Probing the craving neurocircuitry in Cannabis Use Disorder using real-time fMRI neurofeedback

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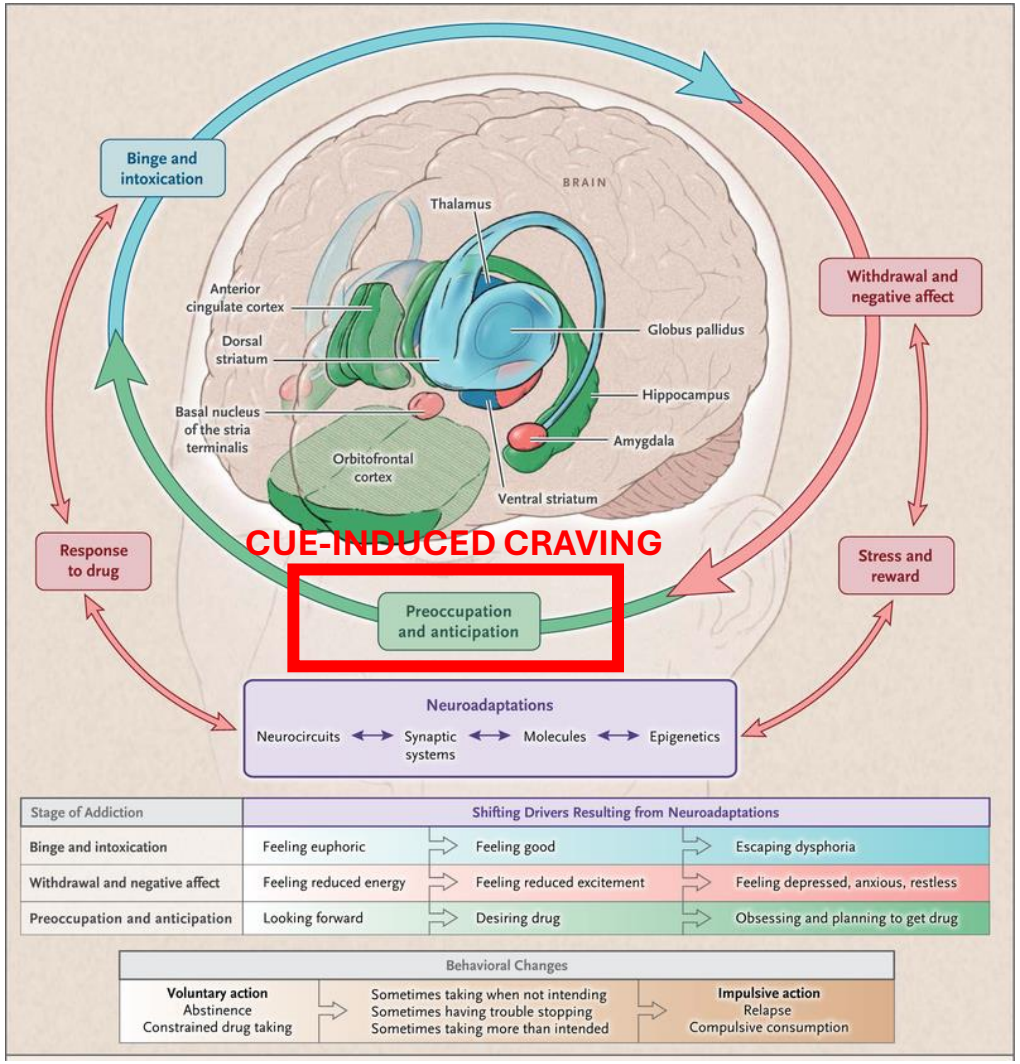
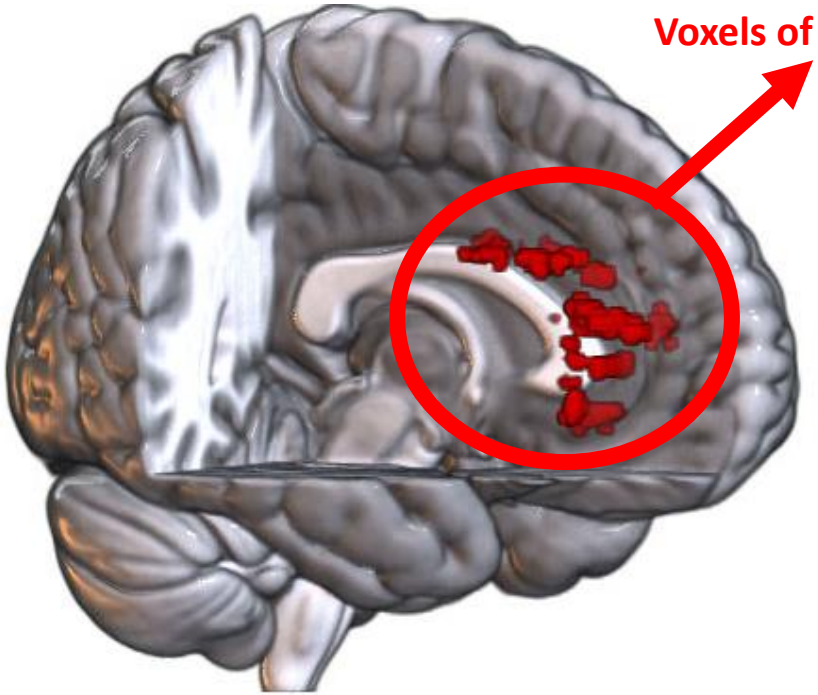
Theoretical framework

Koob & Volkow (NEJM, 2016)

