The who and how of attentional bias in cannabis users: associations with use severity, craving, and interference control

Emese Kroon^{1,2}, Lauren Kuhns^{1,2}, Annette Dunkerbeck³ & Janna Cousijn^{1,2,4}

¹ Neuroscience of Addiction (NofA) Lab, Department of Psychology, University of Amsterdam, The Netherlands

² ADAPT-laboratory, Department of Psychology, University of Amsterdam, the Netherlands

³ Dimence, SCOS, Deventer

⁴ Department of Psychology, Education & Child Studies, Erasmus University Rotterdam, The Netherlands

Correspondence: Emese Kroon, e.kroon@uva.nl, P.O. box 15916, 1001 NK Amsterdam, The Netherlands

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Abstract

Background and Aim. Cognitive and motivational processes are thought to underlie cannabis use disorder (CUD), but research assessing how cognitive processes (e.g. interference control (IC)) interact with implicit motivational processes (e.g. attentional bias (AB)) and explicit motivation (i.e. craving) is lacking. We assessed the presence of AB in cannabis users with varying use severity and tested models of moderation, mediation, and moderated mediation to assess how AB, craving, and IC interact in their association with measures of cannabis use. **Design.** Cross-sectional. **Setting and Participants.** Eight studies performed in the Netherlands including never-sporadic, occasional ($\leq 1/\text{month}$), and regular cannabis users ($\geq 2/\text{week}$), and individuals in treatment for CUD were combined ($N = 560$; 71% male). **Measurements.** All studies included a Classic Stroop task to assess IC, a Cannabis Stroop task to assess AB, and a pre- and post-session measure of craving. Both heaviness of cannabis use (grams per week) and severity of use related problems (CUDIT-R scores) were included. **Findings.** Only those in treatment for CUD showed an AB and group differences in AB were only observed when comparing those in treatment with never to sporadic users. Looking at occasional-regular users, IC was negatively associated with heaviness, but not severity of use. There was no direct association between AB and measures of cannabis use. However, average craving during the session, but not session induced craving, mediated this association between AB and heaviness as well as severity of use; higher AB was associated to heavier use and more severe problems through increased craving. **Conclusions.** AB was only present in cannabis users with the most severe problems and craving mediated the association between AB and both heaviness and severity of use in occasional to regular users. Furthermore, the association of IC with heaviness but not severity of use may point to sub-acute effects.

Key words: attentional bias, craving, interference control, cannabis use, cognition, motivation

INTRODUCTION

Excessive cannabis use and cannabis use disorder (CUD) are considered major health problems. Trends in cannabis legalisation, increasing potency and decreasing harm perceptions (1) highlight the urgency of research into the mechanisms underlying CUD. Traditional theories of addiction propose central roles for both cognitive and motivational processes (2), but research assessing both cognitive and motivational processes and their interactions in cannabis users is lacking.

Increased salience of substance-related cues in substance users is thought to bias behaviour towards substance use, which can present itself as a cue-induced attentional bias (AB) and craving (3). These drug-oriented motivational processes may more easily result in actual substance use in individuals with relatively limited cognitive control (4,5). The classical Stroop task has been used to measure cognitive control (6), in which slower responses on incongruent trials, controlled for congruent trials, are an indication of lower IC. Modified drug Stroop tasks have been developed (e.g. 7) and the extent to which substance-related (e.g. weed or blunt) relative to matched neutral words (e.g. floor or table) slow down color naming is taken as an index of AB, which is expected to relate to substance use history (8).

Several studies investigated the role of IC, AB and craving in cannabis use and CUD. One study using the classical Stroop to measure IC found poorer IC and altered brain activity in weekly to daily users relative to non-sporadic using controls when responding to incongruent trials (9). However, others, found no performance differences when comparing near-daily users and controls (e.g. 10) or only found differences in task-related brain activity in at-risk and treatment samples (e.g. 11–13). Similarly, AB has been identified in cannabis users ranging from lifetime users to those in treatment for CUD (14–16), while others do not observe AB using a Cannabis Stroop even in near daily users and those in treatment for CUD (17–19). Craving, however, has consistently been associated with heavier use (20; review) and has been shown to be predictive of cannabis use and related problems six months later (14). Also, craving has been association with both AB (21; meta-analysis) and IC (e.g. 16) in studies using the Cannabis and Classical Stroop.

