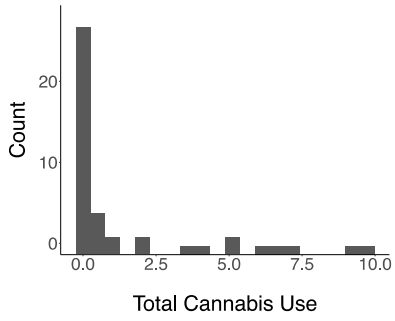
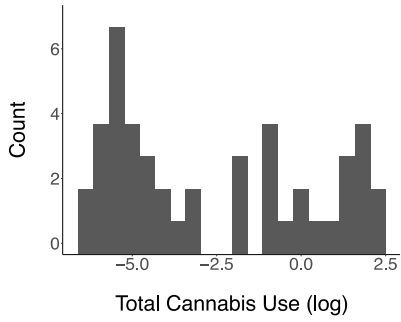


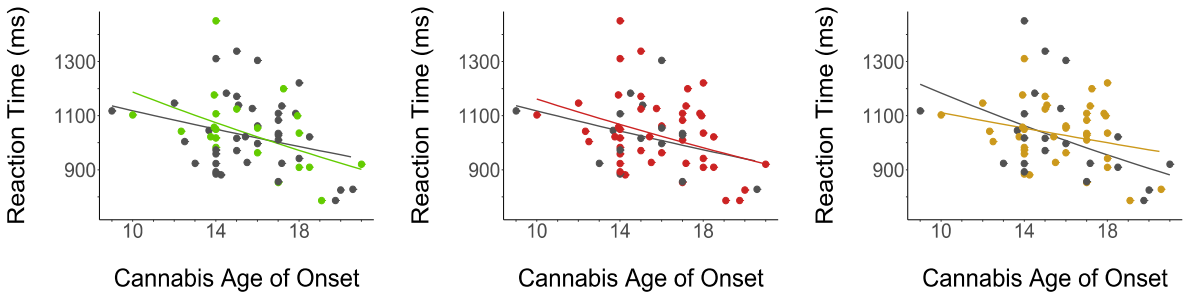
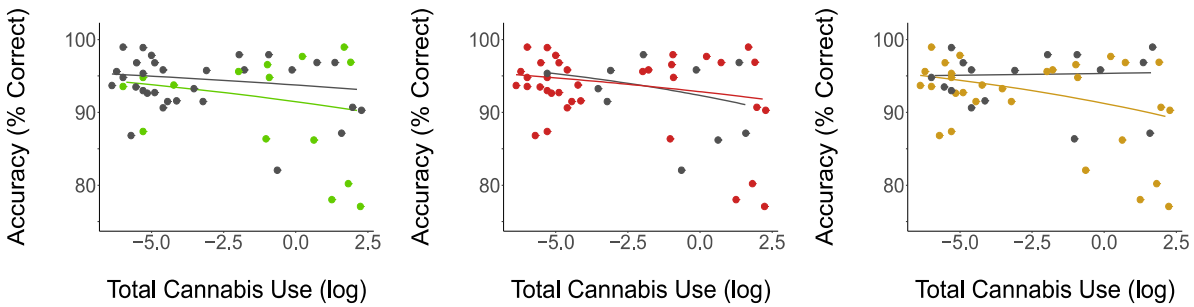
A



B



Supplemental Figure S1. Due to the non-normality of the *raw* total cannabis use distribution, total cannabis use was log transformed in accordance with previous work using cannabis dosage estimates in the MHCPD (1).

