NEUROFUNCTIONAL IMPACT OF **CHRONIC CANNABIS USE** ON **EMOTION**

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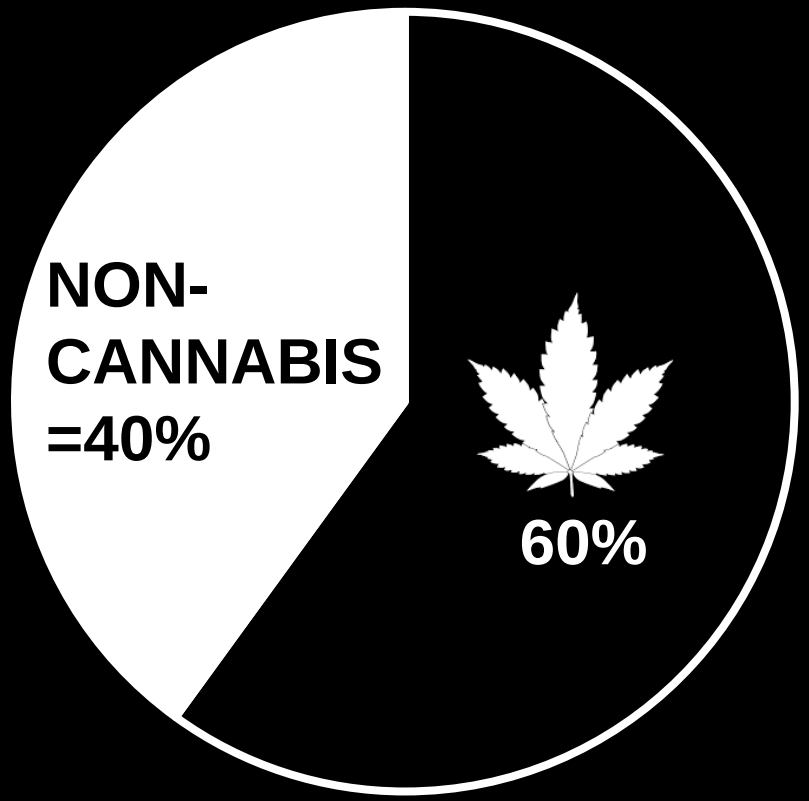


WORLD DRUG REPORT, 2018

PREVALENCE

Acute Effects

- THC → CB_1 receptors
- Well studied effects: perceptual/motor, cognition, emotion

Chronic Effects

- Non-acute, overtime, present without THC
- Cognitive effects well studied: verbal memory[1], theory of mind[2] , and executive functions[3]
- Emotion less understood

EFFECTS OF CANNABIS

1 Battisti et al., 2010
2 Roser et al. 2012;
3 Crean, Crane & Mason, 2011

FUNCTIONAL NEUROIMAGING EVIDENCE

Chronic cannabis use – Mixed Results

Threat-based faces → reduced activity

- Amygdala[1,2,3]
- PCC[1]
- dlPFC[3]

Negative-valence images → increased activity

- mOFC[5]

1 Gruber et al., 2009
2 Cornelius, Aizenstein and Hariri, 2010
3 Heitzeg et al., 2015
4 Wesley et al., 2016
5 Zimmermann et al., 2017

LIMITATION OF PAST STUDIES

- fMRI studies → small sample size

- Inconsistent definition of “chronic cannabis use”

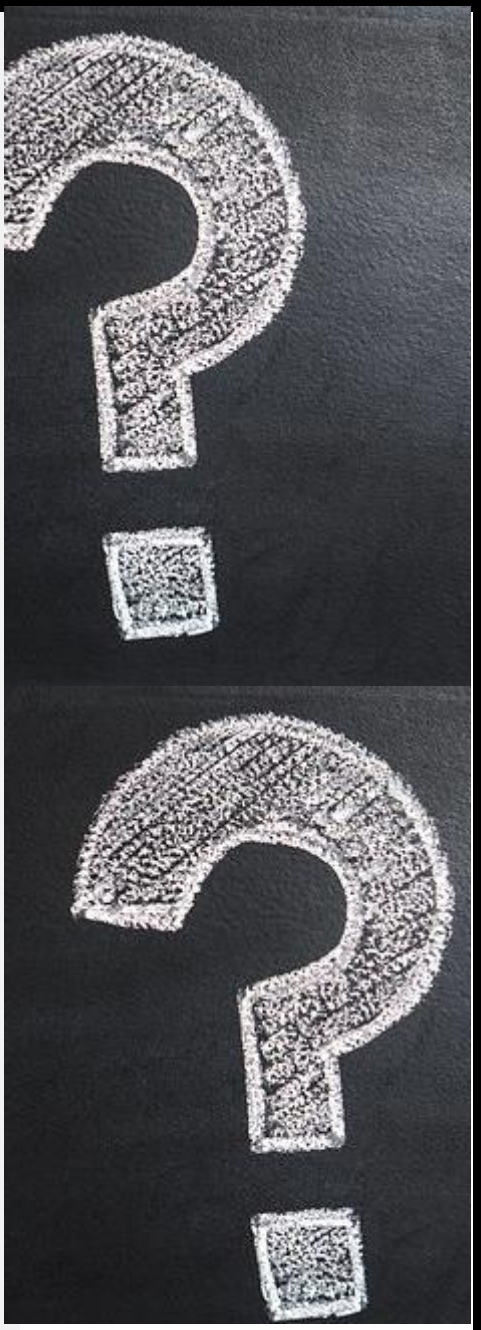
- Continuous and categorical

OUR STUDY

Chronic Cannabis Use → Emotional processing?

- Hypothesis: chronic use of cannabis alters the brain's neurofunctional response to affective stimuli in the limbic system

- Use data from the Human Connectome Project



THE HUMAN CONNECTOME PROJECT

Network Map for the brain.

HUMAN Connectome PROJECT

Comprehensive behavioural data

- Uses reliable and well-validated battery of measures that assess a wide range of human functions (Personality, IQ, Cognitive measures, BMI, etc.)

