Experimental and Clinical Psychopharmacology

Residual Effects of Cannabis Use on Neurocognitive Performance After Prolonged Abstinence: A Meta-Analysis

Amy M. Schreiner and Michael E. Dunn

Online First Publication, June 25, 2012. doi: 10.1037/a0029117

Experimental and Clinical Psychopharmacology

1064-1297/12/$12.00 DOI: 10.1037/a0029117

Residual Effects of Cannabis Use on Neurocognitive Performance After Prolonged Abstinence: A Meta-Analysis

Amy M. Schreiner and Michael E. Dunn
University of Central Florida

Cannabis is the most widely used illicit drug in the U.S., and the number of illicit and licit users is rising. Lasting neurocognitive changes or deficits as a result of use are frequently noted despite a lack of clarity in the scientific literature. In an effort to resolve inconsistencies in the evidence of lasting residual effects of cannabis use, we conducted two meta-analyses. First, we updated a previous meta-analysis on broad nonacute cognitive effects of cannabis use through inclusion of newer studies. In a second meta-analysis, we focused on evidence for lasting residual effects by including only studies that tested users after at least 25 days of abstinence. In the first meta-analysis, 33 studies met inclusion criteria. Results indicated a small negative effect for global neurocognitive performance as well for most cognitive domains assessed. Unfortunately, methodological limitations of these studies prevented the exclusion of withdrawal symptoms as an explanation for observed effects. In the second meta-analysis, 13 of the original 33 studies met inclusion criteria. Results indicated no significant effect of cannabis use on global neurocognitive performance or any effect on the eight assessed domains. Overall, these meta-analyses demonstrate that any negative residual effects on neurocognitive performance attributable to either cannabis residue or withdrawal symptoms are limited to the first 25 days of abstinence. Furthermore, there was no evidence for enduring negative effects of cannabis use.

Keywords: cannabis, marijuana, residual effects, neurocognitive, meta-analysis

The potential for negative effects of cannabis use has been a topic of great interest across scientific disciplines. Cannabis is the most commonly used illicit drug in the U.S. with estimates of 17.4 million current users; an increase of 3 million since 2007 (SAMSHA, 2011). In addition to those using cannabis illicitly, millions of additional individuals consume the drug for medical reasons. As of the end of 2011, 16 states in the U.S. had medical marijuana laws in effect, and many other states were seeking similar legislation. With the number of cannabis users both illicitly and licitly increasing, the question of any potential lasting impact from cannabis use is increasingly important.

While cannabis consists of a large number of cannabinoids, delta-9-tetrahydrocannabinol (typically referred to as "THC" among users, and "Δ-9-THC" among scientists) is the compound thought to be the primary source of effects experienced by users (Grotenhermen, 2003) as well as the likely cause of lasting cognitive effects, if any lasting effects exist. During acute cannabis intoxication, several neurocognitive effects have been regularly identified including effects on learning and memory performance, with mixed evidence for effects on attention, inhibition, and executive functioning (for reviews see Crean, Crane, & Mason, 2011; Gonzalez, 2007; Ranganathan & D'Souza, 2006). While acute intoxication can last several hours, THC is also a fat soluble compound that can be stored in body fat and slowly released into the bloodstream for months (Ellis, Mann, Judson, Schramm, & Taschian, 1985; Grotenhermen, 2003). This characteristic is one element that has encouraged research evaluating potential "residual" neurocognitive effects.

"Residual effects" are those effects observed after acute intoxication has passed, and early attempts to measure residual neurocognitive effects of cannabis use resulted in mixed findings. Several studies were unable to find cognitive effects among moderate to heavy cannabis users (Bowman & Pihl, 1973; Carlin & Trupin, 1977; Grant, Rochford, Fleming, & Stunkard, 1973). Other studies, however, found residual effects on verbal memory, attention, speed and accuracy, and perceptual-motor tasks among cannabis users when compared to controls (Entin & Goldzung, 1973; Fletcher et al., 1996; Soueif, 1976; Varma, Malhotra, Dang, Das, & Nehra, 1988). In a review of empirical literature on residual effects of cannabis, major methodological problems afflicting most of the existing research were identified and may explain these seemingly inconsistent findings (Pope, Gruber, & Yurgelun-Todd, 1995). Problems included failure to specify the abstinence period, confounding variables poorly controlled for (e.g., other drug use, psychiatric symptoms), and testing of participants was not always blind. In addition, the authors emphasized the need to distinguish

Amy M. Schreiner and Michael E. Dunn, Department of Psychology, University of Central Florida.

The current study received no outside financial support or funding during its completion. All authors contributed to the completion of the research and present article. They have all read and approved the final article. The authors have no conflicts of interest that may have impacted the research findings or interpretations. The authors acknowledge their affiliated institute for providing the necessary resources to complete the current study and resultant article (e.g., database access, computers and office space, etc.).

Correspondence concerning this article should be addressed to Michael E. Dunn, PhD, Department of Psychology, P.O. Box 161390, University of Central Florida, Orlando, FL 32816-1390. E-mail: Michael.Dunn@ucf.edu

between two types of potential "residual" effects; active THC metabolites that affect the CNS; and effects that persist after THC and active metabolites have left the body. Overall, the authors concluded that there was a lack of sufficient research into lasting cognitive impacts of cannabis use to draw any conclusions (Pope et al., 1995 p.32). More recent reviews, however, have concluded that there may be evidence for lasting detrimental effects (e.g., Crean et al., 2011; Solowij & Battisti, 2008).

Narrative reviews are inherently limited by the subjectivity of their conclusions and estimates of magnitude and consistency of effects cannot be made (Borenstein, Hedges, Higgins, & Rothstein, 2009). Meta-analysis addresses narrative review limitations by statistically synthesizing data using effect sizes from multiple studies to calculate a summary effect (Borenstein et al., 2009). To date, only one meta-analysis has been focused on evaluating residual neurocognitive effects of cannabis use (Grant, Gonzalez, Carey, Natarajan, & Wolfson, 2003). Using selection criteria that addressed a number of the concerns enumerated by Pope et al. (1995), a global neuropsychological effect, as well as a summary effect for eight neuropsychological domains of functioning were calculated: abstraction/executive, attention, simple reaction time (RT), verbal/language, perceptual-motor, simple motor, learning, and forgetting/retrieval. Results of the meta-analysis revealed a small yet significant effect for global performance, and across domains, only revealed significant negative effects for learning and forgetting/retrieval. However, the abstention period for users across most studies was 72 hours or less prompting the authors to suggest that differences observed may have been largely attributable to the type of residual effect associated with drug residue in the users system instead of being indicative of lasting effects. One included study highlighting the importance of this distinction tested users and nonusers across a 28-day period of abstention and found that while differences were observed in the initial days of abstinence, these differences were no longer significant at Day 28 (Pope, Gruber, Hudson, Huestis, & Yurgelun-Todd, 2001, 2002). Overall, there were not enough studies at that time that measured the type of residual effects indicative of a permanent or very long-term impact on cognitive functioning.

