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9-Tetrahydrocannabinol During Encoding Impairs Perceptual Details yet Spares Context Effects on Episodic Memory

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Abstract

Background: With the growing acceptance of cannabis, it is crucial to understand the drug's effects on episodic memory accuracy and distortion. Here, we investigated the impact of 9-tetrahydrocannabinol (THC), the main psychoactive constituent of cannabis, on a context-based memory illusion.

Methods: In a double-blind, placebo-controlled, within-subjects design, healthy infrequent cannabis users ($N = 24$) memorized object pictures superimposed over scenes (e.g., grey cat on beach) after placebo or THC (15 mg oral) pretreatment. Two days later under sober conditions, memory for the object pictures was tested by asking participants to discriminate between previously seen objects or perceptually similar lures (e.g., different grey cat). Context reinstatement was manipulated by presenting objects on their original or different scenes (e.g., beach or forest).

Results: THC impaired memory for perceptual details of objects compared to placebo, and the context illusion was obtained in each condition: Context reinstatement increased high confidence false recognition along with correct recognition of previously seen objects. Although THC did not interact with these context effects overall, post hoc analyses showed that THC magnified the context illusion when objects were semantically congruent with their encoding contexts but abolished the context illusion when objects were incongruent with their encoding contexts.

Conclusions: These results are consistent with the hypothesis that THC impairs the encoding of specific object information more than item-context associations. As a result, THC may spare the

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distorting effects of context reinstatement on memory. In fact, THC may increase these distorting effects under conditions when objects are semantically congruent with context.

Keywords

THC; cannabis; episodic memory; context reinstatement; false memory; memory illusion

Introduction

With the recent surge in cannabis medicalization and legalization, it is important to determine its acute effects on memory. Here, we focus on episodic memory, or the conscious reexperiencing of information from the past (i.e., “mental time travel”; [1]). Previous work has focused on how cannabis and its main psychoactive constituent, 9-tetrahydrocannabinol (THC), can cause forgetting. More recently, researchers have turned to studying how cannabis and THC can drive memory distortion.

Exactly how THC distorts memory depends on which stage of memory processing it has its influence. When THC is administered only during retrieval (i.e., the memory test) and not during encoding, it increases false memories, as measured by highly confident false alarms to items that were not studied [2]. In contrast, when THC is administered prior to encoding (i.e., the acquisition of information) and memory is tested under sober conditions after a delay, THC reduces memory for studied items (i.e., decreased hit rates), without increasing false alarms [3,4]. In fact, Ballard et al. [3] found that THC during encoding tended to *reduce* false alarms to nonstudied words that were semantically related to studied words in some participants, ostensibly by reducing memory for the related features that would otherwise make these items confusable during retrieval. These findings indicate that THC during memory encoding does not necessarily increase subsequent false memories. They also open the intriguing possibility that THC-induced encoding impairments might interact with subsequent retrieval processes to impact memory distortion.

One way that THC during encoding might distort memory at retrieval, even when in a drug-free state during retrieval, is by impairing memory for perceptually detailed information. People have difficulty discriminating in memory between objects that were previously seen and new objects that are similar but differ in subtle perceptual information (e.g., grey cat vs different grey cat) [5]. This difficulty is reflected in elevated false recognition of nonstudied but similar objects, a kind of memory distortion. We are unaware of any studies investigating effects of THC on perceptual details of objects in episodic memory, but there is reason to predict that THC during encoding would reduce discrimination between studied and similar objects during retrieval, leading to THC-induced increases in false recognition. Cannabinoid 1 (CB1) receptors, the primary target of THC, are particularly dense in the hippocampus [6], a region that supports fine-grained mnemonic discriminations [7]. Moreover, THC may impair visual processing [8,9], which may lead to downstream impairments on episodic memory for objects and also increase false recognition.

In addition to impairing perceptual details in memory, THC during encoding might impair memory for conceptual information that is associated with objects (e.g., forgetting the kind of cat that was studied, or even forgetting that a cat was studied at all). If THC produces a

global impairment on memory encoding, then it might not increase false alarms to similar objects at retrieval, as the conceptual familiarity of both studied and similar objects would be reduced (cf. [3]). Thus, although the literature predicts that THC during encoding will reduce discrimination between same and similar objects in memory, the extent that this will be associated with differences in false recognition (as opposed to decreased hit rates) is unclear. The goal of the present experiment was to investigate these potential THC effects.

