

Cannabis use, cognitive functioning and behaviour problems Lendering, M.F.H.

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Motivational and cognitive inhibitory control in recreational cannabis users.

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Abstract

Substance use disorders have been associated with impaired decision-making and increased impulsive behaviour. Lack of inhibitory control may underlie such higherorder cognitive difficulties and behaviour problems. This study examined inhibitory control in 53 recreational cannabis users and 48 controls. Inhibitory control was tested with two computer tasks, one with a motivational component and one without such a component. Impulsive behaviour was assessed using the Barratt Impulsiveness Scale. Results showed that the recreational cannabis users had poorer motivational inhibition (i.e. were more inclined to 'gamble') than controls. There were no group differences in the cognitive inhibition task. Cannabis users also reported more impulsive behaviour in daily life. This behaviour was related to response style in the motivational inhibition task, but not to performance in the cognitive inhibition task. It is concluded that, among recreational cannabis users, lack of inhibitory control depends on contextual or situational factors, i.e. it becomes evident only when situations or tasks involve a motivational component.

Introduction

Cannabis abusers share a considerable number of neuropsychological weaknesses with abusers of other drugs such as psychostimulants, opoids and alcohol (and with polysubstance abusers) (Fernández-Serrano, Pérez-García, & Verdejo-García, 2011). These include impairments in episodic memory, emotional processing, implicit cognition and executive function (EF). Although there is evidence suggesting some more specific deficits as well, including those regarding prospective memory, processing speed, and complex planning, there are generally abusers of other substances showing these deficits as well (Fernández-Serrano et al., 2011; Grant, Gonzalez, Carey, Natarajan, & Wolfson, 2003; Piechatzek et al., 2009). Many studies have employed tasks or investigated psychological constructs that appear to be built up of multiple, more basic components. One such component is inhibitory control. Next to deficits in memory and processing speed, the most consistently reported basic impairment among cannabis users is a lack of inhibitory control, particularly when required together with other cognitive abilities (Lamers, Bechara, Rizzo, & Ramaekers, 2006; Piechatzek et al., 2009; Solowij et al., 2002; Verdejo-García, Lawrence, & Clark, 2008). Less consistent results were obtained when investigating other executive functions (Piechatzek et al., 2009). When other EF-impairments were reported the tasks that were used often also involved an inhibitory component (Verdejo-Garcia et al., 2007; Whitlow et al., 2004). Whereas deficits in memory and processing speed both appear to be likely consequences of acute and chronic cannabis use, deficient inhibitory control has been considered both a potential consequence of (chronic) cannabis (and other substance) use and as a vulnerability marker predisposing towards substance use. Several studies have suggested a gradual attrition of inhibitory control that could be mediated by structural changes in the prefrontal cortex (e.g. cell death and tissue shrinkage, decreases in neurogenesis and synaptogenesis) (Chanraud et al., 2007; Cowan et al., 2003; Goldstein & Volkow, 2002; Robinson & Kolb, 2004). Alternatively, deficient inhibitory control may be present prior to drug initiation, and represent a vulnerability marker predisposing individuals towards recreational use (and mediate the transition to drug dependence) (Chambers, Taylor, & Potenza, 2003; Dalley et al., 2007; Kreek, Nielsen, Butelman, & LaForge, 2005).

Further indirect evidence for associations between a lack of inhibitory control and cannabis use stems from studies into cannabis and behaviour, which have frequently shown associations with impulsive behaviour in daily life (Clark, Rosier, Robbins & Sahakian, 2009; Malmberg et al., 2010) or with externalizing (e.g. aggressive and delinquent) behaviour characterized by impulsivity deficits (e.g. Fergusson, Horwood & Ridder, 2007; Griffith-Lendering et al., 2011; Nelson & Trainor, 2007). Some of these studies show that the behaviour problems (and subsequently the possible lack of inhibitory control) precede the drug use, providing (indirect) evidence for the vulnerability hypothesis (e.g. Griffith-Lendering et al., 2011).

Despite all the evidence, even inhibitory control deficits among cannabis users have not always been replicated (Clark et al., 2009; Pope, Gruber, Hudson, Huestis, & Yurgelun-Todd, 2001). Although it is generally very difficult to rule out whether sample and methodological differences (e.g. which instruments were used to measure inhibitory control?) accounted for mixed results, it is important to consider differences in the definition of inhibitory control as well. Inhibition is not a unitary construct. Several empirically and statistically-validated taxonomies have been proposed. One of these distinguishes inhibition of prepotent responding, resistance to distractor interference, and resistance to proactive interference (Friedman & Miyake, 2004). For cannabis and other substance (ab-) use, inhibition of prepotent responding may be most relevant, e.g. the ability to resist automatic response tendencies when presented with specific (substance- or non-substance related) cues (Gruber, Silveri, Dahlgren, & Yurgelun-Todd, 2011; Gruber & Yurgelun-Todd, 2005; Tapert et al., 2007). Another taxonomy differentiates cognitive and motivational inhibitory control. Cognitive inhibitory control is required for solving abstract, decontextualized problems, and motivational inhibitory control is required when problems involve regulation of affect and motivation (Huijbregts, Warren, De Sonneville & Swaab, 2008; Sonuga-Barke, 2002; Zelazo & Müller, 2002). There is neuro-anatomical evidence to support this distinction, with relatively more activity in the orbitofrontal cortex (OFC) during tasks involving motivational inhibition and relatively more activity in the dorsolateral prefrontal cortex (DLPFC) and the anterior cingulate cortex (ACC) during tasks involving cognitive inhibition (Krain, Wilson, Arbuckle, Castellanos, & Milham, 2006). The two types of inhibition have also been associated with different dopaminergic pathways: the mesocortical pathway has been associated with cognitive inhibitory control and the mesolimbic pathway with motivational

inhibitory control (Pierce & Kumaresan, 2006; Sonuga-Barke, 2002). Both originate in the ventral tegmental area, but the mesocortical pathway particularly innervates DLPFC, whereas the mesolimbic dopaminergic pathway passes the nucleus accumbens, amygdala, and hippocampus and innervates ventromedial areas/OFC.