In the present study, two meta-analyses of the empirical literature on cannabis-related residual effects on neurocognitive performance were conducted. First, we updated a previous meta-analysis on broad nonacute cognitive effects of cannabis use through inclusion of newer studies. In a second meta-analysis, we focused on evidence for lasting residual effects by including only studies that tested users after at least 25 days of abstinence. In order to increase generalizability across both investigations, the same rigorous selection criteria were used and effects were summarized globally as well as across the eight neuropsychological domains described previously. It is hypothesized that across all studies, there will be an inverse relationship between abstention time and impact on neurocognitive abilities such that the evidence of negative residual effects on cognitive performance among cannabis users, will disappear when looking at studies with a longer abstention period.

Method

In order to identify all relevant studies, a literature search was conducted using the online databases PsycInfo, PsycARTICLES, PubMed, and Medline. The search terms used were (*marijuana* or *marihuana* or *tetra-hydrocannabinol* or *THC* or *cannabis*) AND (*neuro** or *cognit** or *assess** or *abilit** or *effect** or *process** or *impair**) AND (*residual* or *long-term* or *abstinen** or *abstain** or *lasting* or *non-acute* or *persist**). Results were additionally limited to those published in a peer-reviewed journal and to those involving human subjects. The requirement of peer-review was put in place to increase transparency and replicability of results and to ensure studies included have met a minimum degree of methodological rigor (Rosenthal & DiMatteo, 2001). The resulting ~800 citations were evaluated for relevance by review of the title and abstract. The full-text of articles deemed relevant was obtained as well as those for which relevance could not be determined. The references of each full-text article obtained were reviewed for identification of additional studies missed during the database searches. This resulted in a total of 186 full-text articles to be reviewed for inclusion. The articles retained were then reviewed in more detail and categorized broadly based on their relevance. This process resulted in the elimination of 37 articles which were reviews; 25 articles which evaluated acute effects only or in which it was not specified; 13 articles which were brain imaging studies not including neuropsychological measures; 10 articles which were deemed not relevant (i.e., animal studies, case studies, effects of prenatal exposure, effects on emotional processing); and two which were evaluating specific psychiatric populations (i.e., schizophrenia and Tourette's syndrome).

The remaining studies were then reviewed for inclusion using the criteria detailed by Grant, Gonzalez, Carey, Natarajan, and Wolfson (2003): (a) study included a group of cannabis only users, (b) study included a control group consisting of nonusers or with very limited drug experience, (c) study reported necessary information to calculate effect size, (d) study used a valid behavioral measure of neuropsychological functioning, (e) participants are not under the influence of any substances during testing, (f) the use of other substances (past and present) is addressed, (g) history of psychiatric and neurological problems is addressed, (h) the period of abstinence from cannabis before testing is reported. These criteria were selected as they ensure the results of each study are sufficiently answering the research question and also to allow for generalizability across both meta-analyses. A total of 49 studies met all inclusion criteria. One study, Skosnik, Krishnan, Vohs, and O'Donnell (2006) reported results for males and females separately, and therefore these were treated as independent samples. There were also nine studies which shared a sample with another study meeting inclusion criteria. In these instances the samples were not treated as independent and instead combined within the meta-analysis (e.g., Kanayama et al., 2004; Pillay et al., 2004, 2008; Pope et al., 2001, 2002, 2003 all shared participants). Also, due to the significant increase in the number of studies meeting inclusion criteria and in efforts to avoid redundancy with the previous meta-analysis, the present study focused on studies published since 2000. For the overall meta-analysis, this resulted in a final set of 33 independent samples with data from 1,010 current or former cannabis users and 839 controls with no or very limited cannabis use history (see Table 1 for additional information regarding the samples of each included study). Of the total 33 studies meeting inclusion, 13 measured neurocognitive performance after approximately one month of absti-

Table 1
33 Independent Samples Meeting Inclusion Criteria

Study	Users	Control	Quantity/Frequency *M* (*SD*)	Duration *M* (*SD*)	Abstinence period *M* (*SD*)	Domains
[1]Bartholomew, Holroyd, & Heffernan (2010)	45	45	2 joints/week (median)	3 yrs (median)	10.5 days (median)	F
[2]Battisti et al. (2010a, 2010b)	24a; 25b	24a; 23b	435;450 cones/mth 30 days/mth (median)	17 (9.3) yrs 16.4 (9.6) yrs	13 hrs (median)	AE, F
[3]Block et al. (2002)	18	13	18(2)x/week	3.9 (0.4) yrs	≥ 24 hrs	L, F
[4]Chang et al. (2006)*[a]	12 THC−	19	THC−: 26.7 (1.4) day/mth	THC−: 138.8 (24.4) mths	THC−: 38 (18) mths	AE, A, L, F, M, PM, V
	12 THC+		THC+: 27.9 (1.1) day/mth	THC+: 147.6 (33.7) mths	THC+: 4–24 hrs [range]	
[5]Croft et al. (2001)	18	31	7,762.4 (14,480.9) lifetime joints	NR	66.5 (42.4) hrs	AE, A, L, F, M, V
[6]Eldreth et al. (2004)*	11	11	≥ 4x/week	≥ 2 yrs	25 days	AE
[7]Fontes et al. (2011)	107	44	1.8 (2.2) joints/day	9.9 (5.57) yrs	4.3 (6.3) days	AE, M, V
[8]Gouzoulis-Mayfrank et al. (2000)	28	28	20.9 (10.2) days/mth	2.9 (2.0) yrs	96 hrs	AE, A, L, F, PM, SRT, V
[9]Hermann et al. (2007)	13	13	0.7 (0.6) grams/day; 25 (3) days/mth	0.35 grams/day for past 5.6 yrs	29 (29.4) hrs	AE, A, F, PM, V
[10]Hester et al. (2009)	16	16	76.3 (17.7) joints/mth 19.2 (2.6) day/mth	8.2 (1.3) yrs	38.0 (47.7) hrs	AE, A, SRT
[11]Huestegge et al. (2002; 2009; 2010)	17; 20	20	10.5 joints/week	9 (7.4) yrs	30.9 (7.9) hrs	A, V
[12]Jacobsen et al. (2004)*Ψ	7	7	282.8 (523.1) days	NR	10.1 (10.2) mths	A
[13]Jacobsen et al. (2007)*Ψ	20	25	11.2 (10)x/week	NR	4.58 (7) mths	A, F
[14]Kelleher et al. (2004)	22	22	Daily use	4.5 (2.8) yrs	Tested before typical first use of the day	A
[15]Lyons et al. (2004)*	54	54	≥ 1x/week for 1 year; 916 (1,202) days/lifetime	5.8 (5.3) yrs	≥ 1 year since last use; 20 yrs since regular use	AE, A, L, F, M, PM, SRT, V
[16]Mahmood et al. (2010)*Ψ	65	65	16.03 (10.19) days/mth	NR	52.92 (67.36) days	L, F, PM
[17]Medina et al. (2007)*Ψ	31	34	540.64 (380.24) lifetime use episodes	2.91 (2.08) yrs/weekly use	≥ 28 days	AE, A, L, F, PM, V
[18]Messinis et al. (2006)	20 LT 20 ST	24	LT: 20.15 (2.92) days/mth ST: 20.7 (3.4) days/mth	LT: 15.6 (4.81) yrs ST: 6.95 (1.5) yrs	124.55 (76.36) hrs	AE, A, L, F, V
[19]Morgan et al. (2010)	36	38	2.3 (1.3) joints/session; 12.8 (5.1) days/mth	7.6 (5.8) yrs	2.2 (1.1) days	A
[20]Padula et al. (2007)*Ψ	17	17	477.06 (260.07) lifetime use episodes	NR	28 days	A, SRT
[21]Pope et al. (2001; 2002; 2003), Pillay et al. (2004; 2008), & Kanayama et al. (2004)*±	77	87	18,500 lifetime use [11,700–25,600] median and interquartile range	≥ 13 yrs	28 days	AE, L, F, PM, V
[22]Quednow et al. (2006)	19	19	3.89 (4.72)x/week	6.55 (3.67) yrs	6.55 (3.67) days	L, F
[23]Rodgers (2000)*	15	15	4 days/week	11 yrs	1 mth	A, L, F, SRT
[24]Schweinsburg et al. (2008) & Tapert et al. (2007)*±Ψ	15	17	480.7 (277.2) lifetime episodes; 13.5 (11.6) day/mth	2.7 (1.8) yrs since weekly use	60.4 (54.1) days	AE, A, SRT
[25]Schweinsburg et al. (2011)*Ψ	8	22	426.5 (280.1) lifetime episodes; 8.4 (9.3) day/mth	NR	117.6 (153.9) days	L, F
[26]Skosnik et al. (2001)	15	15	1.3x/week	NR	≥ 48 hrs	F, SRT
[27]Skosnik et al. (2006) Females	7	10	9.3 (13.4) joints/week	7.4 (2.1) yrs	≥ 24 hrs	AE, A, PM
[28]Skosnik et al. (2006) Males	7	10	11.2 (14.7) joints/week	7.9 (5.0) yrs	≥ 24 hrs	AE, A, PM
[29]Skosnik et al. (2008)	14	10	9.7 (6.0) joints/week	5.6 (3.5) yrs	≥ 24 hrs	AE, A, PM

