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

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No conflicts of interest

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

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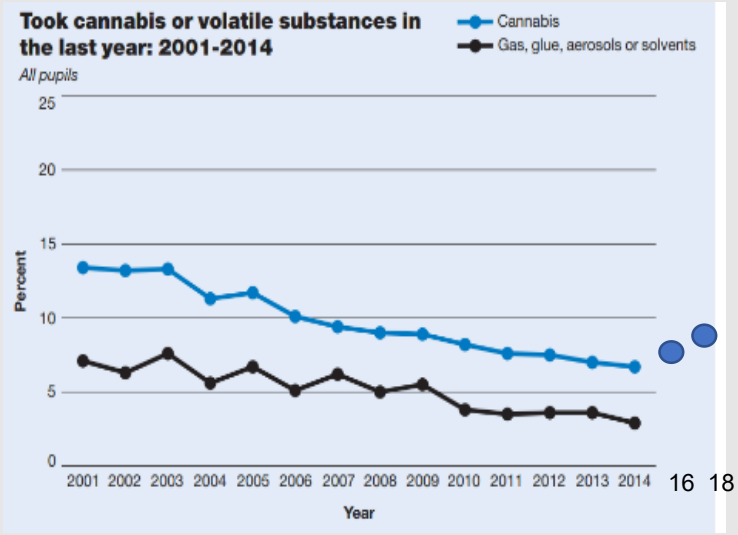
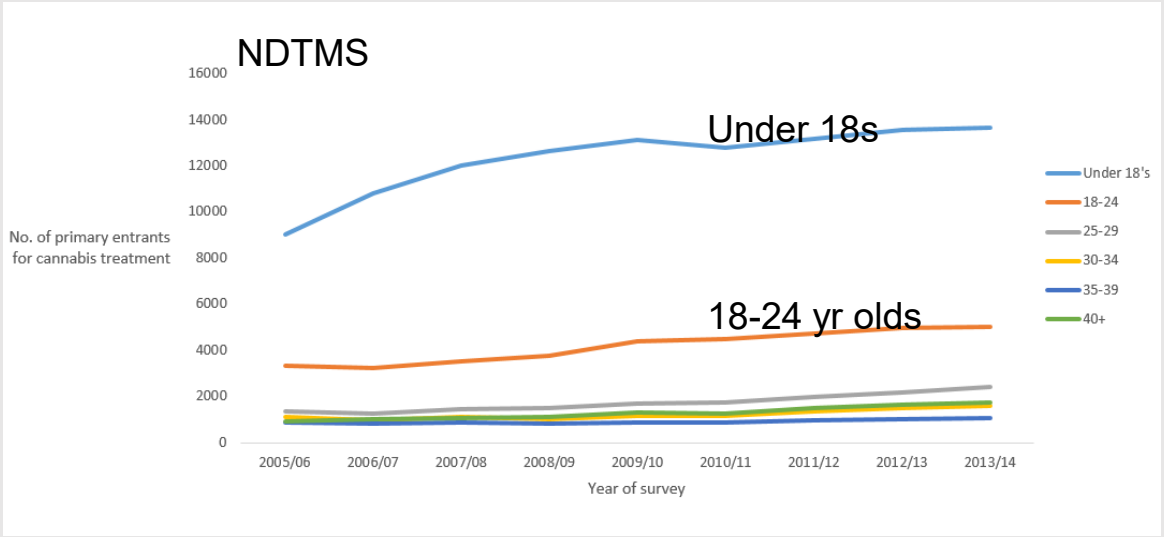
Teenage cannabis use

- 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?