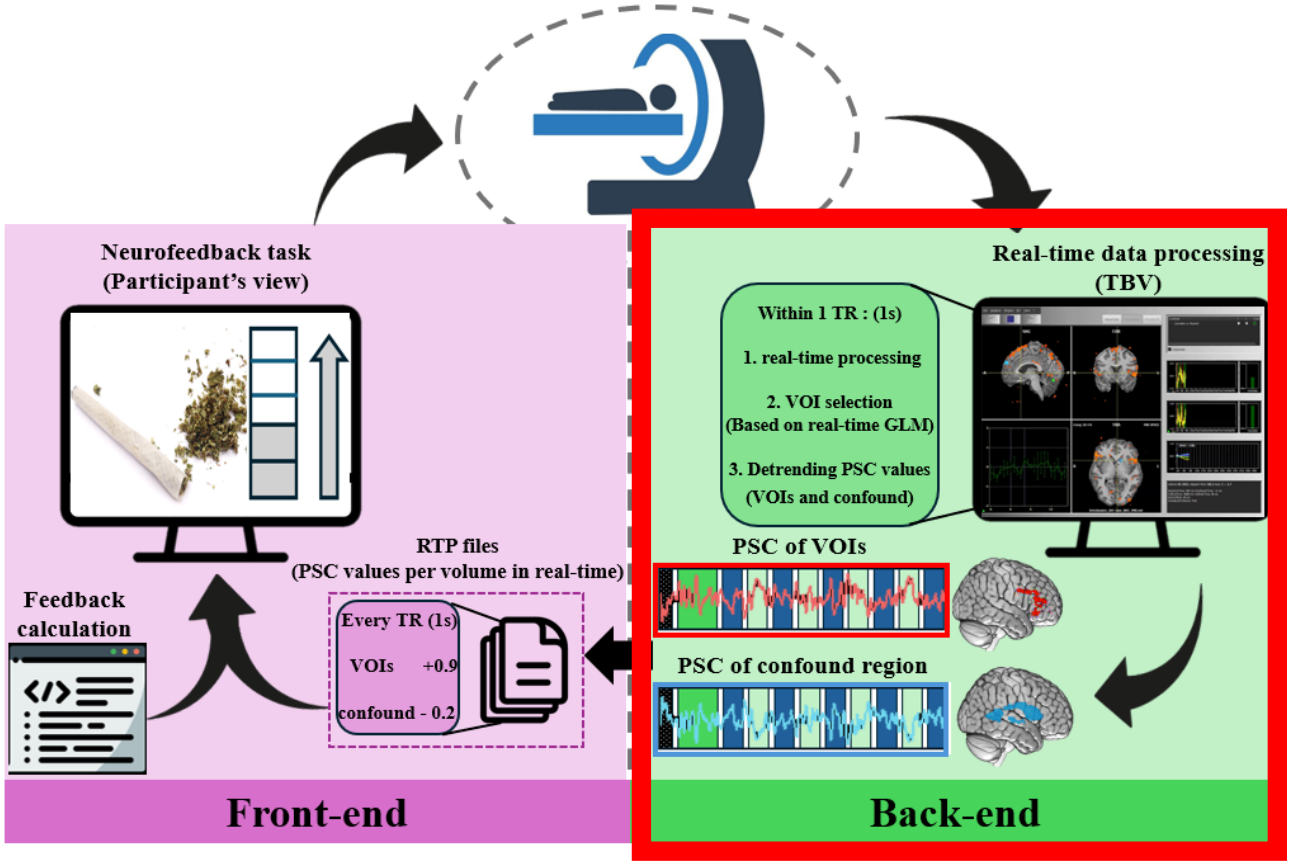


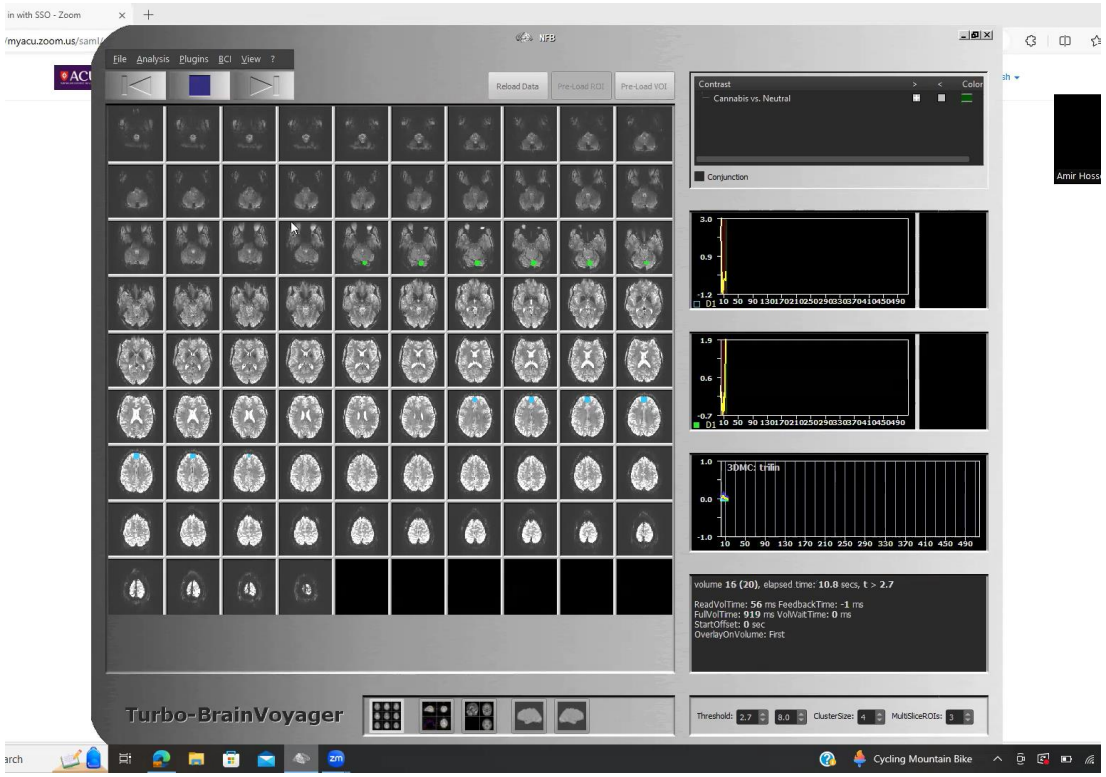
Anterior Cingulate Cortex

Voxels of interest (VOIs)



fMRI-neurofeedback system





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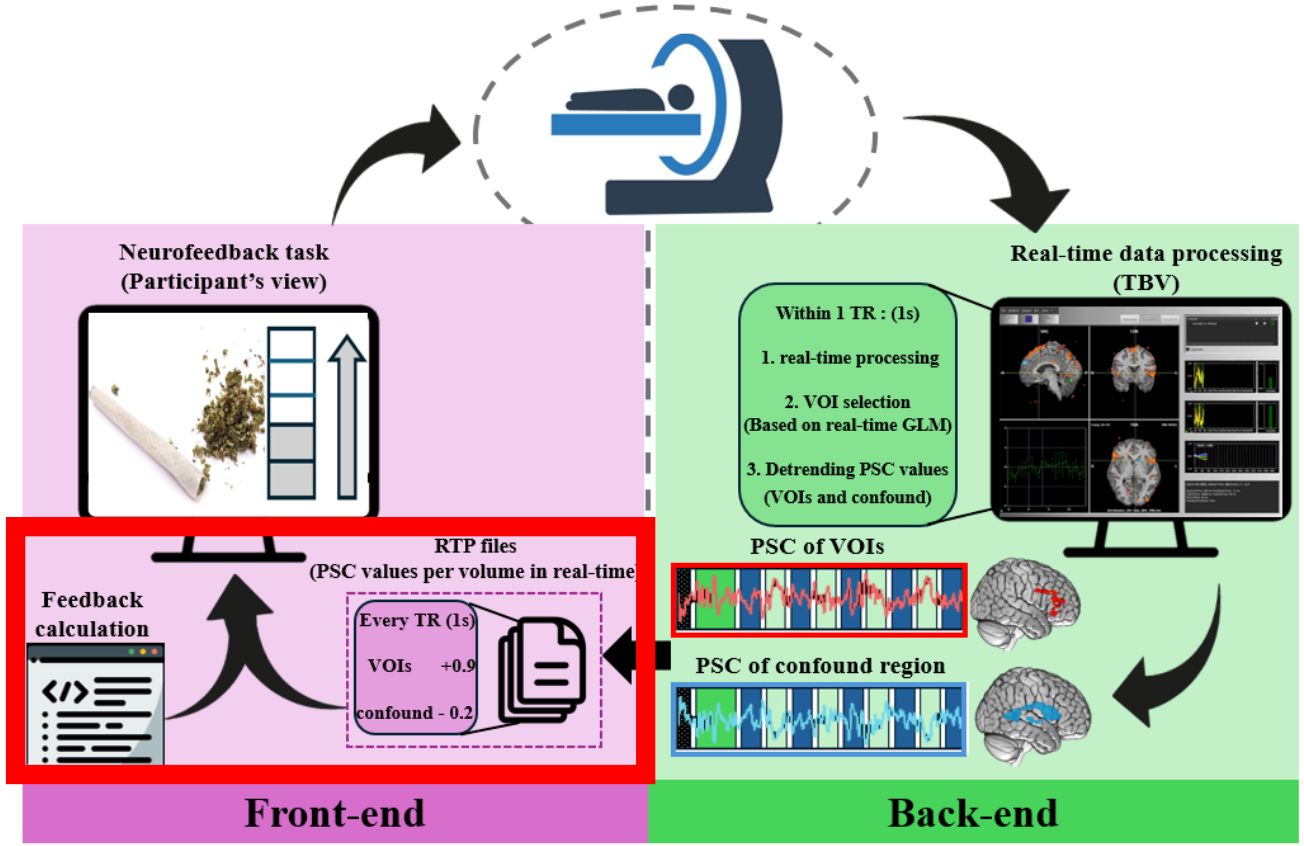

