .001$; controls & cannabis: $p = .008$.
Lifetime cannabis *post hoc* (Bonferroni-adjusted alpha level = .017): inhalant & cannabis: $p = 1.0$; inhalant & controls: $p < .001$; controls & cannabis: $p < .001$.
Age of first cannabis use *post hoc*: inhalant & cannabis: $p = .452$; inhalant & controls: $p = .018$; controls & cannabis: $p = .112$
Regular alcohol use *post hoc* (Bonferroni-adjusted alpha level = .017): inhalant & controls: $p = .171$; inhalant & controls: $p = .184$; controls & cannabis: $p = .003$.
Age of regular alcohol use *post hoc*: inhalant & cannabis: $p = .186$; inhalant & controls: .350; controls & cannabis: .018.

TABLE 2. Go/No Go *d-prime*, and *c* group comparisons

Variable	Descriptive statistic	Inhalant N = 19	Cannabis N = 19	Community controls N = 19	Test statistic	Test statistic value	df	*p*-value
d-prime	Mean (SD)	2.81 (.99)	3.33 (.96)	3.52 (.61)	F	3.79	2,60	.028*
c	Mean (SD)	−.81 (.31)	−.78 (.38)	−.77 (.22)	F	.086	2,60	.917

*Significant result

measures (congruent Stroop effect: reaction times for incongruent trials – reaction times for congruent trials) are described elsewhere (Takagi et al., 2011).

Signal Detection Analysis

SDT separates performance into measures of sensitivity (*d-prime*) and bias (*c*). Sensitivity identifies how well the participant is able to successfully discriminate between correct and incorrect stimuli (e.g., "go" and "no-go" responses) as measured by the proportion of "go" trials to which subject responded "go" (hit rate) and the proportion of "no-go" trials to which subject responded "go" (false alarm rate). Response bias, measured as *c* in the present study, represents a participant's tendency to select one response or the other (Macmillan & Creelman, 2004). When measuring sensitivity (*d-prime*), it is important to account for response bias (*c*) as differences in bias represent different strategies for completing the experiment. For example, a strict criterion (i.e., tendency to respond no, or not respond to a "go" stimuli) would minimize false alarms but increase the likelihood of misses whereas a lax criteria (i.e., tendency to respond yes, or respond to a "go" stimuli) would minimize misses but increase the likelihood of false alarms (Macmillan & Creelman, 2004).

For *d-prime*, a higher value represents higher levels of sensitivity (i.e., more able to successfully identify correct stimuli and reject incorrect stimuli) and for bias, a positive *c* value represents a tendency to say "no" and a negative c value represents a tendency to say "yes". The calculation of *d-prime* and *c* were carried out using the formulas described in Macmillan and Creelman (2004). To avoid problems of division by zero, hit rates and false alarm rates of 1 or 0 were adjusted by 0.05 (Macmillan & Creelman, 2004). For example, a hit rate of 1.0 would be adjusted to .95.

Data Analysis

For all analysis of variance (ANOVA) models that reached significance and met the assumption of homogeneity of variance, Tukey *post hoc* tests were used. For models that violated this assumption, Games–Howell *post hoc* tests were used to account for this violation. For the correlational analysis, if all variables were continuous, Pearson's product-moment correlations were used. If the variables were dichotomous (e.g., have you ever used inhalants regularly: yes or no), point-biserial correlations were used.

RESULTS

The drug-using groups were statistically equivalent on full scale IQ; however, there were significant differences between the groups on verbal IQ (Takagi, Lubman, & Yücel, 2011). We examined the relationship between verbal IQ and all *d-prime* measures; however, they were not significant and verbal IQ was not included as a covariate.

Go/No-Go

One-way independent-groups ANOVA models were performed on the *d-prime* and c, (see Table 2). There were significant differences between the three groups on measures of *d-prime* on the Go/No-Go task. Games–Howell *post hoc* tests revealed significant differences between the inhalant and control groups ($p = .021$, $d = .88$), with inhalant users having a significantly lower d' scores. The *d-prime* score between the inhalant and cannabis groups was not significant ($p = .21$, $d = .55$).