The main question of the present study is whether, among recreational cannabis users, cognitive and motivational inhibitory control can be distinguished, i.e. whether they show specific problems with either cognitive or motivational control. Although based on the existing knowledge cognitive inhibitory control deficits cannot be ruled out, there are several reasons to hypothesize that cannabis users will particularly show problems with motivational inhibitory control. First of all, several different studies have shown motivational deficits in (heavy) cannabis users, both when they were not under the influence of THC, the main active component of cannabis, and when they were (e.g. Cherek, Lane, & Dougherty, 2002; Lane et al., 2005; 2007). Second, many studies provide support for the hypothesis that dysfunctional reward processing, which, by definition, involves motivational inhibition, is central to the phenomenon of substance abuse (Blum et al., 2000; Nestor, Hester, & Garavan, 2010). Examples are studies into implicit cognition which generally involve the memory of the rewarding qualities of certain behaviours (Stacy & Wiers, 2010) and (emotional) decisionmaking (Bechara, 2003; Busemeyer & Stout, 2002), but also studies showing abnormal activation patterns and dopamine dysregulation for substance abusers specifically in the brain regions that are part of the reward circuitry (Kamarajan et al., 2010; Nestor et al., 2010).

In addition to examining user - non-user differences in laboratory measures of inhibitory control, we investigated whether these groups also differ regarding impulsive behaviour in daily life. This has been shown before and we expect to replicate this finding (Churchwell, Lopez-Larson, & Yurgelun-Todd, 2010; Gruber et al., 2011). Based on the fact that the questionnaire used to assess impulsivity in daily life contains items with and without motivational components, we expected associations between both laboratory tasks and outcomes of the questionnaire.

Method

Participants

Participants were classified as cannabis users if they reported using cannabis every month during the past year and as non-users if they reported the use of cannabis zero times during the past year. Based on these criteria (Monshouwer et al., 2006), 53 cannabis users (mean age of 22.6, SD=2.4, with an abstinence period of at least 24 hours) and 48 non-users (mean age 22.3, SD=2.3) were recruited among University of Leiden undergraduate students. Written informed consent was obtained from all participants before the start of the study. Ethical approval for this study was granted by Leiden University's Education and Child Studies Ethics Committee.

Measures

Questionnaires

Cannabis use was assessed by asking participants about their use during the past year and month. Participants also reported on the use of alcohol (weekly yes/no), tobacco (daily yes/no) and other drugs including stimulants (cocaine, (met)amphetamine), opioids (heroin, methadone), and 3,4-methylenedioxymethamphetamine (MDMA: Ecstacy) (past year and past month: yes/no, plus frequency of use during past year/month). Impulsive behaviour in daily life was assessed with the Barratt Impulsiveness Scale (BIS-11; Barrat, 1985), which contains 30 items measuring behavioural impulsivity. Respondents rate statements on a fourpoint scale: rarely/never (1), occasionally (2), often (3), or almost always (4). The BIS-11 has 3 subscales (Barratt, 1985, Miller, Joseph & Tudway, 2004): cognitive impulsivity (8 items, $\alpha = 0.74$), motor impulsivity subscale includes items such as 'I don't pay attention' and 'I have racing thoughts'; the motor impulsivity subscale includes items from the non-planning impulsivity subscale are 'I say things without thinking' and 'I act on impulse'; and examples of items from the non-planning impulsivity subscale are 'I say things without thinking' and 'I get easily bored when solving thought problems' (Stanford et al., 2009).

Neuropsychological tasks

Two computer tasks were performed individually in a quiet room at Leiden University. Participants were seated at a table at a distance of 80 cm from a computer screen.

Cognitive inhibitory control: Response Organization Arrows

In the Response Organization Arrows task (ROA) from the Amsterdam Neuropsychological Tasks (ANT, De Sonneville, 1999), participants had to provide compatible responses in Part 1 of the task and incompatible responses in Part 2 of the task (For an illustration of this task, please see Rowbotham, Pit-ten Cate, Sonuga-Barke & Huijbregts, 2009). An arrow pointing either to the right or the left appeared centrally on the computer screen. In Part 1 (40 trials), a green arrow appeared. When the arrow pointed to the left, participants had to press the lefthand mouse button; when it pointed to the right, participants had to press the right-hand mouse button. In Part 2 (40 trials), the stimulus was a red arrow. When it pointed to the left, participants had to press the right, participants had to press the lefthand mouse button, and when it pointed to the right, participants had to press the lefthand mouse button. A response had to be generated between 200 and 6,000 ms. The fixed post-response interval was 1,200 ms. Error rates were recorded for compatible and incompatible responses.