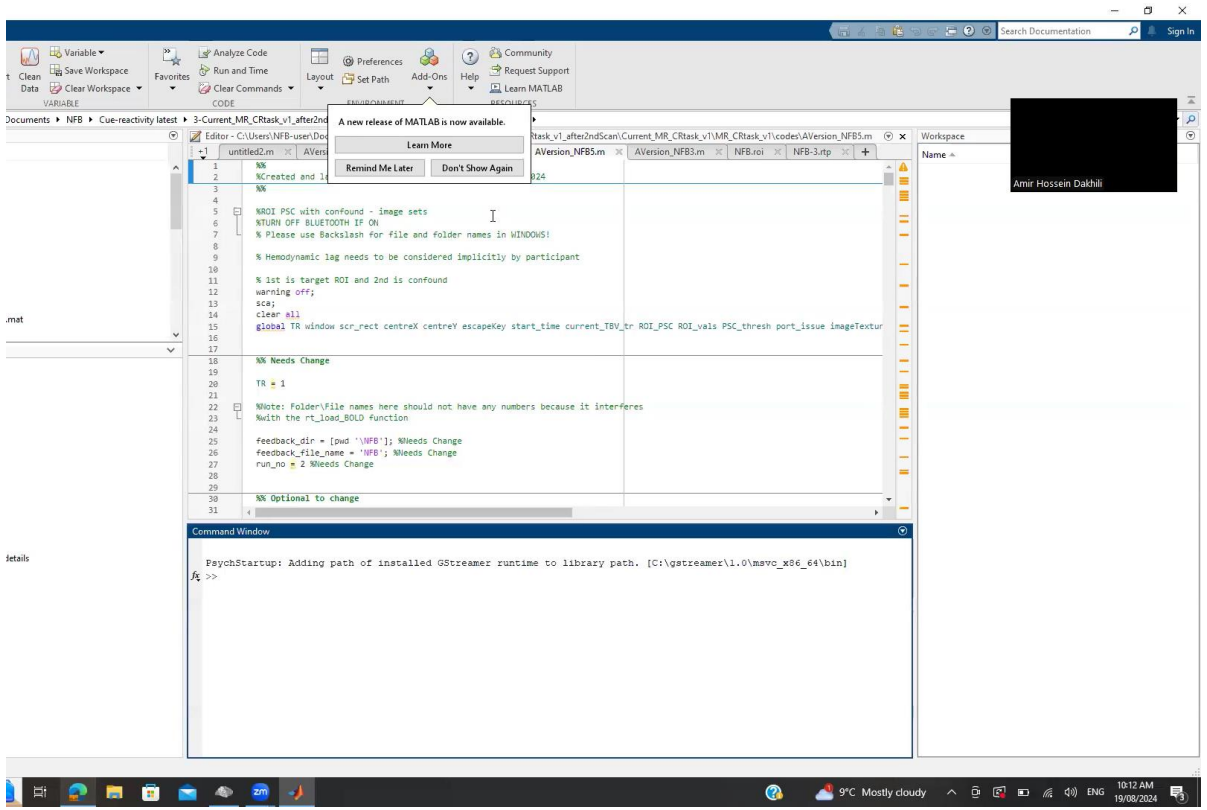

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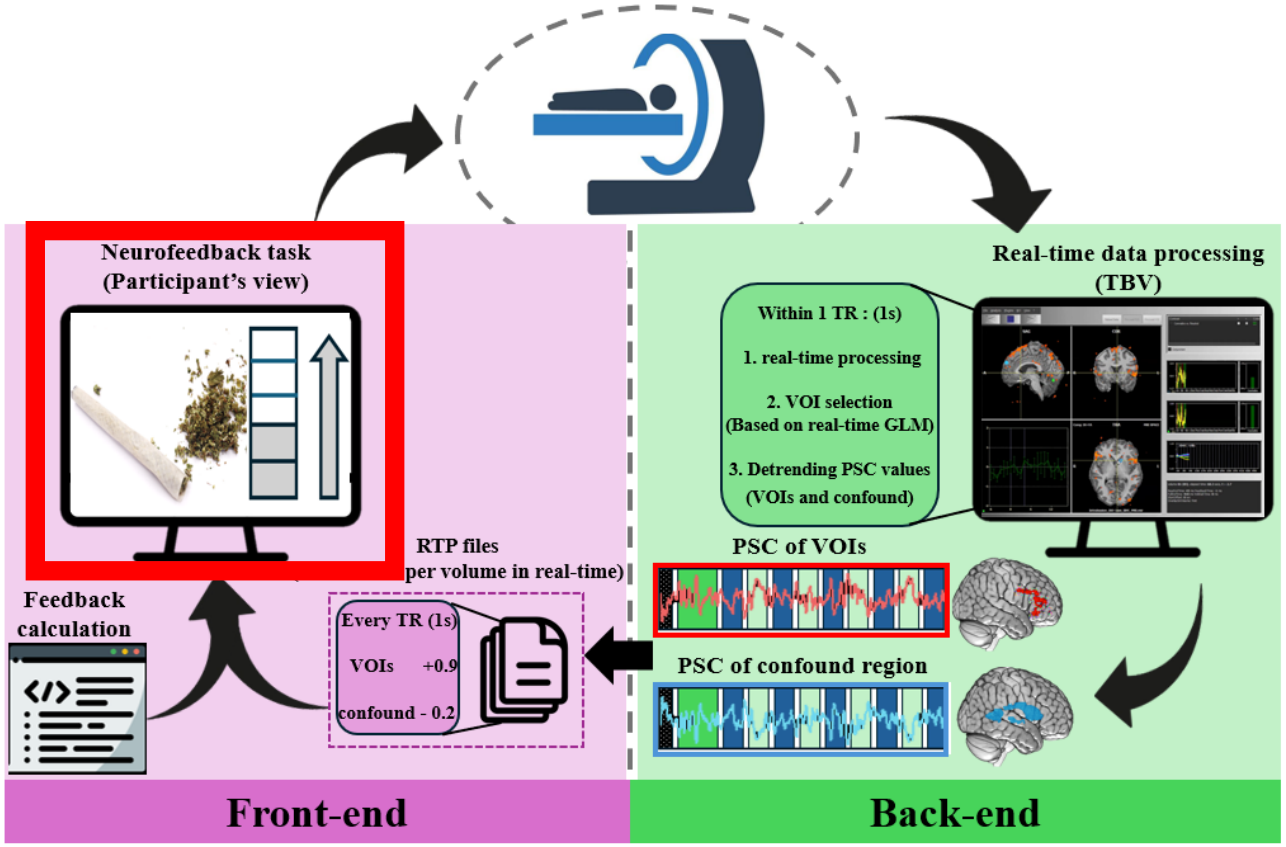
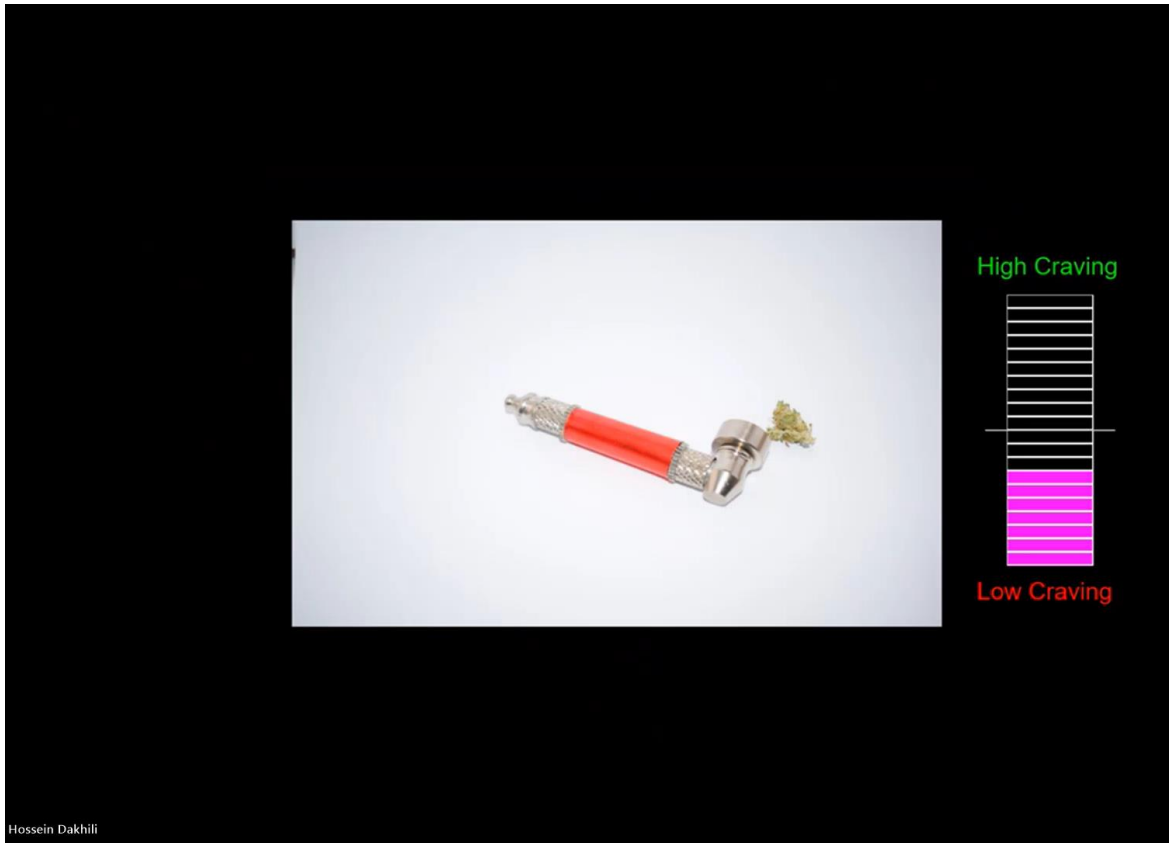
fMRI-neurofeedback system





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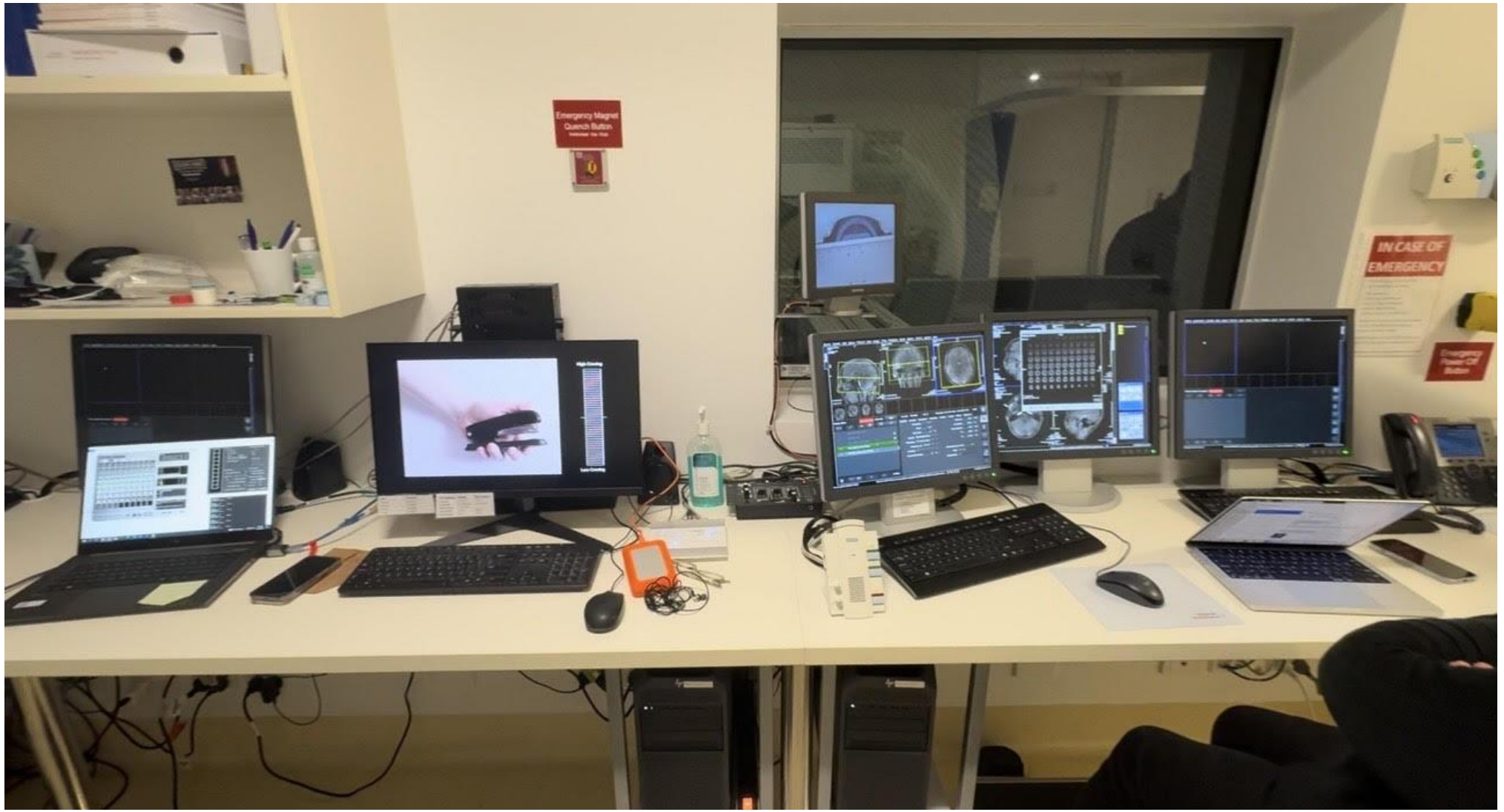
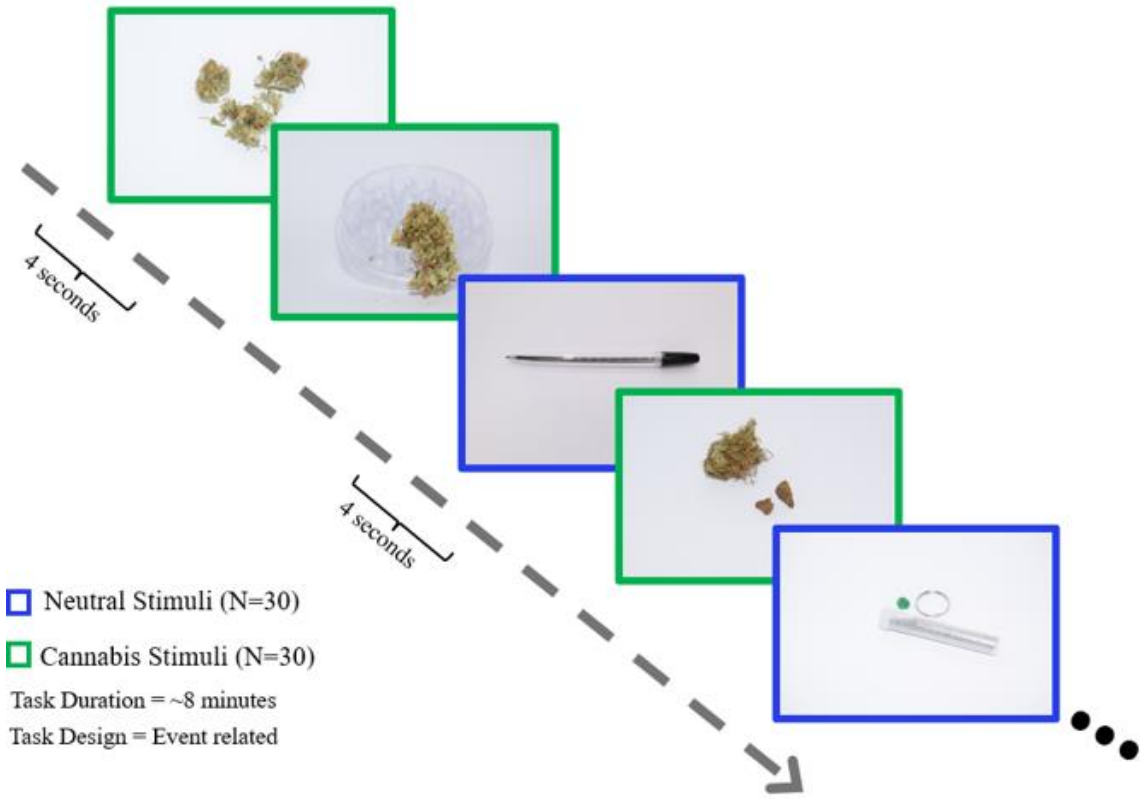
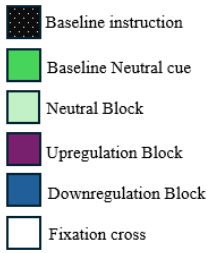
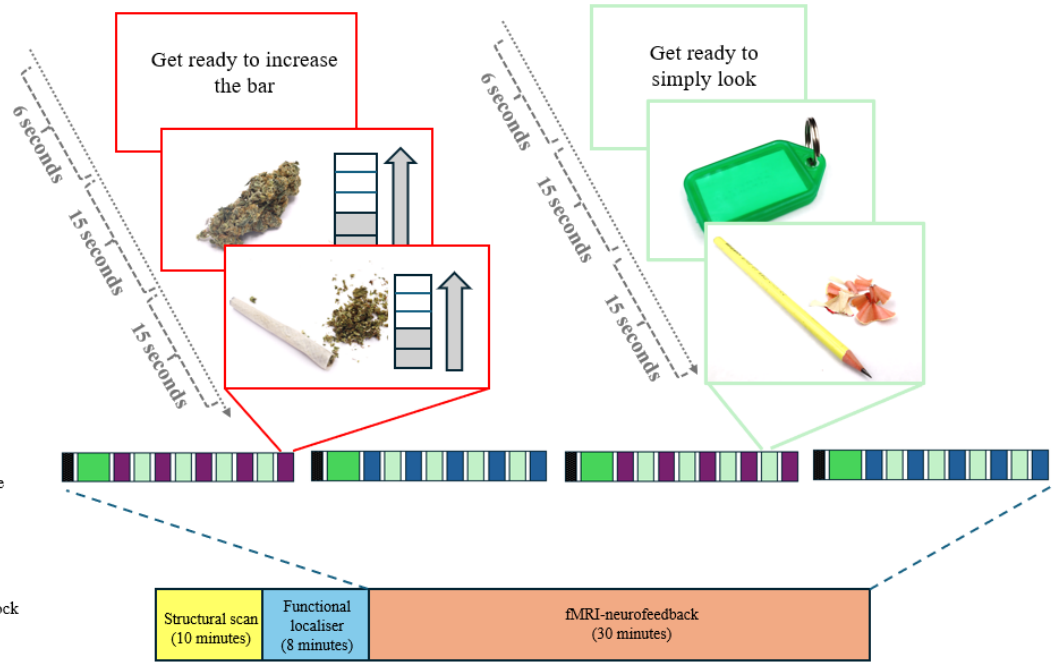