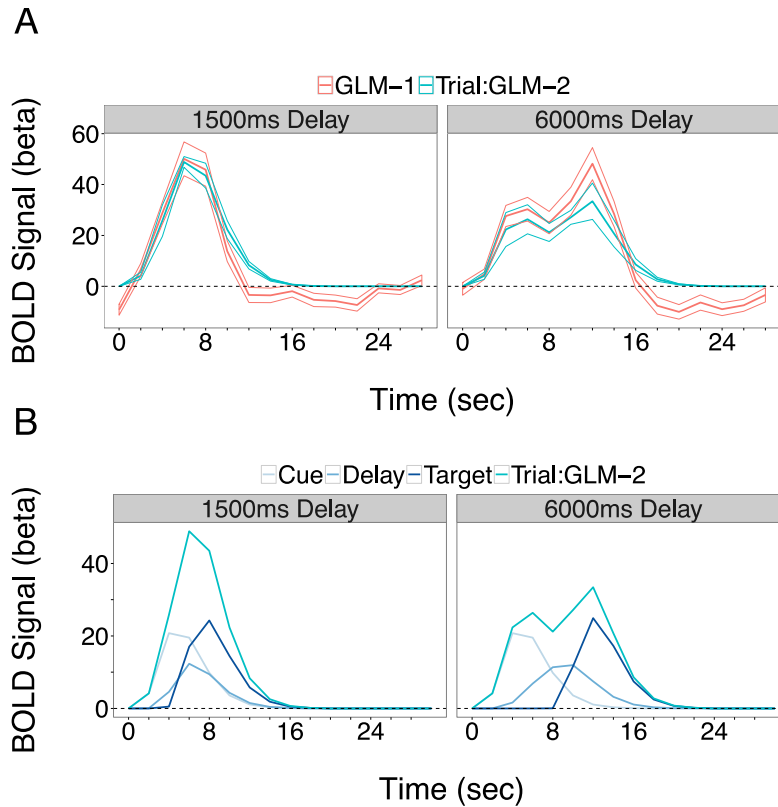
**A****B**

Prenatal Cannabis

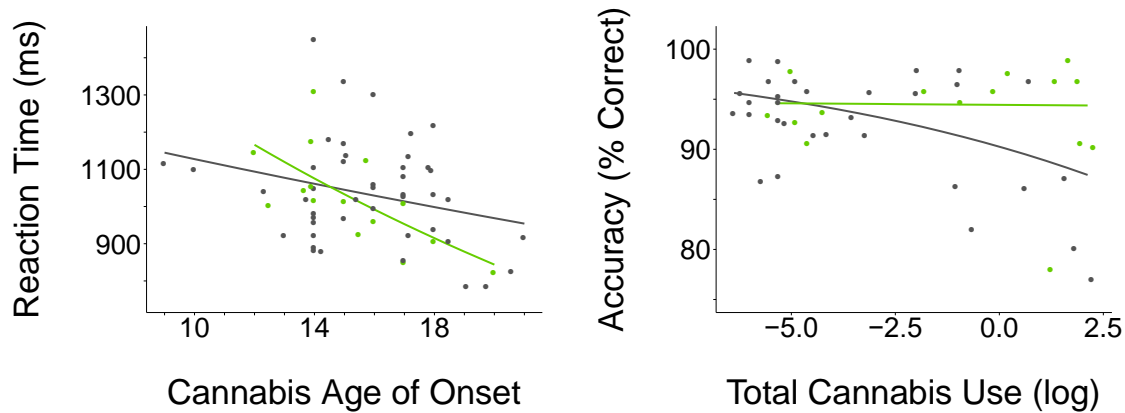
Prenatal Alcohol

Prenatal Cigarette

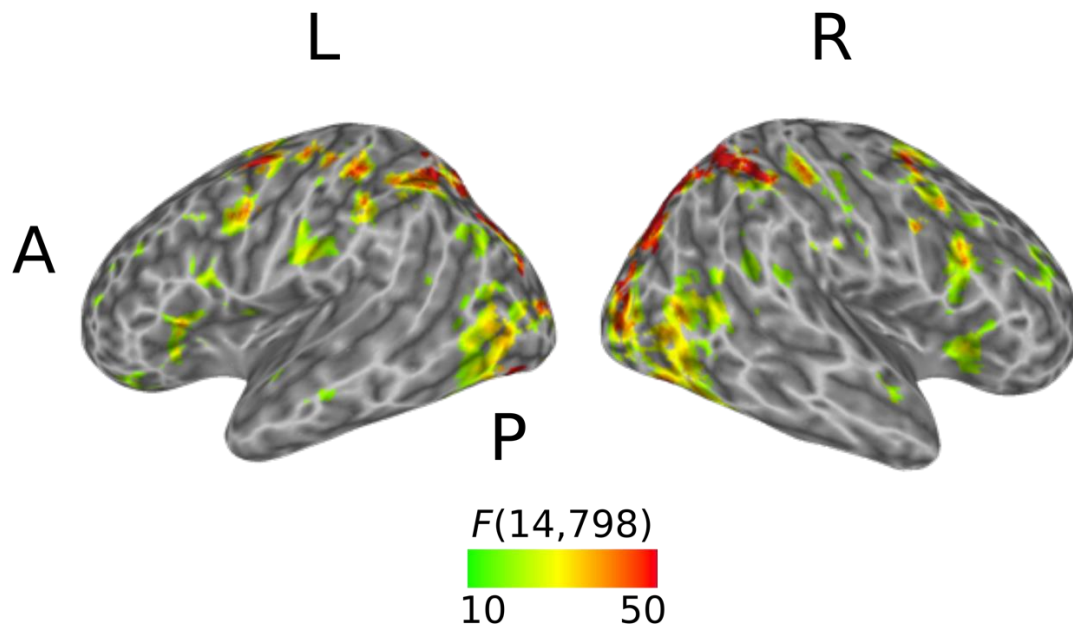
Supplemental Figure S2. Covariate and Moderation Analysis of Prenatal Substance Use measures on Working Memory Performance. Categorical versions of prenatal measures (any exposure) were used to examine whether primary behavior results were influenced or moderated by prenatal substance use. **(A)** Cannabis age of onset was a significant predictor of working memory reaction time (baseline:  $t = -2.99$ ,  $p = .003$ ) and remained significant with the inclusion of prenatal cannabis- (baseline + prenatal cannabis:  $t = -3.04$ ,  $p = .002$ ), prenatal alcohol- (baseline + prenatal alcohol:  $t = -3.04$ ,  $p = .002$ ), and prenatal cigarette- (baseline + prenatal cigarette:  $t = -3.00$ ,  $p = .003$ ) exposure as covariates. Additionally, age of onset WM RT effects did not differ between exposed and unexposed groups (exposure by age of onset interaction) for cannabis- ( $t = -0.22$ ,  $p = .827$ ), alcohol- ( $t = -0.09$ ,  $p = .931$ ) or cigarette- ( $t = 1.08$ ,  $p = .280$ ) prenatal exposure. **(B)** Total cannabis use had a trending, negative relationship with WM accuracy in the baseline model ( $z = -1.93$ ,  $p = .054$ ). However, this was no longer significant with the inclusion of prenatal cannabis as a covariate (baseline + prenatal cannabis:  $z = -1.41$ ,  $p = .159$ ). Nevertheless, prenatal cannabis use was not a significant predictor of WM accuracy (baseline + prenatal cannabis:  $z = -1.23$ ,  $p = .219$ ), ruling out potential mediation. In contrast, the main effect of higher total cannabis use predicting lower WM accuracy remained at a trend while covarying prenatal alcohol- (baseline + prenatal alcohol:  $z = 1.88$ ,  $p = .061$ ) and prenatal cigarette exposure (baseline + prenatal cigarette:  $z = -1.93$ ,  $p = .054$ ). Moderation analysis revealed no significant interactions between exposure measures and total cannabis use predicting WM accuracy (cannabis:  $z = -0.26$ ,  $p = .795$ ; alcohol:  $z = 0.36$ ,  $p = .721$ ; cigarette:  $z = -1.317$ ,  $p = .188$ ).