Motivational inhibitory control: Risky Choice Task

A version of the Risky Choice Task (RCT) (Fairchild et al., 2009; Rogers et al., 2003) was used to measure motivational inhibitory control. Two wheels were presented on screen, each containing eight compartments (Figure 1). These compartments showed either possible gains or possible losses. The relative number of compartments showing gains provided the relative probability of gain for this particular wheel. On eight types of trials, one wheel served as a "control" wheel, providing a 50% chance of winning and a 50% chance of losing. The alternative, "experimental" wheel varied systematically in terms of the probability of a gain (.75 or .25), the magnitude of the possible gain (2 or 8 points), and the magnitude of the possible loss (2 or 8 points). Different combinations of these variables yielded eight trial types varying in the relative expected value (EV) of the experimental wheel (see Figure 1). There were also two trial types with an EV of 0 (the so-called framing trials): one presenting a wheel with 50% chance of winning 8 points, and a 50% chance of winning 0 points, and another wheel with a 100% chance of winning 4 points (positive framing, denoted as EV: 0+). The second presenting a wheel with a 50% chance of losing 8 points and a 50% chance of losing 0 points, and another wheel with a 100% chance of losing 4 points (negative framing; denoted as EV: 0-). All ten trial types were presented twice per block (there were 4 blocks) in a pseudorandom order, and participants played four blocks per session. The control and experimental wheels appeared randomly on the left or right of the display, and participants indicated their choice using a computer mouse. Participants were given ten points at the start of each block and were instructed to try to win as many points as possible. Auditory feedback on wins or losses was provided and the revised points total was presented for two seconds before the next trial (Fairchild et al, 2009).

Figure 1. Example of a trial of the Risky Choice Task. The left wheel represents an experimental wheel (expected value = 5.5 (.75*8 - .25*2)), with a high probability of winning. The right wheel represents a control wheel (expected value = 0 (0.5*1 - 0.5*1)).



Data analyses

First, it was investigated whether control variables should be included in the main statistical analyses as covariates, i.e. whether cannabis users differed from non-users with respect to gender, alcohol-, tobacco-, and other drug use, using Pearson Chi-square analyses, and whether the potential control variables were related to impulsivity as measured by the BIS-11 and performance on the two inhibition tasks. Next, group differences between cannabis users and non-users regarding impulsivity and inhibitory control were investigated. General Linear model (GLM) repeated measures analyses of variance were performed to examine inhibition of prepotent responding in the ROA-task, with group (cannabis users vs. non-users) as between-subjects factor, response type (compatible versus incompatible) as within-subjects factor and error rate as dependent variable. With respect to the RCT, it was first examined whether risky or safe choices increased over time, and whether this depended on the number of points gained. GLM repeated measures analysis was used to investigate points gained during the task, with group (cannabis users vs. non-users) as between-subjects factor and block (block 1 to 4) as within-subjects factor. Next, GLM multivariate analysis of variance was performed to investigate whether cannabis users and non users differed on proportions of

experimental gambles or risky choices (as opposed to control gambles) in general and for each trial type (i.e., for each expected value when the gambling choice was made). Multivariate analysis of variance was also performed to investigate whether cannabis users and non-users differed on the three scales of impulsive behaviour.

In case there were significant differences between controls and cannabis users, we further investigated whether these differences could be attributed to differences between controls and heavy users (defined here as cannabis use 11 times or more in the last month), controls and moderate users (defined here as 1-10 times in the last month) or both, and whether there were significant differences between moderate and heavy users. Because of unequal group sizes and unequal variance distributions for relevant dependent variables between the groups, we used non-parametric statistics, i.e. Kruskal-Wallis tests for analyses involving all three groups simultaneously, and Mann-Whitney tests for comparisons between two groups.

Finally, Pearson correlations were used to investigate possible relationships between impulsive behaviour, cognitive and motivational inhibition.

Results

Cannabis users and non-users differed with respect to gender distribution, tobacco use, and MDMA-use (see Table 1), indicating that, compared to controls, there were relatively more men among the cannabis users and cannabis users were more often daily smokers and monthly MDMA-users. There were no differences regarding alcohol use, and there were no reports of other drug use (e.g. cocaine, amphetamines). Of the factors associated with cannabis use, gender was related to all BIS-11 scales of impulsivity: cognitive impulsivity [t = 3.6, p = .001], motor impulsivity [t = 2.9, p = .005] and non-planning impulsivity [t = 2.8, p = .007]. Men scored higher on all impulsivity measures. Therefore, gender was introduced as a covariate in the group analyses comparing impulsivity in daily life between cannabis users and non-users. Also, smoking was related to experimental gambling when the EV was -1 [t = 2.2, p = .033), to performance in the first part of the ROA-task (t = -2.1, p = .040) and to one BIS-11 scale, i.e. the motor impulsivity scale [t = 3.7, p < .001]. Therefore, smoking was introduced as a covariate to the analyses measuring cognitive inhibitory control, motivational inhibitory control and impulsivity. MDMA-use was unrelated to task outcomes and impulsivity, and therefore omitted from further analyses.

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	Cannabis users	Non users	χ^2
Male	86.8 %	31.2 %	$\chi^2(1) = 32.5 * *$
Daily Smokers	65.3 %	6.1 %	$\chi^2(1) = 37.4**$
Weekly alcohol users	88.7 %	75.0 %	$\chi^2(1) = 3.2$
Monthly MDMA-users	22.6%	4.2%	$\chi^2(1) = 7.2^{**}$
* p <.05; ** p <.01			

Table 1. χ^2 -statistics of cannabis users and non users on control variables (gender, tobacco use and alcohol use).

Cognitive inhibitory control: Response Organization Arrows (ROA)

The repeated measures ANOVA comparing cannabis users and non-users showed no effect for group [F(1,99) = .1, p = .794] regarding error rate. There was no significant interaction between group and condition (task part) on error rate either (F(1,99) = .5, p = .493]. These results indicate that cannabis users and non-users did not differ with respect to cognitive inhibitory control.