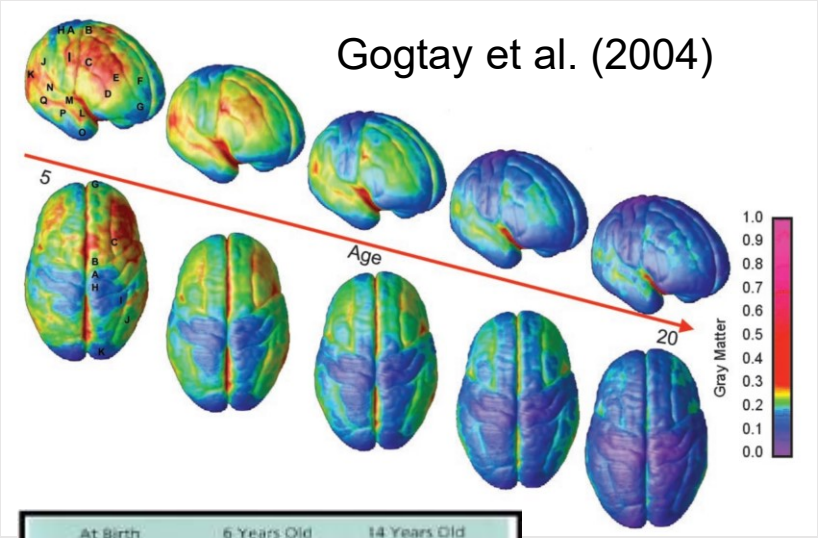


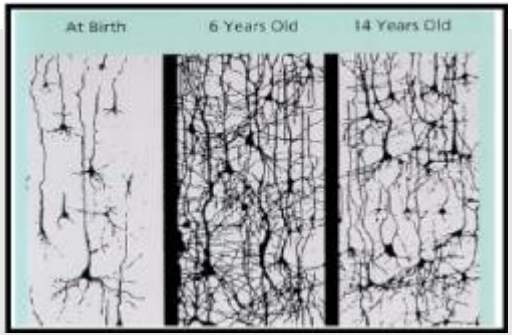
11-15 year olds. Smoking, drinking and drug use among young people in England, NHS Digital

Treatment need for cannabis problems is greatest for teenagers



Adolescent brain development





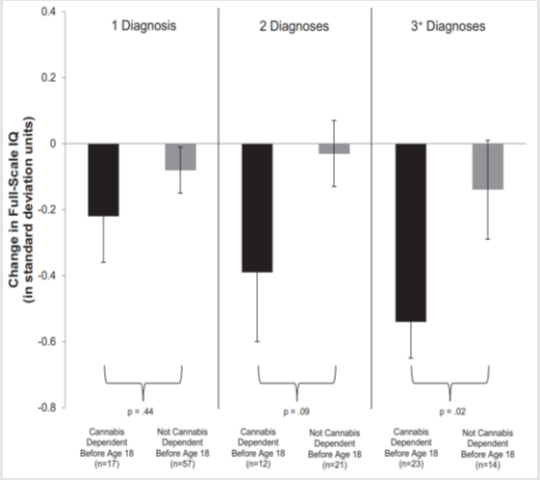
Galvan (2010); Luna et al., 2010); Hurd et al. (2019)

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

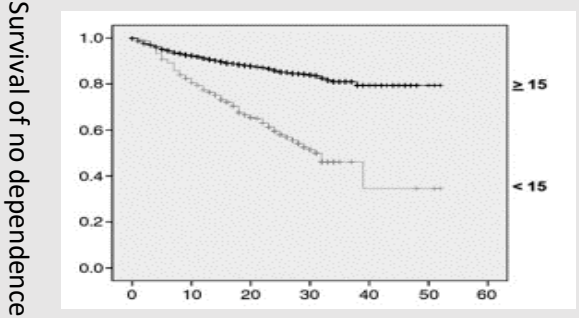
A time of heightened vulnerability?

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.

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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.

Methods

Abstinent from alcohol and cannabis for 12 hours, all other drugs for 24 hours.

Study 1: Longitudinal (n=272)

Baseline	+3 months	+6 months	+9 months	+12 months
β λ *	λ *	λ *	λ *	λ *

Study 2: Longitudinal s/fMRI

(n=140)

Baseline	+12 months

Cannabis user groups: =teenage =adult,

Control groups: =teenage =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.