Table 1 (*continued*)

Study	Users	Control	Quantity/Frequency *M* (*SD*)	Duration *M* (*SD*)	Abstinence period *M* (*SD*)	Domains
[30]Solowij et al. (2002)	51 LT 51 ST	33	2 joints/day; 27.9 [3.5–30] days/mth (median and range)	17.1 (7.9) yrs	17 [7–240] hrs (median and range)	AE, A, L, F
[31]Verdejo-Garcia et al. (2007) & Bolla et al. (2005)*±	11	14	40.1 (22.3) joints/week; 6.3 (1.4)days/week	7.9 (5.6) yrs	25 days	A
[32]Whitlow et al. (2004)	10	10	daily use for 25 out of 30 days	≥ 5 yrs	14.6 (3.1) hrs	A
[33]Yücel et al. (2008)	15	16	636 (565) cones; 28 (4.6) days/mth	19.7 (7.3) yrs of regular use	≥ 12 hrs	L, F

Note. Abstraction/Executive (AE); Attention (A); Learning (L); Forgetting/Retrieval (F); Motor (M); Perceptual-Motor (PM); Simple Reaction Time (SRT); Verbal/Language (VL); Long-term (LT); Short-term (ST); Not Reported (NR).
[a] Only participants in the THC − subgroup were included in the 13 study meta-analysis.
* Study included in both 33 and 13 study meta-analysis. ± Studies shared sample participants and therefore were combined and treated as one independent sample. Ψ Study used an adolescent sample.

nence and therefore met criteria for a second analysis focused on lasting residual effects. These studies included data from 388 current or former cannabis users and 387 controls with no or very limited cannabis use history.

Meta-analysis was conducted using Comprehensive Meta-Analysis Version 2.0 (CMA), a computer program that allows for the computation of multiple effect sizes from a variety of reported data formats (Borenstein, Hedges, Higgins, & Rothstein, 2005). In the present analysis, data was extracted from the primary studies to compute Hedge's *g*. This effect size measure was selected over the commonly used standardized mean difference due to the large number of studies with small sample sizes included. Hedge's *g* is calculated with a correction for the overestimation of effect that can occur in small sample when using Cohen's *d* (Borenstein et al., 2009). CMA also allows for consideration of multiple comparisons within a sample (i.e., heavy users vs. controls and moderate users vs. controls) as well as multiple outcomes. A majority of the studies included reported multiple outcomes across a number of neuropsychological measures. CMA allows for the combination of the effect sizes by averaging across different outcomes within a study to derive a synthetic or summary effect estimate. Thus, an overall neurocognitive performance effect for each study was calculated to evaluate the evidence of a global effect. Due to the lack of overlap in measures across studies, the guidelines for categorizing outcomes described by Grant et al. (2003) were used to also arrive at eight neurocognitive domains for evaluation. These domains were selected in order to be appropriately broad (so as to have a sufficient number of studies falling into each), as well as to allow for generalizability with Grant et al.'s (2003) findings. See Table 2 for descriptions of the domains and examples of measures falling into each.

In order to evaluate variance in effect sizes across studies, the *Q* statistic and I^2 were calculated as tests for heterogeneity. A significant *Q* statistic would indicate that the true effects vary across studies due to multiple population parameters. I^2 is a measure of the proportion of observed variance that is indicative of true effect size differences and is not impacted by the number of studies included (while *Q* is). It reflects the overlap of study effect size confidence intervals, with a large I^2 value reflective of high inconsistency across studies. Lastly, as studies with significant results are more likely to be published and several studies only reported sufficient information for significant results within the study, the fail safe *N* was calculated for significant results. The fail safe *N* determines the number of studies needed with effect sizes of zero to change the significance of the summary effect size (Borenstein et al., 2009).

Given the degree of variability present in the included studies (abstinence length, outcome measures, population characteristics, etc.) a random-effects model was selected. A random-effects model assumes that the true effect size varies between studies included in a meta-analysis. Thus, it is a more conservative approach as it accounts for these likely variations in the true effect sizes of different studies (Borenstein et al., 2009). In addition, it allows for the generalization of results to a wider population. A random-effects model was therefore deemed the more appropriate and preferred model.

Table 2
Examples of Outcome Measures in Assessed Domains

Neurocognitive domain	Outcome measures
Abstraction/Executive	Wisconsin Card Sorting Test; Stroop Test; Raven's Advanced Progressive Matrices; Trail Making Test – Trail B
Attention	Digit Span; Trail Making Test – Trail A; Continuous Performance Task; Iowa Gambling Task*
Forgetting/Retrieval	Wechlser Memory Scale; California Verbal Learning Test – Recall; Rey Auditory Verbal Learning Test – Recall; Rey –Osterrieth Complex Figure Test – Recall; Buschke Selective Reminding Test – Recall
Learning	California Verbal Learning Test – Learning Trials; Rey Auditory Verbal Learning Test – Learning Trials; VIG – Visual Learning
Motor	Finger Tapping Test; Grooved Pegboard
Perceptual-Motor	Block Design; Object Assembly; Rey – Osterrieth Complex Figure Test – Copy
Simple Reaction Time	Signal Detection – Reaction Time
Verbal/Language	Verbal Fluency; Vocabulary; Boston Naming Test

Note. The outcome measures listed are examples. This is not an exhaustive list of tests included in the meta-analysis.
* Although largely believed to test executive functioning, recent evidence suggests the Iowa Gambling Task loads higher on attention and therefore was included within that domain (Gansler, Jerram, Vannorsdall, & Schretlen, 2011).