Supplemental Figure S3. Representative Grand Average Time Series (GLM-1) and Epoch Parameters (GLM-2): R-PPC (B). **(A)** Reconstructed time series from GLM-2 (Trial:GLM-2) captures primary amplitude components of the piecewise time series from GLM-1. **(B)** Individual epoch amplitudes for cue, delay, and target, whose sum creates the time series for GLM-2 (Trial:GLM-2).



Supplemental Figure S4. Covariate and Moderation Analysis of Cannabis Use in the Last Year on Working Memory Performance. As in primary analysis, cannabis use in the last year was treated as a categorical variable (Use: green; No Use: grey). As reported in the primary text, cannabis age of onset remained a significant predictor of WM RT while covarying cannabis use in the last year (full model:  $\chi^2(1) = 9.70$ ,  $z = -3.11$ ,  $p = .002$ ). Cannabis use within the last year was not a significant predictor of WM RT in this model ( $\chi^2(1) = 0.22$ ,  $t = -0.47$ ,  $p = .575$ ) (See Supplemental Table 1). Furthermore, cannabis use in the last year did not significantly moderate the association between cannabis age of onset and WM RT ( $\chi^2(1) = 2.38$ ,  $t = -1.54$ ,  $p = .123$ ). The interaction between cannabis use in the last year and total cannabis use predicting WM accuracy was at a trend ( $\chi^2(1) = 2.74$ ,  $z = 1.66$ ,  $p = .098$ ). However, cannabis use in the last year was not a significant predictor of WM accuracy while covarying total cannabis use (REP group)(full model:  $\chi^2(1) = 1.77$ ,  $z = 1.33$ ,  $p = .183$ ).



Supplemental Figure S5. Main Effect of Time from Cannabis Age of Onset Analysis. L, Left; R, Right; A, anterior; P, posterior. Robust Activation is observed in canonical working memory regions.

Variable	t	$\chi^2_{(1)}$	<i>p-value</i>
Cannabis Age of Onset	-3.11	9.70	.002
Group (REP vs. EXP)	-0.36	.133	.715
Cannabis Use in the Last Year (Use vs. No Use)	-0.47	0.22	.636
Cigarette Use in the Last Year (Use vs. No Use)	0.50	0.25	.615
Highest Level of Education	0.92	0.84	.359
Other Drug (Use vs. No Use)	0.94	0.89	.347
Total Cigarette Use	-1.27	1.61	.205

Supplemental Table 1. Between-subject Fixed Effects from Full Model Predicting Working Memory Reaction Time in the Cannabis Age of Onset Analysis.

