

SI Methods

Subjective measures

Addiction Research Center Inventory (ARCI). The Addiction Research Center Inventory (ARCI) is set of 53 true/false questions to measure drug-specific behavioral and mood effects. These questions include the 49 questions reported in Martin et al. (1) and an additional 4 questions from the Marijuana group sub-scale. The 53-item ARCI measure contains a sub-set of items from the following scales reported by Haertzen (2): The Pentobarbital, Chlorpromazine, & Alcohol Group Scale (PCAG; sedation); The Morphine-Benzedrine Group Scale (MBG; euphoria); the Lysergic Acid Diethylamide Group Scale (LSD; dysphoric /psychotomimetic); the Benzedrine Group Scale (BG; empiric amphetamine scale); Marijuana Group Scale (Ma). In addition, some items in the set of 53 were devised by Martin et al. (1) as part of a revised amphetamine scale. From this set of 53 questions, we focused our analyses on the 12-item “revised Marijuana scale” (3) as this scale is tailored to the effects of cannabis.

Drug Effects Questionnaire (DEQ). The Drug Effects Questionnaire (DEQ) is a set of 5 questions about the current effects of a drug (4). For each question, participants rate how much they feel a drug effect, like the effect, dislike the effect, feel high, and want more of the drug. Participants rate each question on a continuous sliding scale from “not at all/neutral” to “very much.” Participants were instructed to select “not at all/neutral” if they had not yet received a capsule (first time-point).

Visual Analog Scales (VAS). The Visual Analog Scales (VAS) are measures used to assess individual dimensions of subjective mood. These measures were only used in Exp 1. We used a version of this scale with 13 adjectives (5) – anxious, stimulated, sedated, elated, insightful, sociable, confident, lonely, playful, dizzy, loving, friendly, and restless. Participants rated the degree to which they felt each of these adjectives on a continuous sliding scale from “not at all” to “extremely.”

End of Session Questionnaire. The end of session questionnaire (ESQ) asked participants which class of drugs they thought they had received during the current session.

Design

Additional design details for Exp 1. In Exp 1, participants performed the working memory task in two total sessions, but these two sessions were part of a larger, multi-session study, as reported in Doss et al. (6). In this design, participants came into the lab for one orientation pre-session and then a total of six experimental sessions. This multi-session design was used in order to disentangle the effects of THC on long-term memory encoding versus retrieval. To this end, participants performed both a long-term memory retrieval test and a long-term memory encoding test during capsule administration. During Session 1, participants encoded two different sets of stimuli (emotional stimuli; Deese-Roediger-McDermott stimuli). After 48 hours, they returned for Session 2. During Session 2, they took a capsule (THC or placebo), were tested on their memory of the stimuli they had learned during Session 1, encoded a new set of stimuli (object/scene) into long-term memory, and completed the working memory test. Finally, after 48 hours, the participants returned for Session 3 and were tested on their memory of the object/scene stimuli that were learned in Session 2. After a minimum of

72 hours, participants returned for Session 4. Sessions 4-6 followed the exact procedures as Sessions 1-3, with the exception that the specific stimuli used for each long-term memory test were unique (i.e., different images). This six-session design allowed for a within-subjects comparison of the encoding- and retrieval-specific effects of THC on long-term memory performance.

Procedures

Time of abstinence. Participants were instructed that each session would begin with a drug test. In Exp 1, participants were instructed to abstain from using alcohol, prescription drugs (except contraceptives), and over-the-counter drugs for 24 hours prior to the encoding sessions (e.g. Session 1) and to remain abstinent through the corresponding retrieval session (e.g. Session 3). They were instructed to abstain from cannabis starting 1 week before the encoding sessions, and other elicits drugs starting 48 hours before the encoding sessions. In Exp 2, participants were instructed to abstain from the above-named substances for at least 48 hours before each experimental session; participants were also cautioned that a negative drug test would be required to participate in the study, and some substances may take longer than 48 hours to leave the system.

Exp 1. Participants completed other cognitive tasks before completing the working memory task in Exp 1. Cognitive testing began at approximately 120 minutes after capsule consumption. First, participants were tested on their memory for emotional stimuli that had been encoded 48 hours prior (30 min). Second, participants were tested on their memory for the DRM stimuli (5 min). Third, participants encoded a new set of stimuli (object/scene; 20 min). Finally, participants completed the working memory task that is the central focus of this paper.

Exp 2. Participants also completed other cognitive tasks before completing the working memory task in Exp 2; cognitive testing likewise began at ~120 minutes after capsule consumption. Participants completed a series of tasks on a desktop computer and another series of tasks on a mobile phone app. The order of the desktop versus app tasks was counter-balanced. The desktop tasks took approximately 30 min, and the phone tasks took approximately 5 min. After completing both the desktop and phone tasks, participants were allowed to relax for 30 min. Then, they completed both sets of tasks a second time. Finally, participants performed the working memory task (~220 min post-capsule).