Results

33 Studies—Meta-Analysis Overall Residual Effects

The global effect size for all assessed cognitive domains indicated a significant negative effect, ES = −0.29 CI 95% [−0.46 to −0.12] $p < .001$. The summary effect sizes for each study ranged from −1.28–1.83 and as expected there was significant heterogeneity across study effect sizes, Q (32) = 78.54, $p < .001$, I^2 = 59.26, T^2 = 0.13. The summary effect sizes and heterogeneity statistics for the eight measured domains are presented in Table 3. For most of the cognitive domains, there was also a significant negative effect size indicating cannabis related decrease in performance. However, for perceptual-motor and simple RT the effect sizes were not significant. For both domains the summary effects were positive with the 95% confidence intervals including zero. There was also significant heterogeneity for most of the domains with the exception of Abstraction/Executive, Motor, and Perceptual-motor functioning. Overall, the results indicate a small negative residual effect of cannabis use on neuropsychological performance, with significant variability across studies. This negative effect was not evident for the domains of perceptual-motor functioning and simple RT. The fail safe N for the overall effect size was 256 studies. This indicates that 256 studies with an effects size of zero would need to be included in the analysis in order to accept the null hypothesis.

13 Studies—Meta-Analysis Lasting Residual Effects

For studies with at least 1-month of abstinence, a global effect size for all assessed cognitive domains was calculated. The global effect was not significant with zero falling within the confidence interval [ES = −0.12, CI 95% [−0.32 to 0.07] $p = .22$] indicating no evidence for lasting residual effects on overall performance. Similarly, for all eight of the measured cognitive domains, the summary effect size was not significant, including zero within the 95% confidence interval. The study results for each domain are presented in Figure 1. Tests of heterogeneity were not significant for the global neurocognitive effect size [Q (12) = 17.93, $p = .12$, I^2 = 33.09, T^2 = 0.04] or for any of the eight cognitive domains. Overall, results indicate no lasting residual effects of cannabis use on neuropsychological performance.

Metaregression

As both meta-analyses included studies using either exclusively adolescent or adult samples, the potential that age and duration of use moderated observed effect sizes was evaluated. Separate metaregression analyses were conducted for continuous variables of age and duration using the method of unrestricted maximum likelihood for random effects regression (Borenstein et al., 2009). Results showed that neither age nor duration of use were significant moderators for either the 33 study or 13 study meta-analyses.

Discussion

The present investigation used meta-analytic methods to evaluate the presence of residual neurocognitive effects from cannabis use. Two separate analyses were conducted in order to determine whether observed effects were due to drug residue (the presence of metabolites still acting in the CNS) or due to lasting effects on cognitive performance. The first analysis included all 33 studies meeting inclusion criteria and revealed evidence of a small but significant effect both globally and for six of the eight neurocognitive domains. Perceptual-motor and simple RT were the exceptions with positive effect sizes and confidence intervals including zero, indicating no significant observable effect. Therefore, results indicate evidence for small neurocognitive effects that persist after the period of acute intoxication. The second meta-analysis included only the 13 studies whose abstention period was at least 25 days. Results for this analysis revealed no evidence of a significant effect on neurocognitive performance. For the global summary effect and all the cognitive domains measured, the effects sizes all had confidence intervals including zero indicating no evidence of lasting effects on cognitive performance due to cannabis use.

This 33 study meta-analysis expands on the prior meta-analytic investigation into the residual effects of cannabis use (Grant et al., 2003). We were able to replicate the observed negative effects reported for global neurocognitive performance, learning, and forgetting/retrieval as well as replicate the failure to identify duration

Table 3
Domain Effect Sizes and Heterogeneity Statistics

Domain	Meta analysis	Effect size (95% CI)	*Q*-statistic	*df* for *Q*	*p*-value for *Q*	I^2	T^2
Abstraction/Executive	33 Study	−0.21 (−0.38, −0.05)*	23.36	16	0.10	31.51	0.04
	13 Study	−0.10 (−0.29, 0.10)	2.94	5	0.71	0.00	0.00
Attention	33 Study	−0.36 (−0.56, −0.16)***	47.82	22	0.001	53.99	0.12
	13 Study	−0.20 (−0.49, 0.09)	14.79	8	0.06	45.90	0.09
Forgetting/Retrieval	33 Study	−0.25 (−0.47, −0.02)*	58.07	18	<0.001	69.00	0.16
	13 Study	−0.15 (−0.34, 0.04)	8.75	7	0.27	20.02	0.02
Learning	33 Study	−0.35 (−0.55, −0.15)***	25.51	13	0.02	49.03	0.07
	13 Study	−0.16 (−0.33, 0.02)	4.95	6	0.55	0.00	0.00
Motor	33 Study	−0.34 (−0.57, −0.11)**	3.08	3	0.40	2.49	0.001
	13 Study	−0.19 (−0.53, 0.14)	0.09	1	0.77	0.00	0.00
Perceptual-Motor	33 Study	0.02 (−0.15, 0.18)	9.17	9	0.42	1.87	0.001
	13 Study	0.09 (−0.09, 0.27)	4.01	4	0.41	0.20	0.00
Simple Reaction Time	33 Study	0.28 (−0.11, 0.67)	16.66	6	0.01	63.98	0.17
	13 Study	0.07 (−0.21, 0.34)	0.52	3	0.92	0.00	0.00
Verbal/Language	33 Study	−0.23 (−0.47, −0.001)*	19.47	9	0.02	53.77	0.07
	13 Study	−0.10 (−0.31, 0.11)	1.64	3	0.65	0.00	0.00

* $p < .05$. ** $p < .01$. *** $p \leq .001$.

of use as a significant moderator variable. The current results also reveal additional negative effects in the domains of abstraction/executive functioning, attention, verbal/language, and motor functioning. These differences may reflect the large increase in studies meeting inclusion criteria as the chances of committing a Type II error due to insufficient power are reduced with a larger number of primary studies (Borenstein et al., 2009). In addition to increased power, the negative effects observed in the present meta-analysis are strengthened by the more conservative approach taken (i.e., use of random-effects model and presumed high correlation between measures) which results in larger confidence intervals and subsequently makes it more difficult to reject the null hypothesis. However, it is important to consider the distinction between statistical significance and clinical significance. Although small to moderate negative effect sizes are observed, it remains unclear whether these differences translate into practical impairments in functioning (Grant et al., 2003). In addition, these effects do not appear to persist beyond the first 25 days after acute intoxication.

While a residual effect of cannabis use is consistent with the results, a potential withdrawal effect provides an alternative explanation that must be addressed (Grant et al., 2003; Pope et al., 2001). The participants across studies consisted of moderate to heavy cannabis users evaluated over a wide range of abstention periods. However, most users were evaluated somewhere between 4 hrs and 10 days of abstention. This is problematic because in heavy users, cannabis withdrawal symptoms (e.g., irritability, aggression, anxiety, restlessness, etc.) have been shown to peak between Days 2 and 6 of cessation and to last anywhere from 4 to 14 days (Budney, Moore, Vandrey, & Hughes, 2003). These experienced symptoms could therefore impact and explain subsequent performance differences on outcome measures. Despite a majority of studies addressing this potential confound within the discussion of their results, only four independent samples reporting abstention periods of less than 25 days actually measured and accounted for withdrawal symptoms in their study design (Battisti et al., 2010a, 2010b; Hester, Nestor, & Garavan, 2009; Pope et al., 2001; Solowij et al., 2002). The inability to discriminate between these competing explanations of results in half of the primary studies carries over to interpretation of the 33 study meta-analysis results. Therefore, it is unclear whether the observed effect sizes reflect evidence of a cannabis residue effect, the effects of cannabis withdrawal, or both. The likelihood of withdrawal effects impacting the results is greatly reduced in the 13 study meta-analysis that only included data collected after abstention periods of 25 days or longer.