Experimental design



Functional localiser

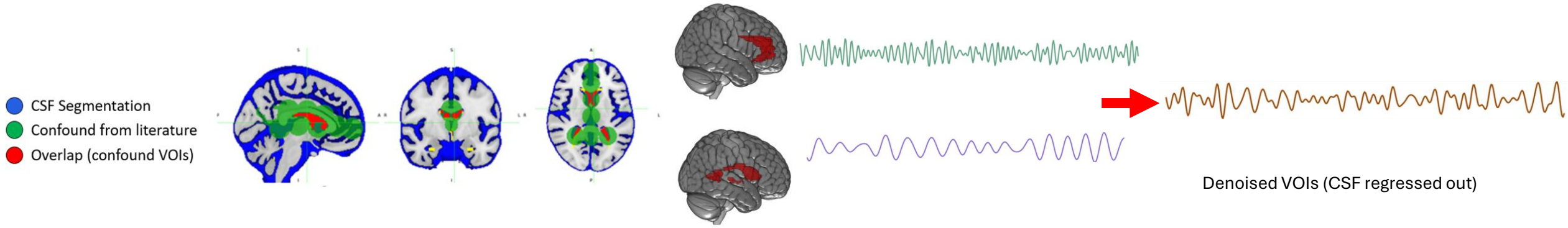




fMRI_neurofeedback

Feedback Signal Characteristics

1. Confound Regression and Denoising



2. Weighted Sliding Window for Signal Stability

Final feedback value

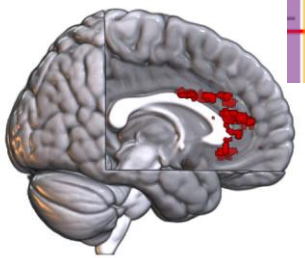
$$A = 0.5\,(V_i) + 0.25\,(V_{i-1}) + 0.125(V_{i-2} + V_{i-3})$$

V_i represents the current TR percent signal change (PSC), and V_{i-1}, V_{i-2} and V_{i-3} are PSC values from the preceding three TRs

Regional Specification Level

=

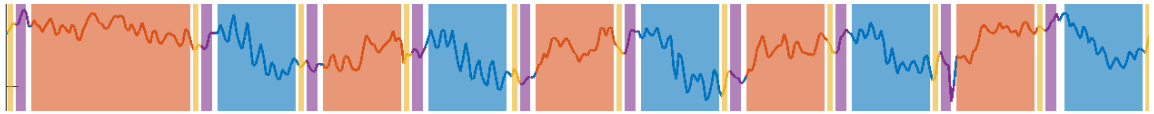
The degree to which BOLD activity during regulation was explained by the neuromodulation signal



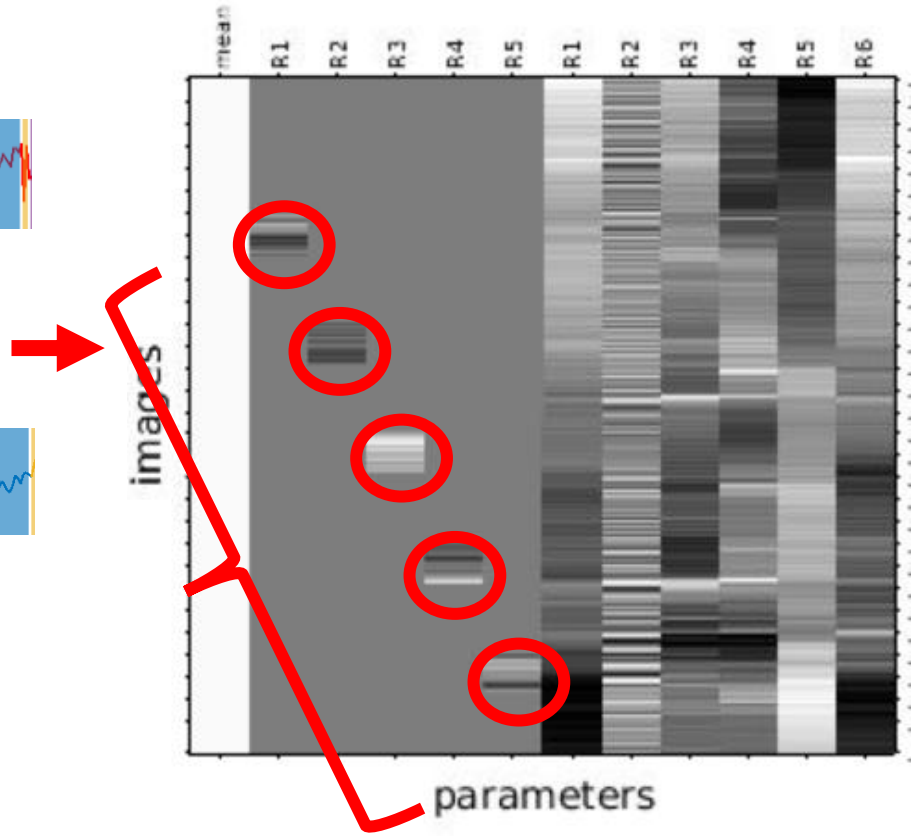
- Fixation Cross
- Instructions
- Regulation
- Neutral