Motivational decision-making: Risky Choice Task (RCT)

Performance data

Firstly, it was investigated whether there were effects for group and group x block (1-4) on points gained during the task. The repeated measures ANOVA comparing cannabis users and non-users showed no effect for group [F(1,97) = .3, p = .567]. There was no significant interaction between group and block regarding points gained during the task either [F(1,97) = 2.8, p = .096]. These results indicate that both groups gained/lost equal amounts of points throughout the task. They also indicate that, as the task progressed, groups did not start to differ in the amount of points won/lost.

Group comparisons on choice of experimental gamble by trial type.

Multivariate analysis of variance showed a significant main group effect of choice of experimental gambles [F(10, 90) = 3.5, p = .001, partial $\eta^2 = .28$]. Overall, cannabis users chose the experimental wheel more often than non-users. Univariate effects per trial type are presented in Table 2. As shown in Table 2, cannabis users chose the experimental wheel more often than non-users chose the experimental wheel more often the experimental wheel more often the experimental wheel more wheel was more risky (i.e. when EVs based on relative probabilities were ambiguous or negative).

After controlling for smoking, there was still a significant main group effect for experimental choice of gambling [F(10, 89) = 2.5, p = .011, partial $\eta^2 = .22$]. As shown in Table 2, all

universate effects that had been significant initially remained significant after controlling for smoking, with the exception of the effect when the EV was .5.

Table 2. Mean proportions of time the experimental gamble was chosen in preference to the control gamble for each risky choice task trial type by group (n=101). The difference in expected value between the experimental and control gambles for each trial type is shown.

Expected	Cannabis users	Non users	F- value	F-value after		
value	(Mean %, SD)	(Mean %, SD)		controlling for		
				smoking		
5.5	98.1 % (5.2)	98.2 % (7.7)	F(1, 99) = .0	F(1, 98) = .1		
4.0	93.8 %(12.6)	90.2 % (20.7)	F(1, 99) = 1.1	F(1, 98) = .2		
1.0	94.5 %(12.4)	95.3 % (12.9)	F(1, 99) = .1	F(1, 98) = .5		
0.5	56.9 % (29.3)	44.0 % (25.1)	F(1, 99) = 5.6*	F(1, 98) = 3.4*		
-0.5	62.6 % (30.8)	61.0 % (34.3)	F(1, 99) = .1	F(1, 98) = .1		
-1.0	18.1 % (19.8)	3.9 % (8.9)	F(1, 99) = 20.9 **	F(1, 98) = 15.7**		
-4.0	23.2% (26.5)	13.5 % (19.3)	F(1, 99) = 4.4 *	F(1, 98) = 4.5*		
-5.5	8.7 % (14.3)	1.0 % (4.6)	F(1, 99) = 12.8 **	F(1, 98) = 11.2**		
0 + frame	87.8 % (19.6)	80.0 % (27.2)	F(1, 99) = 2.8	F(1, 98) = .3		
0 - frame	46.2 % (32.7)	30.2 %(26.6)	F(1, 99) = 7.1 **	F(1, 98) = 5.0**		
$* n < 05 \cdot * * n < 01$						

p <.05; ****** p <.01

Impulsive behaviour: the Barratt Impulsiveness Scale

Multivariate analysis of variance showed a significant main group effect [F(3,96) = 10.0, p =.005, partial $\eta^2 = .24$], indicating more impulsive behaviour in daily life among cannabis users. Univariate effects were found for cognitive impulsivity [F(1,98) = 19.3, p < .001,partial $\eta^2 = .17$]; motor impulsivity [F(1,98) = 18.5, p <.001, partial $\eta^2 = .16$], and nonplanning impulsivity [F(1,98) = 14.4, p < .001, partial $\eta^2 = .13$], with cannabis users scoring higher on each of the three impulsivity types measured: cognitive impulsivity (M=17.1, SD=2.6 vs. M=14.7, SD=2.7), motor impulsivity (M=23.4, SD=3.7 vs. M=20.2, SD=3.9) and non-planning impulsivity (M=26.5, SD = 4.4 vs. M=23.2, SD=4.2).

After controlling for gender and smoking, the multivariate main group effect remained significant [F(3.94) = 4.6, p = .005, partial $\eta^2 = .13$], as well as univariate effects for cognitive impulsivity $[F(1,96) = 10.2, p = .002, \text{ partial } \eta^2 = .10]$ and non-planning impulsivity $[F(1,96) = 8.7, p = .004, \text{ partial } \eta^2 = .08]$. The group difference for motor impulsivity was no longer significant, although a non-significant trend was still present [F(1,96) = 3.8, p = .055, p = .055]partial $\eta^2 = .04$].

Influence of frequency of cannabis use.

Of the cannabis users, 21 had used cannabis up to 10 times in the past month (moderate use: 39.6%), and 32 had used it 11 times or more (heavy use). First of all, Kruskal-Wallis tests with controls, moderate and heavy users confirmed overall group differences (DV: mean percentage of choosing the experimental wheel: χ^2 (2) = 12.0, p = .002). Controls and moderate users differed when the EV was 0.5 (Mann-Whitney U = 309.5, z = -2.5, p = .011) or -1 (U = 306, z = -3.2, p = .001), and in both the positive and negative framing trials (when the EV was 0): U = 345.5, z = -2.3, p = .022, and U = 284.5, z = -2.9, p = .004, respectively. In all instances the cannabis users were more inclined than the non-users to choose the experimental wheel. Controls and heavy users differed when the EV was -5.5 (U = 458.0, z = -4.1, p < .001), -4 (U = 541.0, z = -2.3, p = .019), or -1 (U = 390.0, z = -4.4, p < .001), again in every instance indicating a greater tendency to 'gamble' among cannabis users. Comparisons between the two groups of users did not reveal a consistent pattern: heavy users were more inclined to pick the experimental wheel when the EV was -5.5 (U = 292.0, z = -2.0, p = .049), whereas moderate users were more inclined to gamble than heavy users when the EV was 0 (positive framing: U = 235.0, z = -2.1, p = .037).

