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SUPPLEMENTARY MATERIALS

Cannabidiol reverses attentional bias to cigarette cues in a human experimental model of tobacco withdrawal.

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Running Head: CANNABIDIOL FOR TOBACCO WITHDRAWAL

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Supplementary Method

Participant recruitment

Supplementary Figure 1: flow diagram for study recruitment and assessments. The final sample included 30 participants who completed all three sessions.

Procedure

Supplementary table 1: Schedule of assessments on the satiated and abstinent sessions.

| SATIATED          | TIME | ABSTINENT          | TIME |
|-------------------|------|-------------------|------|
|                  |      |                   |      |
|                  | 0    | Arrival           | 0    | Arrival           |
|                  | 12   | MPSS QSU [1]      | 5    | MPSS QSU HR BP [1] |
|                  | 30   | Cigarette         | 10   | Drug administration |
|                  | 35   | MPSS QSU [2]      | 70   | MPSS QSU HR BP [2] |
|                  | 60   | Visual Probe      | 130  | MPSS QSU HR BP [3] |
|                  | 68   | PRT               | 190  | Visual Probe      |
|                  | 75   | MPSS QSU [3]      | 198  | PRT               |
|                  | -    |                   | 200  | MPSS QSU [4]      |

Supplementary Results

Time since last smoked

There was a significant main effect of abstinence ($F(1,29)= 3289.03, p<.001, \eta^2 p =.99$) where on the satiated session, participants last smoked M: 0.41 (SD: 0.40) hours previously, in comparison to abstinent. There was no main effect of drug ($F(1,29)=0.18, p=.675, \eta^2 p =.006$). Participants last smoked M: 10.97 (SD:0.96) hours previously on the CBD session and M:11.03 (SD:0.95) on the PBO session.
There was a significant main effect of abstinence \((F(1,29)= 167.83, p<.001, \eta^2 p=.84)\) which shows CO was higher in the satiated condition (M: 17.73 ppm SD: 6.63) than in the abstinent conditions. There was no main effect of drug \((F(1,29)=6.13, p=.019, \eta^2 p=.17)\) where CO was 4.27ppm (SD:2.23) for CBD and 4.17 (SD:2.69) for PBO. Thus abstinence was biologically verified.

**MPSS**

*Amount of time spent with urge*

Pre-drug time spent with urges was significantly greater under abstinent than satiated sessions \((F(1,29)=27.96, p<.001, \eta^2 p=.49)\) suggesting abstinence increased the amount of time spent with urges to smoke. There was no different between CBD and PBO, pre-drug administration \((p=0.536; JZS BF in support of the null= 5.86)\). To investigate if CBD attenuated craving in comparison to placebo on abstinent sessions, we conducted an ANOVA that showed a main effect of time \((F(3,87)=8.65, p<.001, \eta^2 p=.23)\) which showed that time spent with urges decreased from T1 (3.17, 95% CI 2.79-3.64) to T3 (2.40, 95% CI 1.97-2.82), and increased from T3 to T4 (2.80, 95% CI 2.38-3.22). However there was no effect of drug \((p=1.00; JZS BF in support of the null= 7.08)\) There was no drug x time interaction \((F(2, 68)=.25, p=.81, \eta^2 p=0.00).\)

*Strength of urges*

Pre-drug strength of urges was significantly greater under abstinent than satiated sessions \((F(1,29)=26.26, p<.001, \eta^2 p=.48)\) suggesting abstinence increased the strength of urges. There was no different between CBD and PBO, pre drug administration \((p=0.879; JZS BF in support of the null= 6.99)\). To investigate if CBD attenuated craving in comparison to placebo on abstinent sessions, we conducted an ANOVA that showed a main effect of time \((F(3,87)=4.33, p=.007, \eta^2 p=.13)\) which showed that time spent with urges decreased significantly from T1 (2.92, 95% CI 2.58-3.25) to T2 (2.40, 95% CI 2.02-2.78), and increased from T2 to T3 (2.48, 95% CI 2.10-2.87) and T4 (2.73, 95% CI 2.31-3.16). However there was no effect of drug \((p=.61; JZS BF in support of the null= 6.20)\) There was no drug x time interaction \((F(3, 87)=0.65, p=0.58, \eta^2 p=0.02).\)

**Side effects**

*Strong Drug effect:* There was no main effect of drug \((F(1,29)=.80, p=.379, \eta^2 p=.03)\) confirmed by Bayesian analysis \((JZS BF: 4.82)\), time \((F(2,58)=.37 p=.695, \eta^2 p =.01)\), or drug x time interaction \((F(2,58)=2.18, p=.123, \eta^2 p=.07)\).

*Good Drug effect:* There was no main effect of drug \((F(1,29)=.10, p=.922, \eta^2 p=.00)\) confirmed by Bayesian analysis \((JZS BF:7.04)\), time \((F(2,58)=2.76, p=.072, \eta^2 p =.09)\), or drug x time interaction \((F(2,58)=2.18, p=.123, \eta^2 p =.07)\).
Willing to take drug again: There was no main effect of drug ($F(1,29)=2.35, p=.136, \eta^2 p=.08$) confirmed by Bayesian analysis (JZS BF: 2.35), time ($F(2,58)=0.42, p=.661, \eta^2 p=.01$), or drug x time interaction ($F(2,58)=1.12, p=.306, \eta^2 p=.040$).

Like drug effect: There was no main effect of drug ($F(1,29)=.01, p=.947, \eta^2 p=.00$) confirmed by Bayesian analysis (JZS BF: 7.06) or drug x time interaction ($F(2,58)=.03, p=.968, \eta^2 p=.00$). There was a main effect of time ($F(2,58)=3.53, p=.036, \eta^2 p=.11$) which showed liking decreased over time.

I have a stomach ache: There was no main effect of drug ($F(1,29)=.00, p=.957, \eta^2 p=.00$) confirmed by Bayesian analysis (JZS BF: 7.07), time ($F(2,58)=.01, p=.988, \eta^2 p=.000$), or drug x time interaction ($F(2,58)=1.44, p=.245, \eta^2 p=.05$).

I have a headache: There was a drug x time interaction ($F(2,58)=3.17, p=.049, \eta^2 p=.099$). Exploration of the interaction showed no significant pairwise comparisons. There was no main effect of drug ($F(1,29)=.04, p=.839, \eta^2 p=.00$) confirmed by Bayesian analysis (JZS BF: 6.93), or time ($F(2,58)=.80, p=.456, \eta^2 p=.03$).