Literature search

We examined the literature to gauge the strength of prior evidence that THC impairs working memory. We searched for all studies using either a Digit Span task, Digit Recall Task, or Spatial *n*-back Task (Tables S1 and S2). In addition, we also report additional recent within-subjects, placebo-controlled studies that used visual working memory tasks and some miscellaneous tasks with a working memory component (Table S3). Inclusion criteria were (1) human subjects, (2) testing $\Delta 9$ -tetrahydrocannabinol, either cannabis (alone, e.g. not mixed with tobacco containing nicotine) or synthetically produced THC, e.g. Marinol® or Dronabinol, (3) placebo-controlled, (4) within-subjects design with randomized order of administration, and (5) report running statistical tests.

We performed our initial literature search in July 2018, and updated it in August 2019. We did not formally exclude papers based on publication date, but we did not find any studies meeting our inclusion criteria from before 1970. We began our search for papers based on previous literature reviews that have discussed the acute effects of THC on working memory (7–12). Importantly, these reviews included two systematic reviews of the effects of THC on behavioral performance. Both papers included a section on the acute effects of THC on working memory performance. Zuurman and colleagues (12) systematically reviewed the literature up until 15 Nov 2007. Broyd and colleagues (11) systematically reviewed the literature from 2004 until February 2015. To supplement these 2 systematic reviews, we performed a mini-systematic review of studies published from 1 Jan 2015 – 29 August 2019. In this mini-review, we searched Scopus for articles (English-language only) containing a word related to a THC manipulation (“cannabis” or “tetrahydrocannabinol”, or “marijuana” or “marihuana”) and a working memory task (“digit span”, “digit recall”, “working memory”, “n-back”, “short-term memory”, or “immediate memory”). To reduce the number of results, we excluded the exact keywords “Nonhuman” and “Animals”.

Beginning with the cited systematic and qualitative reviews, we examined papers cited as containing a working memory task and then looked at the forward- and backwards-citations of these papers for other relevant papers. Working memory task results were often part of a larger test battery and often yielded a null result, so these measures were often not reported in the abstract and reported in a single line (e.g. “no other measures showed significant effects”). We focused, in particular, on finding all studies using the Digit Span task and the Spatial N-back task, which were overwhelmingly the most commonly used tasks. We also include a summary of studies using other commonly used tasks (particularly, visual working memory tasks), but chose not to include some older tasks (e.g., Serial Sevens).

Some studies have been previously discussed in review papers but did not meet our inclusion criteria. For example, Heishman et al. (13) has typically been included in reviews on the acute effects of THC on working memory / cognitive performance (7, 8), but this paper does not report any group-level statistics for the working memory task. They reported that “2 out of 3 subjects showed impairment” but did not quantify this impairment formally at the individual or the group level. Thus, this paper did not meet the inclusion criteria for our literature review. Likewise, other studies cited in some previous reviews did not control for the effects of time on task performance (i.e. they did not counterbalance the administration of THC and placebo).

Many studies that administered THC via cigarette reported the percentage of THC contained in 1 cigarette. To make comparisons across studies easier, we have included the estimated mg of THC in the cigarette that was smoked by participants based on an estimated cigarette weight of 800 mg, based on published work on the weight of NIDA-supplied cigarettes (14). Note, in some studies participants consumed THC as a function of the number of “puffs”. For these studies we cannot report administered THC in mg, as the exact conversion is unknown. We have chosen to include studies in which THC was ingested, smoked, or administered intravenously. In addition, some THC was synthetic (e.g. Dronabinol or Marinol®) and some was

“natural” (e.g. cannabis plant). Previous work has shown that the subjective and physiological effects are comparable for synthetic and natural THC (15). The time course is much slower for ingested THC relative to smoked THC for a comparable dose (e.g. ~8 mg), but the subjective and physiological effects at the peak response are comparable (15). Conversely, a smaller intravenous dose yields stronger physiological and subjective responses relative to an equivalent weight of smoked THC (e.g. 5 mg intravenous vs. 14 mg smoked), but the time course of intravenous and smoked THC is roughly equivalent (16).

SI Results

Literature search

Conditions that were reported separately appear as separate lines in the tables below. For example, most studies separately reported the statistics for forward span versus backward span, and most studies separately reported the statistics for the different doses administered to participants. Because of inconsistent reporting standards across studies, it was not possible to recalculate effects when collapsed across all conditions or to calculate effect sizes for each condition. Where possible, we present exact *p*-values. However, *p*-values were rounded to *p* < .01, *p* < .05, and “not significant” (n.s.) in the vast majority of studies.

Digit span and recall tasks. We found a total of 21 papers that reported a measure of digit span or digit recall and met our inclusion criteria (Table S1). Of these, 15 included a Forward Digit Span Task or a Backward Digit Span Task (17–31). These 15 studies contained a total of 57 conditions (e.g. different drug doses).