Real-time Neuromodulation Signal

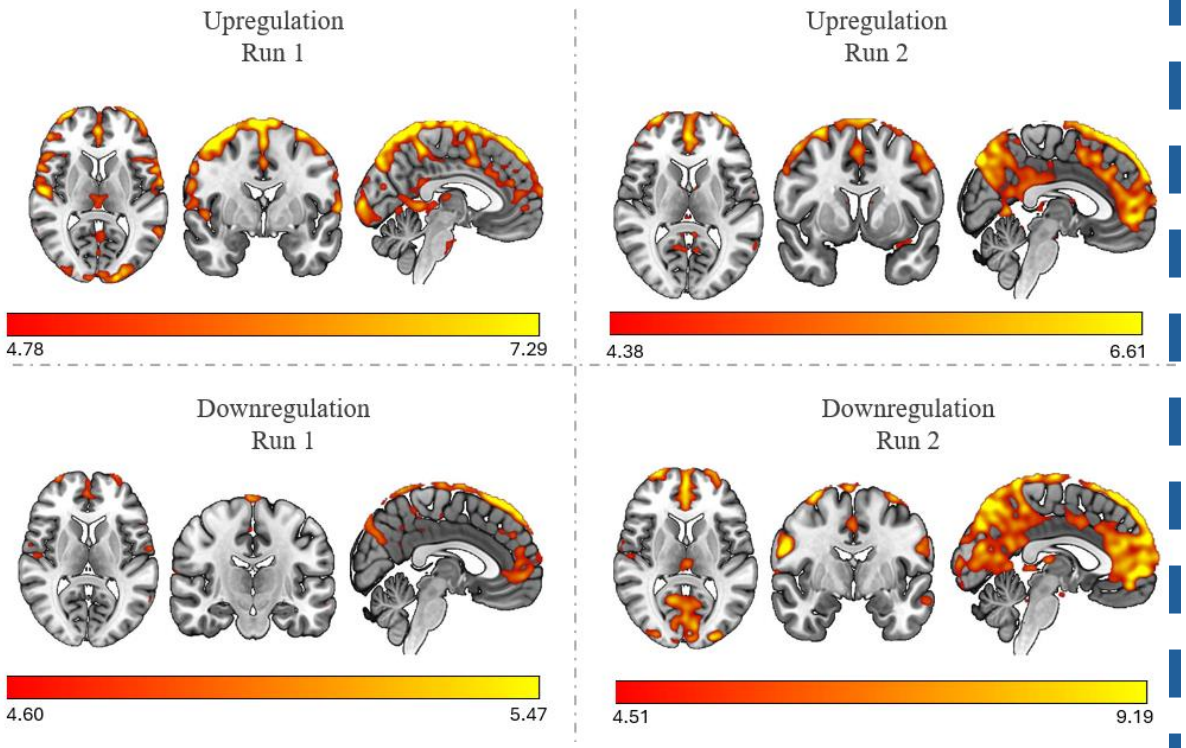
BOLD signal



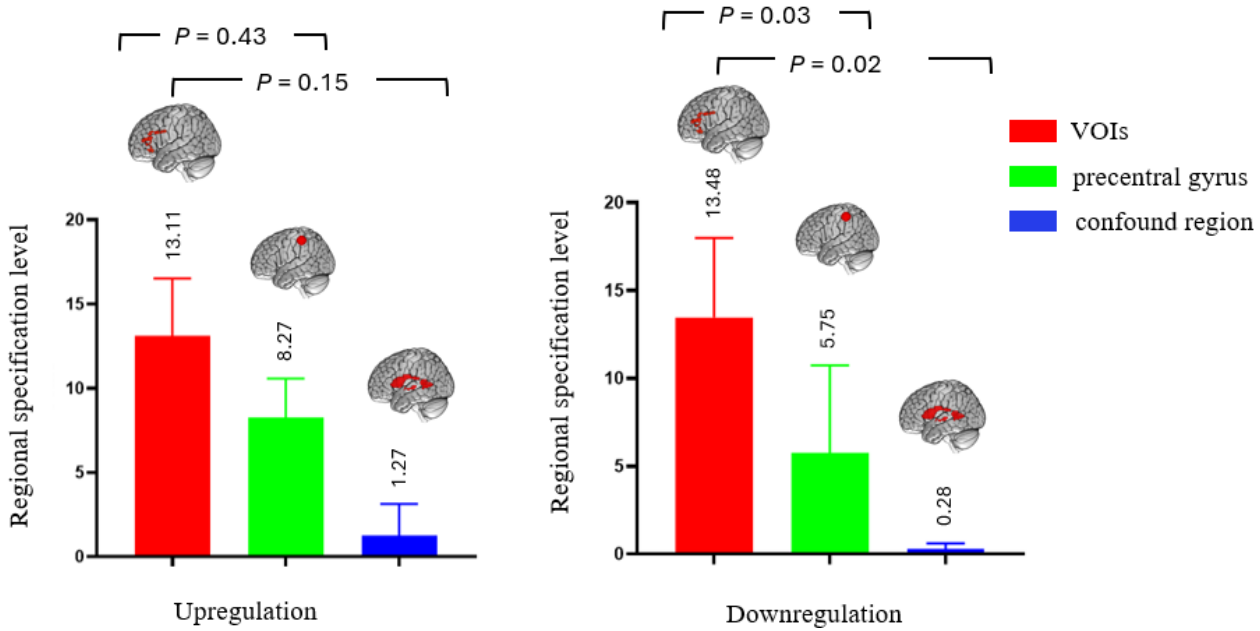
Greater positive beta value => Higher region specificity of the feedback signal



Region specificity of the neuromodulation signal



Whole brain voxel-based



ROI-based

Screening and face-to-face assessment

Participants

- N = 10 (6 female, 4 male)
- Mean age = 23 (2.5)
- Moderate – Severe Cannabis Use Disorder

Inclusion criteria

- Age 18 to 55 years;
- Normal -to-corrected vision;
- Fluent in English
- Able to attend testing at Melbourne Brain Centre (MBCIU), Parkville
- Abstain from drugs (except nicotine) for >12 hrs before testing
- **Daily/almost daily cannabis use for >12 months**
- **Meet criteria for moderate-to-severe CUD (SCID-5-RV, ≥4 symptoms)**
- **≥1 attempt to reduce/quit cannabis in past 12 months**

Screening and face-to-face assessment

Screening

Online

- Demographics (e.g., age, sex, gender, ethnicity, education, employment)
- Medical (e.g., vision, breastfeeding)
- CUDIT (CUD severity)
- MINI-CUD (cannabis disorder)
- ML (motivation level)
- SDS (dependence)
- AUDIT (alcohol use)
- BDI-II (depression)
- DASS (depression/anxiety/stress)
- MINI-Psych (psychiatric screen)
- Strategies used for cravings

Phone

- Confirm identity, eligibility, schedule testing

Face-to-Face Assessment

Descriptives

- Demographics
- MRI screen
- Saliva swab
- IPAQ-SF (physical activity)

Substance use

- CRSEQ (self-efficacy)
- SCID-5 (diagnostic interview)
- CUDIT (CUD severity)
- CUQ (cannabis use history)
- CWS (withdrawal)
- MCQ (craving)
- ML, MTSS (readiness to change)
- MMQ (motives)
- TLFB (timeline use)
- AUDIT (alcohol use)
- FTND (nicotine dependence)
- WSWS2-B (nicotine withdrawal)

Mental Health

- BDI-II (depression)
- CAPE (psychosis symptoms)
- AES (apathy)
- PSS-SF (stress)

Other

- BVS (body vigilance)
- DERS (emotion regulation)
- EHS (handedness)
- TCAQ (thought control)

Pre-MRI

- MCQ (craving)
- STAI-Y (anxiety)
- VAS (craving, anxiety, focus)
- Expectations
- Last substance use

