

Effect of four-week cannabidiol treatment on cognitive function: secondary outcomes from a randomised clinical trial for the treatment of cannabis use disorder

Psychopharmacology

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Secondary outcome analyses

Immediate prose recall

Table S1

Data show model estimates of the effect of dose, time, and dose by time interaction on immediate prose recall.

	Estimate	SE	Df	<i>t</i> -value	Lower CI	Upper CI
Intercept	7.24	0.62	117.48	11.63	5.88	8.38
Placebo	-	-	-	-	-	-
400mg CBD	-0.18	0.87	117.48	-0.20	-1.90	1.72
800mg CBD	0.67	0.88	117.48	0.77	-1.02	2.47
Baseline	-	-	-	-	-	-
Week 4	1.49	0.72	67.34	2.09	0.11	2.83
Dose by time (Placebo, Baseline)	-	-	-	-	-	-
Dose by time (400mg CBD, Week 4)	0.92	1.00	67.32	0.92	-0.95	3.02
Dose by time (800mg CBD, Week 4)	1.57	1.00	66.71	1.57	-0.31	3.50

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Table S2

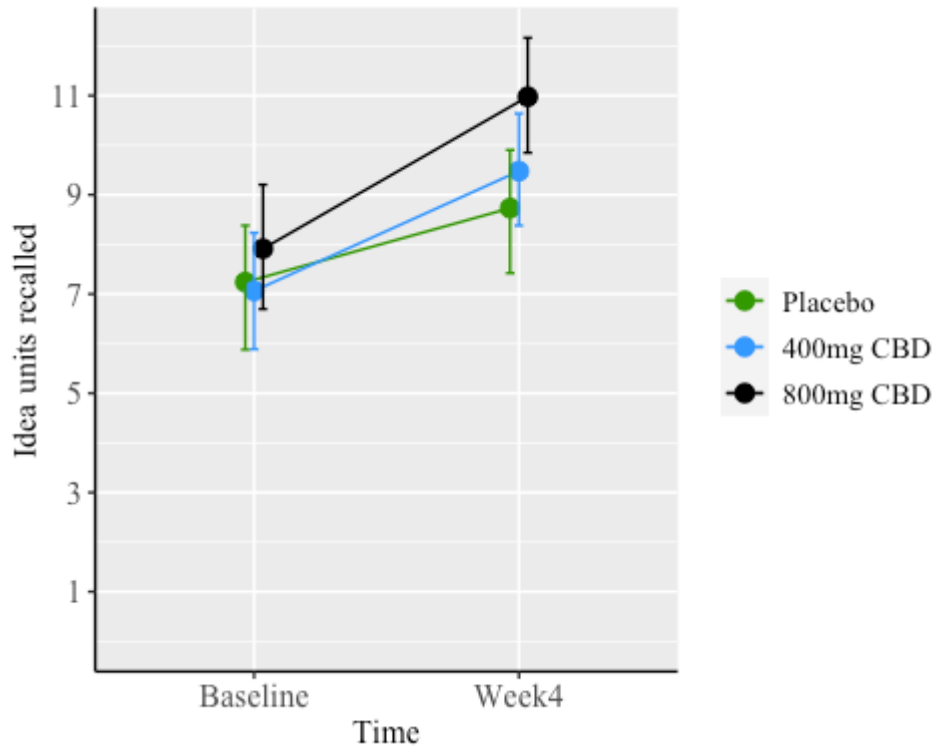
Change from baseline to week 4 (end of treatment) for scores on immediate prose recall, by treatment group.

Contrast	Treatment	Estimate	SE	Df	Lower CI	Upper CI
Week 4 - Baseline	Placebo	0.75	0.36	66.47	0.06	1.41
Week 4 - Baseline	400mg CBD	1.21	0.35	66.42	0.53	1.92
Week 4 - Baseline	800mg CBD	1.53	0.35	65.20	0.82	2.23

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Figure S1

Group means of idea units recalled at the immediate measurement of the prose recall task, by treatment group at baseline and week 4. Error bars represent bootstrapped 95% confidence intervals.



