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Ecological Momentary Assessment of Working Memory Under Conditions of Simultaneous Marijuana and Tobacco Use

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Abstract

Background and aims—The neuropsychological correlates of simultaneous marijuana and tobacco use are largely unknown, which is surprising as both substances have similar neural substrates and have opposing influences on working memory (WM). This study examined the effects of marijuana alone, tobacco alone, and simultaneous marijuana and tobacco use on WM.

Design—Primary aims were tested using a within-subject design, controlling for multiple subject- and momentary-level confounds via ecological momentary assessment (EMA).

Setting—Data collection occurred in the Chicago, USA area in participants' natural environments.

Participants—Participants were 287 community young adults from a larger natural history study, over-sampled for ever smoking, all of whom event-recorded at least one substance use occasion during the study week.

Measurements—Momentary tobacco, marijuana and alcohol use were recorded during multiple EMA across one week of data capture. WM was assessed at the end of each EMA. Contextual variables that may influence WM were recorded via EMA.

Findings—There were main effects for marijuana and tobacco: WM was poorer with marijuana (OR=0.91, 95%CI = 0.84 to 0.99) and better with tobacco (OR=1.11, 95%CI = 1.04 to 1.18). These effects were not qualified by an interaction (OR=1.03, 95%CI = 0.84 to 1.26). Alcohol also reduced WM (OR=0.87, 95%CI = 0.79 to 0.95), and the tobacco by alcohol interaction was significant (OR=0.81, 95%CI = 0.66 to 0.99), indicating that the facilitative effect of tobacco disappeared with concurrent alcohol use.

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Conclusions—Relative to when individuals did not use these substances, working memory (WM) decreased with acute marijuana and alcohol use, and increased with acute tobacco use. However, the putative effect of marijuana on WM and the facilitative effect of tobacco on WM were no longer present when used simultaneously with tobacco and alcohol, respectively. Data suggest that tobacco use may compensate for WM decrements from marijuana among young adults and highlight the importance of further investigating the negative impact of alcohol use on cognition.

Marijuana and tobacco are two of the most widely used drugs in the United States (1), and simultaneous marijuana and tobacco use (i.e., use of both substances at the same time or in close temporal sequence) is popular among young adults (2, 3). Simultaneous marijuana and tobacco use typically takes one of two forms: blunt smoking (smoking cigars with tobacco removed and replaced with marijuana and residual tobacco) or “chasing” (smoking cigarettes/cigarillos immediately after marijuana). Simultaneous users experience more deleterious substance use outcomes than non- and co-users (i.e., individuals who use both but not simultaneously), including greater use severity and cessation difficulties. For example, simultaneous users consume marijuana more frequently and have up to 5.1 times greater odds of being marijuana dependent than co-users (4-7). Qualitative reports also suggest that marijuana reinforces cigarette smoking and interferes with quitting (2), with marijuana users less likely to quit tobacco than non-marijuana users (8).

Interactions between cannabinoid and cholinergic systems on neurochemical and behavioral functioning may partially explain rising rates of simultaneous use. Subchronic nicotine exposure results in region-dependent increases in cannabinoid receptor (CB1) hippocampal expression that persists for one month following nicotine cessation (9). Similarly, animals chronically exposed to nicotine have increased endocannabinoid levels in the limbic forebrain and brainstem (10), and cannabinoid agonists produce greater release and lower turnover of acetylcholine in the hippocampus, cortex and striatum (11-14). Behaviorally, co-administration of marijuana and nicotine in vivo results in acute changes in locomotion, heart rate and body temperature (15), with marijuana's depressant effects potentiated even by sub-clinical doses of nicotine (16). Similarly, administration of Δ9-tetrahydrocannabinol, marijuana's primary psychoactive constituent, may mitigate nicotine withdrawal (17), and nicotine's rewarding effects are diminished among CB1 knockout mice (18). Further, administration of CB1 antagonists reduces dopamine release in the nucleus accumbens, nicotine self-administration, and cue-induced nicotine reinstatement (19-21), and has therefore been suggested as a potentially efficacious pharmacological treatment for nicotine addiction (19, 22).