Table S1. Literature summary of within-subjects, placebo-controlled studies testing Working Memory with a Digit Span (“Span”) or Digit Recall (“Recall”) Task.

Study	Ref.	n	Route	Task	Condition - Task	Condition - Dose	<i>p</i> -value
Tinklenberg et al. 1970	(17)	8	Oral	Span	Forward	20 mg	< .05
						40 mg	< .05
						60 mg	< .05
					Backward	20 mg	<.01
						40 mg	<.01
						60 mg	<.01
Melges et al. 1970	(18)	8	Oral	Span	Forward	Mean: 20, 40, 60 mg	0.05
					Backward	Mean: 20, 40, 60 mg	0.01
Tinklenberg et al. 1972	(32)	15	Oral	Recall	Forward (10 - 20 digits)	26 mg	n.s.
Dornbush & Kokkevi (1976)	(31)	20	Cigarette	Span	Forward	78 mg cannabis leaf, percentage THC not reported (30 minutes)	n.s.
						78 mg cannabis leaf, percentage THC not reported (70 minutes)	n.s.
					Backward	78 mg cannabis leaf, percentage THC not reported (30 minutes)	n.s.
						78 mg cannabis leaf, percentage THC not reported (70 minutes)	n.s.

McDonald et al. 2003	(19)	37	Oral	Span	Forward	7.5 mg	n.s.
						15 mg	n.s.
					Backward	7.5 mg	<.05
						15 mg	<.05
Ballard & de Wit 2011	(20)	11	Oral	Span	Forward	2.5 mg	n.s.
					Backward	2.5 mg	n.s.
Casswell et al. 1973	(21)	12	Cigarette	Span	Forward	3.3. mg	n.s.
						6.6 mg	n.s.
					Backward	3.3 mg	n.s.
						6.6 mg	n.s.
Galanter et al. 1973	(33)	12	Cigarette	Recall	Forward (9 digits)	10 mg "natural"	p<.01
						10 mg synthetic	p<.05
					Backward (9 digits)	10 mg "natural"	p<.01
						10 mg synthetic	p<.01
Cappell & Pliner 1973	(34)	20	Cigarette	Recall	Backward (9 digits)	12 mg	n.s.
Hooker & Jones 1987	(22)	12	Cigarette	Span	Forward	10.7 mg	n.s.
					Backward	10.7 mg THC	n.s.
Chait et al. 1988	(23)	8	Cigarette	Span	Forward	0 to 8 cumulative puffs, 1.4% THC	p<.01
Heishman et al. 1989	(24)	12	Cigarette	Span	Forward	1.3% THC (~10 mg)	p<.01
						2.7% THC (~22 mg)	n.s.
					Backward	1.3% THC (~10 mg)	n.s.
						2.7% THC (~22 mg)	p<.01
Zacny & Chait 1991	(25)	10	Cigarette	Span	Backward	4 puffs 2.3% THC (0 or 20 sec Breathhold Duration)	n.s.
Azorlosa et al. 1992	(26)	7	Cigarette	Span	Forward	4 puffs 1.75 % THC	n.s.
						10 puffs 1.75% THC	n.s.
						25 puffs 1.75% THC	n.s.
						4 puffs 3.55% THC	n.s.
						10 puffs 3.55% THC	n.s.
					Backward	25 puffs 3.55% THC	<.05
						4 puffs 1.75 % THC	n.s.
						10 puffs 1.75% THC	n.s.
						25 puffs 1.75% THC	n.s.
						4 puffs 3.55% THC	n.s.
Chait & Perry 1994	(27)	14	Cigarette	Span	Backward	10 puffs 3.55% THC	s
						10 puffs 3.55% THC	s
						25 puffs 3.55% THC	n.s.
						3.6% THC (~29 mg)	n.s.
Azorlosa et al. 1995	(28)	7	Cigarette	Span	Forward	10 puffs 1.75% THC, 30 - 90 ml puff volume	n.s.
						10 puffs, 3.55% THC, 30 -90 mL puff volume	n.s.
				Span		10 puffs 1.75% THC, 0 - 20 sec Breathhold Duration	n.s.
						10 puffs, 3.55% THC, 0 - 20 sec Breathhold Duration	n.s.
				Span		Backward	10 puffs 1.75% THC, 30 - 90 ml puff volume