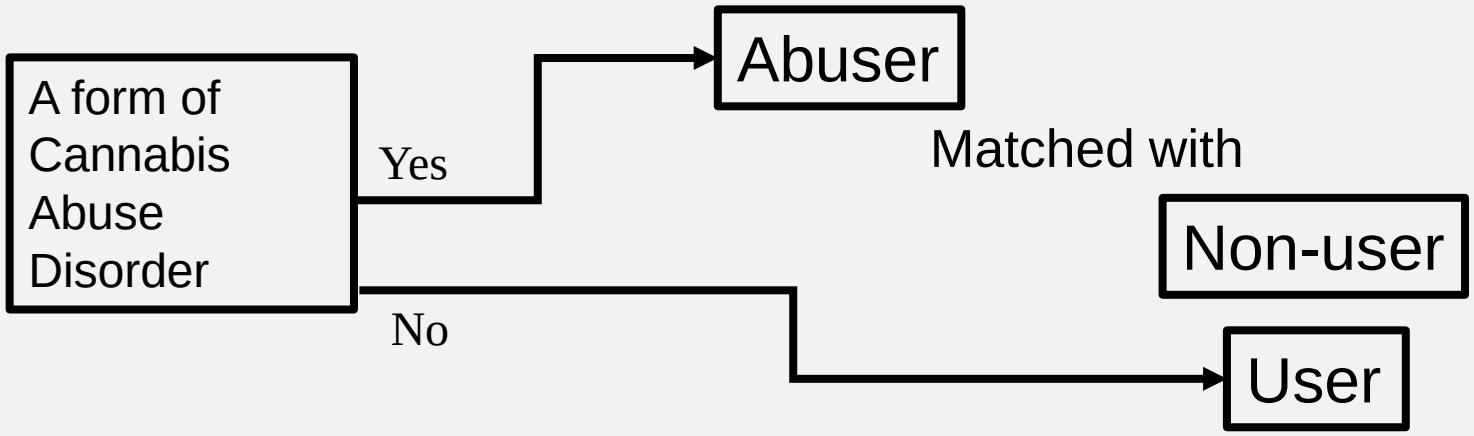
Large-scale neuroimaging

- Collected neuroimaging data for 1200 healthy adults
- Exceptional data quality. High temporal resolution, high maximum gradient strength

METHOD – DATA SELECTION

genetically independent sub-sample analysis - 192 participants into 3 groups

- Exploratory



(each N = 64)

- Case-matched on

1)Age 2)Gender 3)Education status 4)Education attainment

HUMAN Connectome PROJECT

Mapping structural and functional connections in the human brain

GROUP STATS

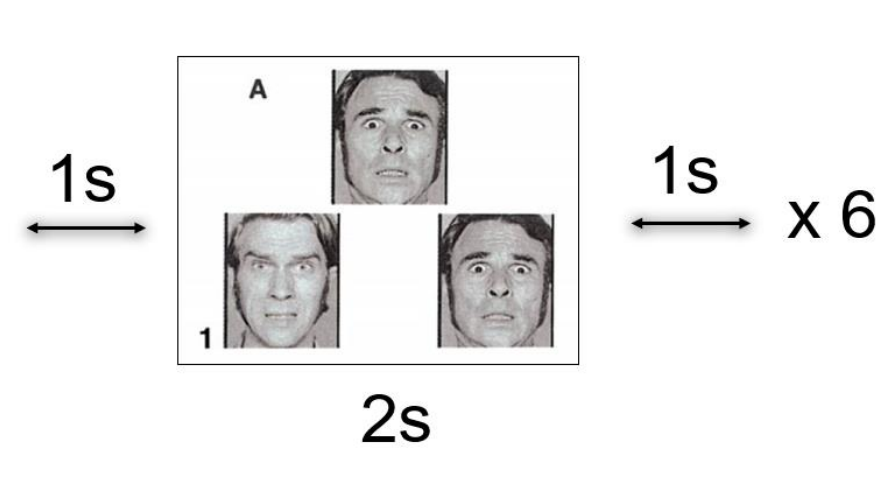
	Gender M/F	Age M(SD)	Education M(SD)	Age of Onset (Years)	Duration of use (Years)	Intensity of Use (5 point scale)
Abuser	44/15	28.4(3.5)	14.5(1.8)	16	12.4	4.3
User	44/15	28.3(3.6)	14.2(2.0)	18.2	10.1	2.4
Non-user	42/17	28.7(3.8)	14.4(1.9)			