Despite pharmacological interactions between cannabinoid and cholinergic systems as well as greater risk for adverse substance use outcomes among simultaneous users, it remains unknown how simultaneous use impacts executive function capacities such as working memory (WM). Studies have only examined co-use of marijuana and tobacco on neurocognition, finding better verbal memory among co-users than among users of marijuana alone (23) and abnormalities in hippocampal and memory correlations (24). Jacobsen and colleagues (25) have come close in addressing brain-behavior relationships with simultaneous use. They found marijuana users who did not smoke a cigarette compared

to ad libitum cigarette smoking had worse delayed recall and WM, and aberrant functional patterns including greater activation in posterior cortical regions and disrupted functional integration of fronto-parietal connectivity (25), which is relevant to efficient verbal WM (26-30). However, this study could not disentangle the mitigating effect of tobacco on neurocognition among marijuana users from the adverse effect of nicotine withdrawal on neurocognition. Therefore, although it is suspected that marijuana disrupts WM and these deficits may be masked in the context of concomitant tobacco use due to independent effects on similar neural substrates that underlie WM, this hypothesis has not been directly tested. Compensatory effects might explain why simultaneous use is reinforcing, elucidate potential barriers to quitting and inform public health efforts aimed at educating young adults on potential risks of marijuana and tobacco co-use.

Associations with alcohol are also important to consider in the context of simultaneous marijuana and tobacco use. Convergent evidence points to probable pharmacokinetic and pharmacodynamic interactions between alcohol and concurrent marijuana or tobacco. This is likely due to overlap in the neurotransmitter systems targeted, including the mesolimbic dopamine pathway for alcohol and marijuana (31-33) and the cholinergic system for alcohol and tobacco (34-36). Studies of co-users of alcohol and marijuana showed worse WM than single substance users (37), though synergistic effects were not found when both substances were acutely administered at low doses (38). With regard to alcohol and tobacco, animal studies have found that pretreatment with nicotine attenuated alcohol's effects on WM (39), and co-administration of sub-clinical doses of alcohol and nicotine resulted in WM impairment (40). Similar effects have been found in humans (41, 42), though synergistic interactions have not been equivocally documented (43, 44). These studies together suggest that alcohol interacts with marijuana and tobacco, but the nature of these effects is incompletely understood. Further, no studies to our knowledge have addressed the neurocognitive consequences of alcohol use when combined with *both* marijuana and tobacco, which is surprising as alcohol commonly co-occurs with and has overlapping risk and protective factors as marijuana and tobacco use (45).

In sum, tobacco consumption among marijuana users may improve aspects of cognition, and this compensatory effect may be especially relevant among young adult marijuana users who are at greater risk to experience cognitive decrements due to ongoing neurodevelopment in regions likely impacted by marijuana and tobacco use. However, no studies have directly tested the impact of simultaneous marijuana and tobacco use on neurocognition. This study aimed to isolate the conjoint effects of marijuana and tobacco on WM from 1) the effects of marijuana alone and 2) the effects of tobacco alone using a within-subject design and an ecologically valid, real-time data capture methodology. Given prior research on the independent and opposing effects of marijuana and tobacco on WM, we hypothesized that, compared to randomly sampled times with no substance use, WM would be enhanced with tobacco, impaired with marijuana, and not significantly different during times of simultaneous tobacco and marijuana use. We also examined whether any of our hypothesized effects varied with concomitant alcohol use. Consideration of the potential separate and interactive effects of marijuana, tobacco and alcohol on WM may have significant implications for pharmacological and behavioral treatment interventions.

Methods

Participants

This project was part of a large natural history study of the social-emotional contexts of tobacco smoking (PI: Mermelstein), which followed high-risk adolescents into young adulthood. The parent project recruited adolescents from 16 Chicago-area high schools, over-sampling for students who had ever smoked a cigarette (83% smoked at baseline), and were thus at risk for smoking escalation. Initial recruitment procedures and participant characteristics are detailed in other publications that utilized the parent project cohort (46-49).

Data for the current study came from parent project participants who completed ecological momentary assessments (EMA) during the five-year follow-up, after individuals had graduated from high school, and who recorded at least one episode of marijuana, tobacco, or alcohol use during the EMA assessment week described below (N=287; 94% of parent EMA project).

Overall Design

The EMA protocol involved a seven-day monitoring period using handheld computers programmed with data collection assessments. This interval length ensured both weekday and weekend sampling and provided an adequate sample of events. Participants were individually trained on using the devices and how to complete two types of assessments: 1) random prompts, which were device-initiated (randomly “beeping” the participant, on average 5-7 times/day throughout participants' waking hours); and 2) tobacco smoke events, which were subject-initiated immediately after using tobacco. Each assessment type took approximately 230 seconds to complete, was completed each day and multiple times throughout the day, had similar questions, and concluded with a WM task (detailed below). Entries were password protected, and time and date stamped. Compliance was assessed directly with the random prompts since each prompt was date and time stamped and the device recorded prompts that were not responded to within three minutes. On average, participants had excellent compliance with an average of 92.6% of random prompts completed, consistent with the adequate compliance criterion set forth by Stone and Shiffman (50). Participants received incentive bonuses for completing more than 85% of all random prompts, which helped to maintain high compliance. At the end of the study week, participants were debriefed with structured interviews and were compensated for participation. All procedures were approved by the University of Illinois at Chicago Institutional Review Board.