Stroop

To explore the possible main effects of trial type (congruent, incongruent) and expectancy (mostly congruent, mostly incongruent) and expectancy by trial type interaction, a two-way repeated-measures ANOVA was performed examining the Stroop reaction time data. Group differences were also examined. There was a significant main effect of trial type ($F\{1,56\} = 180.31$, $p < .001$) and a significant main effect of expectancy ($F\{1,56\} = 12.92$, $p = .001$). Further, the expectancy by trial type interaction was also significant ($F\{1,56\} = 42.16$, $p < .001$). The main effect of group was not significant ($F\{1,2\} = 3.02$, $p = .057$).

Considering the significant interaction, we performed a simple main effects analysis. For trial type, expectancy had a significant effect on the reaction times for both congruent ($F\{1,56\} = 88.7$, $p < .001$) and incongruent trials ($F\{1,56\} = 146.1$, $p < .001$). In contrast, high expectancy for incongruent trials did not have a significant effect on trial type reaction time ($F\{1,56\} = .78$, $p = .382$), but low expectancy for incongruent trials did ($F\{1,56\} = 30.6$, $p < .001$).

For the individual reaction times for the I/C and I/I conditions, only the I/C reaction time was significantly different between the groups (see Table 3). Tukey *post hoc* tests revealed inhalant users performed significantly slower than community controls ($p = .019$, $d = .9$). The remaining comparisons were not significant.

TABLE 3. Stroop effect, reaction times, *d-prime*, and *c* group comparisons for the Stroop

Variable	Descriptive statistic	Inhalant N = 19	Cannabis N = 19	Controls N = 19	Test statistic	Test statistic value	df	*p*-value
Mostly incongruent Stroop effect (I/I – I/C)	Mean (SD)	66.66 (76.12)	93.33 (53.22)	88.02 (67.94)	F	.858	2,54	.430
Reaction Times								
I/C	Mean (SD)	846.77 (116.6)	772.79 (111.3)	736.98 (133.59)	F	4.08	2,54	.022*
I/I	Mean (SD)	913.44 (126.72)	866.12 (126.83)	825.01 (129.5)	F	2.28	2,54	.112
Signal Detection								
I/I, I/C *d-prime*	Mean (SD)	3.26 (.72)	3.7 (.6)	3.7 (.38)	F	3.5	2,54	.037*
I/I, I/C Bias *c*	Mdn.	−0.07	−0.05	−0.05	KW	1.21	2	.547
C/I, C/C *d-prime*	Mean (SD)	3.43 (.74)	3.65 (.62)	3.85 (.46)	F	2.25	2,54	.116
C/I, C/C Bias *c*	Mdn.	−.1	−.22	−.26	KW	2.65	2	.266

Mdn. = median, KW = Kruskal–Wallis, I/C = incongruent/congruent, I/I = incongruent/incongruent, C/I = congruent/incongruent, C/C = congruent/congruent

A one-way ANOVA was performed to assess group differences in mean Stroop effect for the mostly incongruent condition (I/I–I/C). There were no significant differences between the groups with respect to Stroop effect.

Finally, *d-prime* and *c* were calculated for each Stroop condition (high expectancy for congruent stimuli and high expectancy for incongruent stimuli). For the high expectancy for incongruent condition (I/I and I/C), there was a significant difference in *d-prime* scores between the groups. However, Games–Howell *post hoc* tests failed to reveal any significant differences between inhalant and controls ($p = .060$, $d = .79$), inhalant and cannabis users ($p = .137$, $d = .65$) and cannabis and community controls ($p = .988$, $d = .04$).

Correlations

The *d-prime* measures for the I/I and I/C condition of the Stroop and Go/No Go were significant and included in correlational analysis. Further, only the inhalant group was included in the analysis and, to reduce the likelihood of Type I error, only inhalant use measures were examined. The Go/No-Go *d-prime* measure was negatively correlated with lifetime inhalant use (Have you ever used inhalants?) ($r_{pb} = -.306$, $p = .02$) and regular inhalant use (Have you ever used inhalants regularly?) ($r_{pb} = -.406$, $p = .002$) suggesting regular and lifetime inhalant use was significantly associated with lower *d-prime* scores (i.e., less sensitivity). The Go/No-Go d-prime measure was also negatively correlated with frequency of use ($r = -.418$, $p = .033$) and last use amount ($r = -.450$, $p = .021$), suggesting frequent and heavy use of inhalants was significantly associated with lower *d-prime* scores.

