cannTEEN: an observational, longitudinal study investigating how cannabis differentially affects teenagers and adults

Dr Will Lawn

SSA annual conference
Friday 8th November 2019
Clinical Psychopharmacology Unit
University College London

will.lawn@ucl.ac.uk

@Will_Lawn

No conflicts of interest
• Introduction: adolescence as a period of heightened vulnerability to the harmful effects of cannabis?
• Methods and aims of the CannTeen study
• Preliminary cross-sectional results
  • Addiction
  • Psychotic-like symptoms
  • Neural correlates of reward processing
• Discussion
Outline

- Introduction: adolescence as a period of heightened vulnerability to the harmful effects of cannabis?
  - Methods and aims of the CannTeen study
  - Preliminary cross-sectional results
    - Addiction
    - Depression
    - Psychotic-like symptoms
    - Neural correlates of reward processing
  - Discussion
Teenage cannabis use

- 19.3% of 15 year olds in England used cannabis in the last year (NHS Digital).
- Downward trend in England since 2000, but creeping back up since 2014?

Treatment need for cannabis problems is greatest for teenagers
Adolescent brain development

Gogtay et al. (2004)

- Neural, cognitive, emotional and social development continues.
- Endocannabinoid system continues to develop.
- Reward processing and executive functions still maturing.

Galvan (2010); Luna et al., 2010; Hurd et al. (2019)

A time of heightened vulnerability?
Greater vulnerability to cannabis during adolescence?

- IQ and cognition.
- Psychosis.
- Brain structure & function.
- Addiction.

Meier et al. (2012)

Ehlers et al. (2010)
Limitations with existing research

- Lack of direct comparisons between current teenage and adult cannabis users, or inclusion of age-matched controls.

- Often cross-sectional designs with retrospective measures of age-of-onset.

- Lack of research into changes during teenage years, relative to during adult years.

- Crude measures of cannabis use and lacking measures of biological cannabinoid levels.

- No study has compared longitudinal changes in teenage cannabis users with adult cannabis users (who did not use regularly as a teenager), against age-matched controls.
• Methods and aims of the CannTeen study
  • Preliminary cross-sectional results
    • Addiction
    • Psychotic-like symptoms
    • Neural correlates of reward processing
  • Discussion
Aims and general hypotheses of CannTeen

- **Aim:** to investigate the differential associations between cannabis use and mental health, cognition and brain health in teenagers and adults.

- **General hypothesis:** over one year, teenage cannabis users (relative to age-matched controls) will show a worse trajectory than adult cannabis users (relative to age-matched controls) in the above domains.
Abstinent from alcohol and cannabis for 12 hours, all other drugs for 24 hours.

**Study 1: Longitudinal**  (n=272)

<table>
<thead>
<tr>
<th>Baseline</th>
<th>+3 months</th>
<th>+6 months</th>
<th>+9 months</th>
<th>+12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>β</td>
<td>λ*</td>
<td>λ*</td>
<td>λ*</td>
<td>λ*</td>
</tr>
</tbody>
</table>

**Study 2: Longitudinal s/fMRI**  (n=140)

Cannabis user groups:  
- Teenage = teenage
- Adult = adult

Control groups:  
- Teenage = teenage
- Adult = adult

Assessments:  
- β = Baseline
- λ = Longitudinal
- * = Biological assays
- = Brain imaging

**Study 1**
- Observational, longitudinal.
- Four groups.
- n=68 in each. Sex split evenly.
- Once every 3 months, for 1 year.

**Study 2**
- A subset of above participants.
- n=35 in each group.
## Participants

<table>
<thead>
<tr>
<th>Controls</th>
<th>Users</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Teenagers:</strong></td>
<td></td>
</tr>
<tr>
<td>16-17 years</td>
<td>16-17 years</td>
</tr>
<tr>
<td>Used cannabis ≤10 days ever.</td>
<td></td>
</tr>
<tr>
<td>Used tobacco or cannabis ≥1 days.</td>
<td></td>
</tr>
<tr>
<td>No recent (past month) cannabis use</td>
<td></td>
</tr>
<tr>
<td><strong>Adults:</strong></td>
<td></td>
</tr>
<tr>
<td>26-29 years</td>
<td></td>
</tr>
<tr>
<td>Used cannabis ≤10 days ever.</td>
<td></td>
</tr>
<tr>
<td>Used tobacco or cannabis ≥1 days.</td>
<td></td>
</tr>
<tr>
<td>No recent (past month) cannabis use</td>
<td></td>
</tr>
</tbody>
</table>
User participants

Current frequent cannabis use

Adolescent window of vulnerability?

