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.

Did not meet inclusion criteria: (N=75)
Refused to take part or did not attend baseline session: (N=14)

Excluded due to Low CO at SAT: (N=5)
Excluded to positive drug urine screen: (N=2)
Dropped out after baseline: (N=7)

Final Sample who completed all sessions N=30

Procedure

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>
</tr>
<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>
</tr>
<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 ($F(1,29)= 3289.03, p<.001, \eta^2 =.99$) 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 ($F(1,29)=0.18, p=.675, \eta^2 =.006$). 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 ($F(1,29)= 167.83 \ p<.001, \eta^2p= .84$) 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 ($F(1,29)=6.13, \ p=.019, \eta^2p= .17$) 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 $F(1,29)=27.96, \ p<.001, \eta^2p=.49$ 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 ($F(3,87)=8.65, \ p<.001, \eta^2p=.23$) 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 $F(2, 68)=.25, \ p=.81, \eta^2p=0.00$).

**Strength of urges**

Pre-drug strength of urges was significantly greater under abstinent than satiated sessions $F(1,29)=26.26, \ p<.001, \eta^2p=.48$ 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 ($F(3,87)=4.33, \ p=.007, \eta^2p=.13$) 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 $F(3, 87)=0.65, \ p=0.58, \eta^2p=0.02$.

**Side effects**

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

*Good Drug effect:* There was no main effect of drug ($F(1,29)=.10, \ p=.922, \eta^2p=.00$) confirmed by Bayesian analysis ($JZS BF:7.04$), time ($F(2,58)=2.76, \ p=.072, \eta^2p = .09$), or drug x time interaction ($F(2,58)=2.18, \ p=.123, \eta^2p = .07$).
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 ($F(2,58)=.80$, $p=.456$, $\eta^2_p=.03$).