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# Attentional bias to cannabis cues in cannabis users but not cocaine users

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## HIGHLIGHTS

- Signal detection metrics were successfully integrated in a modified visual-probe task using eye-tracking.
- Cannabis-cue attentional bias was selective for cannabis use history.
- Bias was not associated with cue-dependent disruptions in attentional performance.

## ARTICLE INFO

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## ABSTRACT

Attentional bias to drug cues has been associated with the problematic use of drugs, including cannabis. The cognitive mechanisms underlying this bias are not fully understood. The purpose of this study was to determine whether cannabis-cue attentional bias is associated with disruptions in attentional processing. To this end, a novel cannabis-cue visual probe task that incorporated eye tracking technology and attention-based metrics derived from signal detection theory was administered to seventeen individuals who reported daily/near-daily cannabis use. Seventeen individuals with cocaine use disorder were also enrolled as a clinical-control group. Cannabis and neutral images were briefly presented side-by-side on a computer screen, followed by the appearance of a "go" or "no-go" target upon offset of both images to permit assessment of attention-based performance. Cannabis users exhibited attentional bias to cannabis cues, as measured by fixation time and response time, but not cue-dependent disruptions on subsequent attentional performance. Cocaine users did not display an attentional bias to cannabis cues but did display poorer attentional performance relative to cannabis users. These results indicate that attentional bias to cannabis cues is selective to cannabis use history and not associated with impaired attentional processing.

## 1. Introduction

Although global trends vary, the use of cannabis in Western societies is gaining greater public acceptance and recent rates of use are increasing. For example, the percentage of United States (US) survey respondents who favored for some form of cannabis legalization doubled from 31% in 2000 to 61% in 2017 (Pew Research Center, 2018). Since the year 2000, at least 15 countries have decriminalized possession of "personal" or larger amounts of cannabis, and in the US, nine states, plus the District of Columbia, have legalized recreational use. The World Drug Report (2017) indicated that the annual prevalence of cannabis use increased from approximately 3% to 7% in the European Union (EU), and 9% to 14% in the US, from 1990 to 2015. However, frequent regular use (e.g., daily), which increases the risk of developing cannabis use disorder (e.g., Hall, 2009), is reported in only a subset of individuals who report recent use of cannabis (3% of the US population and 1% of the EU population; Center for Behavioral Health Statistics and Quality, 2017; European Monitoring Centre for Drugs and Drug Addiction, 2017).

The factors that contribute to the transition to habitual cannabis use and the maintenance of continued use are not entirely understood. Given the importance of attention to environmental cues in goal-directed behavior, there has been considerable interest in assessing attentional bias to drug stimuli and determining the clinical significance of this bias to uncover its role in the abuse of various substances, including cannabis. Extensive research has demonstrated an attentional

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bias to stimuli specific to the drug abused by the subjects under study across drug types (e.g., Marks et al., 2014 [cocaine]; Miller & Fillmore, 2010, 2011 [alcohol]). Different, and overlapping, theories have been proposed to explain how attentional bias develops (e.g., as a consequence of classical conditioning, sensitization to acquired incentive salience of cues, cues become discriminative stimuli signaling drug availability), but all emphasize that the ability of drug-associated cues to capture the attention of individuals with a history of using that drug is characteristic of problematic drug use (reviewed in Field & Cox, 2008). Consistent with this notion, there is evidence that the magnitude of attentional bias is associated with the presence or degree of a drug use disorder (see below for cannabis examples), though less evidence exists to support a direct link to relapse or the effectiveness of attentional bias training as a therapeutic approach (Christiansen, Schoenmakers, & Field, 2015; Field, Marhe, & Franken, 2014).

Much of the research on cannabis attentional bias has used a modified Stroop task, in which matched drug-related and neutral words that vary in text color are presented individually and the subject is instructed to indicate the color as quickly as possible while ignoring the semantic content of the word. Attentional bias is inferred when response times to accurately indicate the color of drug-related words are slower than for neutral words. A version of the Stroop task using cannabis-related words revealed attentional bias in cannabis users ($\geq 1\times$ past month use) who met dependence criteria ($N = 15$; Cannabis Severity of Dependence Scale [C-SDS; Swift, Copeland, & Hall, 1998]) but not non-dependent users ($N = 13$), and that attentional bias was correlated with subjective craving and frequency of cannabis use (Field, 2005). Greater attentional bias was also observed in adult "heavy" cannabis users ($\geq 1\times$ recent weekly use and $\geq 200$ lifetime uses) who met criteria for cannabis dependence ($N = 17$; Mini-International Neuropsychiatric Interview [MINI; Sheehan et al., 1998]) compared to those who did not meet CUD ($N = 10$), and no cannabis attentional bias was found in control subjects ($N = 26$; Cousijn et al., 2013). Another study using this task reported an attentional bias to cannabis but not alcohol words in adolescent/emerging adult cannabis users ($N = 57$; aged 16–23) receiving outpatient treatment for CUD (Cousijn et el., 2015), demonstrating the selectivity of this bias. These results support the clinical significance of attentional bias to cannabis cues. However, factors other than attentional bias (e.g., slowed cognitive and/or motor processing; Field & Cox, 2008) could contribute to slower response times on addiction versions of the Stroop task, which has prompted the use of other measures.