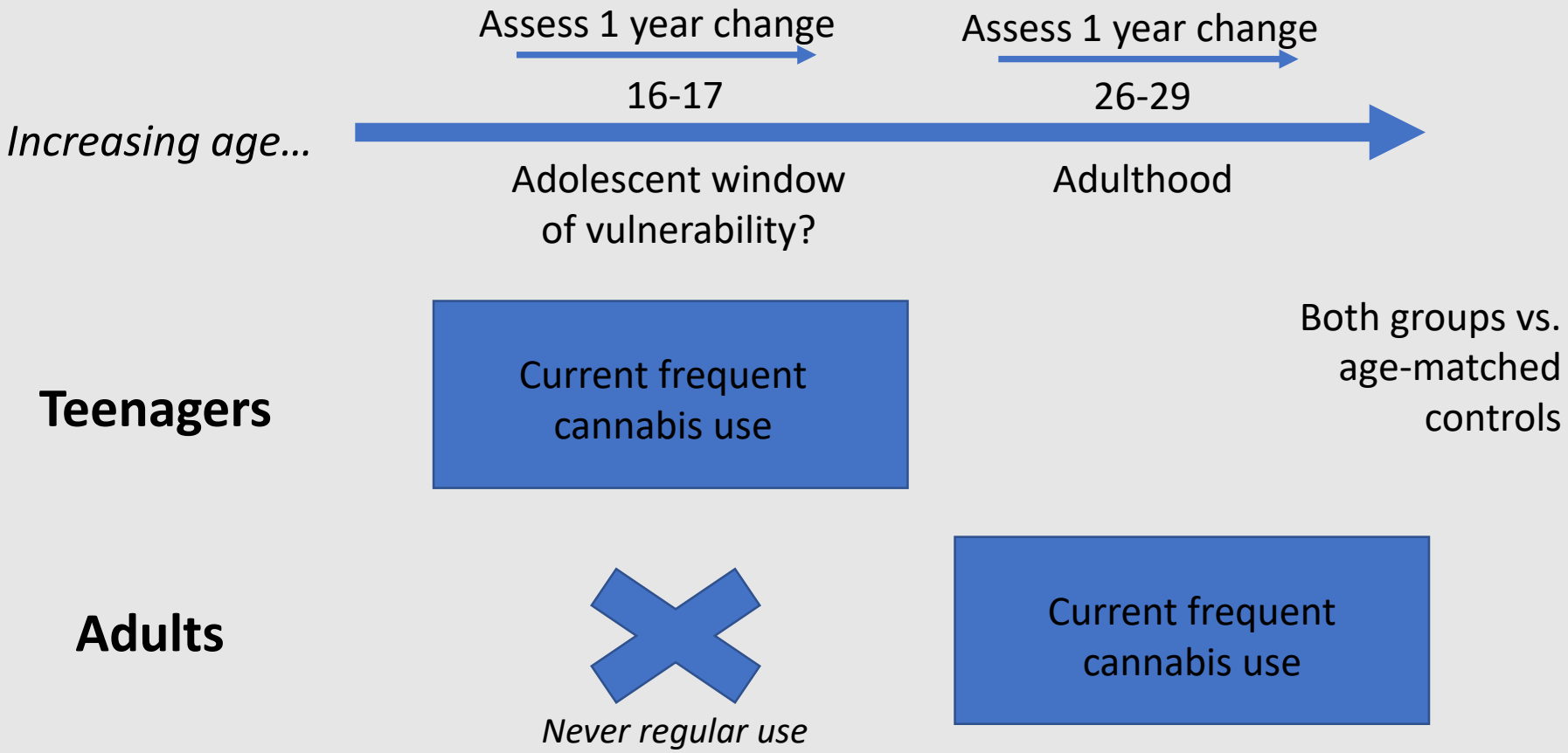
Participants

	Controls	Users
Teenagers:	• 16-17 years • Used cannabis ≤10 days ever. • Used tobacco or cannabis ≥1 days. • No recent (past month) cannabis use	• 16-17 years • Use cannabis 1-7 days per week
Adults:	• 26-29 years • Used cannabis ≤10 days ever. • Used tobacco or cannabis ≥1 days. • No recent (past month) cannabis use	• 26-29 years • Use cannabis 1-7 days per week • *No weekly use before age 18*