These mixed findings could in part be explained by the differential role that AB, craving and IC play across trajectories of cannabis use towards CUD. IC may be lower and AB and craving may be higher in heavier and dependent users (19,20,22–25). Unfortunately, most studies look at these constructs separately and have a limited range of cannabis use severity included in the sample. It remains unclear which cannabis users have an AB and how this relates to craving and IC (e.g. 14). Furthermore, a meta-analysis by Field et al. (2009) found a small but significant association between AB and craving in substance users, indicating that previous studies lack power to detect such small effects (21). To overcome these problems and systematically assess the potential interactions between cognitive and motivational processes in a large sample of cannabis users with variable use frequency, this study combines eight studies conducted in our lab that included a pencil and paper version of the Classical Stroop and the Cannabis Stroop, and assessments of craving.

First, focussing on AB, we will assess whether groups of never-sporadic users, occasional users, regular users and those in treatment for CUD show an AB towards cannabis cues and whether AB differs between these groups. We expect an AB in regular users and those in treatment for CUD only, that differs from the never- and sporadic users (20; review). In occasional to regular users, excluding the CUD group to avoid effects of recent cessation on the outcomes, we will assess whether AB, craving, IC, heaviness of current use, and severity of cannabis use-related problems are indeed associated with each other in this broad range of users.

Second, we will assess *how* the cannabis AB, craving and IC interact in their association with heaviness and severity of cannabis use. We will test different theory informed models; we will assess whether AB, craving and/or IC are predictive of heaviness of cannabis use and/or severity of cannabis use-related problems (Figure 1A; e.g. 26). Then we will assess the proposed moderating role of cognitive processes in overcoming motivational urges (Figure 1B & Figure 1C; ,4,5). AB could increase craving or vice versa, subsequently leading to increased cannabis use or use-related problems (e.g. 3,27). Therefore, we will also separately assess whether AB or craving act as mediators in the association between the other variable with heaviness of use and severity of cannabis-use-related

problems (Figure 1D & Figure 1E). Then, to combine these moderation and mediation models, we will assess whether IC moderates the association of craving and/or AB with heaviness/severity cannabis use in the proposed mediation models (Figure 1F & figure 1G).

METHODS

We combined data from eight studies (19,28,29,30, four studies unpublished) that included similar measures of AB, IC and craving. In all studies, procedures were approved by the ethics committee of the corresponding department and all participants were fully informed and provided informed consent before the start of the experiment.

Participants

Individuals with known color-blindness ($N = 2$) and those that tested positive on drugs other than cannabis during the test session ($N = 7$) were excluded from the analyses, resulting in a total sample of 560 participants (71% male).

Materials

Assessments

Participants reported age, gender, weekly cannabis use in grams (heaviness of use) and completed the cannabis use disorder identification test-revised (CUDIT-R; 31) to assess severity of cannabis use-related problems. Smoking (yes/no), the Fagerström test for Nicotine dependence (FTND; 32) and the alcohol use disorder identification test (AUDIT; 33) were included to assess the severity of drug use other than cannabis.

Craving

Craving was assessed at the start and end of the session using a visual analogue scale or the marijuana craving questionnaire (MCQ; Figure S1; ,34). Session induced craving (start - end score) and average craving were calculated, after which scores were standardized.

Classical Stroop: interference control

The Classical Stroop task included three different cards that were presented in a fixed order (6,35). All cards included ten rows of ten words/blocks which participants were instructed to read over

row-by-row, as fast as possible, according to the card instructions. First, participants were instructed to read the words red, green, blue, and yellow as printed in black (word card). Second, participants were instructed to name the color of the color blocks (color card). Last, participants were instructed to name the incongruent color in which the words red, green, blue, and yellow were printed (color-word card). Reaction times were recorded and IC scores were calculated using this formula: $\text{reaction time color-word card} / ((\text{reaction time word card} + \text{reaction time color card}) / 2)$ (36). Higher scores indicated lower IC.