Another way that THC during encoding might distort retrieval is through interactions with context memory. Reinstating an encoding context during memory retrieval is typically thought to improve memory [10], but in a recent study with no drug manipulation [11], we discovered that context reinstatement can also increase false alarms to similar items that were not studied (i.e., a context illusion). During the encoding phase, perceptually detailed pictures of common objects were superimposed onto scenes that served as context (e.g., grey cat on a beach). At retrieval, participants' memory for specific perceptual details was tested with the same object pictures that they should accept (targets) or similar exemplars that they should reject (e.g., different grey cat; similar lures). The context for these items was reinstated by presenting them on their corresponding scene from encoding (i.e., beach) or a different scene (e.g., forest). Reinstating the encoding context at retrieval, compared to switching the scene at retrieval, boosted hit rates for targets and high confidence false alarm rates for similar lures, despite warning participants to avoid this context illusion.

How might THC during encoding subsequently impact context reinstatement effects at retrieval? Previous findings point to conflicting predictions. One hypothesis is that THC impairs item-context bindings during encoding, thereby reducing the impact of context reinstatement at retrieval. In addition to fine-grained mnemonic discriminations [7], the hippocampus is believed to support item-context bindings [12]. To the extent that item-context bindings during encoding drive the context-reinstatement illusion at retrieval, a THC-impairment of context bindings during encoding might attenuate the context illusion (i.e., reduced contextually driven false alarms, as well as hits). Alternatively, it might be hypothesized from research using associative and source memory tasks that THC will not impact item-context bindings during encoding [13,14]. If THC spares the encoding of item-context bindings, then THC may not alter the impact of context reinstatement at retrieval, or its effects might even be exaggerated (i.e., increased contextually driven hit and false alarms) due to an overreliance on contextual associations to compensate for impaired object memory.

Methods

Participants

Twenty-four healthy volunteers (12 males) aged 18 to 29 years ($M = 22.96$, $SD = 3.61$) with some cannabis experience (4–100 lifetime uses) were recruited from the University of Chicago and surrounding community through advertisements and word-of-mouth referrals. This was the same sample used in [2]. Screening included a physical examination, an electrocardiogram, and a semi-structured interview by a clinical psychologist. Exclusion criteria included any current Axis I DSM-IV disorder, including substance dependence, current use of >5 cigarettes per day, history of psychosis or mania, less than a high school

education, lack of English fluency, a body mass index outside 19–33 kg/m², high blood pressure (>140/90), abnormal electrocardiogram, pregnancy, lactating, or daily use of any medication other than birth control. Women not taking hormonal contraceptives were tested during their follicular phase because hormonal fluctuations can influence drug responses [15]. Demographic and drug use information was obtained during screening (Table 1).

Eligible participants attended an orientation session to consent and practice tasks. Participants were informed there would be memory tests. To minimize drug expectancy effects, participants were informed they could receive a stimulant, sedative, cannabinoid, or placebo. They were instructed to consume their normal amounts of caffeine and nicotine before sessions but abstain from alcohol, prescription drugs (except contraceptives), and over-the-counter drugs for 24 hours, cannabis for 1 week, and other illicit drugs for 48 hours before each session. They were told that urine drug tests would be conducted at each session and positive tests would lead to rescheduling or dismissal. Participants were advised to get their normal amounts of sleep and not eat for two hours before sessions in which a capsule was consumed. Following completion of the study, participants were debriefed and monetarily compensated. The study took place at the University of Chicago Medical Center and was approved by the Institutional Review Board.

Drug

Fifteen mg of THC (Marinol®; Solvay Pharmaceuticals) was placed in opaque size 00 capsules with dextrose filler. Placebo capsules contained dextrose only. This dose of THC is within the range shown to affect memory encoding in prior work [3,4].