For the Stroop, the *d-prime* measure for the I/I and I/C condition was negatively correlated with regular inhalant use ($r_{pb} = -.308$, $p = .02$), amount used in a typical day ($r = -.707$, $p = .005$), and last use amount ($r = -.406$, $p = .04$), suggesting regular, heavy inhalant use was significantly associated with lower *d-prime* score.

DISCUSSION

The aim of the current study was to examine possible deficits in executive control among young, regular inhalant users relative to a cannabis-using control group and a community control group using SDT. On the Go/No-Go task, the inhalant users had significantly lower *d-prime* scores relative to community controls, indicating the inhalant users were less able to successfully discriminate between a "go" and a "no-go" signal. Further, the *d-prime* measure was significantly and negatively correlated with inhalant use measures, suggesting regular, heavy inhalant use was significantly associated with lower *d-prime* scores. There were no significant differences between the groups on the response bias measure, suggesting all three groups adopted a similar strategy for performing the Go/No-Go task (i.e., all three groups adopted a more liberal strategy, tending to respond to "go" signals).

With respect to the Stroop task, for all three groups, the expectancy by trial-type interaction was significant and the main effect of group was not significant, indicating all three groups were able to successfully form expectancies for incongruent stimuli and adjust performance to optimize resolution of response conflict. There were significant differences between the groups on the I/I, I/C *d-prime* measure. *Post hoc* tests failed to reveal any significant differences; however, the comparison between the inhalant users and the community controls approached significance and had a large effect size ($p = .060$, Cohen's $d = .79$), with inhalant users having a lower *d-prime* score. Further, there were significant differences between the groups on RT for the Stroop I/C condition, with inhalant users performing significantly slower relative to community controls. In other words, in the high expectancy for incongruent trials condition, the inhalant users were significantly slower when responding to congruent trials relative to controls and inhalant users were less able to successfully discriminate between congruent and incongruent trials. Finally, the I/I, I/C *d-prime* measure was also significantly and negatively correlated with inhalant use measures, suggesting regular, heavy use was associated

with greater difficulties in decision-making processes. As with the Go/No-Go, there were no significant differences between the groups on bias measure *c*, suggesting similar strategies for performing the Stroop task.

The increase in cognitive demand for the high expectancy incongruent condition requires the deployment of additional cognitive resources. Although the *post hoc* tests did not reveal a significant result, the I/I, I/C *d-prime* results suggest inhalant users were less able to successfully perform the Stroop task in this condition (i.e., successfully discriminate between congruent and incongruent stimuli) relative to controls, suggesting possible executive control deficits. Further, inhalant users were significantly slower in the I/C condition relative to community controls.

When examined in conjunction with the Go/No-Go results, the pattern of performance demonstrated by the inhalant group could represent a deficit in attentional set shifting when compared with controls; a notion that is consistent with previous studies investigating white matter abnormalities in inhalant users (e.g., morphological abnormalities in the corpus callosum; Takagi et al., 2013; Yücel et al., 2010). In other words, once the inhalant users have formed an attentional set (e.g., responding to mostly incongruent stimuli in the I/I, I/C condition), they have difficulties in successfully adjusting to the parameters of a different condition (e.g., the C/I, C/C condition, or not responding to a "no-go" signal). In a practical sense, in situations of high cognitive or emotional demand, inhalant users would be less able successfully shift their attention from one task to the other; this could include shifting focus away from harmful activities such as using inhalants.