Assess 1 year change

Increasing age...

Teenagers

Current frequent cannabis use

Never regular use

Adults

Assess 1 year change

26-29

Both groups vs. age-matched controls

Adulthood
Preliminary cross-sectional analyses

- **Current recruitment.** Very close to completing recruitment for the baseline sample for study 1 (n=255) and study 2 (n=115).

- **Addiction.** MINI for DSM-5 CUD (Sheehan et al., 1998) and CUDIT-R (Adamson et al., 2010).

- **Psychotic-like symptoms.** *(2 week adapted)* Psychotomimetic States Inventory (Mason et al., 2008).

- **Neural correlates of reward processing.** Monetary incentive delay (MID) task (Knutson et al., 2001)
Monetary incentive delay task

Key contrasts:

Reward anticipation (vs. no reward)

Reward feedback (vs. no reward)
Cross-sectional hypotheses

- Age-group by user-group interactions, such that teenage cannabis users have:
  - stronger addiction to cannabis than adult cannabis users.
  - greater psychotic-like symptoms than adult cannabis users.
  - weaker neural response during reward anticipation and feedback.

(relative to age-matched controls)
Outline

- Introduction: adolescence as a period of heightened vulnerability to the harmful effects of cannabis?
- Methods and aims of the CannTeen study
- Preliminary cross-sectional results
  - Addiction
  - Psychotic-like symptoms
  - Neural correlates of reward processing
- Discussion
## Participant demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Teenager</th>
<th>Adult</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>User</td>
<td>Control</td>
</tr>
<tr>
<td>Sex (f/m) [total]</td>
<td>34/29 [63]</td>
<td>30/37 [67]</td>
<td>30/30 [60]</td>
</tr>
<tr>
<td>Age (years) (SD)</td>
<td>17.13 (0.47)</td>
<td>17.10 (0.58)</td>
<td>27.36 (1.02)</td>
</tr>
<tr>
<td>Cannabis frequency (days/week) (SD)</td>
<td>NA</td>
<td>4.44 (1.91)</td>
<td>NA</td>
</tr>
<tr>
<td>Cannabis quantity (grams/day on day of use) (SD)</td>
<td>NA</td>
<td>1.13 (0.84)</td>
<td>NA</td>
</tr>
<tr>
<td>Number of total days of cannabis use (SD)</td>
<td>3.15 (2.89)</td>
<td>NA</td>
<td>4.18 (3.04)</td>
</tr>
<tr>
<td>AUDIT (SD)</td>
<td>4.51 (3.51)</td>
<td>6.21 (4.52)</td>
<td>5.47 (4.36)</td>
</tr>
<tr>
<td>Mother’s education level (SD)</td>
<td>4.89 (1.90)</td>
<td>4.86 (2.07)</td>
<td>4.07 (2.46)</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.001  
Cannabis frequency matched between user groups and age matched between age groups
Addiction within users (DSM)

- Teenage n=67, adult n=64
- DSM: $\chi^2 = 16.56, p < 0.001$

- Logistic regression predicting severe CUD

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds ratio (OR)</th>
<th>95% CI OR</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (teen vs. adult)</td>
<td>3.28</td>
<td>1.26, 8.53</td>
<td>0.015</td>
</tr>
<tr>
<td>Cannabis frequency (dpw)</td>
<td>1.41</td>
<td>1.12, 1.77</td>
<td>0.004</td>
</tr>
<tr>
<td>Cannabis quantity (grams on a day of use)</td>
<td>1.35</td>
<td>0.75, 2.46</td>
<td>0.319</td>
</tr>
<tr>
<td>Sex (male vs. female)</td>
<td>0.80</td>
<td>0.34, 1.90</td>
<td>0.606</td>
</tr>
<tr>
<td>Mother’s education, SES</td>
<td>0.99</td>
<td>0.80, 1.23</td>
<td>0.940</td>
</tr>
</tbody>
</table>
Addiction with users (CUDIT-R)