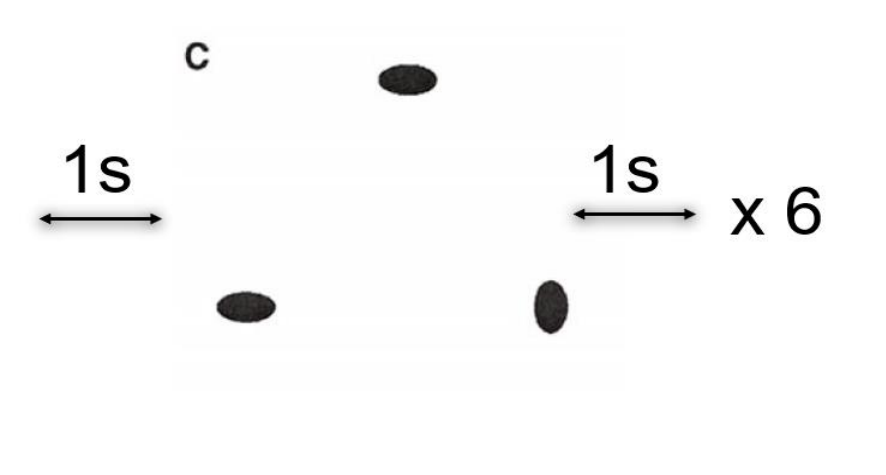
Intentionally matched

Comparable coincidentally: Big Five Personality traits, Household Income, IQ

METHOD – EXPERIMENTAL PARADIGM

Emotional face-matching task (Hariri et al, 2002) – Anger and Fear from IAPS

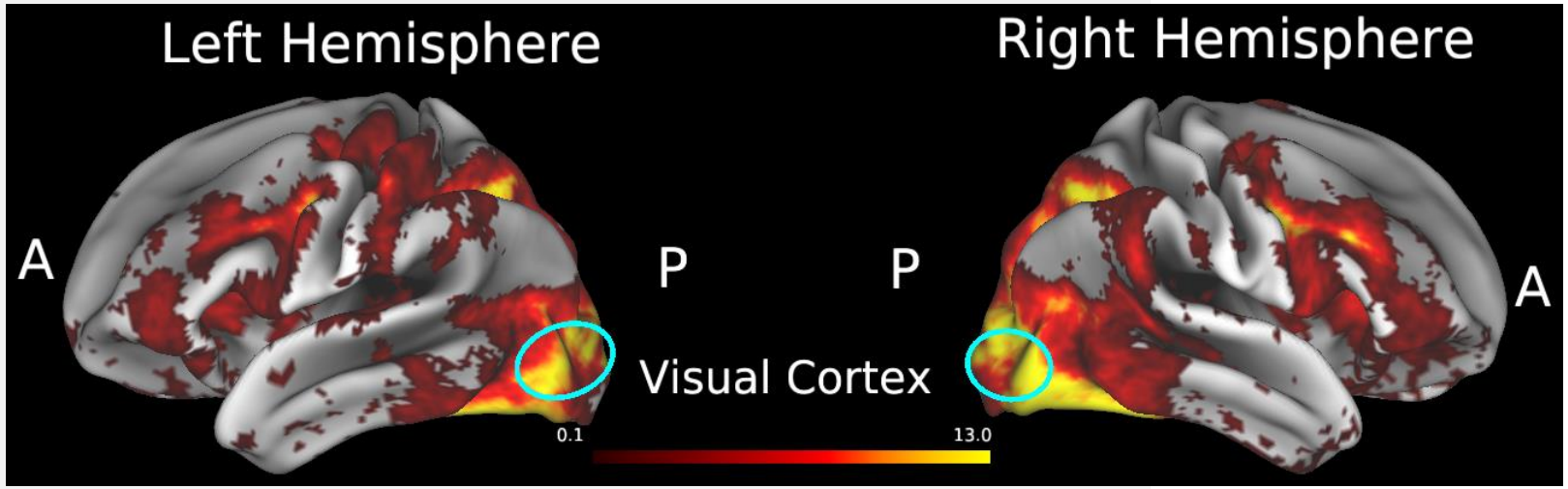


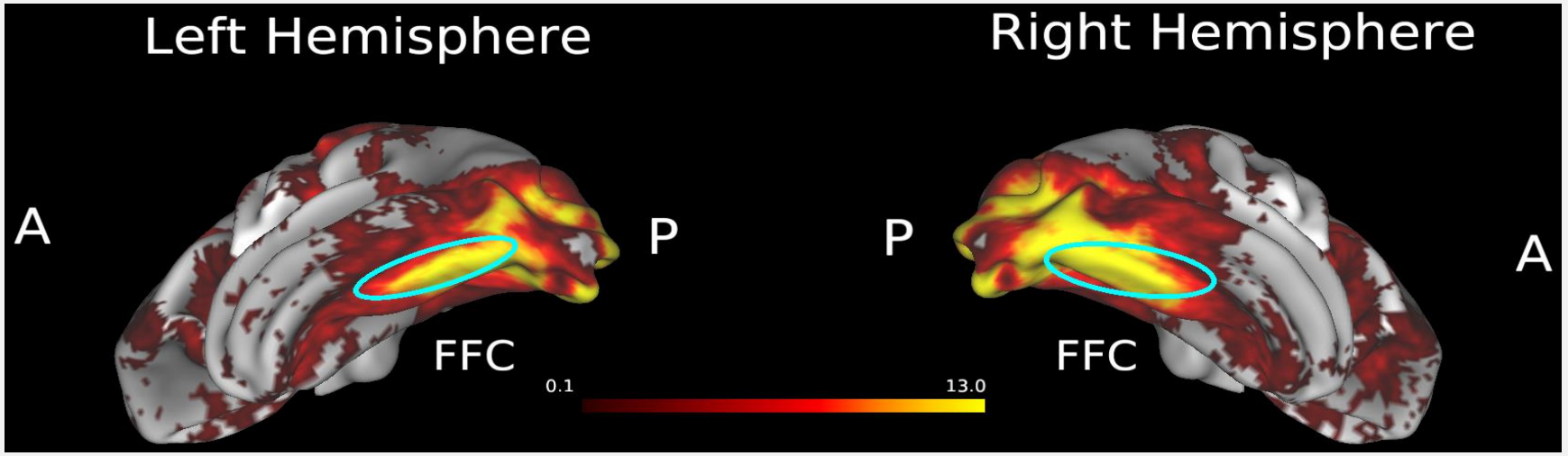


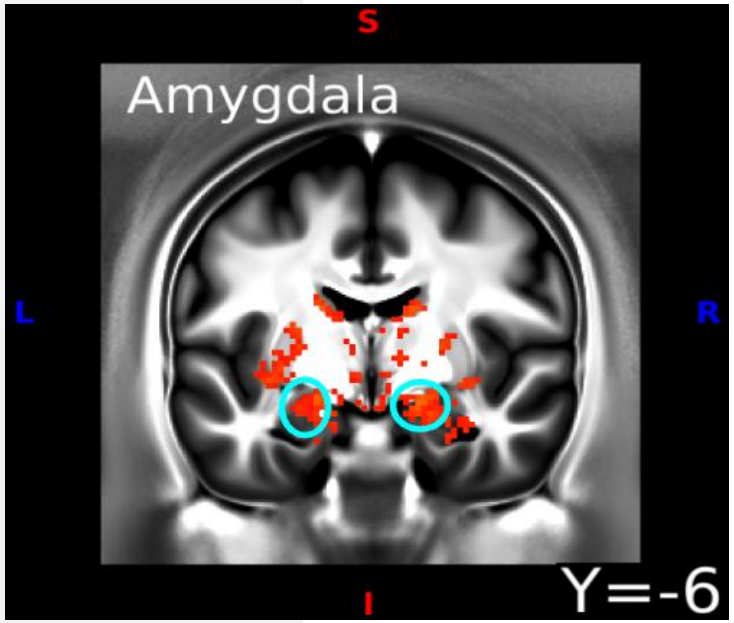
Emotional Task Accuracy in Scanner (%)
Abuser - 98.1
User - 96.5
Non-user - 97.3