Design

This study used a double blind, within-subjects, counterbalanced design in which all participants completed both a placebo arm and a THC arm (three sessions each). The present experiment pertains only to the last two sessions of each arm. During the first session of each arm, participants viewed emotional pictures and verbal stimuli in a drug free state. On the second session, they ingested a capsule containing placebo or THC and two hours later completed memory tests for the emotional pictures and verbal stimuli (described in detail here [2]). Participants then completed the encoding phase of the object-scene stimuli for the present experiment. Afterward, they completed a working memory test with colored square stimuli. At the third session, memory for the object-scene stimuli was tested in a drug-free state. Each session within an arm was separated by 48 hours, and each arm was separated by 5 days, resulting in 7 days between sessions in which a capsule was administered. Drug order was counterbalanced across participants.

Task/Stimuli

This study used a modified version of the widely-used Mnemonic Similarity Task [5] with a context reinstatement manipulation (MS-Doss; [11]). During the encoding phase of the MST, participants view object pictures (e.g., rollerblade, grey cat). During the retrieval phase, they are required to discriminate between the same studied objects (e.g., the same rollerblade; targets), nonstudied objects related to studied objects (e.g., different grey cat; similar lures), and nonstudied objects unrelated to studied objects (e.g., hammer; dissimilar

lures) using “old,” “similar,” and “new” responses, respectively. Object pairs have been normed for their mnemonic similarity based on false alarm rates (i.e., “old” responses) to similar lures.

The MS-Doss uses this same paradigm combined with a context reinstatement manipulation (Figure 1). Specifically, object pictures at both encoding and retrieval were always superimposed on larger context pictures consisting of 20 distinct, high-quality indoor and outdoor scenes (e.g., beach, forest, bathroom). During encoding, participants viewed object pictures yoked to context scenes (e.g., cat on the beach). During retrieval, memory discrimination decisions (“old,” “similar,” “new”) are still made about the objects, but targets and lures can be presented on the scene from encoding (reinstated), or the context can be switched (e.g., cat on a forest; switched) in a rotating fashion (e.g., scene1 to scene2, scene2 to scene3...scene20 to scene1). Each scene was presented equally often across all experimental conditions (i.e., in each experimental arm, 4 objects per encoding scene subsequently in all combinations of reinstated/switched and target/similar conditions and 2 dissimilar lures per scene).

The MS-Doss used 240 object pairs from the MST and divided them into 12 lists (lists AL) of 20 object pairs for counterbalancing stimuli across participants. Lists A-F and G-L were administered during the first and second experimental arms, respectively. Lists within an experimental arm were rotated through item (i.e., target, similar lure, dissimilar) and context conditions (i.e., reinstated, switched) across participants in a Latin square design so that there were 80 objects presented at encoding and 40 targets, 40 similar lures, and 40 dissimilar lures on each memory test. Effort was made to balance semantic content between lists, and there were an equal number of object pairs at the five levels of normed mnemonic similarity in each list.

Procedure

At the beginning of the first and second sessions of each experimental arm, participants completed compliance measures including breath alcohol level (Alco-sensor III, Intoximeters, St. Louis, MO), a urine drug test (ToxCup, Branan Medical Co. Irvine, CA), a pregnancy test (females only; Aimstrip, Craig Medical, Vista, CA), and baseline cardiovascular and mood measures. After compliance measures at the second session of each experimental arm, participants consumed a capsule containing THC or placebo. Cardiovascular and mood measures were taken every 30 minutes for the next 120 minutes. During this time, participants were provided with music and magazines in furnished rooms. They were not allowed to eat, sleep, or work, and they had no access to cell phones or Internet.

After 120 minutes, participants completed memory tasks lasting approximately 35 minutes [2]. These were followed by the encoding phase of the MS-Doss. Each trial began with a scene that covered the entire screen for 750 ms followed by a picture of an object at the center of the screen superimposed over the scene for 2000 ms. Afterward, the object disappeared and just the scene remained for another 750 ms. To encourage item-context associations, participants were to asked decide whether the object belonged in the scene (yes/no) while the object was on the screen. The next trial began after a jittered intertrial

interval (ITI) averaging 2000 ms (range = 1000–5000 ms). Trial order for this phase and the subsequent phase was randomized. This phase lasted approximately 10 minutes. After the encoding phase, participants performed a working memory task (~25 minutes) with colored square stimuli and then were allowed to relax with magazines and music. Participants were allowed to leave 210 min after capsule administration if physiological and subjective measures had returned to baseline.