SSRT**Table S3**

Data show model estimates of the effect of dose, time, and dose by time interaction on SSRT.

	Estimate	SE	Df	<i>t</i> -value	Lower CI	Upper CI
Intercept	257.21	11.19	110.26	22.99	232.78	277.34
Placebo	-	-	-	-	-	-
400mg CBD	-5.50	15.65	110.26	-0.35	-36.47	28.58
800mg CBD	-3.27	15.82	110.26	-0.21	-34.22	28.40
Baseline	-	-	-	-	-	-
Week 4	-18.44	11.90	66.96	-1.55	-41.56	3.52
Dose by time (Placebo, Baseline)	-	-	-	-	-	-
Dose by time (400mg CBD, Week 4)	7.36	16.64	66.94	0.44	-23.80	42.22
Dose by time (800mg CBD, Week 4)	5.01	16.69	66.39	0.30	-26.41	37.22

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Table S4

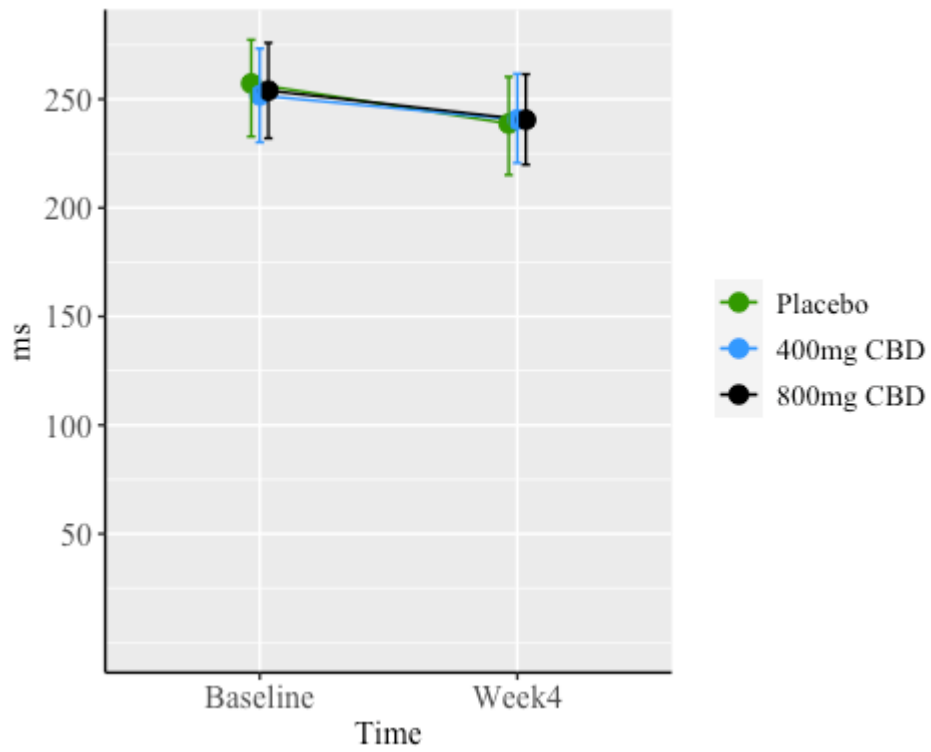
Change from baseline to week 4 (end of treatment) for scores on SSRT, by treatment group.

Contrast	Treatment	Estimate	SE	Df	Lower CI	Upper CI
Week 4 - Baseline	Placebo	-9.22	5.95	66.30	-20.78	1.76
Week 4 - Baseline	400mg CBD	-5.54	5.82	66.26	-16.68	6.46
Week 4 - Baseline	800mg CBD	-6.72	5.85	65.15	-18.60	4.87

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Figure S2

Group means of SSRT score, by treatment group at baseline and week 4. Error bars represent bootstrapped 95% confidence intervals.