TASK RESPONSE

- Faces vs. shapes
- Abuser group



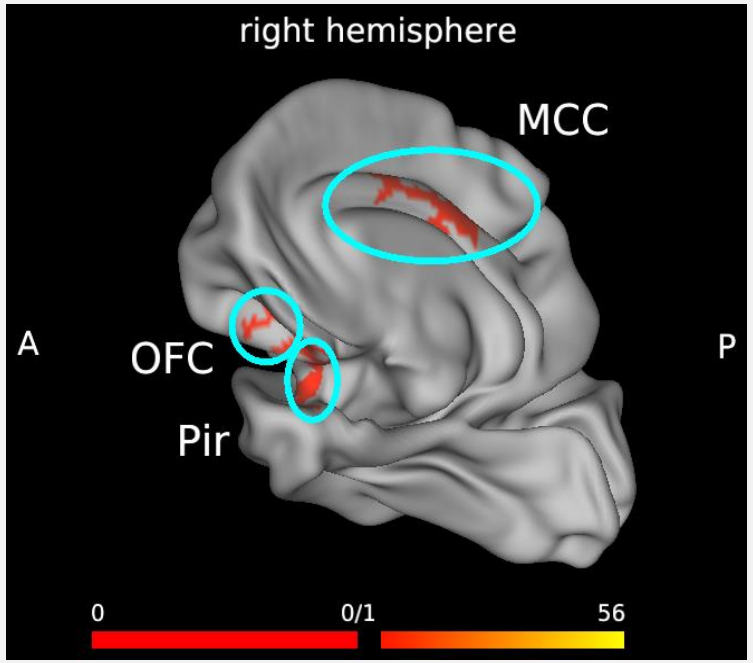




The following findings were significant at a voxel level with minimum cluster size, not significant when we take into account family-wise error correction.

- The effects are simply weak.

ABUSER VS. NON-USER



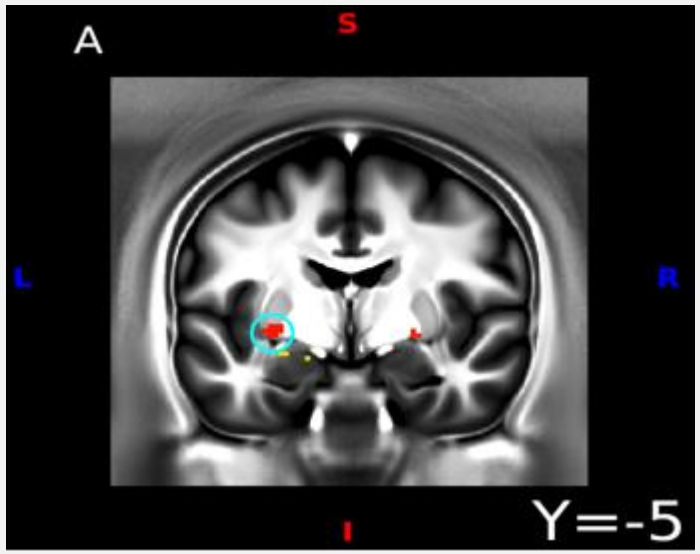
Orbitofrontal Cortex (OFC) – Most support
- decision making and impulse control
- impulsive drug taking behaviour

Abuser vs. Non-user
- MCC
- OFC
- Piriform cortex
- Left putamen
- Left thalamus

User vs. Non-user
- Left amygdala
- IFC
- Left putamen

Abuser vs. User
- No significant difference

ABUSER VS. NON-USER



Left Putamen – well-supported[1,2]

- CB_1 receptors[3] are abundant
- reward anticipation
- Pleasure-related drug-seeking behaviour in chronic cannabis use[1]