Forty-eight hours after the encoding phase, participants returned to the lab for a self-paced memory test for the object picture stimuli (120 items). Each trial again began with a scene for 750 ms before an object appeared superimposed over the scene for 1000 ms. Options for old/similar/new judgements were then displayed on the screen, and after this judgement, options for confidence ratings (five-point scale) were displayed. Participants were warned that although the scenes may help cue their memories, context reinstatement may trick them into thinking a similar object was old and that they should make their responses independent of whether the scene matched the one from the encoding phase. This phase lasted approximately 10 minutes.

Analyses

To confirm expected drug effects, physiological and mood measures were obtained. Heart rate and blood pressure were measured using a portable blood pressure monitor (A&D Medical/Life Source, San Jose, CA). Mood measures included the Addiction Research Centre Inventory (ARCI; [16], the Visual Analog Scales (VAS; [17], the Drug Effects Questionnaire (DEQ; [18]), and an End of Session Questionnaire (ESQ). See Supplemental Information (SI) for a description of each scale. Due to technical malfunctions, one participant's physiological data could not be collected, and another participant's mood data could not be collected. Two-tailed t tests were carried out between drug and placebo conditions to compare changes from baseline measures (i.e., before drug administration - 120 minutes). These data can be found in Table 2.

Key dependent variables were hit rates ($p(\text{"old"}|\text{target})$), false alarm rates ($p(\text{"old"}|\text{similar lure})$), memory accuracy ($p(\text{"old"}|\text{target}) - p(\text{"old"}|\text{similar lure})$). All effects on these measures were similar to high confidence versions (SI; Table 3). Each dependent variable was analyzed separately with 2 (drug during encoding: placebo, THC) $\times$ 2 (context: reinstated, switched) repeated measures ANOVAs. Post hoc analyses included item-context semantic congruency as a factor by conditionalizing items as congruent or incongruent based on each participant's response at encoding (i.e., whether an object belonged in a scene). Bayesian ANOVAs were conducted to support null effects of THC. Thresholds for inference were $p < .05$ and $BF > 3$, and partial eta squared and Cohen's d are reported for significant effects. See SI for analyses of the lure discrimination index (and caveats of this measure), corrected false alarm rates ($p(\text{"old"}|\text{similar lure}) - p(\text{"old"}|\text{dissimilar lure})$), the inclusion of normed mnemonic similarity as a factor, and exploratory correlations between physiological/subjective measures and memory measures.

Data Availability

Data from this study are available from [19].

Results

Primary Analyses

Full data can be found in Table 3. The ANOVAs on hit rates revealed a main effect of drug ($F(1, 23) = 8.67, p = .007, \eta_p^2 = .27$) and context ($F(1, 23) = 23.73, p < .001, \eta_p^2 = .51$). As predicted, THC at encoding decreased hits to studied items, whereas context reinstatement increased hit rates (Figure 2a). The drug by context interaction was not significant ($F(1, 23) = .60, p > .250$), suggesting that THC at encoding did not preclude the memory boost from context reinstatement. Bayesian ANOVAs supported this sparing of item-context bindings, as there was moderate evidence for the model with drug and context as factors relative to the full model (i.e., inclusion of the interaction term; $BF = 3.02$).

THC at encoding did not modulate false alarm rates ($F(1, 23) = 1.24, p > .250$), though it significantly reduced corrected false alarm rates (SI). Thus, there was some evidence that THC reduced false alarms to new objects that were similar to the studied objects, without a concurrent increase in false alarms to dissimilar lures, analogous to previously observed effects [3]. As expected, context reinstatement increased false alarms to similar lures (Figure 2a; $F(1, 23) = 18.60, p < .001, \eta_p^2 = .45$). The context by drug interaction was not significant ($F(1, 23) = .12, p > .250$), again suggesting that THC at encoding did not impact the context illusion. Similar to the results for hit rates, Bayesian ANOVAs supported this sparing of item-context bindings, as there was good evidence for models without the interaction term (BF s reported for models including only context or drug and context, respectively, against the full model; $BF = 7.41$ and 3.50).