With respect to impulsivity in daily life as measured by the BIS-11, Kruskal-Wallis analyses showed group differences for attentional impulsivity (χ^2 (2) = 15.6, p < .001), motor impulsivity (χ^2 (2) = 12.9, p = .002), and non-planning impulsivity (χ^2 (2) = 14.4, p < .001), with both groups of users reporting to be more impulsive than non-users. This was confirmed by significant differences between controls and moderate users on all three dimensions: Attentional: U = 284.0, z = -2.9, p = .004; Motor: U = 262.5, z = -3.2, p = .002; Non-planning: U = 277.0, z = -2.9, p = .004, and between controls and heavy users: Attentional: U = 410.5, z = -3.5, p < .001; Motor: U = 507.0, z = -2.6, p = .010; Non-planning: U = 421.0, z = -3.3, p = .001. There were no significant differences between moderate and heavy users.

Cognitive inhibition, motivational inhibition & impulsive behaviour.

Pearson correlations were used to investigate relationships between inhibition as measured by the two computer tasks and self-reported impulsive behaviour. Performance on the ROA-task was not significantly related to any of the three scales of impulsivity. In contrast, mean percentage of trials the experimental gamble which was chosen in preference to the control gamble in the RCT was associated with the impulsivity scales 'cognitive impulsivity' (r = .24, p=.014) and 'non-planning impulsivity' (r = .21, p=.038), with a trend for 'motor impulsivity' (r = .16, p = .050). All correlations indicated that the higher the percentage of trials the experimental gamble was chosen, the more impulsivity the participant showed in daily life. With respect to specific expected values, attentional impulsivity was significantly correlated with choice for the experimental wheel when the EV was -0.5 (r = .28, p = .003), -4 (r = .25, p = .005, or 0- (r = .22, p = .015), and non-planning impulsivity was significantly correlated with a choice for the experimental wheel when the EV was -1 (r = .20, p = .023), with further trends for five other EVs (0.5, -4, 1, 0+, and 0-).

Discussion

The results of the present study showed that recreational cannabis users differed from nonusers with respect to motivational inhibition. This was particularly evident when the chances of reward were small or relatively difficult to estimate. Contrasting results were observed for the inhibitory control task without reward (or motivational) component: there were no differences whatsoever between cannabis users and non-users. Furthermore, recreational cannabis users reported higher levels of impulsive behaviour in daily life, which, in turn, were related to motivational but not cognitive inhibitory control as measured by the laboratory tasks. It had been expected that both laboratory measures of inhibitory control would be related to impulsivity in daily life, as many questions of the BIS-11 do not appear to involve motivational or affective components. It may be speculated that, when self-reporting on impulsivity, informants generally activate the memory of social contexts where such behaviour had to be suppressed in order to reach a certain goal, i.e. when motivational processes were involved. This could explain the lack of associations between daily life impulsivity reports and cognitive inhibitory control measured in the absence of a socially meaningful context.

Frequency of use did not have a clear influence on the results: there were no differences between moderate and heavy cannabis users regarding daily life impulsivity, and only two

differences regarding measures of motivational inhibitory control, one showing greater gambling tendencies for the heavy users, when chances of a reward were quite small, and one showing greater gambling tendencies for the moderate users, when chances of a reward were difficult to estimate. Together with the type of differences observed between controls and moderate users and between controls and heavy users, respectively, this might indicate that heavy users are the bigger risk-takers, whereas the moderate users are the greater 'doubters', but a more consistent pattern of results would be required to substantiate such inferences.

The finding that cannabis users only experienced deficits in inhibitory control when a motivational component was present might be indicative of relatively strong reward sensitivity that cannot be countered by normal or even good cognitive control skills. For the interpretation of this result it may be relevant to consider group characteristics in more detail. Cannabis users in the present study were considered recreational users (although a number of them reported rather heavy use). Impairments in cognitive inhibitory control have quite clearly been established in addicted individuals, and have been suggested to underlie the transition into addiction (Everitt et al., 2008; Goldstein & Volkow, 2002; Stacy & Wiers, 2010; Wiers et al., 2007). Thus, what may distinguish recreational cannabis users from both non-users and addicted users is a unique involvement of poor motivational inhibition. Non-users could have good motivational inhibition, whereas addicted individuals could have both poor motivational inhibition and weak cognitive control (see also: Kalivas & Volkow, 2005).

Regarding specificity of results, this study does appear to provide evidence for some specific relations between cannabis use and motivational inhibitory control. Concurrent smoking weakened associations to some extent but they remained significant. Alcohol intake did not differ between cannabis users and non-users, whilst MDMA-use was not related to any of the dependent variables. Although the instruments used to measure substance use were similar to those used in other studies into correlates of cannabis use (e.g. Monshouwer et al., 2006), these could be further refined (e.g. establish in more detail the intake amounts), and it would have been preferable to have multiple informants. Moreover, it may be expected that more variation in substance use will be observed in a broader sample of the population. Another consideration here is that cannabis users did show different motivational inhibition compared to non-users, but that the rewards were unrelated to the substance of interest, which is in line with results from other studies (e.g. Kamarajan et al., 2010; Nestor et al., 2010). This appears to contrast with implicit cognition approaches, which generally assume spontaneously activated memory associations and courses of action involving a specific substance (Stacy and Wiers, 2010). Although there is not necessarily a contrast, as implicit cognition was not

examined here (and could therefore just as well produce even stronger evidence for motivational inhibition problems in this sample), this result may be indicative of non-specificity of associations between substance use and motivational inhibitory control (see also Fernández-Serrano et al., 2011).