Variable	z	$\chi^2_{(1)}$	p-value
Total Cannabis Use (log)	-2.50	6.27	.012
Cannabis Age of Onset	0.36	0.13	.720
Cannabis Use in the Last Year (Use vs. No Use)	1.33	1.77	.183
Cigarette Use in the Last Year (Use vs. No Use)	0.88	0.77	.379
Family Income	-0.28	0.08	.777
Highest Level of Education	-1.55	2.41	.120
Other Drug (Use vs. No Use)	-0.90	0.80	.371
Total Alcohol Use	1.61	2.58	.108
Total Cigarette Use	-0.68	0.46	.499

Supplemental Table 2. Between-subject Fixed Effects from Full Model Predicting Working Memory Accuracy in the Total Cannabis Use Analysis. *Note, See Supplementary Figure S2 for Covariate Analysis of Prenatal Cannabis with Total Cannabis Use.*

Variable	t	<i>p-value</i>
Cannabis Age of Onset	2.31	.025
Group (REP vs. EXP)	-0.31	.760
Cannabis Use in the Last Year (Use vs. No Use)	1.29	.203
Cigarette Use in the Last Year (Use vs. No Use)	-0.75	.455
Highest Level of Education	0.55	.584
Other Drug (Use vs. No Use)	-0.68	.498
Total Cigarette Use	0.39	.695

Supplemental Table 3. Full model predicting PPC (A) Cue Epoch BOLD Activation from Cannabis Age of Onset Analysis.



Variable	t	<i>p</i> -value
Total Cannabis Use (log)	2.58	.014
Cannabis Age of Onset	-1.19	.241
Cannabis Use in the Last Year (Use vs. No Use)	-0.72	.479
Prenatal Cannabis Exposure (Any Exposure)	-1.10	.278
Cigarette Use in the Last Year (Use vs. No Use)	0.88	.379
Family Income	-0.13	.895
Highest Level of Education	0.89	.380
Other Drug (Use vs. No Use)	-0.90	.371
Total Alcohol Use	-0.17	.869
Total Cigarette Use	-0.98	.335

Supplemental Table 4. Full model predicting DLPFC Delay Epoch BOLD Activation from Total Cannabis Use Analysis.

### Supplemental Tables 5 & 6: Omission Errors

Omission errors were analyzed using a similar procedure as in accuracy analysis. Generalized linear mixed effects models with a logit link function with maximum likelihood estimation were used. Random intercepts were included for each subject. Baseline models (Table 5 & Table 6) included task conditions (load, delay length, cue validity) and the cannabis measure in question.

Overall, omission errors were fairly rare in the sample (4.02% of all trials). Omission errors did not differ between usage groups (Table 5) and were not associated with Total Cannabis Use (Table 6). Omission errors were not associated with cannabis age of onset in the combined cannabis group (EXP+REP) (Table 6), however an interaction term between group (EXP vs. REP) and age of onset was significant ( $\chi^2(1) = 3.87$ ,  $z = -1.97$ ,  $p = .049$ ). Post-hoc testing demonstrated a significant effect of age of onset in the REP group, where those with later onsets made fewer omission errors, but a non-significant effect of age of onset in the EXP group (Table 6).

#### Supplemental Table 5

	Non-Users (NU) n = 15	Cannabis Experimenters (EXP) n = 14	Cannabis Repeated (REP) n = 46	p-value
<b>Omission Rate</b> (% Trials)	4.03 (4.44)	4.89 (5.82)	4.08 (5.96)	NU > EXP = .836 NU > REP = .664 EXP > REP = .868

#### Supplemental Table 6

Variable	Cannabis Age of Onset (EXP + REP)	Cannabis Age of Onset (EXP)	Cannabis Age of Onset (REP)	Total Cannabis Use (log) (REP)
<b>Omission Rate</b> (% Trials)	$\chi^2(1) = 2.21$ , $z = -1.49$ , $p = .137$	$\chi^2(1) = 1.70$ , $z = -1.30$ , $p = .193$	$\chi^2(1) = 5.33$ , $z = -2.31$ , $p = .021$	$\chi^2(1) = 0.30$ , $z = -0.55$ , $p = .581$

**Note.** Cannabis Age of Onset Effects Presented for full Usage Group (EXP+REP), while covarying group, and EXP and REP groups separately. Age of onset model within REP group covaried total cannabis use. Total cannabis use analyzed only in REP group and covaried cannabis age of onset.

## References

1. Cornelius MD, Goldschmidt L, Day NL, Larkby C (2002): Alcohol, tobacco and marijuana use among pregnant teenagers: 6-year follow-up of offspring growth effects. *Neurotoxicol Teratol.* 24: 703–710.