EMA Measures

EMA contextual covariates—During each EMA assessment, objective and subjective context was queried with a variety of questions using response options in a non-exclusive checklist format. Contextual factors thought to confound WM were included as critical covariates: 1) Proximity to others (0 = with others, 1 = alone); 2) Weekend vs. weekday responding (0 = weekday, 1 = weekend); 3) Watching TV and/or listening to music (0 = no, 1 = yes); 4) At a party (0 = no, 1 = yes); 5) Time of day (1 = 4am-8:59am, 2 = 9am-1:59pm,

3 = 2pm-5:59pm, 4 = 6pm-9:59pm, 5 = 10pm-3:59am); 5) Study day (range: 0-7); 6) Trouble Concentrating (Likert scale item with response options 1-Not at all through 10-Very much); and 7) Negative Affect (average of responses on current feelings of anger, frustration, irritability, sadness and stress, each with continuous response options of 1-Not at all through 10-Very much).

EMA-assessed substance use—In-the-moment use of tobacco was assessed when participants event-recorded a smoking event. Missed episodes of recorded tobacco use were queried during debriefing interviews at the end of the study week. Overall, the agreement between these interviews and the EMA data capture was better than 80%. There were no participants who indicated using tobacco but who did not complete an EMA tobacco use assessment. During both random prompts and smoke events, participants indicated whether they had used marijuana and/or alcohol in the last hour. This design allowed for the capture of occasions of no, single and simultaneous substance use, resulting in eight different drug use categories listed in Table 2. A measure of overall level of tobacco, marijuana and alcohol use was separately derived for each participant based on the proportion of total events across the study week during which use of that substance was reported (0 – 100% of prompts).

EMA WM—Participants completed a brief (~40 seconds) EMA WM task that was administered at the end of each assessment and that was specifically designed to maximize compatibility with EMA (e.g., was brief to minimize disruptions to the participants' lives and to further promote compliance). Visual WM was assessed for a number of reasons including its well-defined neural correlates (51), established associations with substance use (52-54), and excellent psychometric properties, including high test-retest reliability (55, 56). This task was based on visuospatial simple span tasks (57, 58), with an added spatial processing component involving continuously maintaining and updating dot configurations in memory. Participants were presented with between two and four 4×4 grids in sequence, with each grid displayed for one second and containing a random display of five dots. The number of grids presented and the dot configurations within each grid were random. The software was programmed to minimize the likelihood of duplicate displays during the study week. After the final grid presentation, participants attempted to re-create the pattern of dots from the last grid presented on a blank grid using their stylus. This procedure was repeated one additional time for a total of two trials per EMA assessment, each trial with one test grid.

The primary dependent variable was the number of correctly recalled dots in a trial (range 0-5). To account for possible systematic influences that may facilitate associative learning, four parameters of task complexity were created for each pattern to-be-remembered, including the number of interference grids presented, dispersion of the dots on the target grid from a regression line, the number of corner dots in the target grid, and the cumulative distance between dots on the target grid. A full description of the task's development, methods, complexity variables, and psychometric properties can be found in Schuster and colleagues (59). Psychometric evaluation of this task, in brief, indicated that WM performance correlated with laboratory WM measures, particularly visual WM, but not with other laboratory-assessed cognitive capacities.

Analytic Plan

To test for within-person WM differences based on substance use relative to when participants do not use the substance(s) in question, a mixed-effects regression model for repeated ordinal outcomes was fit to the data. This model included random subject effects to account for the correlation between repeated measurements (60). Specifically, a random subject intercept and smoking event effect were included to allow the correlation to vary between the random prompts and the smoking events. The GLIMMIX procedure in SAS 9.2 was used to estimate model parameters by maximum likelihood, and both between- and within-subject factors were entered together to predict WM. Subject-level static covariates including gender and GPA were entered as model covariates. Additionally, the model adjusted for momentary-level covariates that were theoretically linked to WM, including measures of date/time, task complexity, location, social context, affect, and overall level of substance use (tobacco, alcohol, cannabis). Overall substance use levels were created from the momentary-varying reports of substance use based on the decomposition of the between- and within-subjects effects of time-varying covariates as described in Hedeker and Gibbons (61). Specifically, the proportion of total responses in which each of these substances were used represented between-subjects effects, while the deviation of the momentary substance use indicator, relative to a subject's mean, was the within-subjects substance use effect. Primary predictors of interest included the within-subjects main effects for marijuana, tobacco, and alcohol use as well as all two-way and three-way interactions. The model was fit for a six-level ordinal response indicating the number of correctly identified dots in each trial of the WM task. This class of models is useful for analysis of EMA data by allowing multiple observations per subject, multiple levels of nesting (i.e., observations within subjects), multiple subject random effects (e.g., intercept and smoking event indicator), modeling of between-subjects and within-subjects covariates, and extending to non-normal outcomes (e.g., dichotomous, ordinal, counts), which was the case for WM in this study. This approach also allowed for the examination of time trends and practice effects (62, 63).