Cannabis Stroop: attentional bias

The Cannabis Stroop task included two different cards presented in counterbalanced order (29). Each card included eight rows of seven words that were all printed in red, green, blue or yellow. The words on both cards were matched on word length and number of syllables, but on one card the words were neutral (e.g. poster), while the words on the other card were cannabis-related (e.g. stoned). Participants were instructed to name the color in which each word was printed, row by row, from left to right, as fast as they could. A stopwatch was used to record the time needed to complete each card. AB scores were calculated using the following formula: $\text{reaction time cannabis card} - \text{reaction time neutral card}$, with higher scores being indicative of a relatively higher bias for cannabis words.

Procedures

While exact procedures and the order of included measures varied between studies (Figure S1), the Cannabis Stroop was always completed before the Classical Stroop. Also, cannabis-related questionnaires, aside from the pre-session craving, were always completed after the Stroop tasks.

Data Analysis

Grouping & exclusion

Participants were classified as never-sporadic user (no lifetime or no use in the last year), occasional users (maximum of once per month during the last year), regular users (minimum of twice per week during the last year) or CUD (in treatment at the moment of testing; Table 1) using the first

question of the CUDIT-R (31) (note: in study 8, grouping was based on self-reported last year use) and treatment status. Individuals that did not fit any of these groups (N = 8) were excluded (Table S1). IC, AB, craving, grams/week of use and CUDIT-R scores that were more than 3 standard deviations from the mean were excluded to reduce potential effects of outliers.

Attentional bias

One-sample t-tests were run to assess whether there was an AB to cannabis words (whether the AB was different from zero) per group. Then, an ANOVA was performed to assess group differences in AB, with post-hoc independent sample t-tests to explore the differences. Then, in all occasional to regular users, correlation analyses were conducted to assess how heaviness of cannabis use (grams/week), severity of cannabis use-related problems (CUDIT-R score), AB, IC, and session induced (SI) craving were associated with each. Analyses were run in JASP (version 0.14.1.0; ,37).

Attentional bias, interference control and craving: their association with cannabis use

Only current occasional to regular users were included in the following analyses (Table 1; excluding CUD group due to potential effects of recent cessation). Simple and multiple regression analyses were conducted to assess whether AB, IC, and/or SI craving were predictive of heaviness of cannabis use and severity of cannabis use-related problems (Figure 1A). Moderation analyses were conducted to assess whether IC moderates the association between SI craving (Figure 1B) or AB (Figure 1C) and heaviness of cannabis use and severity of cannabis use-related problems. Then, to assess the proposed relation between AB and SI craving in their association with cannabis use outcomes, we ran a mediation analysis to see whether AB mediates the association between SI craving and heaviness of cannabis use or severity of cannabis use related problems (Figure 1D) or the reverse (Figure 1E, Figure S3A). Combining this, moderated-mediation analyses were run to assess whether IC moderates the association between SI craving and AB with heaviness of cannabis use or cannabis use related problems in the proposed mediation models (Figure 1F & Figure 1G, Figure S3B). All included variables were mean centered. Analyses were run in R (version 4.1.2; 38) creating the models (Figure B-G) using the processR (version 0.2.6; 39) package and running them in lavaan (version 0.6-9; 40)

using maximum likelihood estimation. Exclusion criteria, grouping variables and analyses were pre-registered (https://aspredicted.org/7JT_TN7). Exploratory analyses were reported as such and multiple comparison corrections were applied in analyses that were not pre-registered.

RESULTS

Sample characteristics

Groups significantly differed on all variables (see Table 1). Exploratory independent sample t-tests showed varying patterns of differences for all variables with a general tendency of more severe alcohol, cigarette use, and more limited IC in more severe cannabis users and no differences between never-sporadic users and occasional users. Notably, session induced craving was only positive in regular users.

Group differences in attentional bias & correlations between variables

Only the CUD group showed an AB ($t(92) = 2.39, p = .019, d = .25$). The never-sporadic ($t(96) = 1.31, p = .192, d = .13$), occasional ($t(34) = 0.38, p = .704, d = .07$), and regular users ($t(319) = 1.72, p = .087, d = .10$) did not show this AB. AB differed between groups ($F(3,541) = 3.1, p = .026, \eta^2 = .017$; Table 1), with post-hoc analyses revealing a higher bias in CUD (and regular users at $p = .050$) versus never-sporadic users (Figure 2). Exploratory sensitivity analyses adding variables that differed between groups (Table 1) showed that the effect was independent of age and IC but no longer significant after correction for AUDIT and FTND.