Interestingly, there remained no significant differences between the clinical groups on any measure despite more sensitive and sophisticated methods of analysis. This raises the possibility that inhalants may not be more toxic to brain than other psychoactive substances during adolescence and that the adolescent brain is particularly vulnerable to all drugs of abuse (e.g., alcohol and cannabis). This is surprising considering the primary psychoactive substance found in spray paint is toluene, which is hypothesized to be the most toxic commonly misused substance (Hartman, 1995; Yücel et al., 2010). However, there is support for the notion that the adolescent brain is vulnerable to a range of toxic substances (e.g. inhalants, alcohol, cannabis; De Bellis et al., 2005; Pope et al., 2003; Takagi et al., 2011; Takagi et al., 2013), suggesting that any deficits previously identified among inhalant-using populations may reflect adolescent polysubstance use rather than inhalant abuse specifically. This is particularly relevant to inhalant research as inhalant users are almost certainly polysubstance users (Lubman et al., 2006; Sakai, Hall, Mikulich-Gilbertson, & Crowley, 2004; Takagi et al., 2011); therefore, it is difficult to identify any drug-specific or synergistic drug effects.

Moreover, it is possible that, with continued use, chronic inhalant users will develop more significant cognitive and neurobiological abnormalities relative to chronic cannabis users. Alternatively, individuals with certain cognitive profiles may be more likely to develop drug use problems during adolescence. Indeed, early school failure is a major risk factor for adolescent substance misuse. More methodologically rigorous longitudinal studies are required to explore these possibilities.

The limitations of the present study are discussed in detail elsewhere (Takagi et al., 2011). In brief: (1) the study is cross-sectional in design, which limits our ability to determine causality; (2) in order to maximize recruitment of a difficult group and to include a more representative sample, we employed liberal exclusion criteria (e.g., including participants with an IQ < 70); (3) several inhalant users attended alternative schools that did not maintain an academic environment commensurate with mainstream schooling, and this may account for the inhalant group's relatively low IQ score; (4) substance use histories were self-reported, and participants may have downplayed their inhalant use due to the stigma associated with inhalant misuse; (5) and there was no biochemical verification to confirm abstinence from substance use (e.g., urine drug screens), and it is possible that abstinence for longer than 24 hours may also have influenced cognitive performance. However, it is important to note strengths of the present study. The experimental cognitive tasks (Stroop and Go/No-Go) are more sensitive to possible pathology and allow for a more detailed examination of specific cognitive systems (e.g., conflict monitoring with the Stroop; Carter, 2005). Further, SDT is a more sophisticated method for examining cognitive performance and revealed significant differences between inhalant users and controls that were obscured when examining raw error data (Takagi et al., 2011).

In summary, the pattern of performance on the Stroop and Go/No-Go suggests executive dysfunction, with possible deficits in attentional set shifting when compared with controls. As with the previous study, there were no significant differences between inhalant and cannabis users. The results of this study highlight several key notions. First, it is important to consider utilizing experimental cognitive tasks when examining substance-using populations as these tasks are more likely to discriminate subtle pathology when compared to standard measures (e.g., broad measures of intellectual ability). Second, SDT is a more sophisticated and sensitive method of examining cognitive performance when compared to analyzing raw error data. Finally, the lack of significant differences between the clinical groups after employing more sensitive and sophisticated methods of analysis raises important questions regarding the toxicity of inhalants and the vulnerability of the adolescent brain to drugs of abuse (i.e., the adolescent brain is particularly vulnerable to all drugs of abuse). Utilizing well-matched control groups is an important issue for future inhalant studies to consider.

Declaration of Interest

The authors declare no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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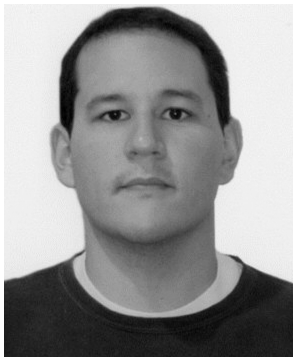

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Professor Dan Lubman has worked across mental health and drug treatment settings in both the UK and Australia. His research is wide ranging and includes investigating the impact of alcohol and drug use on brain function, the relationship between substance use and mental disorder, as well as the development of targeted intervention programs within school, primary care, mental health, and drug treatment settings. He is regularly contacted for policy advice and community comment, and sits on numerous expert reference committees.

Associate Professor Sue Cotton is a Principal Research Fellow in the Centre for Youth Mental Health at the University of Melbourne. She is a NHMRC Career Development Fellow. She is a psychologist (who has training in clinical neuropsychology) and senior biostatistician. Her work involves the integration of the fields of biostatistics, clinical research methodology, psychology, and psychiatric research. Findings from her research activities have contributed to the scientific literature and reflect her areas of strength in these fields.