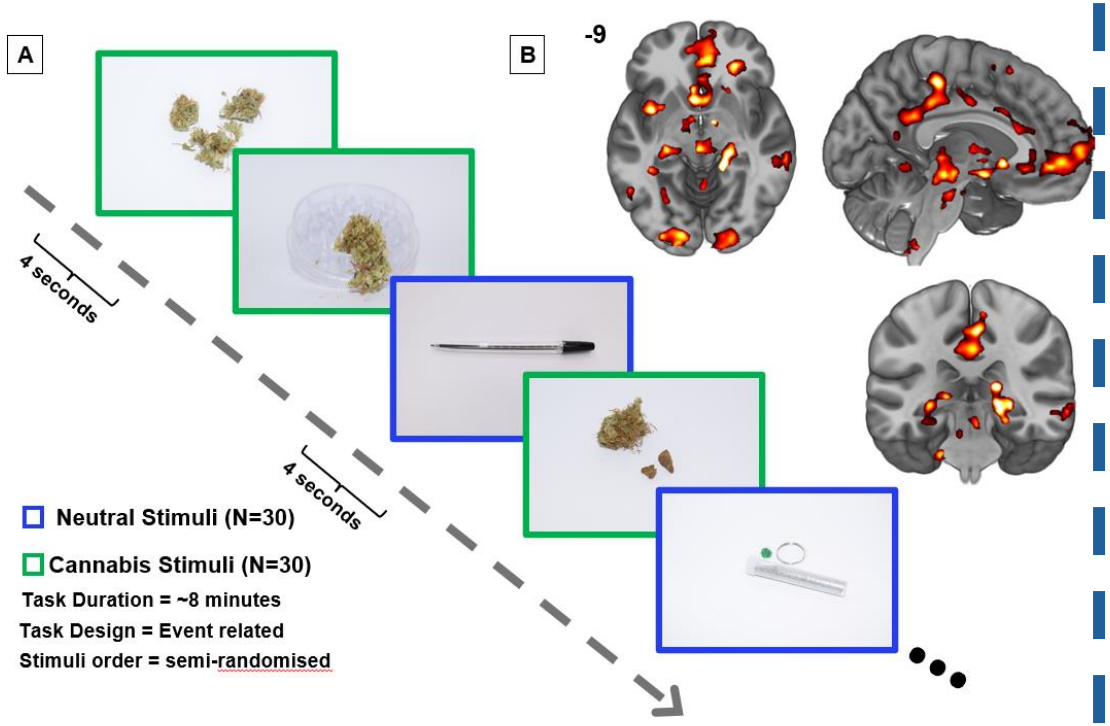
MRI

- T1 structural scan
- fMRI cue-reactivity
- fMRI-neurofeedback

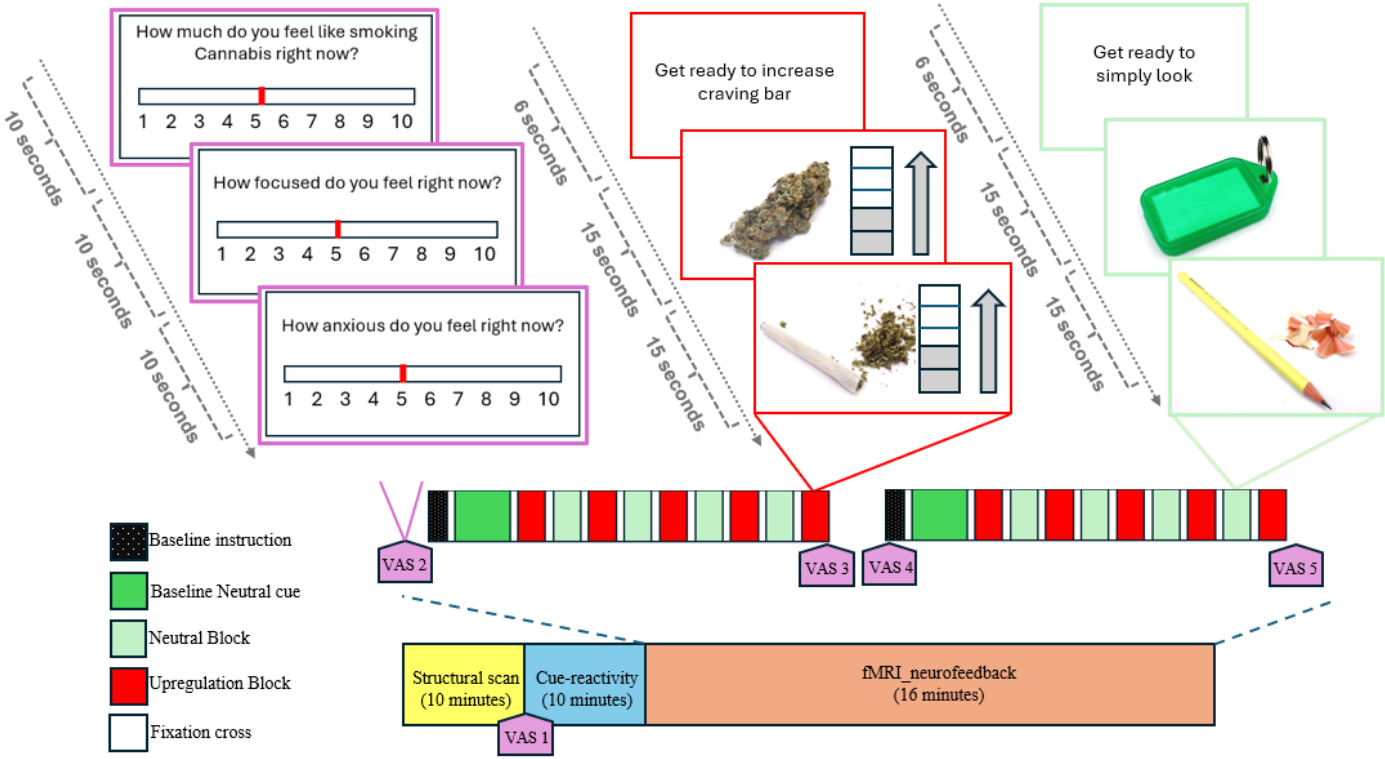
Post-MRI

- MCQ (craving)
- STAI-Y (anxiety)
- VAS (craving, anxiety, focus)
- Expectations
- Cue-reactivity picture rating
- Debrief

Experimental design



Functional localiser



fMRI_neurofeedback

VOIs Mask Characteristics

Individualized ACC neurofeedback masks

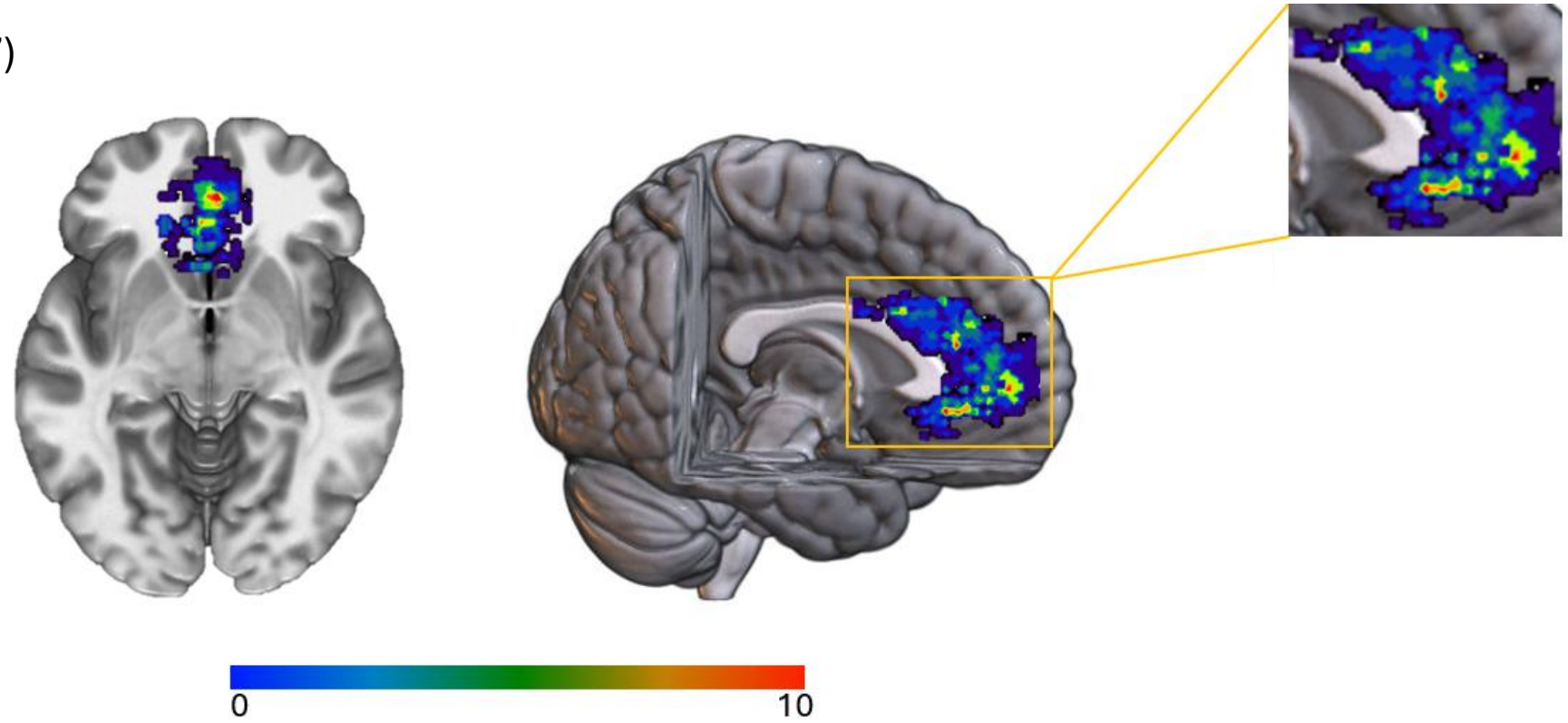
- Functionally defined from **Cannabis > Neutral** contrast in cue-reactivity localizer scan
- Threshold: **t > 2.0**

Mask size variability

- Mean: **830.5 voxels** (SD = 716.7)
- Across 10 participants

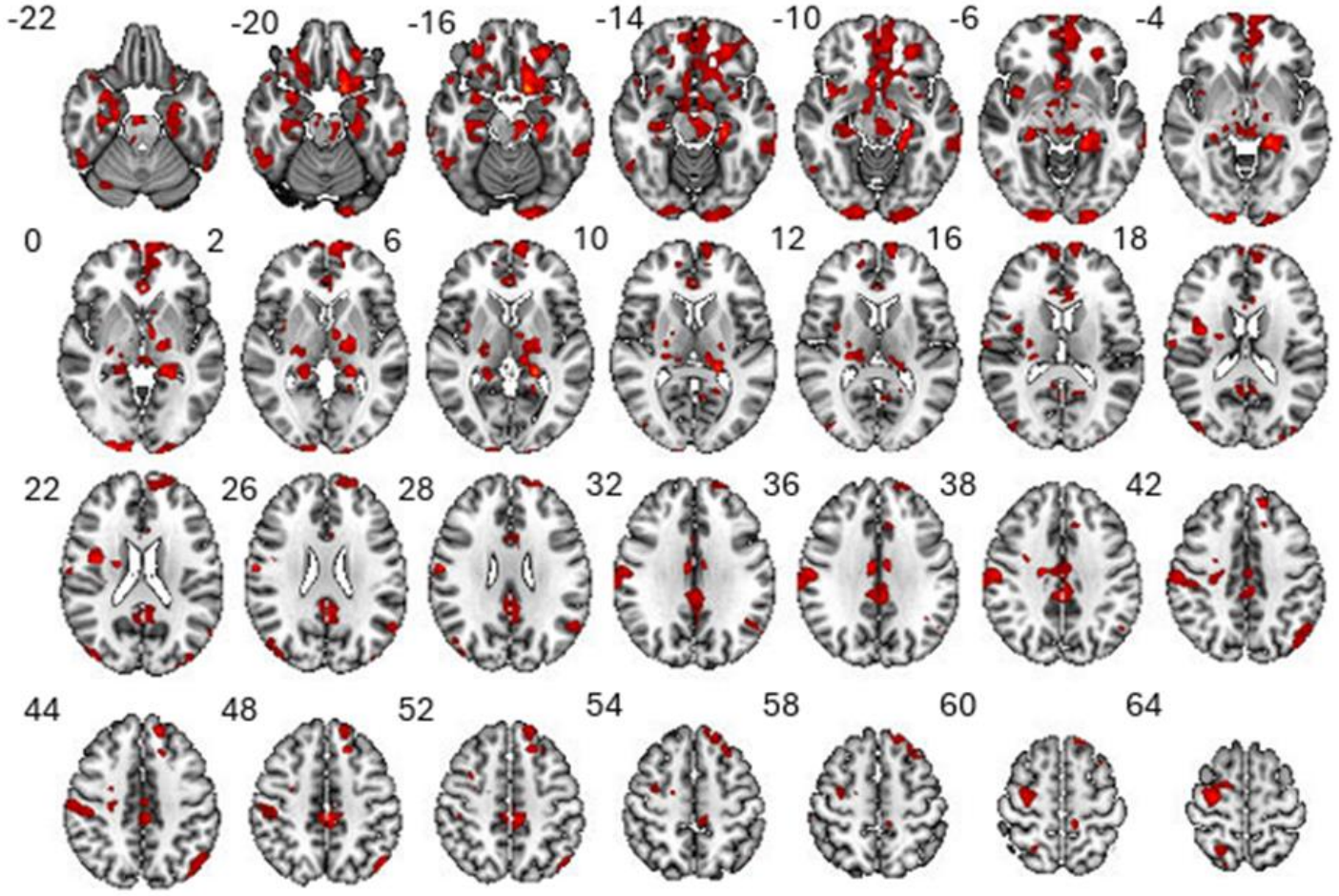
Common activation sites (n = 8)