Abuser vs. Non-user

- MCC
- OFC
- Piriform cortex
- Left putamen
- Left thalamus

User vs. Non-user

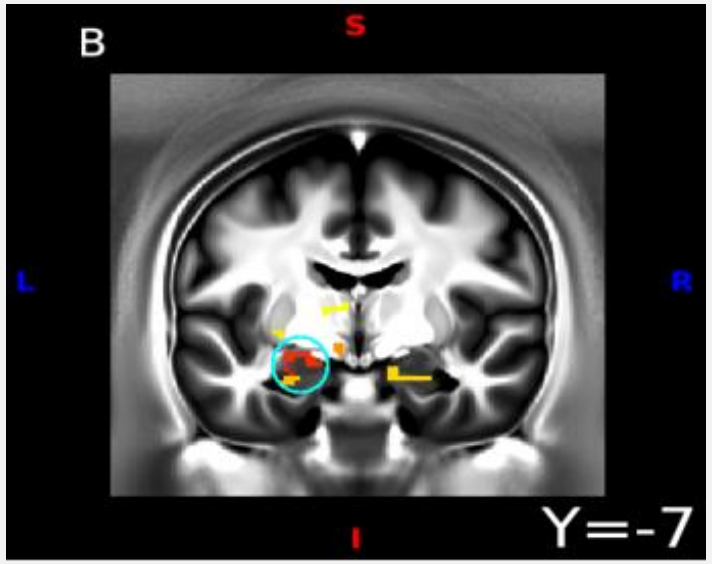
- Left amygdala
- IFC
- Left putamen

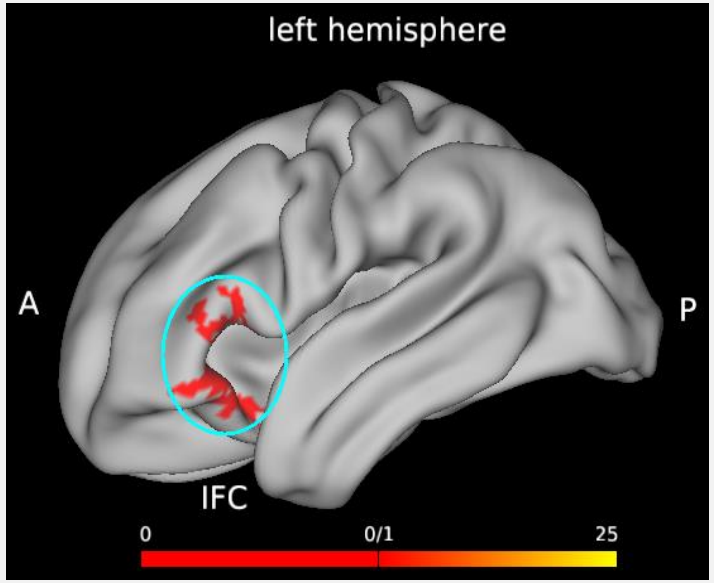
Abuser vs. User

- No significant difference

1 van Hell et al., 2010;
2 Hester, Nestor & Garavan, 2009
3 Hurley, Mash & Jenner, 2003

USER VS. NON-USER





Left amygdala and Inferior Frontal Cortex (IFC)

- Emotional face processing
- Only in users not abusers

- Only in lower doses and not higher doses[1]

- Compensatory effect?

Abuser vs. Non-user

- MCC
- OFC
- Piriform cortex
- Left putamen
- Left thalamus

User vs. Non-user

- Left amygdala
- IFC
- Left putamen

Abuser vs. User

- No significant difference

1 Cornelius et al., 2010

CONCLUSION

Chronic use of cannabis might be associated with altered

- emotional processing (Amygdala, IFC)
- decision making (OFC)
- impulse control (OFC)
- reward anticipation (Putamen)

LIMITATION & FUTURE DIRECTIONS

- Abuser depend on telephone-based, DSM-like diagnosis
- Require self-awareness

- For more sensitive assessment, we will include continuous measures: age of onset, intensity of use

