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 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>
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<tr>
<td>60</td>
<td>Visual Probe</td>
<td>130</td>
<td>MPSS QSU HR BP [3]</td>
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<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 \((F(1,29)= 167.83 \, p<.001, \eta^2p=.84)\) 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 \((p=0.536; \text{JZS BF in support of the null}= 5.86)\). 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 \((p=1.00; \text{JZS BF in support of the null}= 7.08)\) 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 \((p=0.879; \text{JZS BF in support of the null}= 6.99)\). 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 \((p=.61; \text{JZS BF in support of the null}= 6.20)\) 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 \((\text{JZS BF}: \, 4.82)\), 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 \((\text{JZS BF}:7.04)\), 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 ($F(2,58)=.80, p=.456, \eta^2_p=.03$).