As hypothesized, the meta-analysis conducted on studies evaluating users after at least 25 days of abstention found no residual effects on cognitive performance. Effect sizes failed to reach significance across all domains and the heterogeneity between studies present in the first meta-analysis greatly reduced. These results fail to support the idea that heavy cannabis use may result in long-term, persistent effects on neuropsychological functioning. To fully understand these results, however, several potential limitations must be noted. First, these findings are based on 13 studies, and interpretation of these results should be commensurate with the number of studies included. Second, across the 13 studies, mean ages were variable, ranging from 17 to 47 years, with wide ranges of frequency and duration of use. In addition, six of the 13 studies included in this second meta-analysis used adolescent samples exclusively. While frequency of use could not be evaluated due to the high diversity in reporting metric (e.g., days per week, joints per week, cones per week, lifetime episodes, etc.), investigation of potential moderators failed to support age or duration of use as variables impacting observed effect sizes. However, five of the studies using adolescent samples did not report duration and it is unclear whether these samples were comparable to those reporting this variable. As such, further research is needed to evaluate whether duration of use is a potential moderator for effects seen after 25 days of abstinence. There is also some evidence that an earlier age of onset for cannabis use may be related to poorer neurocognitive performance (Pope et al., 2003). It may be that lasting residual effects of cannabis use are dependent on onset of regular use occurring before a certain age or developmental stage. Therefore, caution should be used in generalizing these results to potential subpopulations of cannabis users

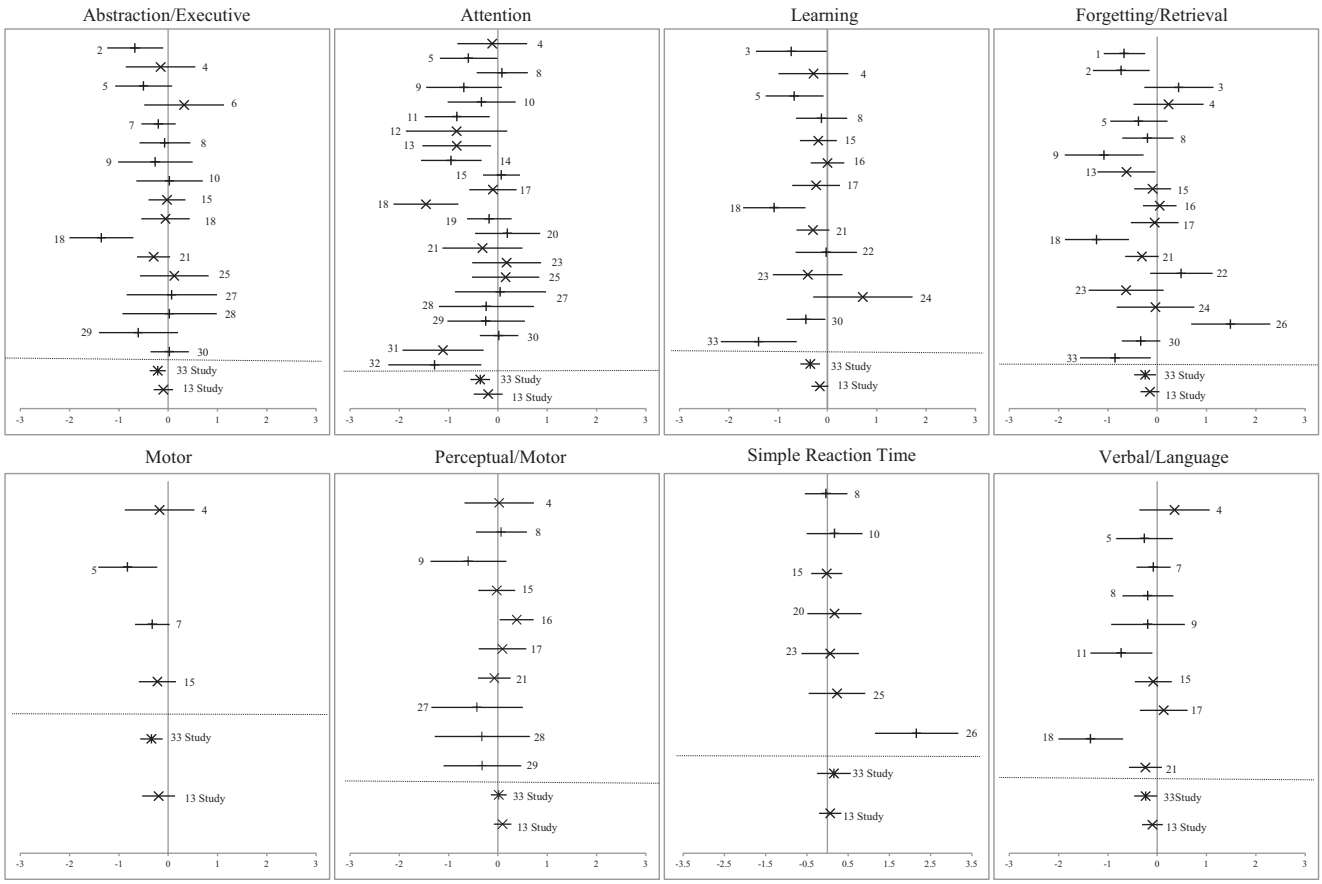

Figure 1. Forest plots for the eight assessed neurocognitive domains. Each domain plot depicts results from both the 33 and 13 study meta-analyses with summary effects at the bottom of each plot. Numeric notations labeling separate effect sizes refer to the independent samples as numbered in Table 1.

such as those with an early age of onset or with more chronic durations of use.

As discussed by Grant et al., (2003), another important consideration is the lack of information regarding users' premorbid performance. It is difficult to interpret scores as notable changes resultant from their cannabis use when their capabilities before onset are unknown. Grant et al., (2003) discusses the possibilities of longitudinal designs as well as twin studies to try and address these issues. Studies utilizing both these methodologies have been published since these issues were raised. Two longitudinal studies examining changes in IQ and specific neurocognitive domains reported negative effects in performance in current heavy cannabis users, but not in former heavy users (Fried, Watkinson, & Gray, 2005; Fried, Watkinson, James, & Gray, 2002). While no specific abstention period was reported for current users (just indications that intoxication was unlikely), former users had not used for at least 3 months. These longitudinal studies were not included in the present study because neither study addressed potential psychiatric or neurological problems. The results of these investigations, however, remain consistent with the present findings which reveal no long-term effects of cannabis use on neurocognitive performance.