THC at encoding reduced memory accuracy (Figure 2b; $F(1, 23) = 5.50, p = .028, \eta_p^2 = .19$), and as we previously observed [11], the magnitude of the boosts in hit and false alarm rates from context reinstatement was similar such that memory accuracy was unaffected by context reinstatement ($F(1, 23) = .12, p > .250$). The drug by context interaction was not significant ($F(1, 23) = .74, p > .250$), and this was strongly supported by Bayesian ANOVAs ($BF = 11.85$). Thus, THC at encoding impairs the encoding of perceptual details, and this effect is not modulated by context reinstatement.

Effects of Item-Context Semantic Congruency

Although THC did not interact with context effects in the above analyses, we also conducted post hoc analyses in which targets and lures were conditionalized on their item-context semantic congruency based on each participant's encoding judgement (see SI for caveats). Data for all dependent variables conditionalized on their item-context semantic congruency can be found in the SI. Drug ($F(1, 23) = 5.66, p = .026, \eta_p^2 = .20$), congruency ($F(1, 23) = 7.73, p = .026, \eta_p^2 = .25$), and context ($F(1, 23) = 19.50, p < .001, \eta_p^2 = .46$) modulated hit rates, as THC at encoding reduced hits and congruent items and context reinstatement increased hits. Although context reinstatement effects on hits were numerically larger for congruent items, the congruency by context interaction was not significant ($F(1, 23) = 1.46$,

$p = .239$). Additionally, the drug by congruency, drug by context, and 3-way interaction were not significant (all F s < 1 , all p s $> .250$).

The effects of congruency on false alarm rates were consistent with hit rates but also revealed potential conditions under which THC at encoding may particularly distort memory or even prevent memory distortion. Drug did not modulate false alarm rates ($F(1, 23) = .54$, $p > .250$), but congruency ($F(1, 23) = 8.22$, $p = .009$, $\eta_p^2 = .26$) and context did ($F(1, 23) = 33.54$, $p < .001$, $\eta_p^2 = .59$), with congruent items and context reinstatement increasing false alarms. The drug by congruency and drug by context interactions were not significant (all F s < 1 , all p s $> .250$). Replicating our prior work [11], context reinstatement was strongly modulated by congruency ($F(1, 23) = 19.28$, $p < .001$, $\eta_p^2 = .46$), with congruent items boosting contextually driven false alarms. Interestingly, the drug by congruency by context interaction was significant ($F(1, 23) = 5.95$, $p = .023$, $\eta_p^2 = .21$). As can be seen in Figure 3, this three-way interaction could be explained by false alarms for objects with semantically congruent contexts and THC at encoding magnifying context reinstatement effects to double that of the placebo condition (placebo: $t(23) = 3.24$, $p = .004$, $d = .66$; THC at encoding: $t(23) = 6.58$, $p < .001$, $d = 1.34$). In contrast, for incongruent item-context pairings, THC at encoding abolished context reinstatement effects on false alarms ($t(23) = .24$, $p > .250$), but context reinstatement effects remain for placebo ($t(23) = 2.62$, $p = .015$, $d = .53$).

Discussion

With this experiment we observed two key findings regarding how THC impacts object and context memory. First, THC impaired memory accuracy for specific perceptual details. This effect was driven by reduced hit rates to studied objects, without a concurrent increase in false alarms to similar lures. In fact, there was evidence that THC reduced false alarms to similar objects (SI), which is an extension of Ballard et al. [3] who found that THC at encoding tended to reduce false alarms to related words. Second, we replicated the distorting effects of context reinstatement on memory [11], and although we did not find an interaction between THC and the context illusion in our primary analyses, THC increased the context illusion for object-scene pairings that were judged to be semantically congruent. A THC-induced impairment in memory for perceptual details of objects might result in an overreliance on object-context associations at retrieval, thereby producing more false alarms to similar objects when the contextual information is made available (i.e., during context reinstatement). However, context-dependent memory distortion was abolished by THC for objects that were incongruent with their contexts, perhaps due to THC causing forgetting of more bizarre object-context associations made at encoding while intoxicated for less commonly paired objects and scenes.