Exclusion criteria for all:

1. Regular use of other illicit drugs.
2. Receiving treatment for mental health condition.
3. History of psychosis.

User participants



Preliminary cross-sectional analyses

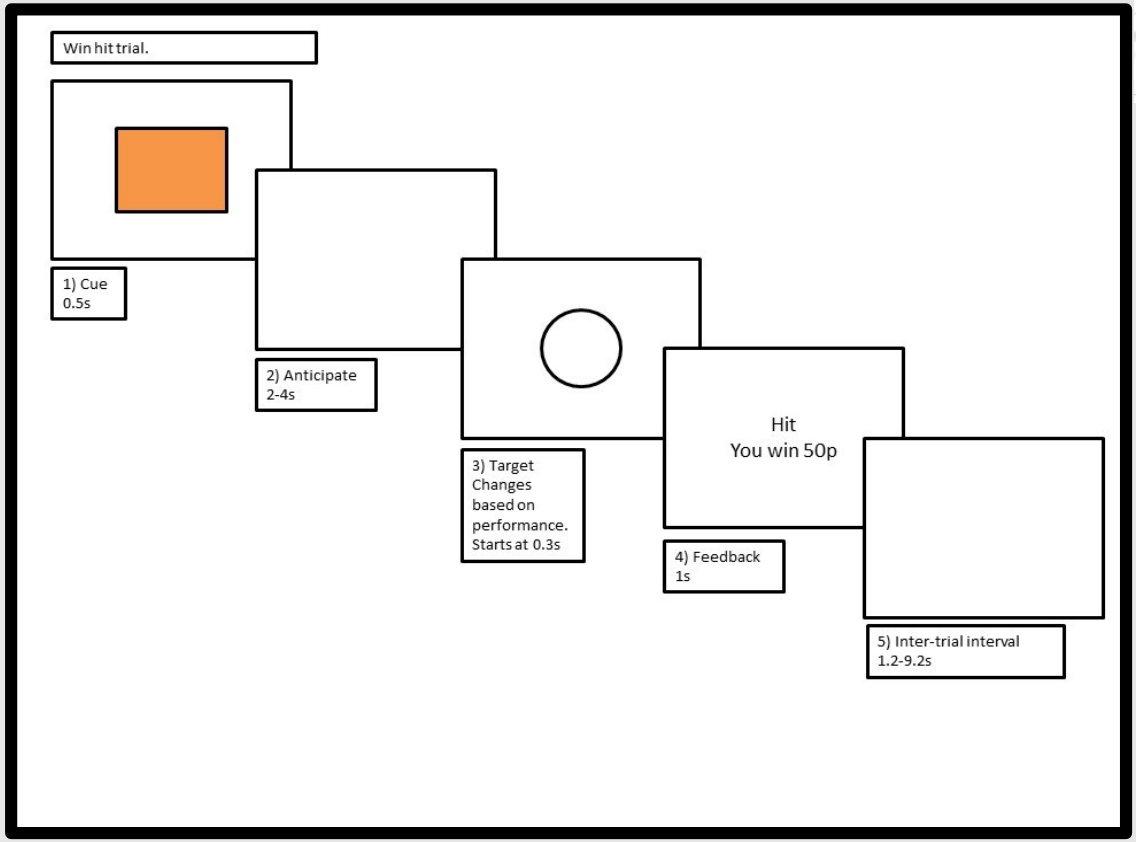
- ***Current recruitment***. Very close to completing recruitment for the baseline sample for study 1 (n=255) and study 2 (n=115).

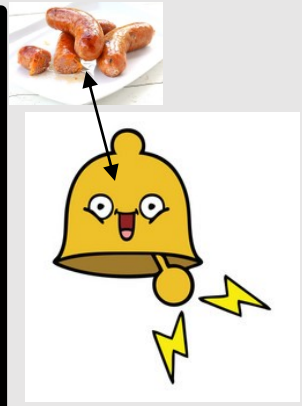
- ***Addiction***. MINI for DSM-5 CUD (Sheehan et al., 1998) and CUDIT-R (Adamson et al., 2010).