						10 puffs, 3.55% THC, 30 -90 mL puff volume	n.s.
				Span		10 puffs 1.75% THC, 0 - 20 sec Breathhold Duration	n.s.
						10 puffs, 3.55% THC, 0 - 20 sec Breathhold Duration	n.s.
Fant et al. 1998	(35)	10	Cigarette	Recall	Recall missing digit (9 digits)	1.8% THC (~14.4 mg)	n.s.
						3.6% THC (~29 mg)	n.s.
Greenwald & Stitzer 2000	(36)	5	Cigarette	Span	Combined	18 puffs, 3.6% THC	0.08
Hart et al. 2001	(29)	18	Cigarette	Span	Forward	1.8% THC (~14.4 mg)	n.s.
						3.6% THC (~29 mg)	n.s.
					Backward	1.8% THC (~14.4 mg)	n.s.
						3.6% THC (~29 mg)	n.s.
				Recall	1 trial of 8 digit recall	1.8% THC (~14.4 mg)	n.s.
						3.6% THC (~29 mg)	<.05
Ramesh et al. 2013	(37)	18	Cigarette	Recall	1 trial of 8 digit recall	2 puffs 5.5%-6.2% THC	n.s.
						4 puffs 5.5%-6.2% THC	n.s.
						6 puffs 5.5%-6.2% THC	n.s.
Morrison et al. 2009	(30)	19	Intravenous	Span	Forward	2.5 mg	p<.05
					Backward	2.5 mg	p<.005

Spatial n-back task. We found a total of 9 papers that reported the results of a spatial n-back task and met our inclusion criteria (Table S2).

Table S2. Literature summary of within-subjects, placebo-controlled studies testing Working Memory with a Spatial *n*-back Task.

Study	Year	n	Route	Dose	Condition - Task	p-value
Ilan et al. 2004	(38)	10	Cigarette	3.5% THC (~28 mg)	0-back	n.s.
					2-back	<.05
Ilan et al. 2005	(39)	23	Cigarette	Mean: 1.8% / 3.6% THC (~14/29 mg)	1-back, 0:20 min	<.05
					1-back, 1:20 min	n.s.
					1-back, 2:20 min	n.s.
					2-back, 0:20 min	<.05
					2-back, 1:20 min	<.05
					2-back, 2:20 min	<.05
Hart et al. 2010	(40)	24	Cigarette	1.8% THC (~14.4 mg)	1-back	n.s.
					2-back	n.s.
				3.9% THC (~31 mg)	1-back	n.s.
					2-back	n.s.
Dumont et al. 2011	(41)	16	Vapor	4 + 6 + 6 mg (90 min intervals)	1-back	<.01
					2-back	n.s.
					3-back	n.s.
Morrison et al. 2011	(42)	16	Intravenous	1.25 mg	Main effect: 0-, 1- and 2- back	.11
Desrosiers et al. 2015	(43)	25	Cigarette	6.8% THC (54 mg)	1-back	n.s.
					2-back	<.05
					3-back	n.s.

Mokrysz et al. 2016	(44)	40	Vapor	.1068 mg / kg (M = ~7.5 mg)	Main effect: 0-, 1- and 2- back	<.001
Hindocha et al. 2017	(45)	24	Cigarette	66.7 mg Bedrobinol (10.7 mg THC)	0-back	n.s.
					1-back	.018
					2-back	<.001
Morgan et al. 2018	(46)	48	Vapor	8 mg THC	Main effect: 1- and 2-back	.012

Other tasks. In Table S3 we report other papers that we include a working memory task (or a task thought to have a considerable working memory component). These papers include all of the miscellaneous visual working memory tasks that we could find (Visual N-back (letters), Memory-Guided Saccade, Delayed Match to Sample, Sternberg Task, Spatial Span, and the CANTAB Spatial Working Memory Task). Some prior work, e.g., Curran et al.(47), has used tasks such as the Serial Sevens Task and a Rapid Visual Information Processing Task; we consider these tasks to be less conventional measures of working memory capacity, and we did not include the Serial Sevens or the Rapid Visual Information Processing Task in our search (but see (8) for more).

Table S3. Literature summary of other visual working memory and working memory tasks.

Study	Ref.	n	Route	Condition - Dose	Task	Condition - Task	p-value
Kollins et al. 2015	(48)	16	Oral	10 mg	Visual N-Back (Letters)	0-back	n.s.
						1-back	n.s.
						2-back	n.s.
						3-back	n.s.
Gilman et al. 2019	(49)	54	Oral	5 – 50 mg (M = 37.8 mg)	Visual N-back (Letters)	Main effect of 0-, and 2- back	n.s., .39
Ploner et al. 2002	(50)	12	Oral	10 mg	Memory Guided Saccade	N/A	* <.05
D'Souza et al. 2004	(51)	22	Intravenous	2.5 mg or 5 mg	Delayed Match to Sample	1-item, "simple shape"	0.02
						1-item, "complex shape"	n.s., 0.28
Lane et al. 2005	(52)	5	Cigarette	2.2% THC (~18 mg)	Delayed Match to Sample	1-item color precision	*** < .001
				3.6% THC (~29 mg)			*** < .001
Makela et al. 2006	(53)	19	Oral	5 mg	Spatial Span	Forward	n.s.
Foltin et al. 1993	(54)	7	Cigarette	27 mg	Sternberg Task	Set Sizes 1 – 6	n.s.
Bossong et al. 2012	(55)	17	Vapor	6 mg, then 3 doses of 1 mg (30 min interval)	Sternberg Task	Set Size 1	n.s.
						Set Size 3	* <.05
						Set Size 5	* <.05
						Set Size 7	n.s., <.10
						Set Size 9	n.s.