- **Dorsal ACC:** MNI [1, 15, 28]
- **Pregenual ACC:** MNI [3, 47, 11]



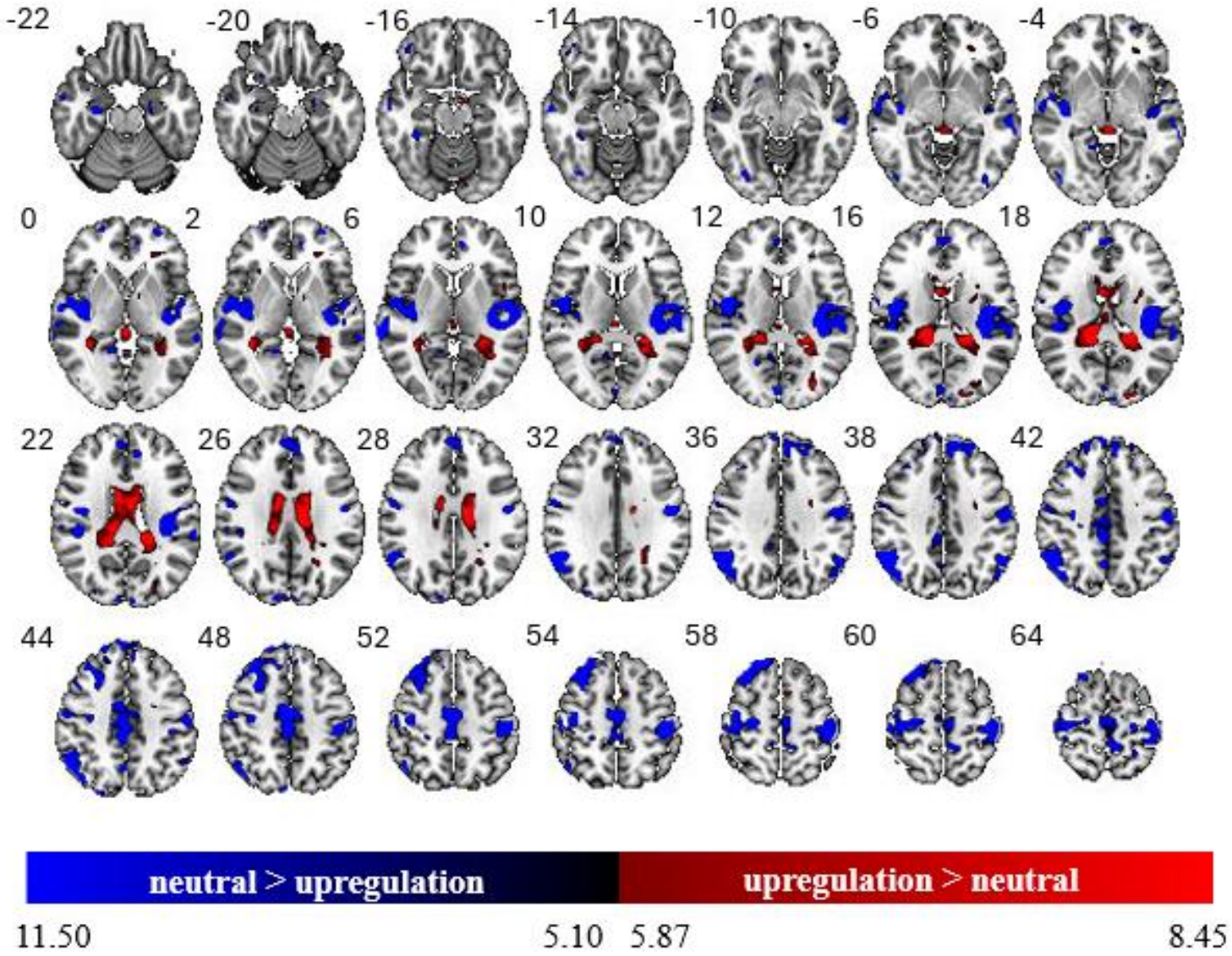
Whole brain analysis

Functional localiser



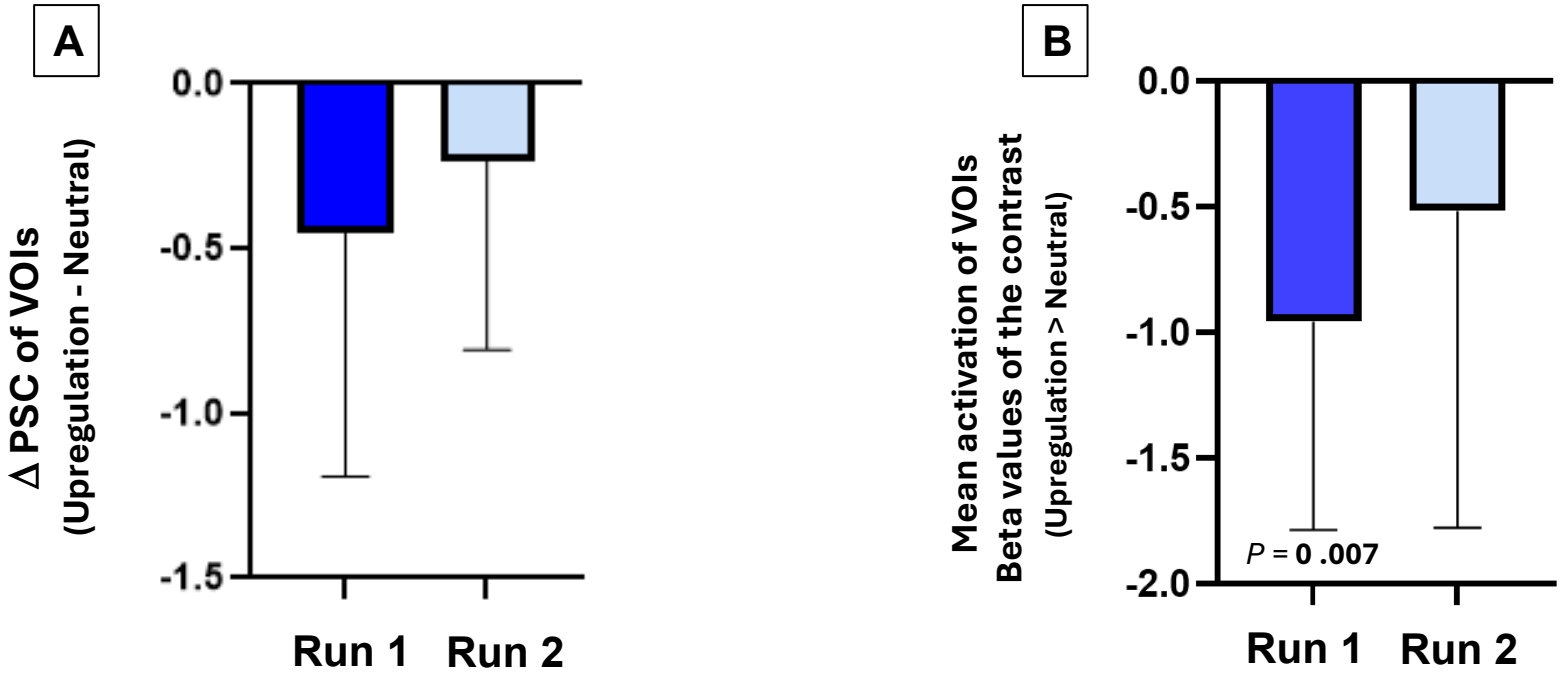
Whole brain analysis

fMRI_neurofeedback

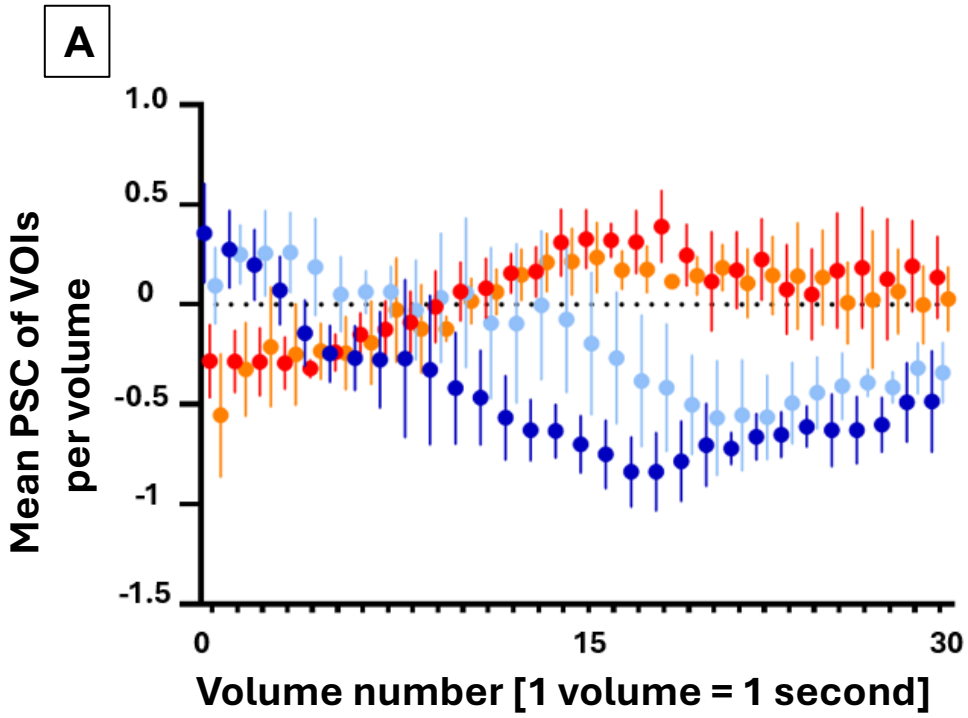


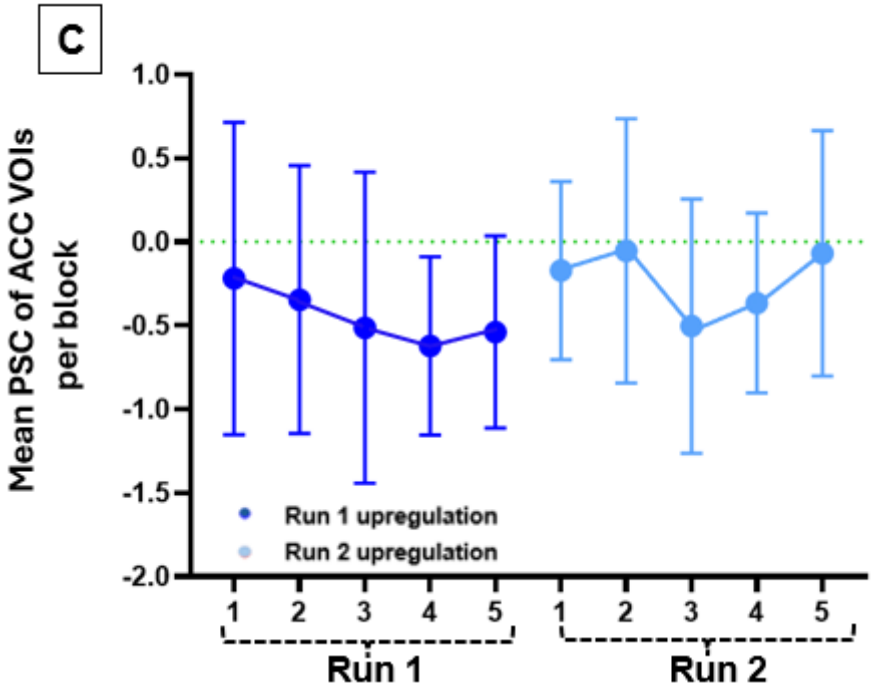