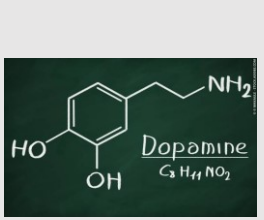
- ***Psychotic-like symptoms***. (*2 week adapted*) Psychotomimetic States Inventory (Mason et al., 2008).

- ***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)

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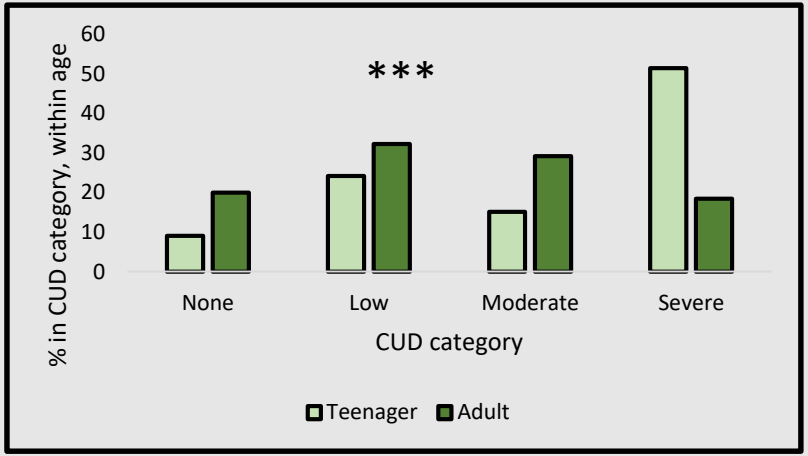
Participant demographics

	Teenager		Adult		Difference
Variable	**Control**	**User**	**Control**	**User**	
Sex (f/m) [total]	34/29 [63]	30/37 [67]	30/30 [60]	31/34 [65]	None
Age (years) (SD)	17.13 (0.47)	17.10 (0.58)	27.36 (1.02)	27.63 (1.19)	Adults > teenagers***
Cannabis frequency (days/week) (SD)	NA	4.44 (1.91)	NA	4.31 (2.02)	None
Cannabis quantity (grams/day on day of use) (SD)	NA	1.13 (0.84)	NA	0.56 (0.63)	Teenagers > adults***
Number of total days of cannabis use (SD)	3.15 (2.89)	NA	4.18 (3.04)	NA	None
AUDIT (SD)	4.51 (3.51)	6.21 (4.52)	5.47 (4.36)	6.35 (4.34)	Users > controls*
Mother's education level (SD)	4.89 (1.90)	4.86 (2.07)	4.07 (2.46)	4.52 (2.14)	Teenagers > Adults*