Trail making task – Part A

Table S5

Data show model estimates of the effect of dose, time, and dose by time interaction on Part A of the trail making task

	Estimate	SE	Df	<i>t</i> -value	Lower CI	Upper CI
Intercept	24.29	1.43	103.83	16.95	21.15	26.90
Placebo	-	-	-	-	-	-
400mg CBD	1.31	2.01	103.83	0.65	-2.57	5.67
800mg CBD	-2.26	2.03	103.83	-1.12	-6.22	1.80
Baseline	-	-	-	-	-	-
Week 4	-3.51	1.43	65.13	-2.45	-6.30	-0.89
Dose by time (Placebo, Baseline)	-	-	-	-	-	-
Dose by time (400mg CBD, Week 4)	-0.74	2.00	65.10	-0.37	-4.49	3.45
Dose by time (800mg CBD, Week 4)	0.94	2.01	64.60	0.47	-2.83	4.80

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Table S6

Change from baseline to week 4 (end of treatment) for scores on part A of the trail making task, by treatment group.

Contrast	Treatment	Estimate	SE	Df	Lower CI	Upper CI
Week 4 - Baseline	Placebo	-1.75	0.72	66.18	-3.15	-0.44
Week 4 - Baseline	400mg CBD	-2.13	0.70	66.13	-3.47	-0.67
Week 4 - Baseline	800mg CBD	-1.28	0.70	65.11	-2.71	0.11

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Trail making task – Part B- Part A

Table S7

Data show model estimates of the effect of dose, time, and dose by time interaction on Part B – Part A of the trail making task

	Estimate	SE	Df	t-value	Lower CI	Upper CI
Intercept	36.94	4.77	120.60	7.75	26.79	45.53
Placebo	-	-	-	-	-	-
400mg CBD	-9.61	6.67	120.60	-1.44	-22.54	4.75
800mg CBD	-10.35	6.74	120.60	-1.54	-23.31	3.31
Baseline	-	-	-	-	-	-
Week 4	1.35	5.67	67.25	0.24	-9.63	11.91
Dose by time (Placebo, Baseline)	-	-	-	-	-	-
Dose by time (400mg CBD, Week 4)	0.52	7.93	67.22	0.07	-14.28	17.09
Dose by time (800mg CBD, Week 4)	12.09	7.96	66.60	1.52	-2.82	27.32

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Table S8

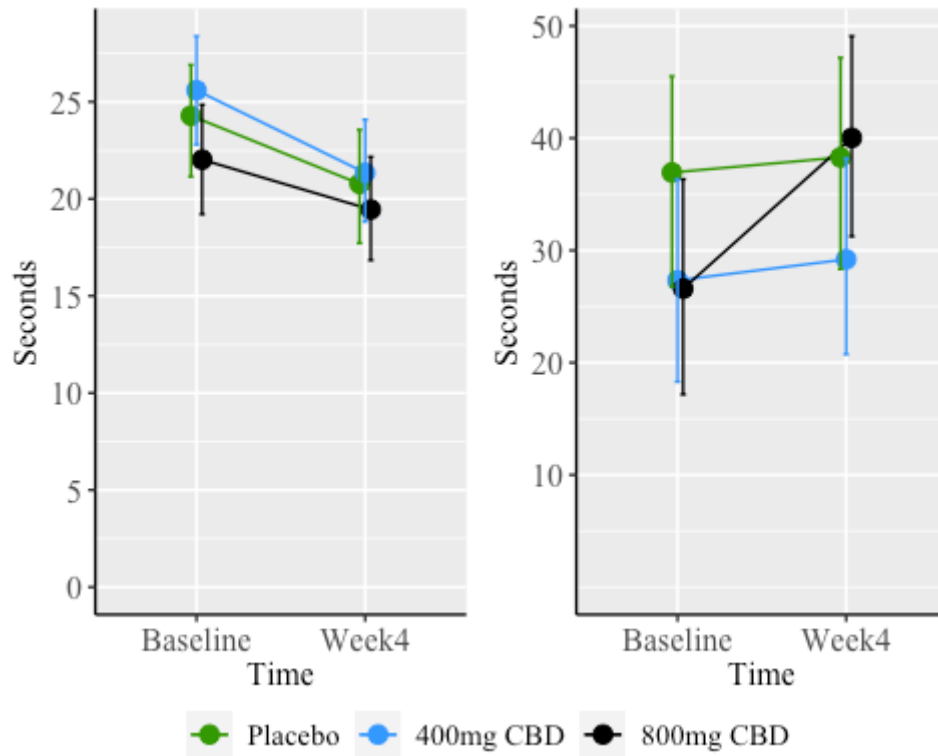
Change from baseline to week 4 (end of treatment) for scores on Part B – Part A of the trail making task, by treatment group.