Results

Descriptive Analyses of Study Sample and EMA Reporting

Sample demographics and substance use are presented in Table 1. This study included 10,669 random prompts and 2,597 smoke assessments, the latter of which came from 86% of the sample (n= 247). The remaining 14% of the sample provided at least one random prompt that indicated current use of alcohol, marijuana, or both concurrently. This resulted in 26,532 ordinal analyzable outcomes (i.e., dots correctly placed in each trial). Participants provided a mean of 37.1 (*SD*= 7.8) random EMA prompts, during which participants reported an average of 3.7 (*SD*= 5.9) marijuana use occasions and 2.84 (*SD*= 3.5) alcohol use occasions (of random prompts: 84% no substance use, 8% marijuana only, 6% alcohol only, 2% concurrent marijuana and alcohol). Participants completed an average of 10.5 (*SD*= 10.9) smoke assessments, with a mean of 1.7 (*SD*= 3.5) co-occurring marijuana reports and 1.1 (*SD*= 1.6) co-occurring alcohol reports (of smoke prompts: 77% tobacco only, 13% concurrent marijuana and tobacco, 7% concurrent alcohol and tobacco, 3% concurrent marijuana, tobacco and alcohol). In the sample of 287 participants, 49% provided at least

one marijuana occasion and 66% provided at least one alcohol occasion. Co-occurring marijuana and alcohol use was reported by 35% of the sample.

Predicting Momentary Fluctuations in WM Capacity

Table 2 illustrates EMA WM performance during drug use categories derived from raw EMA data.

Descriptives of the subject- and momentary-level variables included as model covariates as well as their association with EMA WM performance are in Table 3. Main effects and interactions of within-subject differences in momentary substance use from the mixed effects ordinal regression model predicting the number of correct dots in each task trial are presented in Table 4 and Figure 1. Because the 3-way interaction between marijuana, tobacco and alcohol was not significant ($p=0.48$), the results of the model including only the two-way interactions are presented. Various momentary permutations of substance use were associated with WM, even after accounting for multiple potential confounds. There were significant main effects for marijuana and tobacco: individuals exhibited worse WM (i.e., lower number of correct dots) when using marijuana, and better WM when using tobacco. These main effects were not qualified by a significant interaction, suggesting that the combined use of marijuana and tobacco resulted in WM performance that approached that exhibited during non-substance using occasions. Alcohol reduced WM, and the tobacco by alcohol interaction was significant, indicating that the facilitative effect of tobacco (when used alone) disappeared when there was concurrent alcohol use. Finally, the marijuana by alcohol interaction was not significant. In summary, participants performed poorly when using alcohol and tobacco together, as well as when using alcohol and/or marijuana.

Discussion

This study examined how WM, assessed in real-time, varied by momentary use of tobacco and marijuana, along with their combined use as well as in the context of simultaneous alcohol use. Little is known about WM patterns when marijuana and tobacco are used simultaneously, and no research has characterized WM in the actual context in which substance use occurs. Additionally, preliminary work has examined interactions between alcohol and marijuana or tobacco, but results are inconclusive and no studies have examined how all three substances impact WM when used simultaneously. Therefore, this study addressed three primary questions: does WM fluctuate when individuals use marijuana or tobacco; when used together, does tobacco counteract any adverse impact of marijuana on WM; and, how does concurrent alcohol use alter this neurocognitive profile? This study moves beyond previous research by characterizing within-subject WM variability during situations of no use, single substance use and conjoint use using EMA, which enhances the generalizability of findings due to greater emphasis on ecological validity.