While longitudinal studies allow for measurement of premorbid abilities, monozygotic twin studies allow for control of potential genetic confounds (Grant et al., 2003; Lyons et al., 2004). To date, only one twin study has been conducted looking at the effects of cannabis use on neuropsychological performance. The study compared a participant with a history of regular cannabis use to their monozygotic twin (who had no history of use) on a large neuropsychological battery (Lyons et al., 2004). Within the extensive battery of measures given to the twin pairs, the only significant difference found was on the block design subtest of the WAIS–R. This twin study is included in both the full 33 study meta-analysis and the 13 study meta-analysis as the abstention period for the cannabis using twin was a minimum of 1 year (although the mean was approximately 20 years). The results of this well-matched study again remain consistent with the outcome of the present study, which indicate no evidence of a long-term effect of cannabis use on neurocognitive performance.

One limitation inherent in the research design of the present meta-analysis is the large number of combinations performed to arrive at summary effect sizes. This injects a considerable amount of complexity into the results which can confuse interpretation and potentially obscure findings (Grant et al., 2003). While a global effect size for neurocognitive performance is reported, it is important to note that the specific domain effects size should also be viewed as global. In other words, the reported effect size for

attention is a summary of a number of different outcome measures of attention. Although a significant negative effect size was found for global attention in the 33 study meta-analysis that is not to say this result would generalize to a more specific measure of attention (e.g., divided attention, sustained attention, etc.). These meta-analyses evaluated the presence of a systematic residual effect on cognitive performance within the literature and interpretation of results to more specific outcomes is beyond the scope of the present study.

Future research into the residual effects of cannabis use on neurocognitive performance should focus on continuing to control for important confounds. Most notably, for study designs consisting of abstention periods of less than one month, withdrawal symptoms need to be assessed for and included in subsequent analyses. A majority of the studies on residual effects of cannabis use cannot draw reasonable conclusions about the cause of any observed effects due to this potential confound not being adequately addressed. More evaluations with longer term periods of abstinence are also needed. Although inherently more difficult, studies utilizing monitored abstinence with drug testing would greatly strengthen the literature. Very few of the primary studies were able to conduct monitored abstinence and drug testing. Instead most designs depended on self-reports of cannabis abstinence which increases the potential for error in study conclusions. It may also be beneficial to take the emphasis off abstinence periods, and instead rely on metabolite concentrations when available. Given the unpredictability in strength and potency of the cannabis subjects are using and individual differences in duration and frequency of use, a set number of days abstaining may result in extremely varied metabolite concentrations for different users (Grotenhermen, 2003; Pope et al., 1995). When possible, the assessing and reporting of metabolite concentrations would provide greater information about the role actual drug residue may play in any observed neurocognitive effects.

In sum, two separate meta-analyses were conducted to evaluate the evidence for residual effects on cognitive performance as a result of cannabis use. The first evaluated all investigations into nonacute cognitive performance, while the second aimed to assess whether cannabis use resulted in long-term, lasting effects. While the first meta-analysis revealed a small significant negative effect for general performance and a number of cognitive domains, the clinical significance remains unclear. In addition, primary study designs preclude definitive conclusions as to whether observed results are due to residual effects of cannabis use or due to cannabis withdrawal symptoms. A second meta-analysis focusing on studies with longer abstention periods was conducted and indicated no lasting residual effects on neurocognitive performance as a result of cannabis use. Taken together, the results help to clarify the seemingly inconsistent results present in the literature. Discrepant findings may not be discrepant at all but instead reflect difference in effect size due to variable periods of abstention across studies. Whether differences seen in the initial days or weeks of abstinence are due to drug residue effects or withdrawal effects, after approximately 1 month these effects do not persist for the moderate to heavy user.

References

References marked with an asterisk (*) indicate studies included in the meta-analysis.

*Bartholomew, J., Holroyd, S., & Heffernan, T. M. (2010). Does cannabis use affect prospective memory in young adults? *Journal of Psychopharmacology, 24,* 241–246. doi:10.1177/0269881109106909

*Battisti, R. A., Roodenrys, S., Johnstone, S. J., Pesa, N., Hermens, D. F., & Solowij, N. (2010a). Chronic cannabis users show altered neurophysiological functioning on Stroop task conflict resolution. *Psychopharmacology, 212,* 613–624. doi:10.1007/s00213-010-1988-3

*Battisti, R. A., Roodenrys, S., Johnstone, S. J., Respondek, C., Hermens, D. F., & Solowij, N. (2010b). Chronic use of cannabis and poor neural efficiency in verbal memory ability. *Psychopharmacology, 209,* 319–330. doi:10.1007/s00213-010-1800-4

*Block, R. I., O'Leary, D. S., Hichwa, R. D., Augustinack, J. C., Ponto, L., Ghoneim, M. M., . . . Andreasen, N. C. (2002). Effects of frequent marijuana use on memory-related regional cerebral blood flow. *Pharmacology, Biochemistry and Behavior, 72,* 237–250. doi:10.1016/S0091-3057(01)00771-7

*Bolla, K., Eldreth, D., Matochik, J., & Cadet, J. (2005). Neural substrates of faulty decision-making in abstinent marijuana users. *Neuroimage, 26,* 480–492. doi:10.1016/j.neuroimage.2005.02.012

Borenstein, M., Hedges, L. V., Higgins, J. P., & Rothstein, H. R. (2005). *Comprehensive Meta-Analysis (Version 2.0*) [Computer Software]. Englewood, NJ: Biostat.

Borenstein, M., Hedges, L. V., Higgins, J. P., & Rothstein, H. R. (2009). *Introduction to meta-analysis.* West Sussex, UK: John Wiley and Sons, Ltd. doi:10.1002/9780470743386

Bowman, M., & Pihl, R. O. (1973). Cannabis: Psychological effects of chronic heavy use: A controlled study of intellectual functioning in chronic users of high potency cannabis. *Psychopharmacologia, 29,* 159–170. doi:10.1007/BF00422648

Budney, A. J., Moore, B. A., Vandrey, R. G., & Hughes, J. R. (2003). The time course and significance of cannabis withdrawal. *Journal of Abnormal Psychology, 112,* 393–402. doi:10.1037/0021-843X.112.3.393

Carlin, A. S., & Trupin, E. W. (1977). The effect of long-term chronic marijuana use on neuropsychological functioning. *International Journal of the Addictions, 12,* 617–624.

*Chang, L., Yakupov, R. R., Cloak, C. C., & Ernst, T. T. (2006). Marijuana use is associated with a reorganized visual-attention network and cerebellar hypoactivation. *Brain: A Journal of Neurology, 129,* 1096–1112. doi:10.1093/brain/awl064

Crean, R. D., Crane, N. A., & Mason, B. J. (2011). An evidence-based review of acute and long-term effects of cannabis use on executive cognitive functions. *Journal of Addiction Medicine, 5,* 1–8. doi:10.1097/ADM.0b013e31820c23fa

*Croft, R. J., Mackay, A. J., Mills, A. D., & Gruzelier, J. H. (2001). The relative contributions of ecstasy and cannabis to cognitive impairment. *Psychopharmacology, 153,* 373–379. doi:10.1007/s002130000591

*Eldreth, D., Matochik, J., Cadet, J., & Bolla, K. (2004). Abnormal brain activity in prefrontal brain regions in abstinent marijuana users. *Neuroimage, 23,* 914–920. doi:10.1016/j.neuroimage.2004.07.032

Ellis, G. M., Jr., Mann, M. A., Judson, B. A., Schramm, N. T., & Taschian, A. (1985). Excretion patterns of cannabinoid metabolites after last use in a group of chronic users. *Clinical Pharmacology & Therapeutics, 38,* 572–578. doi:10.1038/clpt.1985.226

Entin, E. E., & Goldzung, P. J. (1973). Residual effects of marihuana usage on learning and memory. *The Psychological Record, 23,* 169–178.