*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: χ_3=16.56, p<0.001

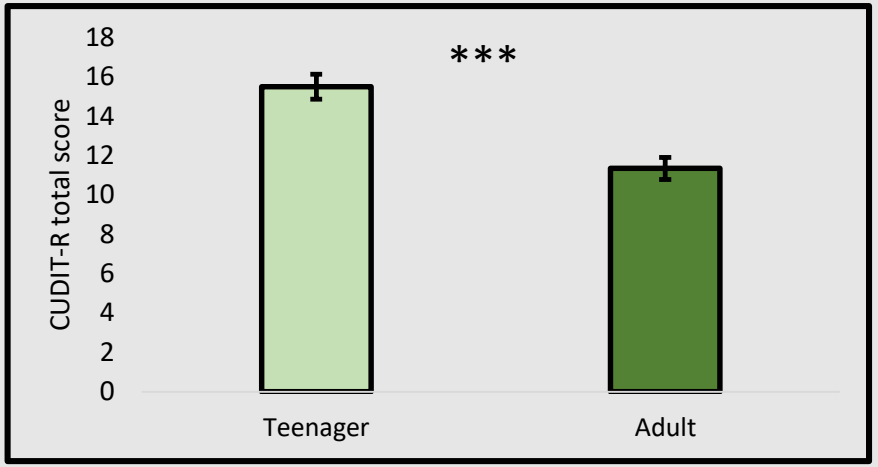


- Logistic regression predicting severe CUD

Predictor	Odds ratio (OR)	95% CI OR	p value
Age (teen vs. adult)	*3.28*	*1.26, 8.53*	*0.015*
Cannabis frequency (dpw)	*1.41*	*1.12, 1.77*	*0.004*
Cannabis quantity (grams on a day of use)	1.35	0.75, 2.46	0.319
Sex (male vs. female)	0.80	0.34, 1.90	0.606
Mother's education, SES	0.99	0.80, 1.23	0.940

Addiction with users (CUDIT-R)

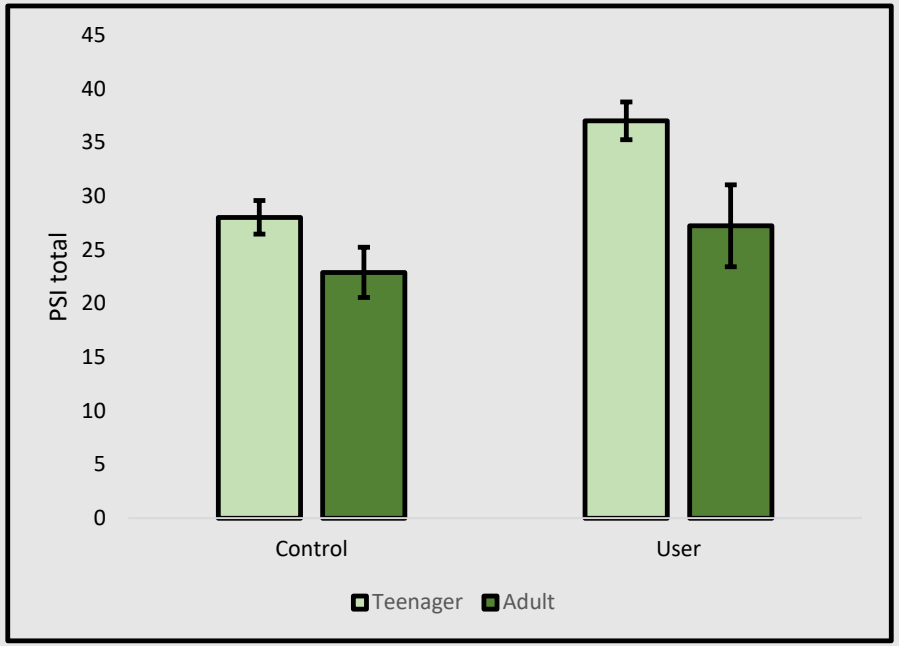
- Teenage n=67, adult n=65
- t_{130}=4.85, p<0.001, d=0.60



- Linear regression predicting CUDIT-R score

Predictor	Unstandardised beta	SE (b)	p value
Age (teen vs. adult)	*3.07*	*0.86*	*0.001*
Cannabis frequency (dpw)	*1.03*	*0.20*	*<0.001*
Cannabis quantity (grams on a day of use)	*1.72*	*0.57*	*0.003*
Sex (male vs. female)	-1.03	0.79	0.20
Mother's education, SES	-0.248	0.20	0.21