Contrast	Treatment	Estimate	SE	Df	Lower CI	Upper CI
Week 4 - Baseline	Placebo	0.67	2.84	66.55	-4.82	5.95
Week 4 - Baseline	400mg CBD	0.93	2.77	66.50	-4.44	6.53
Week 4 - Baseline	800mg CBD	6.72	2.79	65.23	1.05	12.25

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Figure S3

Group means of time taken to complete Part A of the Trail making Task (3a), and Part B – A (3b), by treatment group at baseline and week 4. Error bars represent bootstrapped 95% confidence intervals.



Digit Span

Table S9

Data show model estimates of the effect of dose, time, and dose by time interaction on digit span.

	Estimate	SE	Df	<i>t</i> -value	Lower CI	Upper CI
Intercept	6.96	0.26	97.79	27.26	6.40	7.43
Placebo	-	-	-	-	-	-
400mg CBD	0.63	0.36	97.79	1.76	-0.07	1.39
800mg CBD	0.43	0.36	97.79	1.20	-0.27	1.17
Baseline	-	-	-	-	-	-
Week 4	0.18	0.23	66.20	0.78	-0.28	0.61
Dose by time (Placebo, Baseline)	-	-	-	-	-	-
Dose by time (400mg CBD, Week 4)	-0.16	0.33	66.18	-0.50	-0.77	0.52
Dose by time (800mg CBD, Week 4)	0.04	0.33	65.74	0.11	-0.58	0.66

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Table S10

Change from baseline to week 4 (end of treatment) for digits repeated on the digit span test, by treatment group.

Contrast	Treatment	Estimate	SE	Df	Lower CI	Upper CI
Week 4 - Baseline	Placebo	0.09	0.12	66.00	-0.14	0.30
Week 4 - Baseline	400mg CBD	0.01	0.11	65.97	-0.21	0.25
Week 4 - Baseline	800mg CBD	0.11	0.11	65.08	-0.12	0.33

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Backwards digit span

Table S11

Data show model estimates of the effect of dose, time, and dose by time interaction on backwards digit span.

	Estimate	SE	Df	<i>t</i> -value	Lower CI	Upper CI
Intercept	5.17	0.27	109.54	19.23	4.59	5.66
Placebo	-	-	-	-	-	-
400mg CBD	-0.17	0.38	109.54	-0.46	-0.92	0.65
800mg CBD	-0.04	0.38	109.54	-0.11	-0.79	0.72
Baseline	-	-	-	-	-	-
Week 4	-0.15	0.29	65.75	-0.53	-0.71	0.38
Dose by time (Placebo, Baseline)	-	-	-	-	-	-
Dose by time (400mg CBD, Week 4)	0.41	0.40	65.72	1.02	-0.34	1.25
Dose by time (800mg CBD, Week 4)	0.76	0.40	65.17	1.90	0.01	1.54