Antonio Verdejo-Garcia is an associate professor in the School of Psychology and Psychiatry at Monash University (Melbourne, Australia). He has an MSc in Psychological and Biomedical aspects of Health and Illness and a PhD in Psychology. His PhD training focused on Clinical Neuropsychology and Neuroscience, and included research internships in the following international centers: University of Iowa Hospitals and Clinics (Iowa, USA), Behavioural and Clinical Neuroscience Institute, University of Cambridge (Cambridge, UK) and Johns Hopkins Medical Institute (Baltimore, USA). After obtaining his PhD by the University of Granada, Antonio has held a competitive post-doctoral research fellow position in the IMIM-Hospital del Mar, Barcelona, where he developed strategic research collaborations in the fields of genetics, pharmacology, and functional neuroimaging as well as senior lecturer and associate professor positions in the Department of Clinical Psychology of the University of Granada. His current research program is focused on the role of executive functions in addiction treatment outcomes.

Raquel Vilar is an associate professor of Psychology at the University of Granada. She is a member of several research projects about addictions and obesity, and has published about 20 papers in several journals. Her actual areas of interest are the neuropsychological characterization of obese individuals and drug dependents, and the efficacy of the Brief Motivational Intervention.

Prof Yücel is a clinical neuropsychologist currently appointed as a professorial fellow within the School of Psychological Sciences, Monash University where he directs the Monash Clinical and Imaging Neuroscience (MCIN) laboratory. He also holds an appointment within the National Health and Medical Research Council (NHMRC) of Australia fellowship scheme. He is an expert in the area of biological psychiatry and addiction neuroscience.

GLOSSARY

Cognitive control: Refers to processes that allow information processing and behavior to vary adaptively from moment to moment depending on current goals, rather than remaining rigid and inflexible.

d-Prime: A sensitivity index used in signal detection theory.

Inhalants: Inhalants are chemical substances that give off fumes or vapors at room temperature.

Signal Detection Theory: A statistical technique designed to locate a signal against a background of noise.

REFERENCES

Achenbach, T. (1997). *Manual for the Child Behavior Checklist/4–18 and 1991 profile* Vermont: University of Vermont, Department of Psychiatry.

Carter, C. (2005). Applying new approaches from cognitive neuroscience to enhance drug development for the treatment of impaired cognition in schizophrenia. *Schizophrenia Bulletin, 31*(4), 810–815.

Carter, C., Macdonald, A., Botvinick, M., Ross, L., Stenger, V., Noll, D., & Cohen, J. (2000). Parsing executive processes: Strategic vs. evaluative functions of the anterior cingulate cortex. *Proceedings of the National Academy of Sciences of the United States of America, 97*(4), 1944–1948.

De Bellis, M., Narasimhan, A., Thatcher, D., Keshavan, M., Solof, P., & Clark, D. (2005). Prefrontal cortex, thalamus, and cerebellar volumes in adolescents and young adults with adolescent-onset alcohol use disorders and comorbid mental disorders. *Alcoholism: Clinical and Experimental Research, 29*(9), 1590–1600.

Green, D., & Swets, J. (1966). *Signal Detection Theory and Psychophysics*. New York, NY: Wiley.

Haatveit, B., Sundet, K., Hugdahl, K., Ueland, T., Melle, I., & Andreassen, O. (2010). The validity of d prime as a working memory index: Results from the "Bergen n-back task". *Journal of Clinical and Experimental Neuropsychology, 32*(8), 871–880.

Hartman, D. (1995). *Neuropsychological Toxicology* (2nd ed.). New York, NY: Plenum Press.

Lubman, D., Hides, L., & Yücel, M. (2006). Inhalant misuse in youth: Time for a coordinated response. *Medical Journal of Australia, 185*(6), 327–330.

Macmillan, N., & Creelman, C. (2004). *Detection Theory: A User's Guide (2nd ed.)*. Malwah, NJ: Lawrence Erlbaum Associates, Inc.