Consistent with hypotheses, WM was worse with marijuana and better with tobacco. Findings support previous theory and research suggesting that acute and chronic exposure to marijuana is linked with selective, dose-dependent negative influences on WM in animal (e.g., 64, 65) and human models (e.g., 66, 67), whereas tobacco enhances WM (e.g., 68-70). Additionally and consistent with central hypotheses, marijuana was not associated with

diminished WM when used with tobacco. More specifically, although there was an overall effect for marijuana worsening WM, WM was comparable to non-use occasions when marijuana and tobacco were used simultaneously. These findings, alongside data from animal models on functional interactions between cannabinoid and cholinergic systems (11-13, 71), together provide convincing preliminary evidence in favor of a compensatory theory. This theory, which hypothesizes that tobacco counteracts marijuana-induced WM decrements, is based largely on the fact that marijuana and tobacco target similar neuroanatomical structures that are central to WM, namely the hippocampus and prefrontal cortex (72, 73), and exert opposing independent influences on memory and WM (e.g., (66, 67, 74, 75). Although experimental investigations demonstrate that concomitant marijuana and tobacco use is linked with altered behavior (15-18, 21, 23), few studies specifically examine simultaneous use on neurocognition. Therefore, these data provide first steps in understanding whether tobacco mitigates WM impairments from acute marijuana use, and does so using an EMA paradigm allowing for a first-of-its kind real-life replication of laboratory findings.

Associations between acute marijuana and tobacco use and WM persisted after adjusting for multiple potential confounds including task complexity, demographics, background/ contextual variables, and overall substance use. Employing this conservative model with multiple controls was critical as many of these factors may adversely influence WM. For instance, Speck and colleagues (76) demonstrated that gender moderated both performance and functional organization during WM tasks. The fact that significant effects were detected above and beyond the influence of multiple confounds speaks to the specificity and the robustness of these associations.

Intriguing effects emerged regarding alcohol's relationship to WM, despite no a priori hypotheses on this relationship. First, people who drank more during the week exhibited better WM than those who drank less (see proportion of alcohol prompts in Table 4). However, the drinking heaviness variable was only a proxy (not absolute) measure of level of alcohol use: the proportion of drinking episodes assessed via EMA was modestly correlated with amount of past month drinking indicated on a single-item retrospective recall question collected through the parent project. (r =0.37), suggesting that this variable may be an adequate albeit not ideal measure of level of alcohol use. In contrast, acute drinking episodes were associated with worse WM, suggesting that the pharmacology of alcohol and/or the contexts surrounding alcohol use are likely adverse contributors to WM. These exploratory findings are consistent with alcohol being associated with decrements in cognition (77-81; however, 43, 82-84) likely due to a narrowing of attentional control and impaired capacity to engage in controlled, effortful processing (85-88). WM decrements with alcohol use may be attributable to the alcohol's depressant effects, such as inhibition of glutamatergic transmission (89). Surprisingly, alcohol was not associated with WM decrements when used in combination with marijuana and tobacco, which may be due to a number of different unmeasured factors including dosing effects, sampling variations, or contexts associated with this three-drug use combination. However, the insignificant three-way interaction should be interpreted with caution given the relatively small number of prompts attained in this substance use category (n=78; 0.06% of all prompts). Further

research is warranted to better determine the acute influence of alcohol on WM in real-world settings and in the context of use of other common substances.

Results should be examined in the context of several limitations. First, the EMA-based cognitive assessment is novel and it is possible that this was not an accurate WM measure. Yet, substantial work has already been conducted establishing the acceptability and validity of this paradigm. Schuster and colleagues (59) found that even after adjusting for IQ, task performance was associated standardized laboratory WM measures but not processing speed or verbal abilities, providing preliminary evidence supporting the task's validity. Regardless, future studies are warranted that both stringently establish the psychometric properties of this task and implement redundant measures of WM and neurocognition into EMA to determine the sensitivity and specificity of effects observed in this study. Second, different results may have emerged if other unmeasured variables were modeled (e.g., concurrent use of other substances; substance use dose). For example, it is conceivable that participants smoked less marijuana during tobacco-marijuana occasions than with marijuana alone, which would impact the marijuana effects, and this possibility needs to be specifically considered in next step studies. However, we statistically controlled for a multitude of theoretically relevant variables that may have confounded results and rates of past 90-day use of other substances was extremely low (less than 5%). Additionally, studies with specific hypotheses about how real-time negative affect interacts with real-time substance use are warranted, especially as this study found a significant negative relationship between momentary negative affect and WM. Third, there were fewer occasions of (and fewer participants who reported) simultaneous substance use as compared to occasions of no or single substance use, and concerns for possible sampling variations may be minimized by specifically targeting populations that report regular simultaneous marijuana and tobacco use. Fourth, the potential for self-initiated (i.e., tobacco with and without marijuana and/or alcohol) versus randomly prompted (i.e., marijuana and alcohol without tobacco) responses should be considered as a potential cross-substance confound. Fifth, despite the fact that participants were well-trained on EMA data capture (i.e., many had completed prior waves of EMA through the parent study) and the concordance between the debriefing interviews and EMA data was high (>80%), it cannot be completely guaranteed that participants event-recorded tobacco every time used, thereby representing potentially unmeasured confounding. Finally, overall WM performance was negatively skewed and this task was given multiple times a day over one week; therefore, task learning might have influenced findings and/or resulted in a ceiling effect. However, controlling for multiple practice effect parameters minimized this concern.