As mentioned, the instruments used to assess drug use could be further refined. A similar argument could be made about the instruments that were used to assess cognitive outcomes. It should be noted, however, that the choice for these instruments was based on earlier studies investigating the cognitive constructs that are of interest here (Fairchild et al., 2009; Rogers et al., 2003; Rowbotham et al., 2009). The cognitive inhibition task used in the present study, which is a variant of the well-established Eriksen flanker-paradigm, is a standardized task with good reliability and validity scores (De Sonneville, 1999; Rowbotham et al., 2009). In order to measure inhibitory control in a motivational context, the most widely used task is the Iowa Gambling Task (IGT; Bechara et al., 1994), which indeed has shown differences between substance (ab-)using individuals and controls (Bolla, Eldreth, Matochik, & Cadet, 2005; Verdejo-Garcia et al., 2008; Whitlow et al., 2004). It has however been argued that IGT performance deficits particularly reflects decision-making impairments, which, in turn involves multiple neuropsychological processes, including working memory, reversal learning, and sensitivity to reward/punishment (Busemeyer & Stout, 2002; Dunn, Dalgleish, & Lawrence, 2006). Since we wanted to clearly contrast cognitive and motivational inhibition, we used a version of the Risky Choice Task (Rogers et al., 2003). In this task it is more difficult to use a strategy based on cognitive assertions, i.e. built-up knowledge of rewards and punishments (Fairchild et al., 2009). It should however be acknowledged that it might have been preferable to have multiple tasks or questionnaires for each construct we tested, or perhaps, regarding the outcome measures, to have had two laboratory tasks differing purely with respect the requirement of motivational inhibitory control (cf. Daniel & Pollmann, 2010; Vadhan et al., 2009).

Despite the obvious opportunities to expand this research, it may be concluded from the present study that motivational inhibitory control in recreational cannabis users differs from that of non-users, and that the relatively poor impulse control cannabis users show in their daily lives is associated with this specific type of inhibitory control deficit.

References

Barratt, E. S (1985). Impulsiveness subtraits: arousal and information processing. In J. T. Spence, & C. E. Itard, (Eds.), *Motivation, Emotion and Personality* (pp. 43-68). North Holland: Elsevier.

Bechara, A. (2003). Risky business: Emotion, decision-making, and addiction. *Journal of Gambling Studies*, *19*, 23-51.

Bechara, A., Damásio, A. R., Damásio, H., & Anderson, S. W. (1994). Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition*, *50*, 7–15.

Blum, K., Braverman, E.R., Holder, J.M., Lubar, J.F., Monastra, V.J., Miller, D., Lubar, J.O., Chen, T.J., & Comings, D.E. (2000). Reward deficiency syndrome: a biogenetic model for the diagnosis and treatment of impulsive, addictive, and compulsive behaviors. *Journal of Psychoactive Drugs*, *32*, *Suppl: i-iv*, 1-112.

Bolla, K.I., Eldreth, D.A., Matochik, J.A., & Cadet, J.L. (2005). Neural substrates of faulty decision-making in abstinent marijuana users. *Neuroimage, 26,* 480-492.

Busemeyer, J.R., & Stout, J.C. (2002). A contribution of cognitive decision models to clinical assessment: Decomposing performance on the Bechara gambling task. *Psychological Assessment*, *14*, 253-262.

Chambers, R.A., Taylor, J.R., & Potenza, 2003. Developmental neurocircuitry of motivation in adolescence: A critical period of addiction vulnerability. *American journal of psychiatry*, *160*, 1041-1052.

Chanraud, S., Martelli, C., Delain, F., Kostogianni, N., Douaud, G., Aubin, H.J., Reynaud, M., & Martinot, J.J. (2007). Brain morphometry and cognitive performance in detoxified alcohol-dependents with preserved psychosocial functioning. *Neuropsychopharmacology, 32*, 429-438.

Cherek, D.R., Lane, S.D., & Dougherty, D.M. (2002). Possible amotivational effects following marijuana smoking under laboratory conditions. *Experimental and Clinical Psychopharmacology*, *10*, 26-38.

Churchwell, J.W., Lopez-Larson, M., & Yurgelun-Todd, D.A. (2010). Altered frontal cortical volume and decision making in adolescent cannabis users. *Frontiers in Psychology*, *1*, 225.

Clark, L., Rosier, J.P., Robbins, T.W., & Sahakian, B.J. (2009). Disrupted 'reflection' impulsivity in cannabis users but not current or former ecstacy users. *Journal of Psychopharmacology*, 23, 14-22.

Cowan, R.L., Lyoo, I.K., Sung, S.M., Ahn, K.H., kim, M.J., Hwang, J., Haga, E., Vimal, R.L., Lukas, S.E., & Renshaw, P.F. (2003). Reduced cortical gray matter density in human MDMA (ecstacy) users: A voxel-based morphometry study. *Drug and Alcohol Dependence*, *72*, 225-235.

Dalley, J.W., Fryer, T.D., Brichard, L., Robinson, E.S., Theobald, D.E., Laane, K., Pena, Y., Murphy, E.R., Shah, Y., Probst, K., Abakumova, I., Aigbirhio, F.I., Richards, H.K., Hong, Y., Baron, J.C., Everitt, B.J., & Robbins, T.W. (2007). Nucleus accumbens D2/3 receptors predict trait impulsivity and cocaine reinforcement. *Science*, *315*, 1267-1270.