Variations of a visual probe task have been used to measure biased visuo-spatial attention to cannabis-related images in cannabis users. In one version of this task, cannabis and matched neutral images are briefly presented side-by-side. Upon offset of the images, a visual probe (e.g., an X) replaces one of the images and subjects must make a choice response based on the probe location. Attentional bias is inferred if subjects respond more quickly to probes replacing cannabis images. An early study using a visual probe task revealed attentional bias to cannabis-related words in cannabis users ($N = 16$; median cannabis cigarettes used per month = 16) with higher craving scores (upper half of a median split on the Marijuana Craving Questionnaire; Heishman, Singleton, & Liguori, 2001), but not in cannabis users with lower craving scores and non-users ($N = 15$; Field, Mogg, & Bradley, 2004a). A more recent study using a visual probe task demonstrated attentional bias to cannabis images in individuals with cannabis use disorder ($N = 12$; CUDIT-R and the Diagnostic and Statistical Manual of Mental Disorders-IV [DSM-IV; American Psychiatric Association, 2000]) compared to controls ($N = 13$; Vujanovic, Wardle, Liu, Dias, & Lane, 2016). These results using visual probe tasks are consistent with cannabis Stroop studies, though both procedures are restricted to response time as a measure of attentional bias, which appears to have limited internal and test-retest reliability (Ataya et al., 2012; Spiegelhalder et al., 2011). Further, visual probe tasks only index final gaze direction rather than the total time that attention was directed towards the stimulus.

To overcome those limitations, eye-tracking technology has been combined with visual probe tasks to provide a more ecologically valid and objective measure of attentional allocation. Fixation (or gaze) time derived from this task is generally a more sensitive measure of attentional bias than response time (e.g., Field, Eastwood, Bradley, & Mogg, 2006; Marks et al., 2014; Miller & Fillmore, 2010, 2011) and has greater internal reliability (Ataya et al., 2012; Field & Christiansen, 2012), though fewer studies have used this technology, likely due to the added expense and complexity. One prior study in cannabis users ($N = 23$; $\geq 1\times$ recent weekly use; $\geq 3$ on the C-SDS, indicative of dependence) and controls ($N = 23$) found that cannabis users had longer fixation times towards cannabis images compared to neutral images, whereas fixation times for the different cue types did not differ in non-using controls (Field et al., 2006).

This disproportionate orientation towards drug cues could be associated with compromised attentional processing; for example, an inability to disengage from drug cues and discriminate relevant environmental stimuli (Field & Cox, 2008; Franken, 2003; Waters, Sayette, Franken, & Schwartz, 2005). The present study sought to further address whether cannabis-cue attentional bias is associated with compromised attentional processing by incorporating signal detection metrics into a visual probe task, along with eye tracking, in daily or near-daily cannabis users ($\geq 25$ days per month). "Go" and "no-go" visual probe targets were presented to subjects following the offset of cannabis and neutral images, which permitted the calculation of d' (a measure of the ability to discriminate the visual probe targets) and criterion c (a measure of response bias). We predicted that responses to targets behind neutral cues would be suboptimal in cannabis users due to disproportionate sustained attention to cannabis cues. A prior study that used a visual probe task variant designed to determine whether the presentation of differently-valenced probes impacted cannabis cue attentional bias failed to find impairments in signal detection in cannabis users compared to controls (Vujanovic et al., 2016). The present study therefore also enrolled cocaine users who met DSM-IV criteria for cocaine abuse or dependence as a clinical control group of individuals with a distinct drug use history associated with attention-based performance impairments (reviewed in Potvin, Stavro, Rizkallah, & Pelletier, 2014) to determine whether the task variant was sensitive to group differences.

## 2. Materials and methods

### 2.1. Subjects and procedures

Thirty-four adult men and women who could speak/read English were recruited from the local community through newspaper, radio and website advertisements, as well as word-of-mouth. The cannabis group consisted of seventeen subjects who reported daily or near-daily cannabis use (at least 25 out of the past 30 days; as defined in Budney, Vandrey, Hughes, Moore, & Bahrenburg, 2007). The cocaine group consisted of seventeen subjects who met criteria for a DSM-IV cocaine-use disorder (cocaine dependence $N = 13$; cocaine abuse $N = 4$) and reported smoked crack cocaine as their typical method of cocaine use, and who used cannabis fewer than five days in the past month. All subjects completed detailed demographic, substance-use history and medical history questionnaires, and a computerized version of Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders-IV (SCID; First, Spitzer, Gibbon, & Williams, 1996) during screening. Subjects in the cannabis group endorsed between 0 and 7 DSM-IV cannabis dependence items (mean = 3.9 items). All but one subject in the cannabis group met DSM-IV criteria for cannabis dependence. None of the subjects in the cocaine group met DSM-IV criteria for a cannabis use disorder. Potential subjects were excluded if they had a serious medical or psychiatric condition (e.g., schizophrenia) or were currently prescribed psychiatric medication, were dependent on any drug that could produce withdrawal (e.g., alcohol, opioids or