Despite limitations, this study suggests that tobacco use may compensate for WM decrements from marijuana among young adults. The attenuation of cognitive decrements may be an important mechanism by which tobacco use is reinforced among marijuana users. Particularly given the numerous documented health risks from tobacco, these results may have relevance in informing the development of more tailored and targeted intervention efforts for the growing number of individuals who use both marijuana and tobacco. This may be especially relevant among the average young adult smoker, as studied here, who is a light and non-daily cigarette user. Findings from this study also highlight the importance of further investigating the putative impact of alcohol (particularly in the context of concurrent

tobacco use) on WM. Strengths of this study include within-subject comparisons to examine cognitive shifts under different substance use conditions and use of real-time data capture methodology, allowing for simultaneous modeling of contextual factors that may interrupt WM. This is the first study to assess WM under ecologically valid conditions while young adults are using substances. Additionally information on WM fluctuations during marijuana, tobacco and alcohol use occasions supports the sensitivity of the WM task to detect drug effects in an EMA paradigm. Future work will assess whether these effects change as individuals progress to substance dependence and develop tolerance. Additionally, related lines of inquiry will examine whether WM fluctuations impact perceived intoxication, affect and subsequently reinforce continued substance use and serve as a barrier for quitting.

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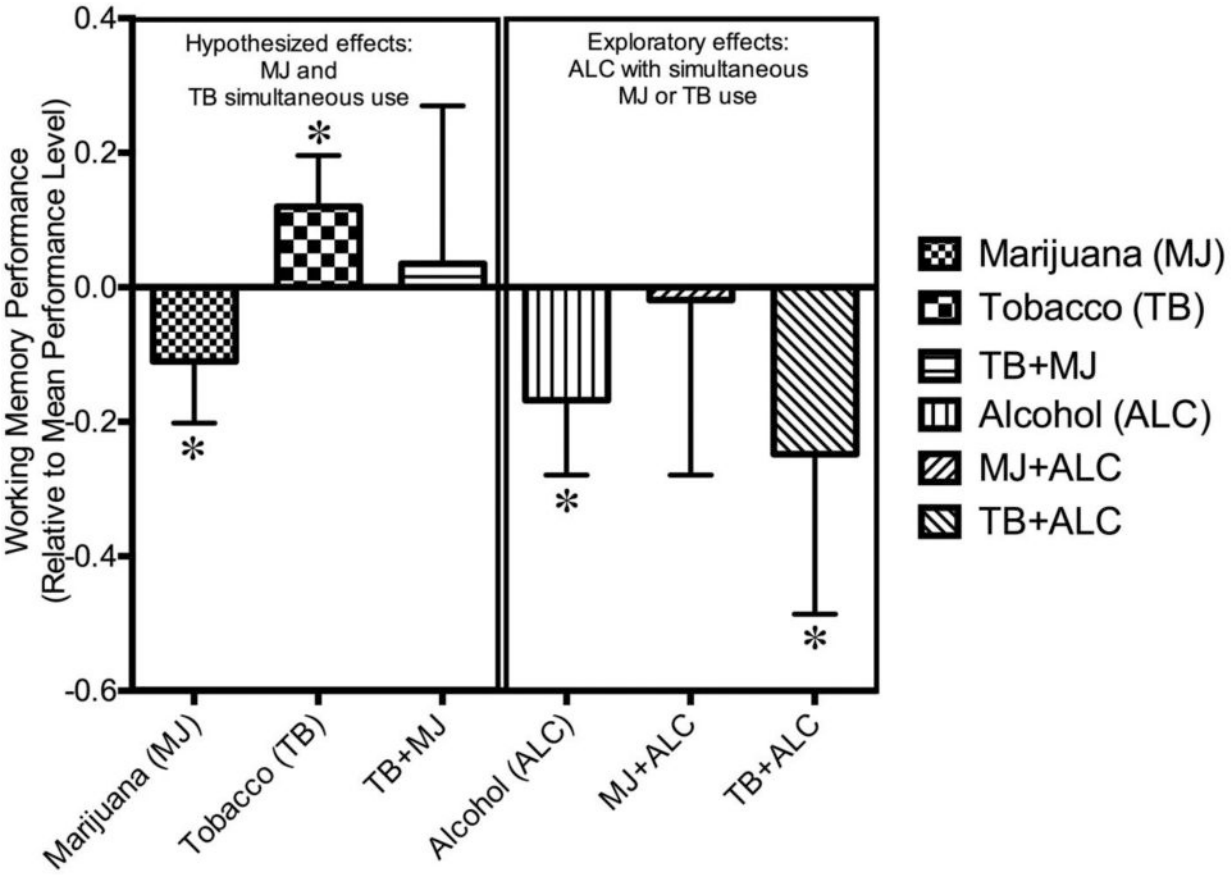