Fletcher, J., Page, J., Francis, D., Copeland, K., Naus, M., Davis, C., . . . Satz, P. (1996). Cognitive correlates of long-term cannabis use in Costa Rican men. *Archives of General Psychiatry, 53,* 1051–1057. doi:10.1001/archpsyc.1996.01830110089011

*Fontes, M., Bolla, K., Cunha, P., Almeida, P., Jungerman, F., Laranjeira,

R., . . . Lacerda, A. (2011). Frontal Assessment Battery (FAB) is a simple tool for detecting executive deficits in chronic cannabis users. *Journal of Clinical and Experimental Neuropsychology, 33,* 523–531. doi:10.1080/13803395.2010.535505

Fried, P., Watkinson, B., & Gray, R. (2005). Neurocognitive consequences of marihuana–a comparison with pre-drug performance. *Neurotoxicology and Teratology, 27,* 231–239. doi:10.1016/j.ntt.2004.11.003

Fried, P., Watkinson, B., James, D., & Gray, R. (2002). Current and former marijuana use: Preliminary findings of a longitudinal study of effects on IQ in young adults. *CMAJ: Canadian Medical Association Journal (Journal De L'association Medicale Canadienne), 166,* 887–891.

Gansler, D., Jerram, M., Vannorsdall, T., & Schretlen, D. (2011). Does the Iowa gambling task measure executive function? *Archives of Clinical Neuropsychology: The Official Journal of the National Academy of Neuropsychologists, 26,* 706–717.

Gonzalez, R. (2007). Acute and non-acute effects of cannabis on brain functioning and neuropsychological performance. *Neuropsychology Review, 17,* 347–361. doi:10.1007/s11065-007-9036-8

*Gouzoulis-Mayfrank, E., Daumann, J., Tuchtenhagen, F., Pelz, S., Becker, S., Kunert, H., . . . Sass, H. (2000). Impaired cognitive performance in drug free users of recreational ecstasy (MDMA). *Journal of Neurology, Neurosurgery & Psychiatry, 68,* 719–725. doi:10.1136/jnnp.68.6.719

Grant, I., Gonzalez, R., Carey, C. L., Natarajan, L., & Wolfson, T. (2003). Non-acute (residual) neurocognitive effects of cannabis use: A meta-analytic study. *Journal of the International Neuropsychological Society, 9,* 679–689. doi:10.1017/S1355617703950016

Grant, I., Rochford, J., Fleming, T., & Stunkard, A. (1973). A neuropsychological assessment of the effects of moderate marihuana use. *Journal of Nervous and Mental Disease, 156,* 278–280. doi:10.1097/00005053-197304000-00008

Grotenhermen, F. (2003). Pharmacokinetics and pharmacodynamics of cannabinoids. *Clinical Pharmacokinetics, 42,* 327–360. doi:10.2165/00003088-200342040-00003

*Hermann, D., Sartorius, A., Welzel, H., Walter, S., Skopp, G., Ende, G., & Mann, K. (2007). Dorsolateral prefrontal cortex N-acetylaspartate/total creatine (NAA/tCr) loss in male recreational cannabis users. *Biological Psychiatry, 61,* 1281–1289. doi:10.1016/j.biopsych.2006.08.027

*Hester, R., Nestor, L., & Garavan, H. (2009). Impaired error awareness and anterior cingulate cortex hypoactivity in chronic cannabis users. *Neuropsychopharmacology, 34,* 2450–2458. doi:10.1038/npp.2009.67

*Huestegge, L., Kunert, H. J., & Radach, R. (2010). Long-term effects of cannabis on eye movement control in reading. *Psychopharmacology, 209,* 77–84. doi:10.1007/s00213-009-1769-z

*Huestegge, L., Radach, R. R., & Kunert, H. J. (2009). Long-term effects of cannabis on oculomotor function in humans. *Journal of Psychopharmacology, 23,* 714–722. doi:10.1177/0269881108091601

*Huestegge, L., Radach, R., Kunert, H., & Heller, D. (2002). Visual search in long-term cannabis users with early age of onset. *Progress in Brain Research, 140,* 377–394.

*Jacobsen, L. K., Mencl, W., Westerveld, M., & Pugh, K. R. (2004). Impact of cannabis use on brain function in adolescents. In R. E. Dahl & L. Spear (Eds.), *Adolescent brain development: Vulnerabilities and opportunities* (pp. 384–390). New York, NY: New York Academy of Sciences.

*Jacobsen, L. K., Pugh, K., Constable, R., Westerveld, M., & Mencl, W. (2007). Functional correlates of verbal memory deficits emerging during nicotine withdrawal in abstinent adolescent cannabis users. *Biological Psychiatry, 61,* 31–40. doi:10.1016/j.biopsych.2006.02.014

*Kanayama, G., Rogowska, J., Pope, H. G., Gruber, S. A., & Yurgelun-Todd, D. A. (2004). Spatial working memory in heavy cannabis users: A functional magnetic resonance imaging study. *Psychopharmacology, 176,* 239–247. doi:10.1007/s00213-004-1885-8

*Kelleher, L. M., Stough, C., Sergejew, A. A., & Rolfe, T. (2004). The effects of cannabis on information-processing speed. *Addictive Behaviors, 29,* 1213–1219. doi:10.1016/j.addbeh.2004.03.039

*Lyons, M. J., Bar, J. L., Panizzon, M. S., Toomey, R. R., Eisen, S. S., Xian, H. H., & Tsuang, M. T. (2004). Neuropsychological consequences of regular marijuana use: A twin study. *Psychological Medicine: A Journal of Research in Psychiatry and the Allied Sciences, 34,* 1239–1250. doi:10.1017/S0033291704002260

*Mahmood, O. M., Jacobus, J., Bava, S., Scarlett, A., & Tapert, S. F. (2010). Learning and memory performance in adolescent users of alcohol and marijuana: Interactive effects. *Journal of Studies on Alcohol and Drugs, 71,* 885–894.