Use the whole HCP dataset

- Include genetic relatedness

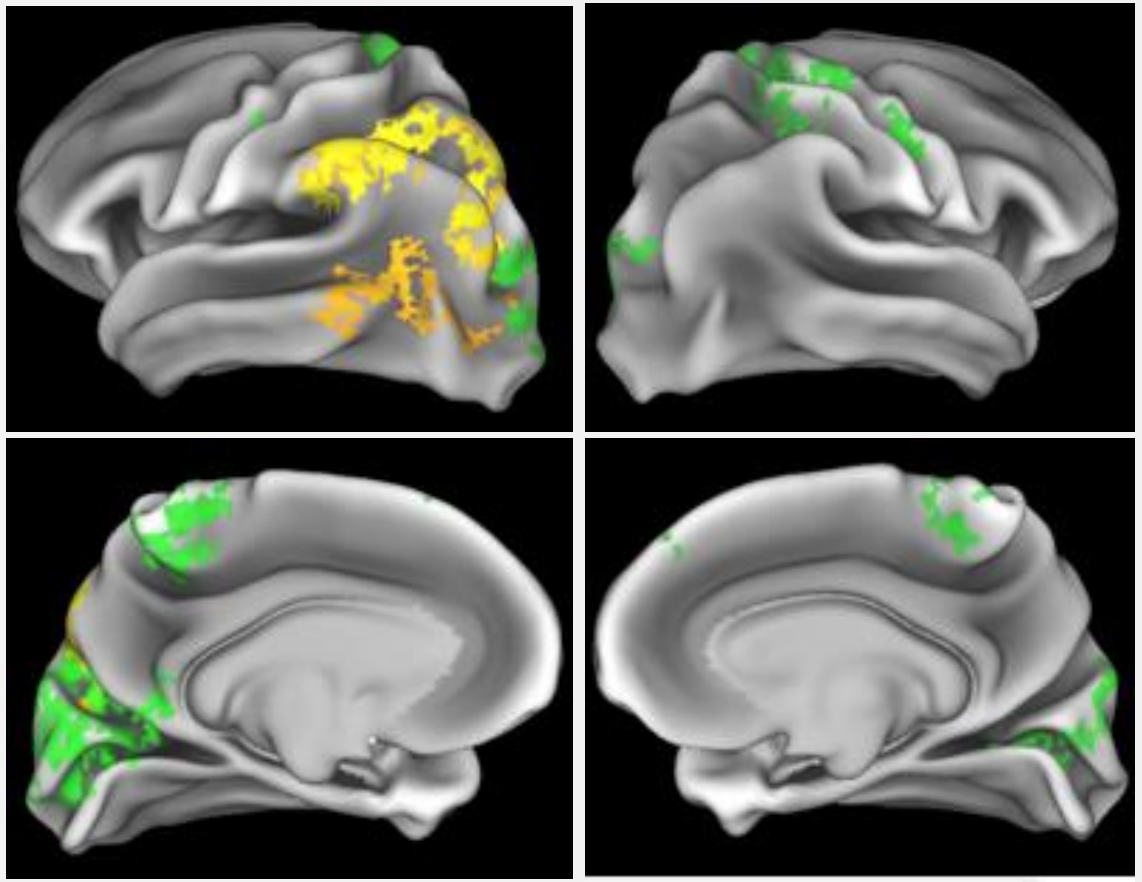
QUESTION

ONGOING ANALYSES

- Stripped down to 59 each group, Excluded

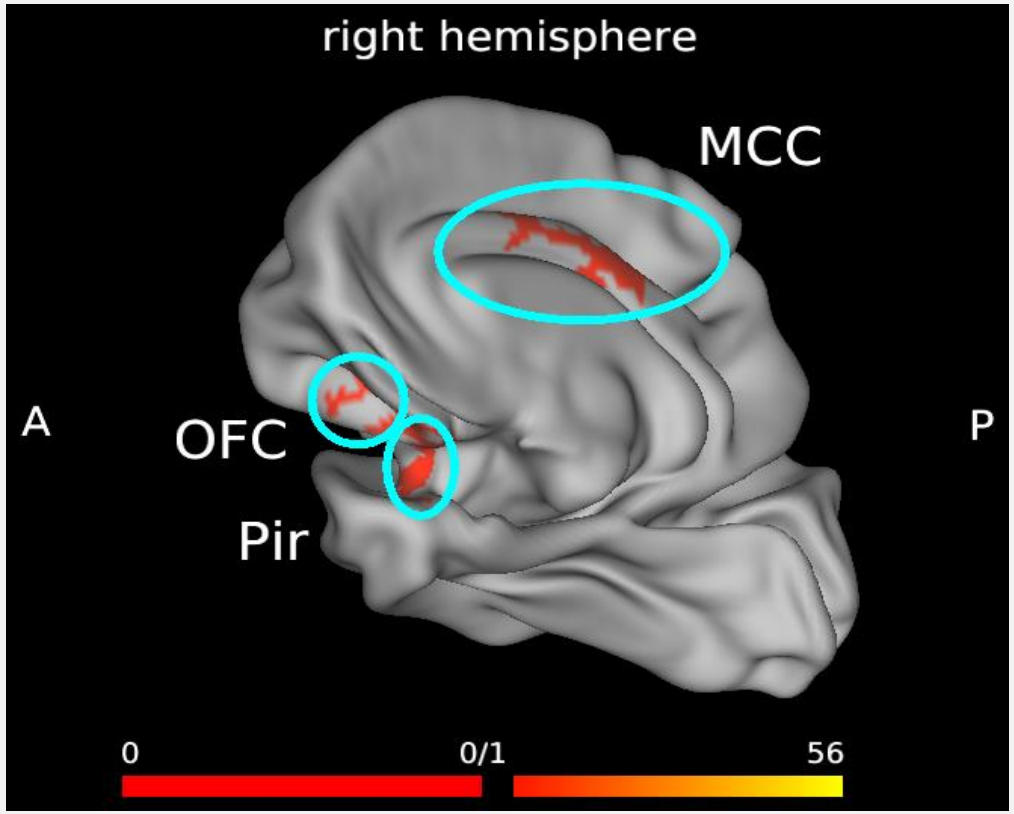
1. Current psychiatric disorders
2. Urine test positive for drugs other than THC
3. Other variables (such as tobacco use and alcohol use)

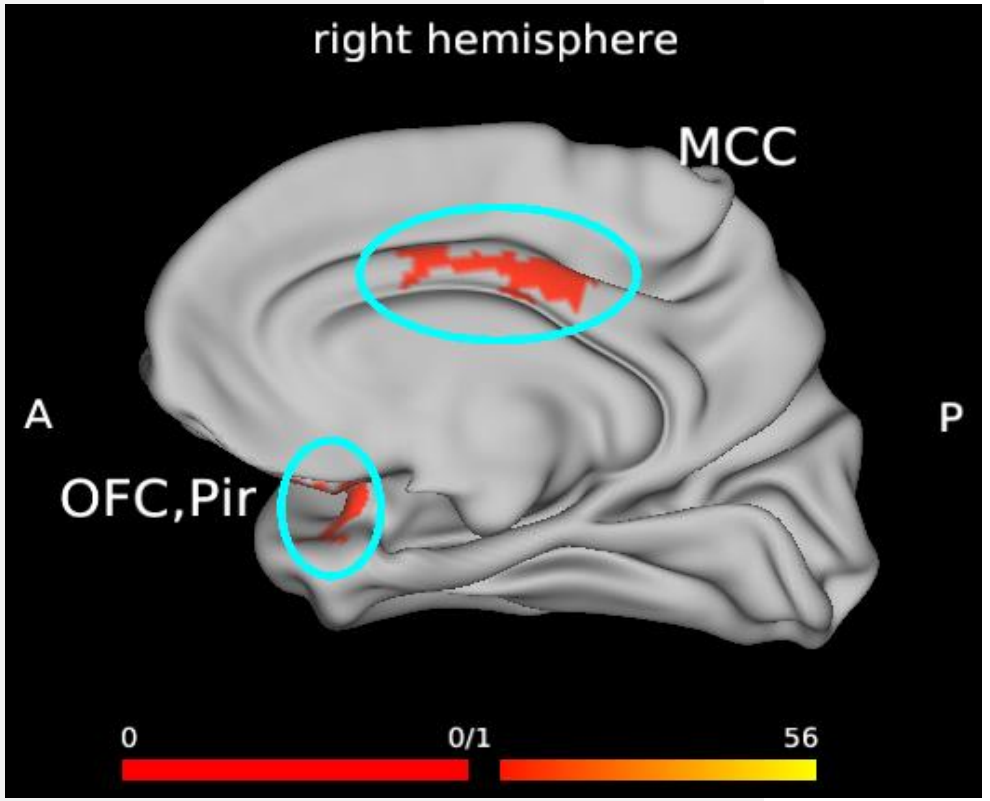
- Ignore group, use alcohol and intensity of cannabis use