Figure 1.

Figure 1 depicts the mean change in working memory performance under different substance use combinations, compared to mean performance levels. Error bars represent 95% confidence intervals. **Represents significant changes from non-use occasions.*

Table 1

Descriptives of Study Sample

	N =287
Demographics	
Age	21.3 (.8)
% Female	54%
Ethnicity/Race	
Caucasian	65%
Black	11%
Hispanic	16%
Other	7%
Education	
Some High School	4%
High School Diploma or GED	22%
Vocational/Technical School	2%
Some College or Beyond	72%
Mental Health	
BIS-11 Total Score (M, SD)	34.7 (7.5)
CESD Total Score [Md, IQR]	12 [7, 21]
MASQ Total Score [Md, IQR]	25 [20, 30]
ASRS, % of Scores ≥4	20%
Tobacco Use	
Percent Lifetime Cigarettes (100 or more)	88%
Ever Daily Tobacco Use, % Yes	81%
Current Daily Tobacco Use, % Yes	41%
Number of Days Smoked Cigarettes in the Past Month [Md, IQR]	25 [7, 30]
Number of Cigarettes on Days Smoked [Md, IQR]	4 [2, 10]
mFTQ Total Score [Md, IQR]	2 [2,4]
Marijuana Use	
Ever Use, % Yes	91%
Frequency of Use in Past 90 Days	
0 Times	29%
Once a Month or Less	16%
More than Once a Month but Less than Once a Week	10%
One or More Times a Week but Not Every Day	22%
Every Day	23%
CUDIT-R, Total Score [Md, IQR]	7 [2, 13.71]
Alcohol Use	
Ever Use, % Yes	98%
Frequency of Use in Past 90 Days	
0 Times	4%
Once a Month or Less	8%

	N =287
More than Once a Month but Less than Once a Week	25%
One or More Times a Week but Not Every Day	59%
Every Day	4%
Other Substance Use	
Ever Use, % Yes	
Cocaine	35%
Amphetamines	24%
Hallucinogens	47%
Inhalants	46%
IV Drugs	2%

Note. M, Mean; SD, Standard Deviation; Md, Median; IQR, Interquartile range; BIS-11, Barratt Impulsiveness Scale-11th version; CESD, Center for Epidemiological Studies-Depression; MASQ, Mood and Affect Symptom Questionnaire; ASRS, Adult ADHD Self-Report Scale; NDSS, Nicotine Dependence Syndrome Scale; mFTQ, Modified Fagerstrom Tolerance Questionnaire; CUDIT-R, Marijuana Use Disorders Identification Test-Revised

Table 2

Percent of Participants by Number of Correctly Recalled Dots in EMA Working Memory Task and EMA Substance Use Type

	Number of Dots Correctly Recalled						
	n	**0**	**1**	**2**	**3**	**4**	**5**
Random Prompt							
No Substance Use	9003	2%	5%	8%	10%	17%	58%
Marijuana Only	851	2%	6%	10%	13%	17%	52%
Alcohol Only	617	1%	3%	7%	10%	18%	61%
Marijuana and Alcohol	198	3%	7%	10%	11%	19%	50%
Smoke Prompt							
Tobacco Only	1998	2%	4%	8%	10%	17%	59%
Marijuana and Tobacco	329	3%	6%	7%	12%	17%	55%
Alcohol and Tobacco	192	2%	4%	11%	12%	19%	52%
Marijuana, Alcohol and Tobacco	78	3%	5%	4%	10%	22%	56%

Note. Table 2 illustrates the number of correct responses during drug use categories derived from raw EMA data. Primary analyses (presented in Tables 3-4), considered effects of substance(s) collapsed across other substance use categories.