- Teenage n=67, adult n=65
- \( t_{130} = 4.85, p < 0.001, d = 0.60 \)
- Linear regression predicting CUDIT-R score

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Unstandardised beta</th>
<th>SE (b)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (teen vs. adult)</td>
<td>3.07</td>
<td>0.86</td>
<td>0.001</td>
</tr>
<tr>
<td>Cannabis frequency (dpw)</td>
<td>1.03</td>
<td>0.20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cannabis quantity (grams on a day of use)</td>
<td>1.72</td>
<td>0.57</td>
<td>0.003</td>
</tr>
<tr>
<td>Sex (male vs. female)</td>
<td>-1.03</td>
<td>0.79</td>
<td>0.20</td>
</tr>
<tr>
<td>Mother’s education, SES</td>
<td>-0.248</td>
<td>0.20</td>
<td>0.21</td>
</tr>
</tbody>
</table>
Psychotic-like symptoms

- Teenagers > adults ($F_{1,250}=15.157$, $p<0.001$, $n_p^2=0.057$).

- Users > controls ($F_{1,250}=12.131$, $p=0.001$, $n_p^2=0.046$)

- No interaction between age-group and user-group.

- Additive, rather than interactive, effect of age-group and user-group.

<table>
<thead>
<tr>
<th></th>
<th>Teenage</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>63</td>
<td>60</td>
</tr>
<tr>
<td>User</td>
<td>66</td>
<td>65</td>
</tr>
</tbody>
</table>
MID – whole brain – anticipate – overall task

- Supplementary motor area
- Anterior cingulate cortex
- Thalamus
- Caudate (dorsal striatum)
- Insula

Clusterwise corrected, $z>2.3$, $p<0.05$

<table>
<thead>
<tr>
<th></th>
<th>Teenage</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>32</td>
<td>34</td>
</tr>
<tr>
<td>User</td>
<td>23</td>
<td>26</td>
</tr>
</tbody>
</table>
MID – whole brain – feedback – overall task

- Posterior cingulate cortex
- Paracingulate gyrus
- Orbitofrontal cortex
- Frontal pole
MID – whole brain – feedback – users > controls

Bilateral frontal pole
Outline

• Introduction: adolescence as a period of vulnerability to the harmful effects of cannabis?
• Methods and aims of the CannTeen study
• Preliminary cross-sectional results
  • Addiction
  • Psychotic-like symptoms
  • Neural correlates of reward processing
• Discussion
Summary of results

- Teenage cannabis users are more likely to have cannabis use disorder than adult cannabis users.

- Teenagers (vs. adults) and cannabis users (vs. controls) have more subclinical psychotic-like symptoms. But no differential association between cannabis use and psychotic-like symptoms for teenagers and adults.

- Cannabis users have greater brain activity than controls in the frontal pole when winning money, but no relationship with age and no interaction between age and user-group.
Discussion

• Window of adolescent vulnerability for developing cannabis use problems.
  • Why teenage vulnerability?
  • Dare to delay?
  • Or different populations?

• Additive effect on subclinical psychotic-like symptoms of being a teenager and a cannabis user.

• Cannabis users neurally hypersensitive to reward feedback.

• Strengths and limitations of existing, cross-sectional data.

• Longitudinal changes to come.
Thanks for listening! Acknowledgements

**Funding:**
MRC

**The CannTeam:**
Dr Claire Mokrysz*
Dr Tom Freeman*
Katherine Petrilli
Rachel Lees*
Dr Anya Borissova
Dr Matt Wall
Dr Michael Bloomfield
Prof Val Curran
Many MSc students

*special thanks!

will.lawn@ucl.ac.uk

[Image of people]