Matarazzo, J., & Herman, D. (1984). Relationship of education and IQ in the WAIS—R standardization sample. *Journal of Consulting and Clinical Psychology, 52*(4), 631–634.

Oades, R. D. (2000). Differential measures of 'sustained attention' in children with attention-deficit/hyperactivity or tic disorders: Relations to monoamine metabolism. *Psychiatry Research, 93*(2), 165–178.

Pope, H., Gruber, A., Hudson, J., Cohane, G., Huestis, M., & Yurgelun-Todd, D. (2003). Early-Onset cannabis use and cognitive deficits: What is the nature of the association. *Drug and Alcohol Dependence, 69*, 303–310.

Rosenberg, N., Grigsby, J., Dreisbach, J., Busenbark, D., & Grigsby, P. (2002). Neuropsychologic impairment and MRI abnormalities associated with chronic solvent abuse. *Clinical Toxicology, 40*(1), 21–34.

Sakai, J., Hall, S., Mikulich-Gilbertson, S., & Crowley, T. (2004). Inhalant use, abuse and dependence among adolescent patients: Commonly comorbid problems. *Journal of the American Academy of Adolescent Psychiatry, 43*(9), 1080–1088.

Scott, K. D., & Scott, A. A. (2013). Adolescent inhalant use and executive cognitive functioning. *Child: Care, Health and Development*. **AQ3**

See, J., Warm, J., Dember, W., & Howe, S. (1997). Vigilance and signal detection theory: An empirical evaluation of five measures of response bias. *Human Factors: The Journal of the Human Factors and Ergonomics Society, 39*(1), 14–29.

Swets, J. (1996). *Signal Detection Theory and ROC Analysis in Psychology and Diagnostics*. Mahwah, NJ: Lawrence Earlbaum Associates.

Takagi, M., Lubman, D., Cotton, S., Baliz, Y., Tucker, A., & Yücel, M. (2011). Executive control among adolescent inhalant and cannabis users. *Drug and Alcohol Review, 30*(6), 629–637.

Takagi, M., Lubman, D., & Yücel, M. (2008). Interpreting neuropsychological impairment among adolescent inhalant users: Two case reports. *Acta Neuropsychiatrica, 20*(1), 41–43. **AQ4**

Takagi, M., Lubman, D., & Yücel, M. (2011). Solvent-induced leukoencephalopathy: A disorder of adolescence? *Substance Use & Misuse, 46*(S1), 95–98.

Takagi, M., Lubman, D. I., Walterfang, M., Barton, S., Reutens, D., Wood, A., & Yucel, M. (2013). Corpus callosum size and shape alterations in adolescent inhalant users. *Addiction Biology, 18*(5), 851–854.

Takagi, M., Yucel, M., Cotton, S. M., Baliz, Y., Tucker, A., Elkins, K., & Lubman, D. I. (2011). Verbal memory, learning, and executive functioning among adolescent inhalant and cannabis users. *Journal of Studies on Alcohol and Drugs, 72*(1), 96–105.

Tsoi, D. T., Lee, K. H., Khokhar, W. A., Mir, N. U., Swalli, J. S., Gee, K. A., ... Woodruff, P. W. (2008). Is facial emotion recognition impairment in schizophrenia identical for different emotions? A signal detection analysis. *Schizophrenia Research, 99*(1-3), 263–269.

Vilar-Lopez, R., Takagi, M., Lubman, D., Cotton, S., Bora, E., Verdejo-Garcia, A., & Yucel, M. (2013). The effects of inhalant misuse on attentional networks. *Developmental Neuropsychology, 38*(2), 126–136.

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology, 54*(6), 1063–1070.

Yücel, M., Takagi, M., Walterfang, M., & Lubman, D. (2008). Toluene misuse and long-term harms: A systematic review of the neuropsychological and neuroimaging literature. *Neuroscience & Biobehavioral Reviews, 32*, 910–926.

Yücel, M., Zalesky, A., Takagi, M., Bora, E., Fornito, A., Ditchfield, M., ... Lubman, D. (2010). White-Matter abnormalities in long-term inhalant abusing adolescents. *Journal of Psychiatry and Neuroscience, 35*(6), 409–412.