Theunissen et al. 2015	(56)	15	Vapor	.138 mg/kg (M = ~9.3 mg)	Sternberg Task	Set Sizes 1, 2, & 4	n.s.
Ranganathan et al. 2019	(57)	74	Intravenous	.05 mg/kg	CANTAB Spatial Working Memory Task	Total errors combined for set sizes 4+ (other set sizes not reported)	*** < .001

(31)

Demographic information, subjective measures, and physiological measures

Demographic characteristics of participants are shown in Table S4. Mean values for each of the physiological and subjective measures are shown in Tables S5 and S6.

Table S4. Demographic data for Exps 1 and 2.

	Experiment 1	Experiment 2
<i>Age (years)</i>	22.70 (.72)	23.52 (.90)
<i>Education (years)</i>	15.13 (.35)	15.57 (.33)
<i>BMI</i>	24.77 (.76)	23.31 (.43)
<i>Caffeine (cups/day)</i>	1.43 (.28); n = 22	1.69 (0.22); n = 21
<i>Nicotine (cigarettes/day in the five users)</i>	.19 (.07); n = 5	2.80 (0.85); n = 5
<i>Alcohol (drinks/week)</i>	6.57 (1.38); n = 21	8.61 (1.65); n = 21
<i>Cannabis (uses/month)</i>	2.11 (.35); n = 9	7.67 (1.86); n = 13
<i>Lifetime uses of Cannabis</i>	27.13 (5.27); n = 23	641.19 (470.95); n = 21
<i>Last use of cannabis before Placebo session (days)</i>	118.61 (41.48); n = 23	7.82 (1.82); n = 17
<i>Last use of cannabis before THC session (days)</i>	116.20 (41.48); n = 23	6.76 (.98); n = 17 10.67 (1.69); n = 18

Age, education, and past month recent substance use are listed as mean (SEM). For recent substance use, the mean and SEM were calculated using only subjects who reported any recent use of the drug (n for each drug type is shown). Two subjects in Exp 2 had missing data for the lifetime use of Cannabis question. Remaining participants reported no recent use of the drugs.

Table S5. Values for heart rate and subjective measure in Exp 1 and Exp 2. Scores are change scores for at the time of the working memory test relative to baseline. Bonferonni corrections are done within measure (3 comparisons for heart rate + blood pressure; 5 comparisons for DEQ).

	Exp 1			Exp 2			
	Placebo	High (15 mg)	$p_{\text{uncorrected}}$ ($p_{\text{bonferroni}}$)	Placebo	Low (7.5 mg)	High (15 mg)	$p_{\text{uncorrected}}$ ($p_{\text{bonferroni}}$)
Physiological							
Heart Rate	-7.77 (9.25)	0.73 (11.50)	.002 (.006)	-8.22 (7.27)	-4.57 (12.42)	6.48 (12.59)	<.001 (<.001)
Systolic Blood Pressure	-2.46 (10.92)	0.55 (7.97)	.31 (.93)	-3.04 (9.44)	-1.57 (9.97)	-2.13 (11.95)	.875 (1.0)
Diastolic Blood Pressure	-1.86 (8.04)	-0.09 (9.25)	.53 (1.0)	0.04 (9.44)	1.83 (15.82)	-2.00 (9.32)	.51 (1.0)
ARCI	.41 (1.47)	4.73 (3.45)	<.001	.27 (.83)	2.18 (2.72)	3.59 (2.89)	<.001
DEQ							
Feel	4.55 (7.45)	45.73 (30.96)	<.001 (<.001)	2.86 (6.97)	24.41 (30.14)	37.23 (30.28)	<.001 (<.001)
Like	11.41 (21.73)	34.05 (31.37)	.001 (.005)	11.82 (24.42)	34.86 (28.58)	30.64 (27.99)	<.001 (<.001)
Dislike	8.73 (18.06)	26.09 (26.45)	.006 (.03)	6.32 (14.30)	16.50 (23.20)	33.82 (32.63)	.002 (.01)
High	3.05 (8.57)	41.91 (30.47)	<.001 (<.001)	1.82 (4.99)	26.09 (31.11)	38.82 (31.71)	<.001 (<.001)
More	7.55 (17.79)	20.64 (21.80)	.002 (.01)	10.09 (22.24)	18.36 (24.39)	14.95 (23.58)	.197 (.985)

Table S6. Values for the Visual Analog Scales (VAS) in Exp 1. Scores are change scores for at the time of the working memory test relative to baseline. Bonferroni corrections are for the 13 comparisons in the VAS measure.