Focussing on occasional and regular users, correlational analysis revealed a positive association between heaviness of cannabis use (Gram/week) and severity of cannabis use (CUDIT-R scores; $r_s(347) = .49, p < .001$). CUDIT-R score was not associated with any of the other variables (highest $r_s = .10$, with $p = .06$), but gram/week was positively associated with Classical Stroop scores ($r_s(343) = .20, p < .001$), indicating worse IC in more severe users. No other correlations between IC, craving and AB were observed (highest $r_s = .08$, with $p = .16$).

Attentional bias, interference control and craving: their association with cannabis use

In line with the correlational results, simple regression analyses (Figure 1A) showed an association between poorer IC and gram/week ($R^2 = .037$, $F(1, 343) = 14.23$, $\beta = .015$, $\beta_{SE} = .004$, $t = 3.772$, $p < .001$), but not CUDIT-R score ($R^2 = -.003$, $F(1, 350) = .023$, $\beta = .004$, $\beta_{SE} = .027$, $t = .150$, $p = .881$). AB and craving did not directly predict gram/week or CUDIT-R score (Table S2; Figure S2).

Moderation (Figure 1B & Figure 1C; Table S3), mediation (Figure 1D & Figure 1E; Table S4) and moderated-mediation (Figure 1F & Figure 1G; Table S5) models revealed no other associations than the consistently present direct association between IC and gram/week (Figure S2).

Exploratory analyses: the role of average session craving

As session induced changes in craving do not necessarily reflect absolute feelings of craving, but rather to what extent the session affected craving in the individual, we re-ran the correlations, simple regressions, moderation, mediation, and moderated-mediation models with average session (AS) craving instead of session induced craving.

Correlational and simple regression analyses showed that AS craving was positively associated with gram/week ($r_s(330) = .30$, $p < .001$; $R^2 = .057$, $F(1, 330) = 20.93$, $\beta = .977$, $\beta_{SE} = .214$, $t = 4.575$, $p < .001$) and CUDIT-R ($r_s(338) = .26$, $p < .001$; $R^2 = .074$, $F(1, 338) = 28.19$, $\beta = 1.75$, $\beta_{SE} = .331$, $t = 5.309$, $p < .001$) of use. Furthermore, higher AS craving during the session was associated with higher AB ($r_s(336) = .15$, $p = .006$) and lower IC (i.e. higher Stroop score; $r_s(333) = .18$, $p = .001$).

Moderation analyses revealed similar associations, also including the association between IC and heaviness of use (Table S7). However, mediation analyses revealed that AS craving mediated the association between AB and both gram/week (indirect effect: $\beta = .050$, $\beta_{SE} = .020$, $z = 2.556$, $p = .011$) and CUDIT-R score (indirect effect: $\beta = .083$, $\beta_{SE} = .032$, $z = 2.602$, $p = .009$; Table S7). These mediations were stable across the moderated-mediation models (CUDIT-R – indirect effect: $\beta = .089$, $\beta_{SE} = .033$, $z = 2.655$, $p = .008$; gram/week – indirect effect: $\beta = .049$, $\beta_{SE} = .019$, $z = 2.552$, $p = .011$), but IC did not act as a moderator but rather was directly associated with gram/week only (Table S7; Figure 4).

DISCUSSION

We assessed the presence of AB in cannabis users with different levels of use and how AB interacted with craving and IC in its relationship with heaviness and severity of cannabis use. A clear strength of this study is the inclusion of a large sample with a large range of cannabis use severity ($N = 560$). Only those users in treatment for CUD showed an AB (significantly > 0), which was significantly higher compared to never-sporadic users, but not compared to occasional and regular users. Poorer IC was consistently associated with heavier cannabis use, but not the severity of use related problems. However, in contrast to our hypotheses, IC did not moderate the association between AB and craving in their association with measures of cannabis use. Moreover, session induced craving did not mediate the association between AB (nor vice versa) and measures of cannabis use, yet results changed when using average craving instead; craving mediated the association between AB and heaviness as well as severity of use.