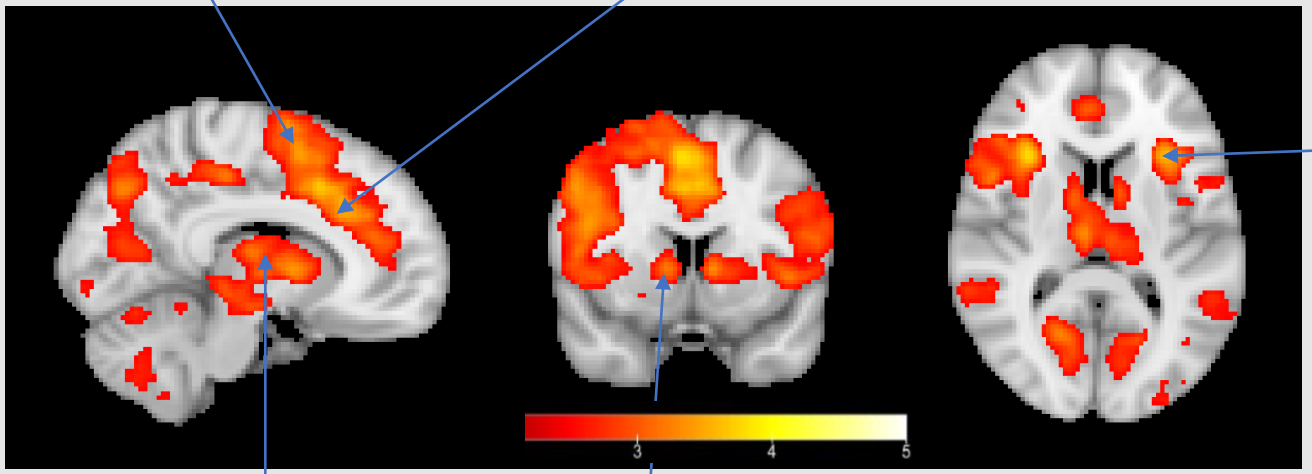
Psychotic-like symptoms



n	Teenage	Adult
Control	63	60
User	66	65

- 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.

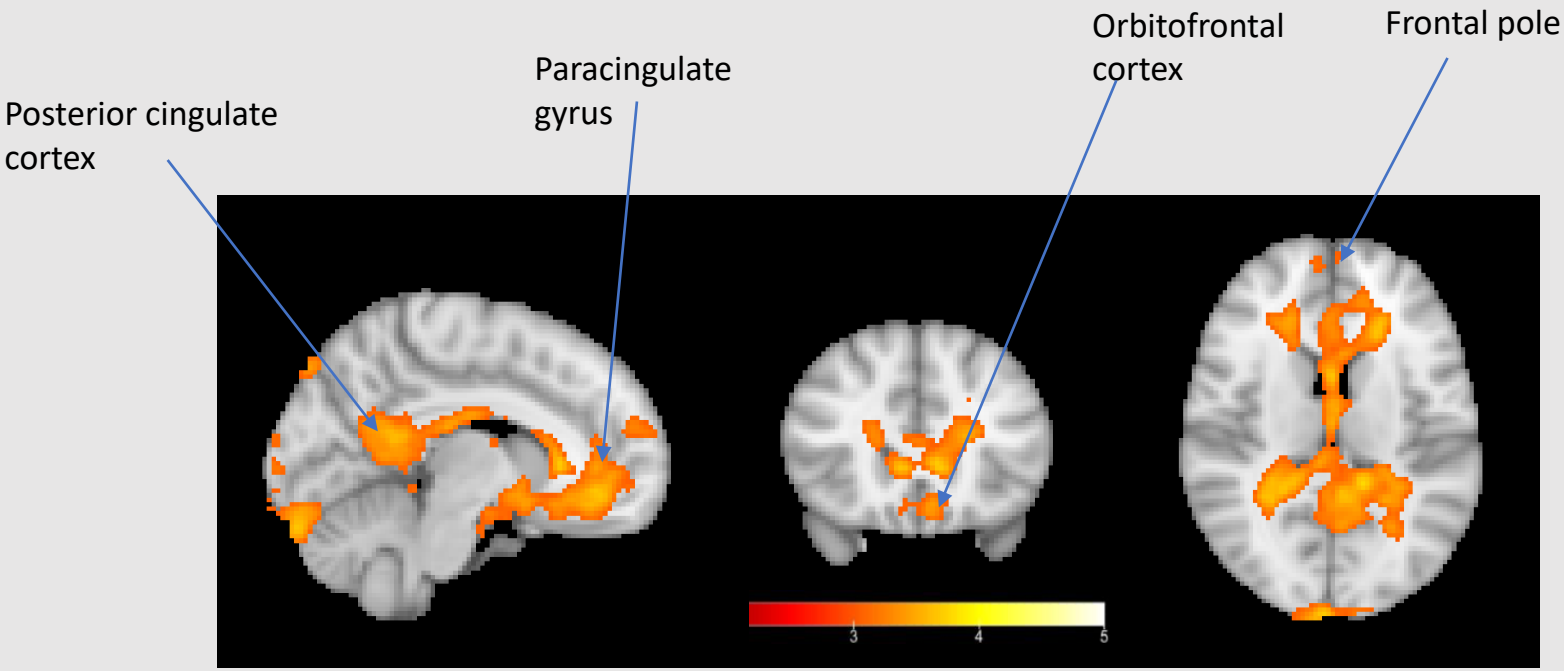
MID – whole brain – anticipate – overall task