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Table S12

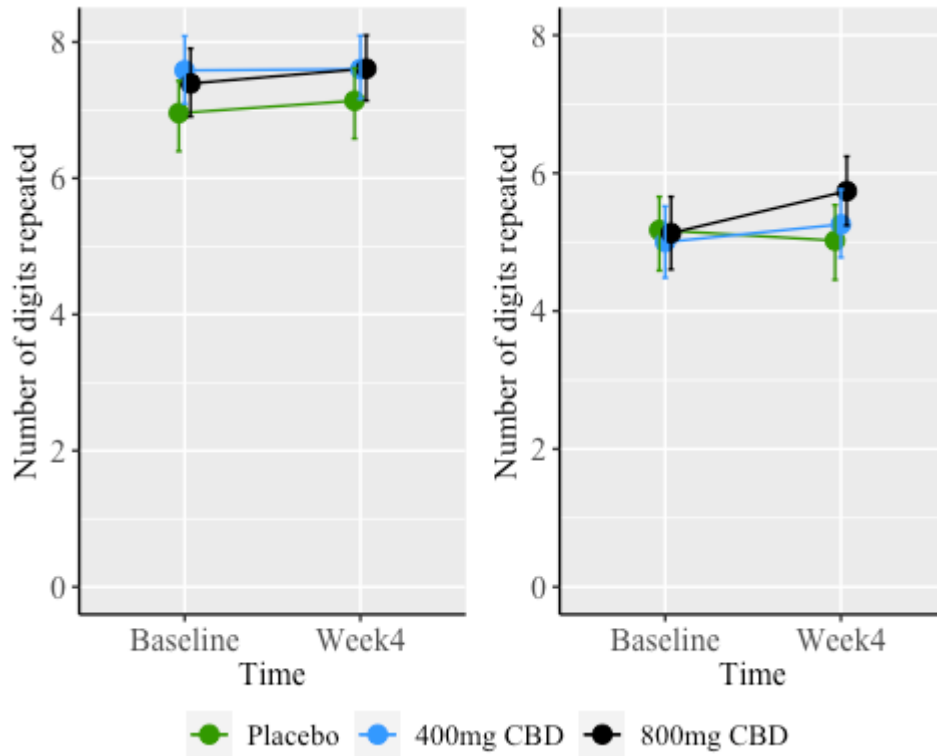
Change from baseline to week 4 (end of treatment) for digits repeated backwards, by treatment group

Contrast	Treatment	Estimate	SE	Df	Lower CI	Upper CI
Week 4 - Baseline	Placebo	-0.08	0.14	66.30	-0.35	0.19
Week 4 - Baseline	400mg CBD	0.13	0.14	66.25	-0.14	0.42
Week 4 - Baseline	800mg CBD	0.30	0.14	65.15	0.02	0.58

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Figure S4

Group means on forward and backward digit span by treatment group, at baseline and week 4. Error bars represent bootstrapped 95% confidence intervals.



Letter (phonemic) fluency

Table S13

Data show model estimates of the effect of dose, time, and dose by time interaction on letter fluency.

	Estimate	SE	Df	<i>t</i> -value	Lower CI	Upper CI
Intercept	12.57	0.99	106.49	12.73	10.40	14.38
Placebo	-	-	-	-	-	-
400mg CBD	0.89	1.38	106.49	0.65	-1.82	3.88
800mg CBD	-0.13	1.40	106.49	-0.09	-2.85	2.64
Baseline	-	-	-	-	-	-
Week 4	-0.31	1.01	66.61	-0.30	-2.27	1.54
Dose by time (Placebo, Baseline)	-	-	-	-	-	-
Dose by time (400mg CBD, Week 4)	-0.88	1.41	66.58	-0.63	-3.52	2.07
Dose by time (800mg CBD, Week 4)	0.13	1.41	66.07	0.09	-2.53	2.85