Our results suggest that AB may be a clinical marker of CUD severity, while IC may generally be poorer in heavier users regardless of CUD problem severity. However, the associations between AB, craving IC and cannabis use are complex. Looking at Figure 1, AB appears higher in more frequent users, but AB did not directly relate to our measures of cannabis use (also not when exploratively including the CUD group in the regression analysis). It only did through its positive association with craving; those with higher AB might have higher, potentially more ‘trait-like’ levels of craving, triggering a higher general likelihood to use. Most studies indicate that the relationship between craving and AB is likely reciprocal (3), however, our results in which AB affects use *through* craving are in line with earlier research in alcohol users in which training to increase AB resulted in increased craving and subsequent use (41). The indirect effects of AB via craving could also explain why some studies did not find direct associations between AB and measures of use (e.g. 25, alcohol Stroop; 42, cocaine Stroop). However, our findings are cross-sectional and were only significant for average craving, not session induced craving. Studies investigating the temporal dynamics between AB and craving are needed to further investigate this.

The specific presence of AB in the treatment (most severe) group, could explain some of the null findings of previous studies (e.g. 43) and could indicate its potential value as a clinical marker. However, research evaluating the relevance of assessing AB for other substance use disorders in clinical settings are inconsistent (e.g. 27,44) - while some studies show AB to be associated with worse treatment outcomes or increased relapse rate (45, heroin; 46, cocaine; 47, alcohol) this is not (45, cocaine; 48, tobacco) the case in all studies - and studies on the value of AB as a marker of CUD severity and treatment outcomes are largely lacking. Hence, further research is required to systematically assess the clinical relevance of AB to cannabis cues in clinical and non-clinical samples of cannabis users.

It must be noted that the group differences disappeared when controlling for AUDIT and FTND. Poly substance use is very common (49) and the higher use of alcohol and tobacco might arise from the same underlying factors as their heavy cannabis use. Including AUDIT and FTND as covariates is suboptimal for it likely deletes cannabis use-relevant variance. Furthermore, it seems theoretically unlikely that alcohol and tobacco use directly affect AB for cannabis words, but further research with samples (more closely) matched on these variables are needed to confirm this.

Partially in line with our expectations, we consistently found lower IC to be associated with heavier cannabis use (small-medium effect; $r_s = .20$). While it is often argued that this could indicate of a lack of control over use (4,5), the lack of association with severity of cannabis use related problems and the lack of interactions with AB and craving may indicate that this association is a result of current heaviness of use and the associated sub-acute effects. Some earlier studies also failed to find a moderating role if IC (e.g. 19,24). Cannabis intoxication has been found to negatively affect Stroop performance (e.g. 50) and there is evidence that several cognitive functions recover with increased abstinence (e.g. 51). In line with this, an exploratory check in the CUD group, of which the majority have been abstinent for multiple days (53% at least 7 days of abstinence), showed that there is no association between IC and heaviness of use in the CUD group (Table S9). Further research is needed to assess (sub)acute effects and the potential for recovery.

Several limitations of this study should be noted. While combining different studies increases the sample size and allows for more complex models to be tested, it also introduces differences in methodology between studies. This could have affected the results of session induced craving as sessions in all studies had different length and content aside from the measures we included. However, the difference in the results when including two different measures of craving (session induced vs. average craving during the session) highlight the importance of the exact measures included and the potential incomparability of those measures. Furthermore, it must be investigated whether our results generalize to other measures of cognitive functioning and AB and whether these effects generalize to more ecologically valid situations in which AB could affect craving and cannabis use.

Our results show that AB as measured by the Cannabis Stroop was only present in those cannabis users with the most severe problems but that, even in less severe cannabis users, the size of the AB was associated with higher craving and in turn higher cannabis use and related problems. While systematic research into the clinical relevance of these associations is crucial, these results highlight the potential importance of AB in both heaviness and severity of cannabis use as well as the mechanisms by which AB through increased craving could affect efforts to reduce or stop using cannabis.

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Figure 1. Visual representation of hypotheses.