The present results can be weighed against our understanding of the neurobiology of THC and memory. In the medial temporal lobe, CB1 receptors are most densely distributed in the hippocampus [6], a structure thought to support both the encoding of high resolution perceptual information [20] and item-context bindings [12]. Although agonism and antagonism of hippocampal CB1 receptors impair and enhance long-term potentiation,

respectively [21], activation of CB1 via THC was not found to impact associative memory in humans [13], and blocking CB1 via rimonabant has been found to impair associative memory in mice [22]. Such findings suggest that there does not appear to be a one-to-one mapping between activation of hippocampal CB1 receptors and global episodic memory dysfunction.

Some researchers have suggested that cannabis, as well as ketamine, may be appropriate models for psychosis, considering both drugs produce psychotomimetic effects and cognitive impairments that occur in psychosis [23]. However, our findings suggest the episodic memory encoding impairments of THC do not model those of psychosis. Whereas patients with first-episode psychosis exhibit a reduction in context reinstatement effects [24], we did not observe this effect with THC at encoding. Moreover, a recent study that used the MST found comparable impairments in memory for perceptual details in patients with first episode psychosis and in healthy volunteers under ketamine [25]. Both of these effects were considerably larger than what we found with THC, again suggesting that THC has a different mechanism of action.

Our findings and others also have implications for eyewitness testimonies involving an individual under the influence of cannabis (“highwitness testimonies”), the prevalence of which may increase with the acceptance of cannabis. Although overall less details may be remembered, one implication of our study is that context reinstating techniques aimed at driving memory retrieval may distort memory more so in intoxicated individuals, at least in those cases where items and contexts are semantically congruent. Interestingly, it has also been shown that cannabis administered during both encoding and retrieval (with a delay in between), a type of context reinstatement, can partially rescue memory impairments [26]. Nevertheless, THC at retrieval robustly increases false memories [27], an effect that could interact with contextual associations at retrieval via enhanced semantic activation [28,29]. This possibility may be particularly detrimental to posttraumatic stress disorder, which has a high incidence of cannabis use and inappropriate memory retrieval from overgeneralized memory cues.

Future work testing the effects of THC on encoding, retrieval, and both phases with memory distorting manipulations such as context reinstatement or conceptual fluency [30,31] will help address the boundary conditions of THC-induced memory distortion. Such considerations highlight the complexity of drug effects on episodic memory. Depending on what kinds of information are impacted at what stage of memory will be critical in determining whether a drug manipulation will render one more or less susceptible to false memories.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Schematic of experiment and the MS-Doss task. Participants encoded object-scene stimuli approximately 2.5 hours after capsule administration followed by a memory test for the objects two days later. Objects could be the same pictures from encoding (Targets), similar exemplars of an object from encoding (Similar Lures), and novel exemplars (Dissimilar Lures). Additionally, context reinstatement was manipulated by pairing the object with the original scene from encoding (Reinstated) or switched to a different scene (Switched).

Figure 2.

Hit and false alarm rates as a function of drug condition and context reinstatement (a) and memory accuracy ($p(\text{"old"}|\text{Target}) - p(\text{"old"}|\text{Sim. Lure})$) and lure discrimination index ($p(\text{"similar"}|\text{Sim. Lure}) - p(\text{"similar"}|\text{Dis. Lure})$) as a function of drug condition, averaged over context condition (b). Paired scatter points in (a) highlight the significant effect of context reinstatement across drug conditions (asterisks indicate $p < .001$). Paired scatter points in (b) highlight the THC-induced impairments of specific perceptual details in memory (asterisks indicate $p < .05$). Horizontal bars and error bars within violin plots are means and 95% CIs, respectively.

Figure 3.

False alarm rates ($p(\text{"old"}|\text{Sim. Lure})$) as a function of drug condition and context reinstatement conditionalized on their item-context semantic congruency (based on each participant's judgments at encoding). Paired scatter points highlight the significant effect of context reinstatement. Single and double asterisks indicate moderate and strong effects of context reinstatement, respectively. Horizontal bars and error bars within violin plots are means and 95% CIs, respectively.

Table 1.