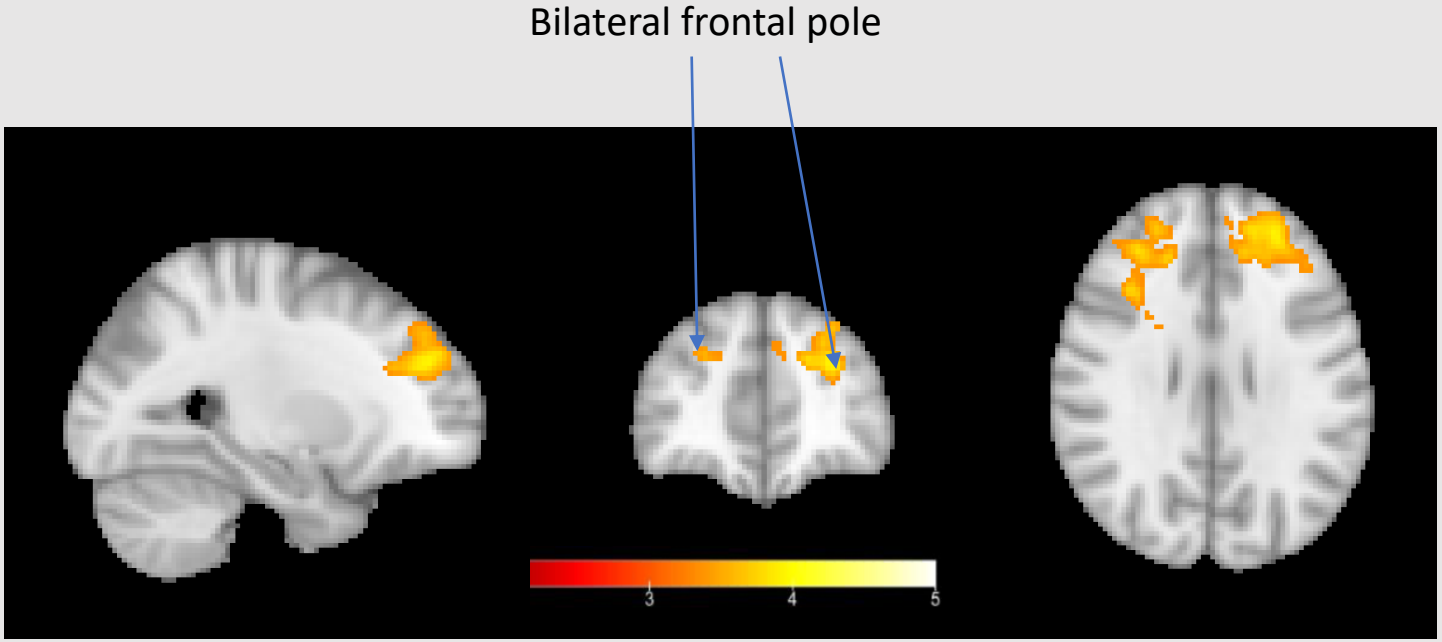
n	Teenage	Adult
Control	32	34
User	23	26

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

MID – whole brain – feedback – overall task



MID – whole brain – feedback – users > controls



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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

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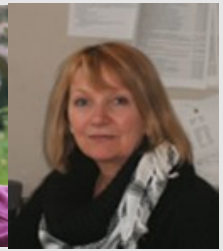

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