Table 1. Sample characteristics							
Variables	Groups						Occasional & Regular (N=358)
	Never- Sporadic (N = 97)	Occasional (N = 35)	Regular (N = 323)	CUD (N = 97)	Group Difference	Pairwise Difference [#]	
Gender, % <i>male</i>	57.7	45.7	75.9	77.7	$\chi^2(3, N = 549) = 24.9, p < .001$	2, 3, 4, 5	72.9
Age, <i>M(SD)</i>	22.7(3.2)	21.9(2.7)	23.3(6.0)	20.6(3.0)	$F(3,539) = 7.2, p < .001, \eta^2 = .04$	3, 6	23.2(5.8)
CUDIT-R, <i>M(SD)</i>	-	2.0(1.5)	15.4(5.2)	21.6(6.6)	$F(2,441) = 169.0, p < .001, \eta^2 = .43$	4, 5, 6	14.1(6.4)
Gram/Week, <i>M(SD)</i>	-	.3(1.2)	4.7(4.0)	9.2(7.9)	$F(2,415) = 46.0, p < .001, \eta^2 = .18$	4, 5, 6	4.2(4.0)
Age of onset, <i>M(SD)</i>	-	16.9(2.3)	15.7(2.3)	15.6(2.2)	$F(2,429) = 3.7, p < .001, \eta^2 = .02$	4, 5	15.8(2.4)
Smoking, % smokers	19.6	40.0	64.1	85.3	$\chi^2(3, N = 550) = 97.5, p < .001$	2, 3, 4, 5, 6	61.7
FTND, <i>M(SD)</i>	1.3(1.8)	1.9(1.7)	2.8(2.3)	4.1(2.2)	$F(3,344) = 13.6, p < .001, \eta^2 = .11$	2, 3, 5, 6	2.7(2.3)
AUDIT, <i>M(SD)</i>	5.6(3.3)	6.4(2.7)	8.8(5.6)	9.3(6.9)	$F(3,481) = 6.5, p < .001, \eta^2 = .06$	2, 3	8.6(5.5)
Session induced craving, <i>M(SD)</i>	-.22(.52)	-.00(1.4)	.64(2.4)	-.27(.95)	$F(3,528) = 8.7, p < .001, \eta^2 = .05$	2, 6	.58(2.3)
Average session craving, <i>M(SD)</i>	-.80(.29)	-.71(.55)	.31(1.0)	-.0003(1.0)	$F(3,528) = 45.1, p < .001, \eta^2 = .20$	2, 3, 4, 5, 6	.21(1.0)
Interference control, <i>M(SD)</i>	27.5(12.9)	26.9(12.8)	32.1(12.3)	34.8(12.2)	$F(3,540) = 7.3, p < .001, \eta^2 = .04$	2, 3, 5	31.6(12.5)
Attentional bias, <i>M(SD)</i>	-.45(3.4)	-.18(2.8)	.33(.95)	1.1(4.4)	$F(3,541) = 3.1, p = .026, \eta^2 = .02$		.28(3.4)
	Never-sporadic vs. occasional				$t(130) = .42, p = .673, d = .08$		
	Never-sporadic vs. regular				$t(415) = 1.96, p = .050, d = .23$		
	Never-sporadic vs. CUD				$t(188) = 2.71, p = .007, d = .39$		
	Occasional vs. regular				$t(353) = .85, p = .398, d = .15$		
	Occasional vs. CUD				$t(126) = 1.59, p = .114, d = .32$		
	Regular vs. CUD				$t(411) = 1.74, p = .084, d = .20$		
Note: AUDIT: alcohol use disorder identification test; CUD: cannabis use disorder; CUDIT-R: cannabis use disorder identification test; FTND: Fagerström test for nicotine dependence; M = mean, SD = standard deviation; [#] Pairwise differences (p < .05) after Bonferroni correction; Pairwise comparisons: 1 = never-sporadic vs. occasional, 2 = never-sporadic vs. regular, 3 = never-sporadic vs. CUD, 4 = occasional vs. regular, 5 = occasional vs. CUD, 6 = regular vs. CUD;

Figure 2. Group differences in attentional bias (AB). Error bars presenting standard error (SE) of the mean.