Daniel, R., & Pollmann, S. (2010). Comparing the neural basis of monetary reward and cognitive feedback during information-integration category learning. *Journal of Neuroscience*, *30*, 47-55.

De Sonneville, L.M.J. (1999). Amsterdam Neuropsychological Tasks: a computer-aided assessment program. In Den Brinker, B.P.L.M., Beek, P.J., Brand, A.N., Maarse, S.J., & Mulder, L.J.M. (Eds.), *Computers in Psychology; Cognitive Ergonomics, Clinical Assessment and Computer-assisted Learning* (pp. 187-203). Swets and Zeitlinger, Lisse.

Dunn, B.D., Dalgleish, T., & Lawrence, A.D. (2006). The somatic marker hypothesis: A critical evaluation. *Neuroscience and Biobehavioral Reviews*, *30*, 239-271.

Everitt, B.J., Belin, D., Economidou, D., Pelloux, Y., Dalley, J.W., & Robbins, T.W. (2008). Neural mechanisms underlying the vulnerability to develop compulsive drug-seeking habits and addiction. *Philosophical transactions of the Royal Society of London, 363*, 3125-3135.

Fairchild, G., Van Goozen, S.H.M., Stollery, S.J., Aitken, M.R.F., Savage, J., Moore, S.C., & Goodyer, I.M. (2009). Decision making and executive function in male adolescents with early-onset or adolescence-onset conduct disorder and control subjects. *Biological Psychiatry*, *66*, 162-168.

Fergusson, D. M., Horwood, L. J., & Ridder, E. M., (2007). Conduct and attentional problems in childhood and adolescence and later substance use, abuse and dependence: Results of a 25-year longitudinal study. *Drug and Alcohol Dependence*, *88*, 14-26.

Fernández-Serrano, M.J., Pérez-García, M., Verdejo-García, A. (2011). What are the specific vs. generalized effects of drugs of abuse on neuropsychological performance? *Neuroscience and Biobehavioral Reviews*, *35*, 377-406.

Friedman, N., & Miyake, A. (2004). The relations among inhibition and interference control functions: A latent-variable analysis. *J. Exp. Psychol. Gen., 133,* 101-135.

Goldstein, R.Z, & Volkow, N.D. (2002). Drug Addiction and its Underlying Neurobiological Basis: Neuroimaging Evidence for the Involvement of the Frontal Cortex. *American Journal of Psychiatry*, *159*, 1642-1652.

Grant, I., Gonzalez, R., Carey, C.L., Natarajan, L., & Wolfson, T. (2003). Non-acute (residual) neurocognitive effects of cannabis use: A meta-analytic study. *Journal of the International Neuropsychological Society*, *9*, 679-689.

Griffith-Lendering, M.F.H., Huijbregts, S.C.J., Mooijaart, A., Vollebergh, W.A.M., & Swaab,H. (2011). Cannabis use and development of externalizing and internalizing behaviorproblems in early adolescence: A TRAILS-study. *Drug and Alcohol Dependence, in press*

Gruber, S.A., Silveri, M.M., Dahlgren, M.K., & Yurgelun-Todd, D. (2011). Why so impulsive? White matter alterations are associated with impulsivity in chronic marijuana smokers. *Experimental and Clinical Psychopharmacology*, *19*, 231-242.

Gruber, S.A., Yurgelun-Todd, D.A. (2005). Neuroimaging of marijuana smokers during inhibitory processing: a pilot investigation. *Brain Research. Cognitive Brain Research, 23*, 107–118.

Huijbregts, S.C.J., Warren, A.J., De Sonneville, L.M.J., & Swaab-Barneveld, H. (2008). Hot and cool forms of inhibitory control and externalizing behavior in children of mothers who smoked during pregnancy: An exploratory study. *Journal of Abnormal Child Psychology, 36*, 323-333.

Kalivas, P.W., & Volkow, N.D. (2005). The neural basis of addiction: A pathology of motivation and choice. *American Journal of Psychiatry*, *162*, 1403-1413.

Kamarajan, C., Rangaswamy, M., Tang, Y., Chorlian, D.B., Pandey, A.K., Roopesh, B.N., Manz, N., Saunders, R., Stimus, A.T., & Porjesz, B. (2010). Dysfunctional reward processing in male alcoholics: An ERP study during a gambling task. *Journal of Psychiatric Research*, *44*, 576-590.

Krain, A.L., Wilson, A.M., Arbuckle, R., Castellanos, F.X., & Milham, M.P. (2006). Distinct neural mechanisms of risk and ambiguity: A meta-analysis of decision-making. *NeuroImage*, *32*, 477-484.

Kreek, M.J., Nielsen, D.A., Butelman, E.R., & LaForge, K.S. (2005). Genetic influences on impulsivity, risk taking, stress responsivity and vulnerability to drug abuse and addiction. *Nature Neuroscience*, *8*, 1450-1457.

Lamers, C.T.J., Bechara, A., Rizzo, M., & Ramaekers, J.G. (2006). Cognitive function and mood in MDMA/THC users, THC users and non-drug using controls. *Journal of Psychopharmacology, 20,* 302-311.

Lane, S.D., Cherek, D.R., Tcheremissine, O.V., Steinberg, J.L., & Sharon, J.L. (2007). Response perseveration and adaptation in heavy marijuana-smoking adolescents. *Addictive Behaviors*, *32*, 977-90.

Lane, S.D., Cherek, D.R., Peitras, C.J., & Steinberg, J.L. (2005). Performance of heavy marijuana-smoking adolescents on a laboratory measure of motivation. *Addictive Behaviors, 30*, 815-828.