GROUP RESULTS

- Abusers vs. Non-Users





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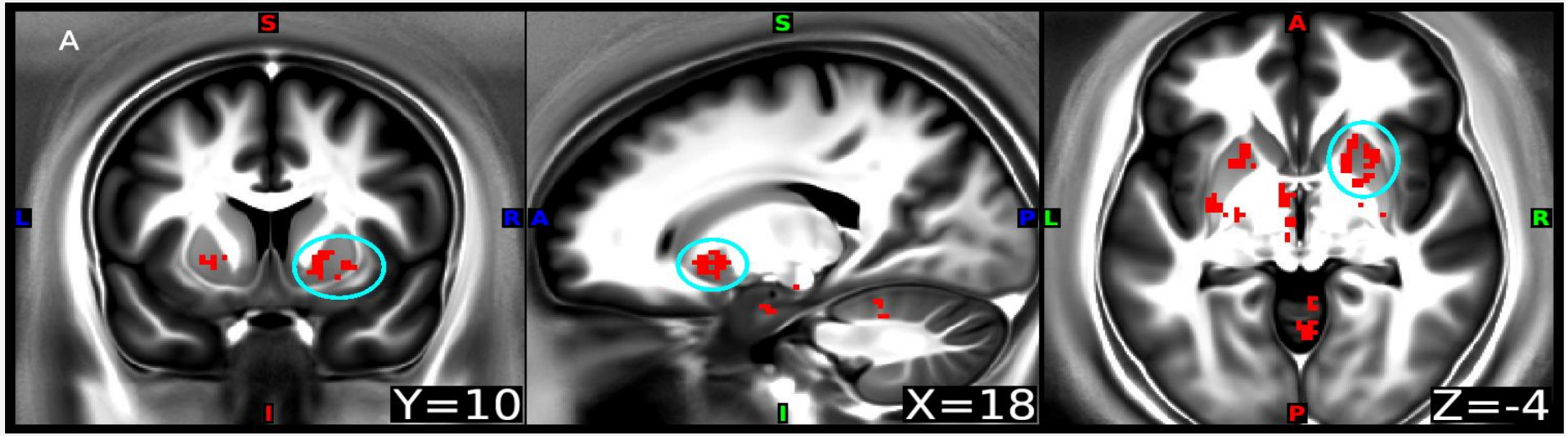
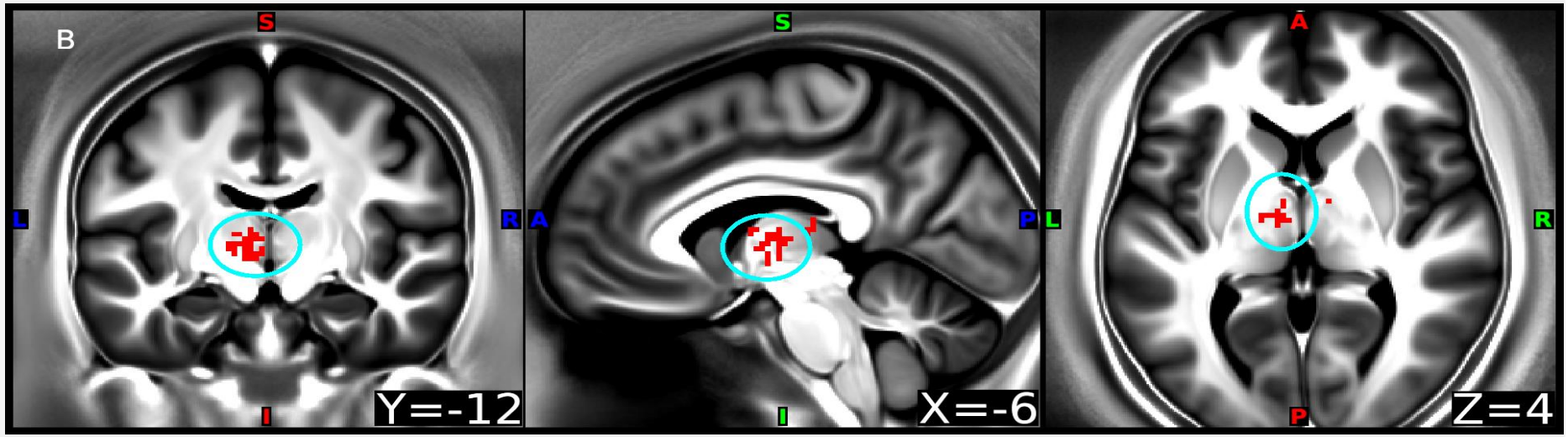


