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SUPPLEMENTARY MATERIALS

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

Hindocha, C1*, Freeman, T.P1,2, Grabski, M1,3, Stroud, J.B1, Crudgington, H1, Davies, A.C.1, Das, R.K1, Lawn, W1, Morgan, C.J.A1,4, Curran, H.V.1

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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.

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

<table>
<thead>
<tr>
<th>TIME</th>
<th>SATIATED</th>
<th>TIME</th>
<th>ABSTINENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Arrival</td>
<td>0</td>
<td>Arrival</td>
</tr>
<tr>
<td>12</td>
<td>MPSS QSU [1]</td>
<td>5</td>
<td>MPSS QSU HR BP [1]</td>
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<tr>
<td>30</td>
<td>Cigarette</td>
<td>10</td>
<td>Drug administration</td>
</tr>
<tr>
<td>60</td>
<td>Visual Probe</td>
<td>130</td>
<td>MPSS QSU HR BP [3]</td>
</tr>
<tr>
<td>68</td>
<td>PRT</td>
<td>190</td>
<td>Visual Probe</td>
</tr>
<tr>
<td>75</td>
<td>MPSS QSU [3]</td>
<td>198</td>
<td>PRT</td>
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<tr>
<td>-</td>
<td>-</td>
<td>200</td>
<td>MPSS QSU [4]</td>
</tr>
</tbody>
</table>

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.
CO
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 ($F(2,58)=.80, p=.456, \eta^2_p=.03$).