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Table S14

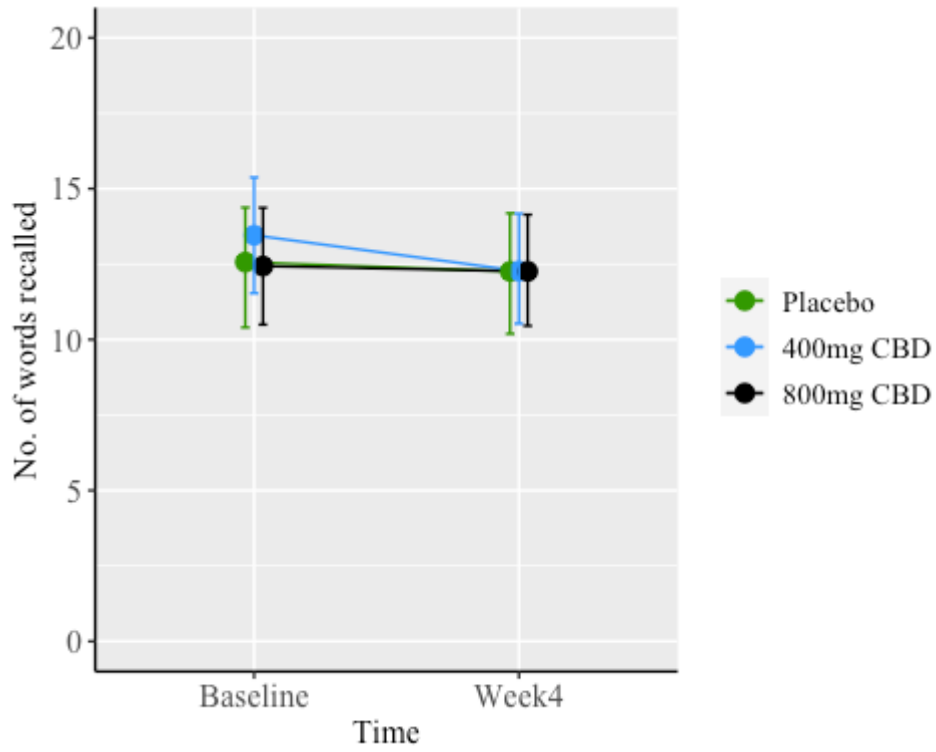
Change from baseline to week 4 (end of treatment) for number of letter words recalled, by treatment group.

Contrast	Treatment	Estimate	SE	Df	Lower CI	Upper CI
Week 4 - Baseline	Placebo	-0.15	0.50	66.22	-1.14	0.77
Week 4 - Baseline	400mg CBD	-0.59	0.49	66.17	-1.54	0.43
Week 4 - Baseline	800mg CBD	-0.09	0.50	65.12	-1.09	0.89

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Figure S5

Group means of number of words recalled on the letter fluency task by treatment group, at baseline and week 4. Error bars represent bootstrapped 95% confidence intervals.



Category (semantic) fluency

Table S15

Data show model estimates of the effect of dose, time, and dose by time interaction on category (semantic) fluency.

	Estimate	SE	Df	<i>t</i> -value	Lower CI	Upper CI
Intercept	13.48	0.89	104.00	15.15	11.53	15.10
Placebo	-	-	-	-	-	-
400mg CBD	1.23	1.24	104.00	0.99	-1.16	3.92
800mg CBD	-0.26	1.26	104.00	-0.21	-2.72	2.27
Baseline	-	-	-	-	-	-
Week 4	2.60	0.88	66.61	2.96	0.88	4.21
Dose by time (Placebo, Baseline)	-	-	-	-	-	-
Dose by time (400mg CBD, Week 4)	-1.37	1.23	66.59	-1.11	-3.67	1.21
Dose by time (800mg CBD, Week 4)	-1.34	1.23	66.09	-1.09	-3.66	1.03