VAS	Placebo	High (15 mg)	p _{uncorrected}	p _{bonferroni}
Anxious	-7.78 (31.26)	3.59 (13.19)	.15	1.0
Stimulated	-8.73 (26.85)	15.32 (27.92)	.02	.26
Sedated	-3.91 (35.16)	-4.14 (25.42)	.98	1.0
Elated	-12.68 (25.83)	7.86 (28.63)	.05	.65
Insightful	-10.91 (28.29)	11.27 (28.53)	.04	.52
Sociable	-12.86 (19.12)	9.77 (22.51)	.001	.013
Confident	-9.41 (23.00)	6.91 (22.75)	.02	.26
Lonely	-3.09 (23.73)	1.59 (10.45)	.44	1.0
Playful	-11.82 (21.41)	14.96 (26.51)	.004	.052
Dizzy	-6.86 (25.17)	4.73 (23.66)	.17	1.0
Loving	-5.09 (31.03)	6.27 (24.83)	.24	1.0
Friendly	-10.77 (27.62)	14.82 (24.94)	.003	.039
Restless	-7.55 (38.98)	8.27 (29.31)	.11	1.0

References

1. W. R. Martin, J. W. Sloan, J. D. Sapira, D. R. Jasinski, Physiologic, subjective, and behavioral effects of amphetamine, methamphetamine, ephedrine, phenmetrazine, and methylphenidate in man. *Clin. Pharmacol. Ther.* **12**, 245–258 (1971).
2. C. A. Haertzen, Development of Scales Based on Patterns of Drug Effects, Using the Addiction Research Center Inventory (ARCI). *Psychological Reports* **18**, 163–194 (1966).
3. L. D. Chait, M. W. Fischman, C. R. Schuster, ‘Hangover’ effects the morning after marijuana smoking. *Drug and Alcohol Dependence* **15**, 229–238 (1985).
4. M. E. Morean, *et al.*, The drug effects questionnaire: psychometric support across three drug types. *Psychopharmacology* **227**, 177–192 (2013).
5. M. F. Folstein, R. Luria, Reliability, validity, and clinical application of the visual analogue mood scale¹. *Psychological Medicine* **3**, 479 (1973).
6. M. K. Doss, J. Weafer, D. A. Gallo, H. de Wit, Δ 9-Tetrahydrocannabinol at Retrieval Drives False Recollection of Neutral and Emotional Memories. *Biological Psychiatry* (2018) <https://doi.org/10.1016/j.biopsych.2018.04.020> (June 25, 2018).
7. N. P. Vadhan, M. R. Serper, M. Haney, Effects of Δ -THC on Working Memory: Implications for Schizophrenia? *Prim psychiatry* **16**, 51–99 (2009).

8. M. Ranganathan, D. C. D'Souza, The acute effects of cannabinoids on memory in humans: a review. *Psychopharmacology* **188**, 425–444 (2006).
9. H. V. Curran, *et al.*, Keep off the grass? Cannabis, cognition and addiction. *Nature Reviews Neuroscience* **17**, 293–306 (2016).
10. L. D. Chait, J. Pierri, “Effects of smoked marijuana on human performance: A critical review” in *Marijuana/Cannabinoids: Neurobiology and Neurophysiology*, L. Murphy, A. Bartke, Eds. (1992), pp. 387–423.
11. S. J. Broyd, H. H. van Hell, C. Beale, M. Yücel, N. Solowij, Acute and Chronic Effects of Cannabinoids on Human Cognition—A Systematic Review. *Biological Psychiatry* **79**, 557–567 (2016).
12. L. Zuurman, A. E. Ippel, E. Moin, J. M. A. van Gerven, Biomarkers for the effects of cannabis and THC in healthy volunteers. *British Journal of Clinical Pharmacology* **67**, 5–21 (2009).
13. S. J. Heishman, M. A. Huestis, J. E. Henningfield, E. J. Cone, Acute and residual effects of marijuana: Profiles of plasma THC levels, physiological, subjective, and performance measures. *Pharmacology Biochemistry and Behavior* **37**, 561–565 (1990).
14. L. D. Chait, J. Pierri, Some physical characteristics of NIDA marijuana cigarettes. *Addict Behav* **14**, 61–67 (1989).
15. S. R. Wachtel, M. A. ElSohly, S. A. Ross, J. Ambre, H. de Wit, Comparison of the subjective effects of Δ 9-tetrahydrocannabinol and marijuana in humans. *Psychopharmacology* **161**, 331–339 (2002).
16. J. E. Lindgren, A. Ohlsson, S. Agurell, L. Hollister, H. Gillespie, Clinical effects and plasma levels of delta 9-tetrahydrocannabinol (delta 9-THC) in heavy and light users of cannabis. *Psychopharmacology (Berl.)* **74**, 208–212 (1981).
17. J. R. Tinklenberg, F. T. Melges, L. E. Hollister, H. K. Gillespie, Marijuana and Immediate Memory. *Nature* **226**, 1171–1172 (1970).
18. F. T. Melges, J. R. Tinklenberg, L. E. Hollister, H. K. Gillespie, Marijuana and Temporal Disintegration. *Science* **168**, 1118–1120 (1970).
19. J. McDonald, L. Schleifer, J. B. Richards, H. de Wit, Effects of THC on Behavioral Measures of Impulsivity in Humans. *Neuropsychopharmacology* **28**, 1356–1365 (2003).