*Medina, K., Hanson, K. L., Schweinsburg, A. D., Cohen-Zion, M., Nagel, B. J., & Tapert, S. F. (2007). Neuropsychological functioning in adolescent marijuana users: Subtle deficits detectable after a month of abstinence. *Journal of the International Neuropsychological Society, 13,* 807–820. doi:10.1017/S1355617707071032

*Messinis, L., Kyprianidou, A., Malefaki, S., & Papathanasopoulos, P. (2006). Neuropsychological deficits in long-term frequent cannabis users. *Neurology, 66,* 737–739. doi:10.1212/01.wnl.0000201279.83203.c6

*Morgan, C., Rothwell, E., Atkinson, H., Mason, O., & Curran, H. (2010). Hyper-priming in cannabis users: A naturalistic study of the effects of cannabis on semantic memory function. *Psychiatry Research, 176,* 213–218. doi:10.1016/j.psychres.2008.09.002

*Padula, C. B., Schweinsburg, A. D., & Tapert, S. F. (2007). Spatial working memory performance and fMRI activation interaction in abstinent adolescent marijuana users. *Psychology of Addictive Behaviors, 21,* 478–487. doi:10.1037/0893-164X.21.4.478

*Pillay, S. S., Rogowska, J., Kanayama, G., Gruber, S., Simpson, N., Pope, H., & Yurgelun-Todd, D. (2008). Cannabis and motor function: FMRI changes following 28 days of discontinuation. *Experimental and Clinical Psychopharmacology, 16,* 22–32. doi:10.1037/1064-1297.16.1.22

*Pillay, S. S., Rogowska, J., Kanayama, G., Jon, D., Gruber, S., Simpson, N., . . . Yurgelun-Todd, D. A. (2004). Neurophysiology of motor function following cannabis discontinuation in chronic cannabis smokers: An fMRI study. *Drug and Alcohol Dependence, 76,* 261–271. doi:10.1016/j.drugalcdep.2004.05.009

*Pope, H. G., Gruber, A. J., Hudson, J. I., Cohane, G., Heustis, M. A., & Yurgelun-Todd, D. (2003). Early-onset cannabis use and cognitive deficits: What is the nature of the association? *Drug and Alcohol Dependence, 69,* 303–310. doi:10.1016/S0376-8716(02)00334-4

*Pope, H. G., Gruber, A. J., Hudson, J. I., Huestis, M. A., & Yurgelun-Todd, D. (2001). Neuropsychological performance in long-term cannabis users. *Archives of General Psychiatry, 58,* 909–915. doi:10.1001/archpsyc.58.10.909

*Pope, H. G., Gruber, A. J., Hudson, J. I., Huestis, M. A., & Yurgelun-Todd, D. (2002). Cognitive measures in long-term cannabis users. *Journal of Clinical Pharmacology, 42,* 41S–47S.

Pope, H. G., Gruber, A. J., & Yurgelun-Todd, D. (1995). The residual neuropsychological effects of cannabis: The current status of research. *Drug and Alcohol Dependence, 38,* 25–34. doi:10.1016/0376-8716(95)01097-I

*Quednow, B., Jessen, F., Kuhn, K., Maier, W., Daum, I., & Wagner, M. (2006). Memory deficits in abstinent MDMA (ecstasy) users: Neuropsychological evidence of frontal dysfunction. *Journal of Psychopharmacology (Oxford, England), 20,* 373–384. doi:10.1177/0269881106061200

Ranganathan, M., & D'Souza, D. (2006). The acute effects of cannabinoids on memory in humans: A review. *Psychopharmacology, 188,* 425–444. doi:10.1007/s00213-006-0508-y

*Rodgers, J. (2000). Cognitive performance amongst recreational users of 'ecstasy.' *Psychopharmacology, 151,* 19–24. doi:10.1007/s002130000467

Rosenthal, R., & DiMatteo, M. R. (2001). Meta-analysis: Recent developments in quantitative methods for literature reviews. *Annual Review of Psychology, 52,* 59–82. doi:10.1146/annurev.psych.52.1.59

*Schweinsburg, A., Nagel, B., Schweinsburg, B., Park, A., Theilmann, R., & Tapert, S. (2008). Abstinent adolescent marijuana users show altered fMRI response during spatial working memory. *Psychiatry Research, 163,* 40–51. doi:10.1016/j.pscychresns.2007.04.018

*Schweinsburg, A., Schweinsburg, B., Nagel, B., Eyler, L., & Tapert, S. (2011). Neural correlates of verbal learning in adolescent alcohol and marijuana users. *Addiction, 106,* 564–573. doi:10.1111/j.1360-0443.2010.03197.x

*Skosnik, P. D., Edwards, C., O'Donnell, B., Steffen, A., Steinmetz, J., & Hetrick, W. (2008). Cannabis use disrupts eyeblink conditioning: Evidence for cannabinoid modulation of cerebellar-dependent learning. *Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology, 33,* 1432–1440. doi:10.1038/sj.npp.1301506

*Skosnik, P. D., Krishnan, G. P., Vohs, J. L., & O'Donnell, B. F. (2006). The effect of cannabis use and gender on the visual steady state evoked potential. *Clinical Neurophysiology, 117,* 144–156. doi:10.1016/j.clinph.2005.09.024

*Skosnik, P. D., Spatz-Glenn, L., & Park, S. (2001). Cannabis use is associated with schizotypy and attentional disinhibition. *Schizophrenia Research, 48,* 83–92. doi:10.1016/S0920-9964(00)00132-8

Solowij, N., & Battisti, R. (2008). The chronic effects of cannabis on memory in humans: A review. *Current Drug Abuse Reviews, 1,* 81–98. doi:10.2174/1874473710801010081

*Solowij, N., Stephens, R. S., Roffman, R. A., Babor, T., Kadden, R., Miller, M., . . . Vendetti, J. (2002). Cognitive functioning of long-term heavy cannabis users seeking treatment. *Journal of the American Medical Association, 287,* 1123–1131. doi:10.1001/jama.287.9.1123

Soueif, M. (1976). Differential association between chronic cannabis use and brain function deficits. *Annals Of The New York Academy Of Sciences, 282,* 323–343.

Substance Abuse and Mental Health Services Administration (2011). *Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings*. Rockville, MD: NSDUH Series H-41, HHS Publication No. (SMA) 11–4658.

*Tapert, S. F., Schweinsburg, A. D., Drummond, S. A., Paulus, M. P., Brown, S. A., Yang, T. T., & Frank, L. R. (2007). Functional MRI of inhibitory processing in abstinent adolescent marijuana users. *Psychopharmacology, 194,* 173–183. doi:10.1007/s00213-007-0823-y

Varma, V. K., Malhotra, A. K., Dang, R., & Das, K. (1988). Cannabis and cognitive functions: A prospective study. *Drug and Alcohol Dependence, 21,* 147–152. doi:10.1016/0376-8716(88)90061-0

*Verdejo-Garcia, A., Benbrook, A., Funderburk, F., David, P., Cadet, J., & Bolla, K. I. (2007). The differential relationship between cocaine use and marijuana use on decision-making performance over repeat testing with the Iowa Gambling Task. *Drug and Alcohol Dependence, 90,* 2–11. doi:10.1016/j.drugalcdep.2007.02.004

*Whitlow, C., Liguori, A., Livengood, L., Hart, S., Mussat-Whitlow, B., Lamborn, C., . . . Porrino, L. (2004). Long-term heavy marijuana users make costly decisions on a gambling task. *Drug and Alcohol Dependence, 76,* 107–111. doi:10.1016/j.drugalcdep.2004.04.009

*Yücel, M., Solowij, N., Respondek, C., Whittle, S., Fornito, A., Pantelis, C., & Lubman, D. I. (2008). Regional brain abnormalities associated with long-term heavy cannabis use. *Archives of General Psychiatry, 65,* 694–701. doi:10.1001/archpsyc.65.6.694

Received January 30, 2012
Revision received May 15, 2012
Accepted May 16, 2012 ■