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Table S16

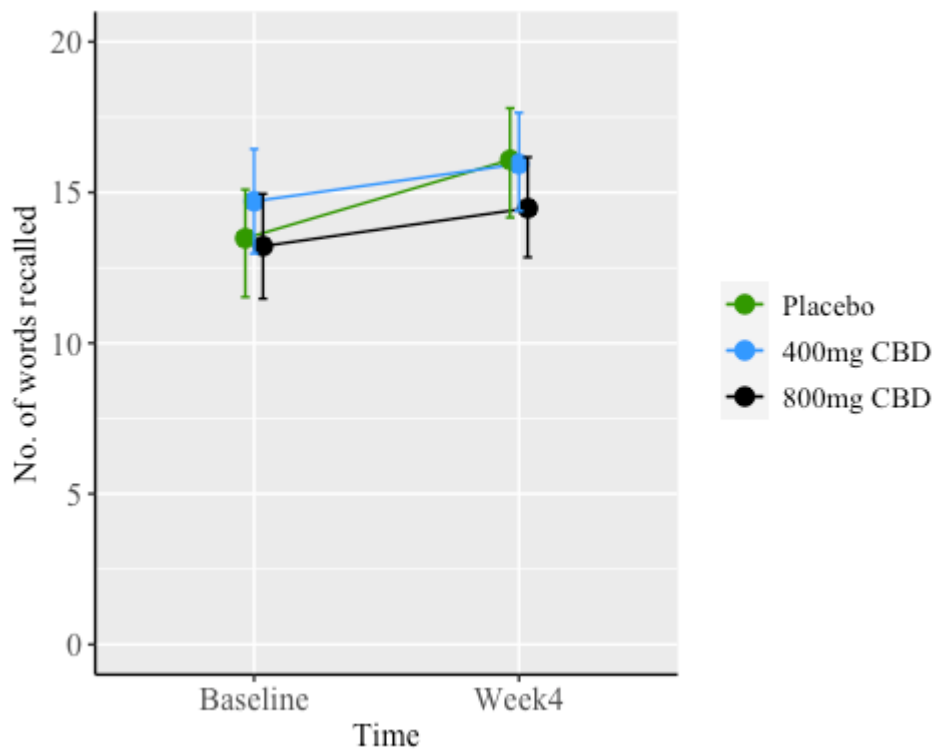
Change from baseline to week 4 (end of treatment) for number of category (semantic) words recalled, by treatment group.

Contrast	Treatment	Estimate	SE	Df	Lower CI	Upper CI
Week 4 - Baseline	Placebo	1.30	0.44	66.16	0.44	2.11
Week 4 - Baseline	400mg CBD	0.62	0.43	66.11	-0.21	1.51
Week 4 - Baseline	800mg CBD	0.63	0.43	65.11	-0.25	1.49

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Figure S6

Group means of number of words recalled on the category fluency task by treatment group, at baseline and week 4. Error bars represent bootstrapped 95% confidence intervals.



Drug Fluency**Table S17**

Data show model estimates of the effect of dose, time, and dose by time interaction on drug (cannabis) fluency.

	Estimate	SE	Df	<i>t</i> -value	Lower CI	Upper CI
Intercept	18.78	1.14	88.96	16.51	16.36	20.91
Placebo	-	-	-	-	-	-
400mg CBD	0.68	1.59	88.96	0.42	-2.53	4.08
800mg CBD	-0.43	1.61	88.96	-0.27	-3.61	2.91
Baseline	-	-	-	-	-	-
Week 4	-1.42	0.89	66.13	-1.60	-3.17	0.21
Dose by time (Placebo, Baseline)	-	-	-	-	-	-
Dose by time (400mg CBD, Week 4)	-0.27	1.24	66.12	-0.22	-2.59	2.32
Dose by time (800mg CBD, Week 4)	1.07	1.24	65.78	0.86	-1.26	3.46