20. M. E. Ballard, H. de Wit, Combined effects of acute, very-low-dose ethanol and delta(9)-tetrahydrocannabinol in healthy human volunteers. *Pharmacology Biochemistry and Behavior* **97**, 627–631 (2011).
21. S. Casswell, D. F. Marks, Cannabis and Temporal Disintegration in Experienced and Naive Subjects. *Science* **179**, 803–805 (1973).
22. W. D. Hooker, R. T. Jones, Increased susceptibility to memory intrusions and the Stroop interference effect during acute marijuana intoxication. *Psychopharmacology* **91**, 20–24 (1987).
23. L. D. Chait, R. L. Corwin, C. E. Johanson, A cumulative dosing procedure for administering marijuana smoke to humans. *Pharmacology Biochemistry and Behavior* **29**, 553–557 (1988).
24. S. J. Heishman, M. L. Stitzer, J. E. Yingling, Effects of tetrahydrocannabinol content on marijuana smoking behavior, subjective reports, and performance. *Pharmacology Biochemistry and Behavior* **34**, 173–179 (1989).
25. J. P. Zacny, L. D. Chait, Response to marijuana as a function of potency and breathhold duration. *Psychopharmacology* **103**, 223–226 (1991).
26. J. L. Azorlosa, S. J. Heishman, M. L. Stitzer, J. M. Mahaffey, Marijuana smoking: effect of varying delta 9-tetrahydrocannabinol content and number of puffs. *J. Pharmacol. Exp. Ther.* **261**, 114–122 (1992).
27. L. D. Chait, J. L. Perry, Acute and residual effects of alcohol and marijuana, alone and in combination, on mood and performance. *Psychopharmacology* **115**, 340–349 (1994).
28. J. L. Azorlosa, M. K. Greenwald, M. L. Stitzer, Marijuana smoking: effects of varying puff volume and breathhold duration. *J. Pharmacol. Exp. Ther.* **272**, 560–569 (1995).
29. C. Hart, Effects of Acute Smoked Marijuana on Complex Cognitive Performance. *Neuropsychopharmacology* **25**, 757–765 (2001).
30. P. D. Morrison, *et al.*, The acute effects of synthetic intravenous Δ 9-tetrahydrocannabinol on psychosis, mood and cognitive functioning. *Psychological Medicine* **39**, 1607 (2009).
31. R. L. Dornbush, A. Kokkevi, ACUTE EFFECTS OF CANNABIS ON COGNITIVE, PERCEPTUAL, AND MOTOR PERFORMANCE IN CHRONIC HASHISH USERS. *Ann NY Acad Sci* **282**, 313–322 (1976).