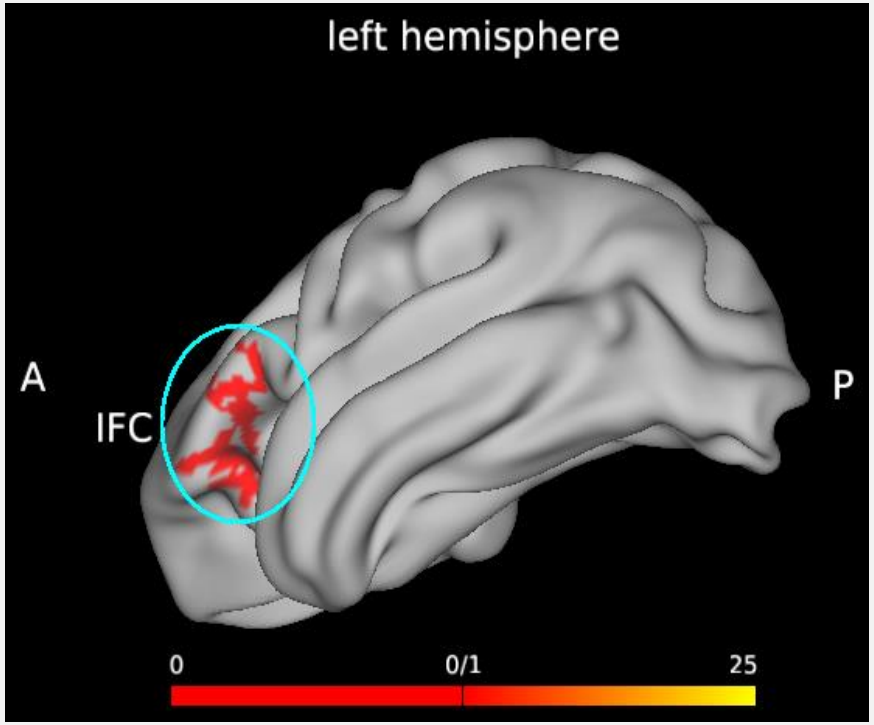
Left putamen

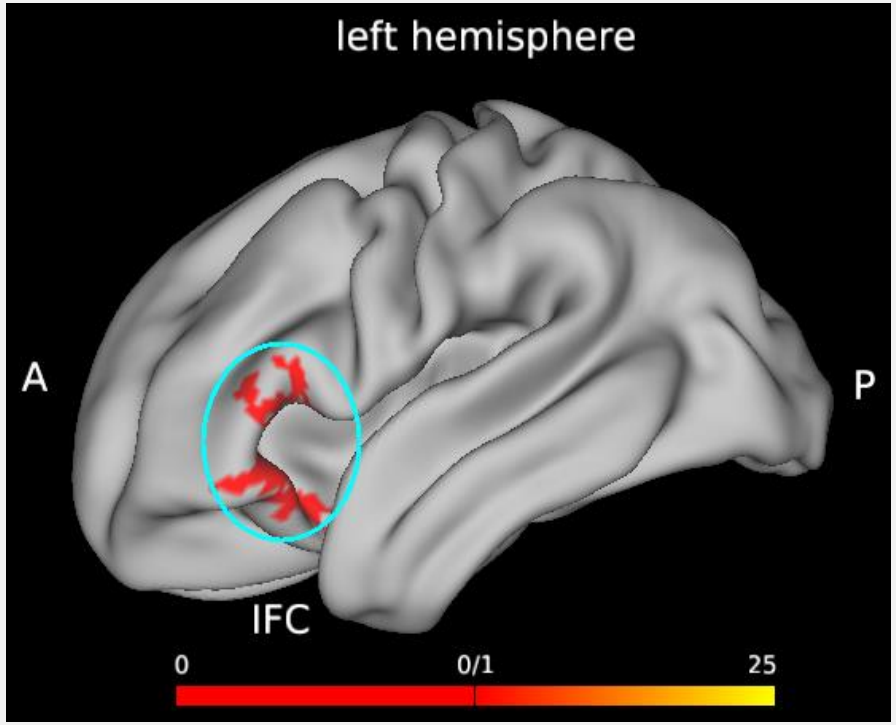


Left thalamus

GROUP RESULTS

- Users vs. Non-Users





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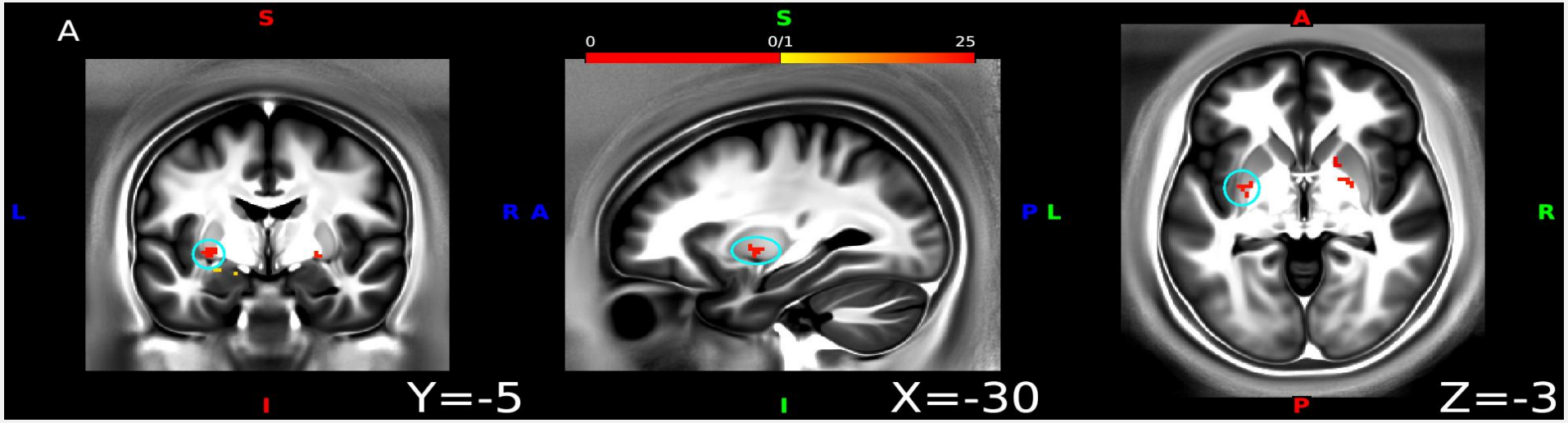

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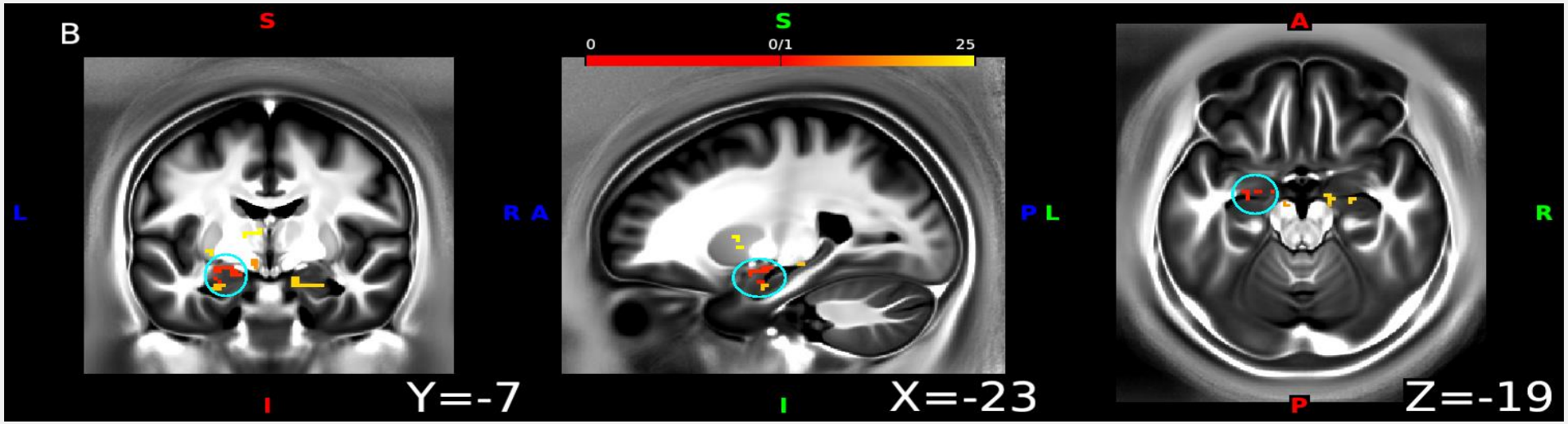

Left amygdala