Demographic characteristics and drug use histories of study participants.

	Mean (SD)
<i>Age (years)</i>	22.96 (3.61)
<i>Education (years)</i>	15.25 (1.75)
<i>BMI</i>	24.86 (3.59)
<i>Caffeine (cups/day)</i>	1.41 (1.29)
<i>Nicotine (cigarettes/day in the five users)</i>	.19 (.15)
<i>Alcohol (drinks/week)</i>	6.01 (6.17)
<i>Cannabis (uses/month)</i>	.79 (1.22)
<i>Lifetime uses of Cannabis</i>	26.67 (24.78)
<i>Days since last use of cannabis before Placebo session</i>	296.17 (891.35)
<i>Days since last use of cannabis before THC session</i>	293.85 (891.82)

Table 2.

Mean (95% CI of mean) changes from pre-capsule to 120 minutes post-capsule for physiological and mood measures. Last four columns are statistics based on differences between THC and placebo conditions. ARCI = Addiction Research Centre Inventory, VAS = Visual Analog Scales, DEQ = Drug Effects Questionnaire, ESQ = End of Study Questionnaire.

	Placebo	THC	95% CI	t(22)	p	d
<i>Physiology</i>						
Heart Rate	-7.52 [-11.47, -3.58]	.39 [-4.52, 5.30]	[3.02, 12.81]	3.35	.003	.77
Systolic BP	-2.43 [-7.05, 2.18]	.57 [-2.80, 3.93]	[-2.71, 8.71]	1.09	.287	.32
Diastolic BP	-1.74 [-5.15, 1.67]	.09 [-3.84, 4.01]	[-3.71, 7.36]	.68	.501	.21
<i>ARCI</i>						
Marijuana scale	.50 [-.13, 1.13]	4.65 [3.19, 6.12]	[2.68, 5.84]	5.59	.000	1.59
<i>VAS</i>						
Anxious	-7.21 [-19.85, 5.43]	2.52 [-3.48, 8.52]	[-5.46, 25.46]	1.34	.194	.41
Stimulated	-8.17 [-18.66, 2.33]	12.57 [-.54, 25.67]	[.78, 40.70]	2.15	.042	.75
Sedated	-3.58 [-17.78, 10.61]	-3.96 [-14.70, 6.79]	[-17.15, 16.72]	.03	.979	.01
Elated	-13.29 [-23.76, -2.83]	7.65 [-4.45, 19.76]	[.70, 40.34]	2.15	.043	.79
Insightful	-10.88 [-22.30, .55]	10.13 [-2.15, 22.42]	[.71, 41.11]	2.15	.043	.76
Sociable	-11.21 [-19.58, -2.83]	9.17 [-.42, 18.76]	[7.63, 33.15]	3.31	.003	.97
Confident	-7.67 [-17.47, 2.13]	5.74 [-4.17, 15.65]	[-.38, 27.51]	2.02	.056	.58
Lonely	-2.92 [-12.50, 6.67]	1.48 [-2.94, 5.90]	[-7.24, 16.45]	.81	.428	.25
Playful	-10.92 [-19.66, -2.18]	14.22 [2.91, 25.52]	[8.70, 42.17]	3.15	.005	1.07
Dizzy	-6.29 [-16.48, 3.90]	4.52 [-5.48, 14.53]	[-5.03, 27.20]	1.43	.168	.46
Loving	-4.42 [-16.99, 8.15]	5.78 [-4.76, 16.32]	[-7.96, 29.35]	1.19	.247	.37
Friendly	-9.96 [-21.16, 1.25]	13.70 [2.91, 24.48]	[8.66, 39.52]	3.24	.004	.92
Restless	-6.67 [-22.45, 9.11]	7.61 [-4.85, 20.07]	[-4.08, 33.65]	1.63	.118	.43
<i>DEQ</i>						
Feel drug effect	5.63 [2.24, 9.01]	46.52 [33.34, 59.71]	[28.65, 54.30]	6.71	.000	1.85
Like drug effect	12.08 [3.08, 21.08]	35.61 [21.97, 49.25]	[11.07, 35.37]	3.96	.001	.88
Dislike drug effect	9.79 [2.10, 17.48]	25.57 [14.34, 36.79]	[5.62, 28.29]	3.10	.005	.71
Feel high	4.21 [-.12, 8.53]	42.91 [29.87, 55.96]	[25.42, 51.71]	6.09	.000	1.73
Want more drug	8.67 [.90, 16.43]	22.96 [12.57, 33.35]	[6.41, 21.51]	3.83	.001	.67
<i>ESQ (percent who guessed receiving)</i>						
stimulant	4.17	12.5				
sedative	25	16.67				
cannabinoid	0	70.83				
placebo	70.83	0				

Table 3.