32. J. R. Tinklenberg, Marihuana and Alcohol: Time Production and Memory Functions. *Archives of General Psychiatry* **27**, 812 (1972).
33. M. Galanter, δ 9-Transetrahydrocannabinol and Natural Marihuana: A Controlled Comparison. *Archives of General Psychiatry* **28**, 278 (1973).
34. H. D. Cappell, P. L. Pliner, Volitional control of marijuana intoxication: A study of the ability to “come down” on command. *Journal of Abnormal Psychology* **82**, 428–434 (1973).
35. R. V. Fant, S. J. Heishman, E. B. Bunker, W. B. Pickworth, Acute and residual effects of marijuana in humans. *Pharmacol. Biochem. Behav.* **60**, 777–784 (1998).
36. M. K. Greenwald, M. L. Stitzer, Antinociceptive, subjective and behavioral effects of smoked marijuana in humans. *Drug Alcohol Depend* **59**, 261–275 (2000).
37. D. Ramesh, M. Haney, Z. D. Cooper, Marijuana’s dose-dependent effects in daily marijuana smokers. *Experimental and Clinical Psychopharmacology* **21**, 287–293 (2013).
38. A. B. Ilan, M. E. Smith, A. Gevins, Effects of marijuana on neurophysiological signals of working and episodic memory. *Psychopharmacology* **176**, 214–222 (2004).
39. A. B. Ilan, A. Gevins, M. Coleman, M. A. ElSohly, H. de Wit, Neurophysiological and subjective profile of marijuana with varying concentrations of cannabinoids: *Behavioural Pharmacology* **16**, 487–496 (2005).
40. C. L. Hart, *et al.*, Neurophysiological and cognitive effects of smoked marijuana in frequent users. *Pharmacology Biochemistry and Behavior* **96**, 333–341 (2010).
41. G. Dumont, *et al.*, Acute psychomotor, memory and subjective effects of MDMA and THC co-administration over time in healthy volunteers. *Journal of Psychopharmacology* **25**, 478–489 (2011).
42. P. D. Morrison, *et al.*, Disruption of Frontal Theta Coherence by Δ 9-Tetrahydrocannabinol is Associated with Positive Psychotic Symptoms. *Neuropsychopharmacol* **36**, 827–836 (2011).
43. N. A. Desrosiers, J. G. Ramaekers, E. Chauchard, D. A. Gorelick, M. A. Huestis, Smoked Cannabis’ Psychomotor and Neurocognitive Effects in Occasional and Frequent Smokers. *Journal of Analytical Toxicology* **39**, 251–261 (2015).
44. C. Mokrysz, T. P. Freeman, S. Korkki, K. Griffiths, H. V. Curran, Are adolescents more vulnerable to the harmful effects of cannabis than adults? A placebo-controlled study in human males. *Translational Psychiatry* **6**, e961–e961 (2016).

45. C. Hindocha, T. P. Freeman, J. X. Xia, N. D. C. Shaban, H. V. Curran, Acute memory and psychotomimetic effects of cannabis and tobacco both 'joint' and individually: a placebo-controlled trial. *Psychological Medicine* **47**, 2708–2719 (2017).
46. C. J. A. Morgan, *et al.*, Individual and combined effects of acute delta-9-tetrahydrocannabinol and cannabidiol on psychotomimetic symptoms and memory function. *Transl Psychiatry* **8**, 181 (2018).
47. V. Curran, C. Brignell, S. Fletcher, P. Middleton, J. Henry, Cognitive and subjective dose-response effects of acute oral Δ 9 -tetrahydrocannabinol (THC) in infrequent cannabis users. *Psychopharmacology* **164**, 61–70 (2002).
48. S. H. Kollins, *et al.*, An exploratory study of the combined effects of orally administered methylphenidate and delta-9-tetrahydrocannabinol (THC) on cardiovascular function, subjective effects, and performance in healthy adults. *Journal of Substance Abuse Treatment* **48**, 96–103 (2015).
49. J. M. Gilman, *et al.*, Delta-9-tetrahydrocannabinol intoxication is associated with increased prefrontal activation as assessed with functional near-infrared spectroscopy: A report of a potential biomarker of intoxication. *NeuroImage* **197**, 575–585 (2019).
50. C. J. Ploner, *et al.*, Oculomotor effects of delta-9-tetrahydrocannabinol in humans: implications for the functional neuroanatomy of the brain cannabinoid system. *Cereb. Cortex* **12**, 1016–1023 (2002).
51. D. C. D'Souza, *et al.*, The Psychotomimetic Effects of Intravenous Delta-9-Tetrahydrocannabinol in Healthy Individuals: Implications for Psychosis. *Neuropsychopharmacology* **29**, 1558–1572 (2004).
52. S. D. Lane, D. R. Cherek, L. M. Lieving, O. V. Tcheremissine, Marijuana Effects On Human Forgetting Functions. *Journal of the Experimental Analysis of Behavior* **83**, 67–83 (2005).
53. P. Makela, *et al.*, Low Doses of Δ -9 Tetrahydrocannabinol (THC) Have Divergent Effects on Short-Term Spatial Memory in Young, Healthy Adults. *Neuropsychopharmacology* **31**, 462–470 (2006).
54. R. W. Foltin, M. W. Fischman, P. A. Pippen, T. H. Kelly, Behavioral effects of cocaine alone and in combination with ethanol or marijuana in humans. *Drug and Alcohol Dependence* **32**, 93–106 (1993).
55. M. G. Bossong, *et al.*, Effects of Δ 9-Tetrahydrocannabinol on Human Working Memory Function. *Biological Psychiatry* **71**, 693–699 (2012).

56. E. L. Theunissen, *et al.*, Rivastigmine but not vardenafil reverses cannabis-induced impairment of verbal memory in healthy humans. *Psychopharmacology* **232**, 343–353 (2015).
57. M. Ranganathan, *et al.*, Highs and lows of cannabinoid-dopamine interactions: effects of genetic variability and pharmacological modulation of catechol-O-methyl transferase on the acute response to delta-9-tetrahydrocannabinol in humans. *Psychopharmacology* (2019) <https://doi.org/10.1007/s00213-019-05273-5> (August 31, 2019).