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Table S18

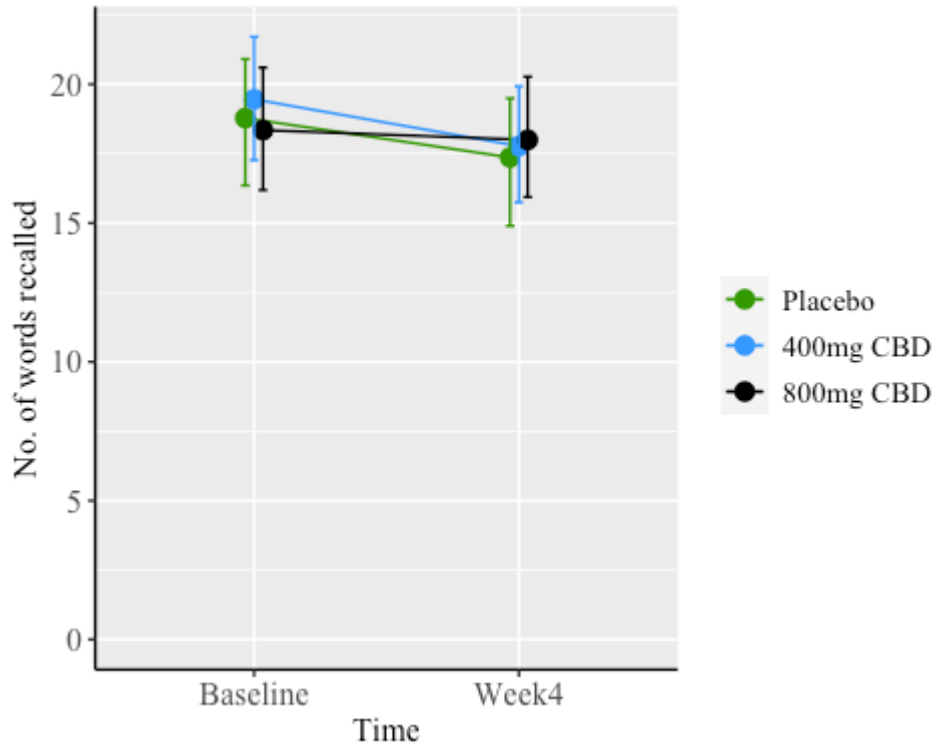
Change from baseline to week 4 (end of treatment) for number of drug (cannabis) words recalled, by treatment group.

Contrast	Treatment	Estimate	SE	Df	Lower CI	Upper CI
Week 4 - Baseline	Placebo	-0.71	0.44	65.76	-1.59	0.10
Week 4 - Baseline	400mg CBD	-0.84	0.43	65.73	-1.68	0.05
Week 4 - Baseline	800mg CBD	-0.17	0.44	65.04	-1.06	0.69

CI = 95% confidence interval, bootstrapped. SE = Standard Error. Df = Degrees of freedom.

Figure S7

Group means of number of words recalled on the drug fluency task by treatment group, at baseline and week 4. Error bars represent bootstrapped 95% confidence intervals.



Exploratory Bayes Factors

Table S19

Omnibus Bayes Factors for dose by time interaction in all models with null findings at 95% confidence interval level

Outcome	Bayes Factor
Prose Recall Delayed	0.057
Prose Recall Immediate	0.121
SSRT	0.041
TMT Part A	0.057
TMT Part B – Part A	0.153
Digit Span	0.048
Letter fluency	0.052
Category fluency	0.073
Drug fluency	0.076

Bayes Factors between 0.10-0.05 indicate strong evidence for the null hypothesis (1).

Bayes Factors between 0.33–0.10 indicate substantial evidence for the null hypothesis.

1. Jarosz AF, Wiley J. What are the odds? A practical guide to computing and reporting Bayes factors. *J Probl Solving*. 2014;7(1):2.