Mean [95% CI] proportion of “old” and “similar” responses to targets, similar lures, and dissimilar lures ($p(\text{“old”}|\text{Target})$ and $p(\text{“old”}|\text{Sim. Lure})$ are referred to in the main text as hit and false alarm rates, respectively), as well as memory accuracy ($p(\text{“old”}|\text{Target}) - p(\text{“old”}|\text{Sim. Lure})$), corrected false alarm rate ($p(\text{“old”}|\text{Sim. Lure}) - p(\text{“similar”}|\text{Dis. Lure})$), and lure discrimination index ($p(\text{“similar”}|\text{Sim. Lure}) - p(\text{“similar”}|\text{Dis. Lure})$). High confidence versions of these metrics include only responses with the highest confidence level in the numerator. Sim. = similar, Dis. = Dissimilar, FA = False Alarm, LDI = Lure Discrimination Index.

	Placebo		THC at Encoding	
	Reinstated	Switched	Reinstated	Switched
<i>All Responses</i>				
$p(\text{“old”} \text{Target})$	.65 [.58, .73]	.56 [.46, .66]	.58 [.51, .65]	.45 [.39, .52]
$p(\text{“old”} \text{Sim. Lure})$	.42 [.35, .49]	.32 [.26, .37]	.39 [.32, .45]	.29 [.23, .35]
$p(\text{“old”} \text{Dis. Lure})$	.05 [.03, .06]		.08 [.05, .11]	
$p(\text{“similar”} \text{Target})$	.22 [.18, .27]	.23 [.16, .30]	.24 [.19, .29]	.27 [.21, .33]
$p(\text{“similar”} \text{Sim. Lure})$	.36 [.29, .44]	.38 [.33, .44]	.29 [.23, .35]	.33 [.27, .39]
$p(\text{“similar”} \text{Dis. Lure})$	.21 [.17, .25]		.21 [.17, .25]	
Memory Accuracy	.23 [.16, .30]	.24 [.17, .32]	.19 [.15, .24]	.16 [.10, .22]
Corrected FA Rate	.37 [.30, .45]	.27 [.21, .32]	.31 [.24, .37]	.21 [.16, .26]
LDI	.15 [.08, .23]	.17 [-.11, .24]	.09 [.02, .15]	.12 [.05, .19]
<i>High Confidence Responses</i>				
$p(\text{“old”} \text{Target})$	.33 [.23, .43]	.27 [.17, .37]	.27 [.19, .34]	.15 [.10, .21]
$p(\text{“old”} \text{Sim. Lure})$	.18 [.12, .24]	.09 [.04, .14]	.15 [.09, .20]	.06 [.03, .09]
$p(\text{“old”} \text{Dis. Lure})$	.01 [.00, .01]		.01 [.00, .02]	
$p(\text{“similar”} \text{Target})$	.02 [.01, .03]	.01 [.00, .02]	.01 [.00, .03]	.01 [.00, .02]
$p(\text{“similar”} \text{Sim. Lure})$	.08 [.03, .12]	.05 [.01, .09]	.03 [.01, .04]	.01 [.00, .02]
$p(\text{“similar”} \text{Dis. Lure})$	.01 [.00, .02]		.01 [.00, .01]	
Memory Accuracy	.15 [.08, .21]	.18 [.11, .24]	.12 [.07, .16]	.09 [.06, .13]
Corrected FA Rate	.18 [.12, .24]	.09 [.04, .14]	.14 [.09, .19]	.05 [.02, .09]
LDI	.07 [.02, .11]	.04 [.00, .07]	.02 [.01, .03]	.00 [.00, .01]