Malmberg, M., Overbeek, G., Monshouwer, K., Lammers, J., Vollebergh, W.A., & Engels, R.C. (2010). Substance use risk profiles and associations with early substance use in adolescence. *Journal of Behavioral Medicine*, *33*, 474-485.

Miller, E., Joseph, S., & Tudway, J. (2004). Assessing the component structure of four self-report measures of impulsivity. *Personality and Individual Differences*, *37*, 349–358.

Monshouwer, K., Van Dorsselaer, S., Verdurmen, J., Ter Bogt, T., De Graaf, R., & Vollebergh, W. (2006). Cannabis use and mental health in secondary school children. Findings from a Dutch survey. *British Journal of Psychiatry*, *188*, 148-153.

Nelson, R.J., & Trainor, B.C. (2007). Neural mechanisms of aggression. *Nature Reviews Neuroscience*, *8*, 536-546.

Nestor, L., Hester, R., & Garavan, H. (2010). Increased ventral striatal BOLD activity during non-drug reward anticipation in cannabis users. *Neuroimage, 49,* 1133-1143.

Piechatzek, M., Indlekofer, F., Daamen, M., Glasmacher, C., Lieb, R., Pfister, H., Tucha, O., Lange, K.W., Wittchen, H-U., & Schütz, C.G. (2009). Is moderate substance use associated with altered executive functioning in a population-based sample of young adults? *Human*. *Psychocopharmacology*, *24*, 650-665.

Pierce, R.C., & Kumaresan, V. (2006). The mesolimbic dopaminergic system: The final common pathway for the reinforcing effect of drugs of abuse? *Neuroscience and Biobehavioral Reviews*, *30*, 215-238.

Pope, H.G., Gruber, A.J., Hudson, J.L., Huestis, M.A., & Yurgelun-Todd, D. (2001). Neuropsychological performance in long-term cannabis users. *Archives of General Psychiatry*, *58*, 909-915.

Robinson, T.E., & Kolb, B. (2004). Structural plasticity associated with exposure to drugs of abuse. *Neuropharmacology*, *42 (Suppl. 1)*, 33-46.

Rogers, R.D., Turnbridge, E.M., Bhagwagar, Z., Drevets, W.C., Sahakian, B.J., & Carter, C.S. (2003). Tryptophan depletion alters the decision-making of healthy volunteers through altered processing of reward cues. *Neuropsychopharmacology*, *28*, 153-162.

Rowbotham, I., Pit-ten Cate, I.M., Sonuga-Barke, E.J.S., & Huijbregts, S.C.J. (2009). Cognitive control in adolescents with neurofibromatosis type 1. *Neuropsychology*, *23*, 50–60.

Solowij, N., Stephens, R.S., Roffman, R.A. et al (2002). Cognitive functioning of long-term heavy cannabis users seeking treatment. *Journal of the American Medical Association, 287,* 1123-1131.

Sonuga-Barke, E.J. (2002). Psychological heterogeneity in AD/HD: A dual pathway model of and cognition. *Behavioural Brain Research*, *130*, 29-36.

Stacy, A.W., & Wiers, R.W. (2010). Implicit cognition and addiction: A tool for explaining paradoxical behavior. *Annual Review of Clinical Psychology*, *6*, 551-575.

Stanford M.S., Mathias C.W., Dougherty D.M., Lake S.L., Anderson N.E., & Patton, J.H. (2009). Fifty years of the Barratt Impulsiveness Scale: An update and review. *Personality and Individual Differences*, *47*, 385–395.

Tapert, S.F. Schweinsburg, A.D., Drummond, S.P., Paulus, M.P., Brown, S.A., Yang, T.T. & Frank, L.R. (2007). Functional MRI of inhibitory processing in abstinent adolescent marijuana users. *Psychopharmacology*, *194*, 173-83.

Vadhan, N.P., Hart, C.L., Haney, M., Van Gorp, W.G., & Foltin, R.W. (2009). Decisionmaking in long-term cocaine users: Efects of a cash monetary contingency on gambling task performance. *Drug and Alcohol Dependence*, *102*, 95-101.

Verdejo-Garcia, A., Benbrook, A., Funderburk, F., David, P., Cadet, J.L., & Bolla, K.I. (2007). The differential relationship between cocaine use and marijuana use on decision-making performance over repeat testing with the Iowa Gambling Task. *Drug and Alcohol Dependence*, *90*, 2-11.

Verdejo-Garcia, A., Lawrence, A.J., & Clark, L. (2008). Impulsivity as a vulnerability marker for substance-use disorders: review of findings from high-risk research, problem gamblers and genetic association studies. *Neuroscience and Biobehavioral Reviews, 32*, 777-810.

Whitlow, C.T., Liguori, A., Livengood, L.B., Hart, S.L., Mussat-Whitlow, B.J., Lamborn, C.M., Laurienti, P.J., & Porrino, L.J. (2004). Long-term heavy marijuana users make costly decisions on a gambling task. *Drug and Alcohol Dependence*, *76*, 107-111.

Wiers, R.W., Bartholow, B.D., Van den Wildenberg, E., Thush, C., Engels, R.C.M.E., Sher, K.J., Grenard, J., Ames, S.L., & Stacy, A.W. (2007). Automatic and controlled processes and the development of addictive behaviors in adolescents: A review and a model. *Pharmacology, Biochemistry and Behavior, 86*, 263-283.

Zelazo, P.D., & Müller, U. (2002). Executive function in typical and atypical development. In U. Goswami (Ed.), *Handbook of Childhood Cognitive Development* (pp. 445-469). Oxford, Blackwell.