Table 3

Descriptives of Covariates Included in Random-Effect Ordinal Regression Model and Association with Number Correctly Recalled Dots on EMA Working Memory Task

Effect	Descriptives	Estimate	p-value	Marginal OR	95% CI
Task Complexity					
Trial	--	0.07	0.008	1.06	(1.02,1.11)
Number of Grids	--				
2		0	--	--	--
3		0.21	<0.0001	1.20	(1.13, 1.26)
4		0.30	<0.0001	1.29	(1.23, 1.36)
Dispersion of Dots from Regression Line	.4 (.2)	0.37	<0.0001	1.37	(1.25, 1.50)
Number of Corner Dots	1.3 (.8)	0.40	<0.0001	1.41	(1.36, 1.46)
Distance between Dots	21.5 (3. 1)	-0.15	<0.0001	0.88	(0.87, 0.89)
Contextual/Background Factors					
Gender (B/S)	54% Female	0.07	0.61	1.06	(0.85, 1.31)
GPA	3.6 (.7)	0.38	<0.0001	1.39	(1.20, 1.61)
Alone	52.3%	0.16	<0.0001	1.15	(1.09, 1.20)
Weekend Responding	28.2%	-0.04	0.12	0.96	(0.92, 1.01)
Watching TV/Listening to Music	34.6%	0.18	<0.0001	1.17	(1.11, 1.23)
At a Party	2.1%	-0.17	0.06	0.86	(0.74, 1.01)
Time of Day					
4am-8:59am	3%	-0.24	0.003	0.82	(0.71, 0.93)
9am-1:59pm	24%	0	--	--	--
2pm-5:59pm	29%	-0.12	0.0006	0.90	(0.85, 0.96)
6pm-9:59pm	31%	-0.08	0.03	0.93	(0.88, 0.99)
10pm-3:59am	13%	-0.09	0.05	0.93	(0.85, 1.00)
Study Day		0.30	<0.0001	1.29	(1.24, 1.34)
0	10%				
1	16%				
2	15%				
3	14%				

Effect	Descriptives	Estimate	p-value	Marginal OR	95% CI
4	14%				
5	13%				
6	13%				
7	5%				
Study Day (Quadratic)	--	-0.03	<0.0001	0.97	(0.97, 0.98)
Trouble Concentrating	3.1 (2.6)	-0.01	0.20	0.99	(0.98, 1.00)
Negative Affect	3.0 (2.1)	-0.03	0.001	0.98	(0.96, 0.99)
Overall Substance Use					
Proportion Marijuana Prompts (B/S)	.1 (.2)	-0.36	0.36	0.74	(0.38, 1.42)
Proportion Tobacco Prompts (B/S)	.2 (.2)	0.62	0.14	1.71	(0.84, 3.48)
Proportion Alcohol Prompts (B/S)	.1 (.1)	2.67	<0.0001	9.97	(3.22, 30.91)

Note. All descriptive values are means and standard deviations, unless otherwise specified. Between-subject effects (B/S) are specifically denoted. All other covariates represent within-subject effects. Grade point average, GPA (on 4-point scale); Trouble concentrating (Likert scale item with response options 1-Not at all through 10-Very much); Negative affect (average of responses on current feelings of anger, frustration, irritability, sadness and stress, each with continuous response options of 1-Not at all through 10-Very much); Overall substance use separately derived for each participant based on the proportion of total prompts across the study week during which use of that substance was reported.

Table 4

Main Effects and Interactions of Momentary Substance Use From Random-Effect Ordinal Regression Model Predicting Proportion of Correctly Recalled Dots on EMA Working Memory Task

Effect	Estimate	p-value	Marginal OR	95% CI
Marijuana	-0.11	0.03	0.91	(0.84, 0.99)
Alcohol	-0.17	0.003	0.87	(0.79, 0.95)
Tobacco	0.12	0.002	1.11	(1.04, 1.18)
Marijuana*Tobacco	0.04	0.77	1.03	(0.84, 1.26)
Marijuana*Alcohol Use	-0.001	0.99	1.00	(0.79, 1.27)
Tobacco*Alcohol	-0.25	0.04	0.81	(0.66, 0.99)

Note. All predictors represent within-subject effects. This model includes adjustment for all covariates in Table 3. This model was run initially with main effects of marijuana, tobacco and alcohol as well as all two-way and three-way interactions; however, the three-way interaction was not significant (p=.48) and was therefore removed from the model.