Activation of VOIs

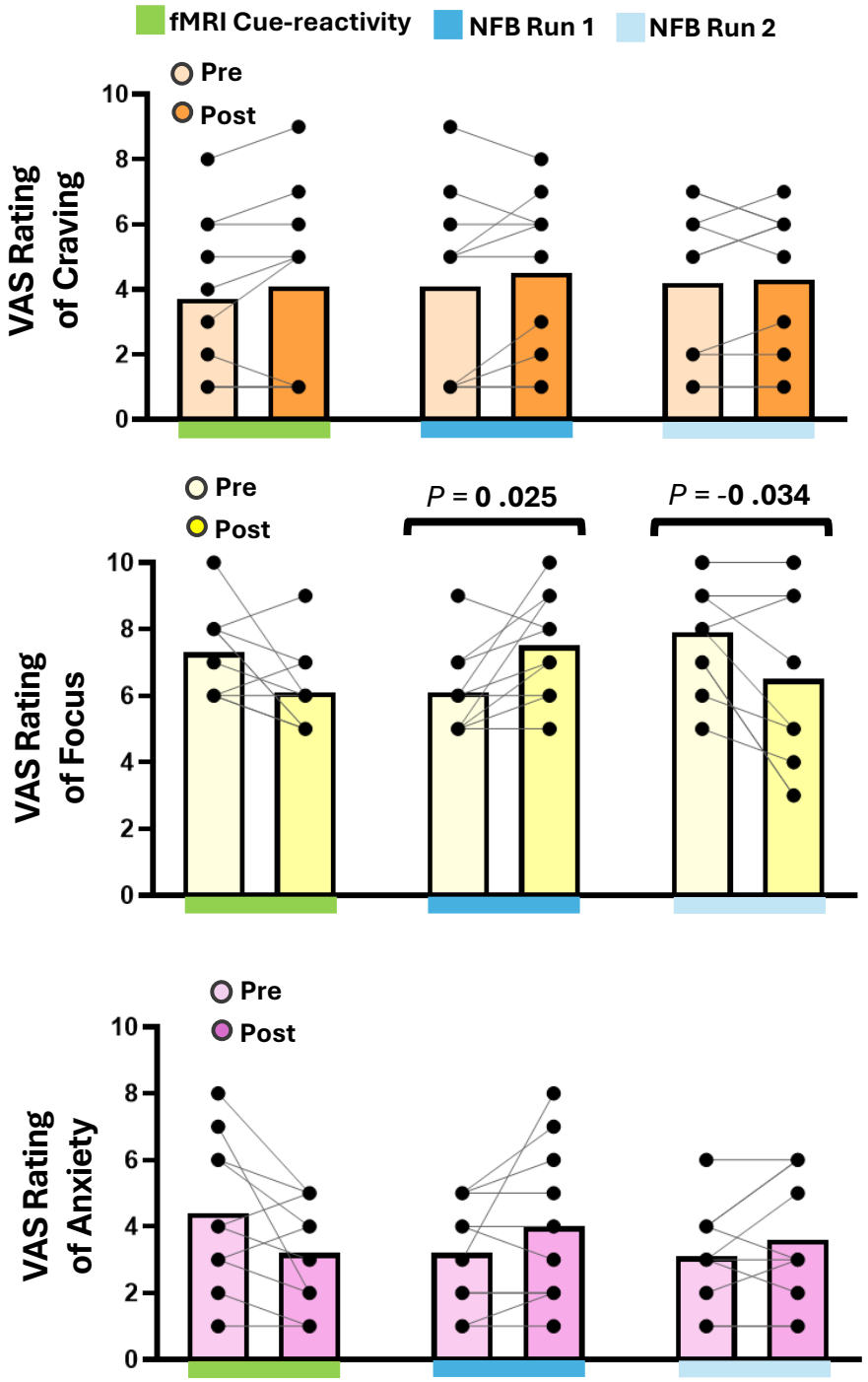
Upregulation vs Neutral

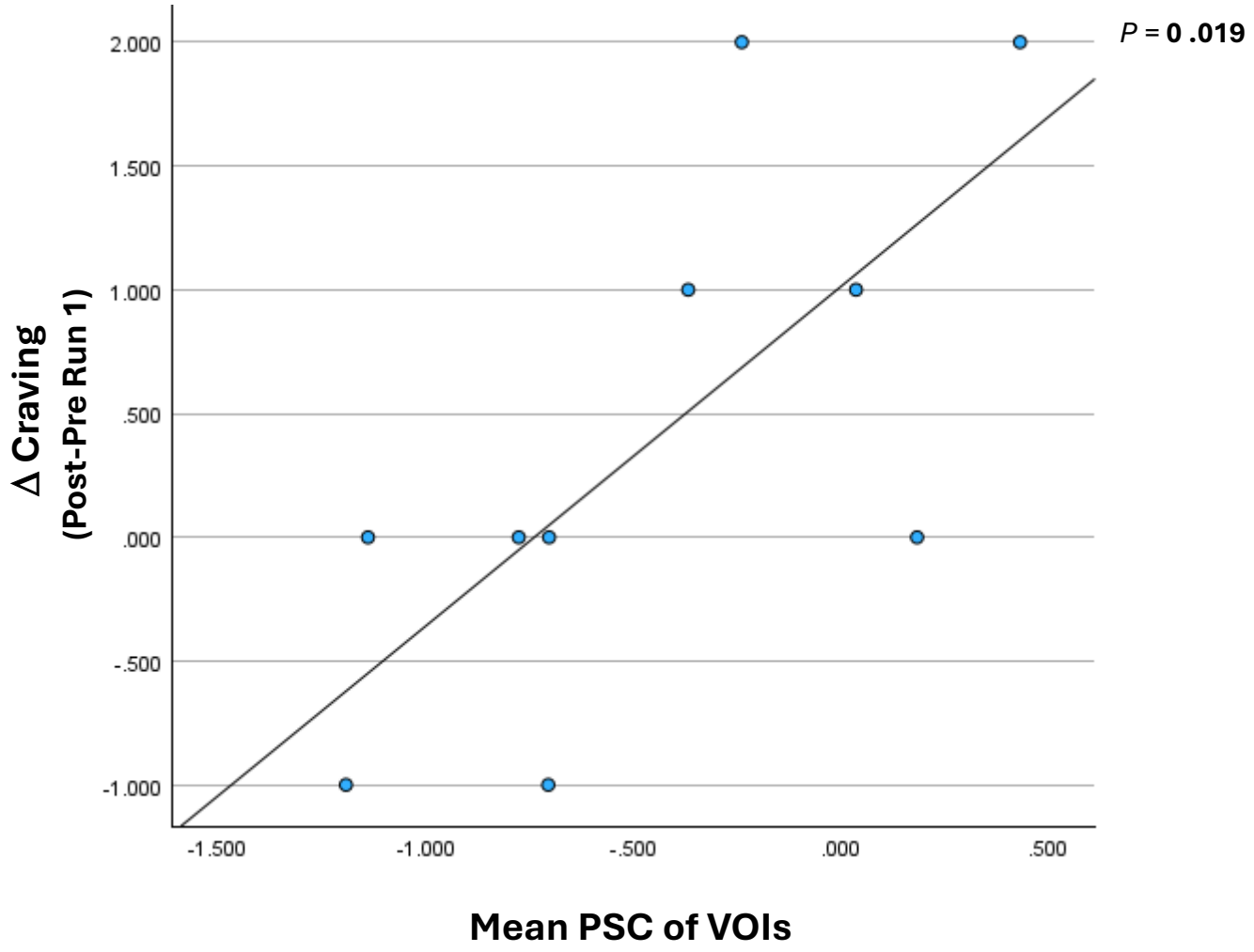


Mean PSC of VOIs

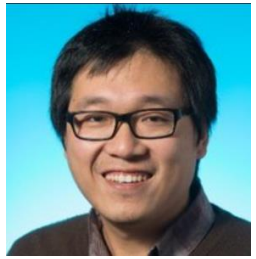





fMRI Cue-reactivity
NFB Run 1
NFB Run 2
Pre
Post
VAS Rating of Craving
10
8
6
4
2
0
Pre
Post
P = 0 .025
P = -0 .034
VAS Rating of Focus
10
8
6
4
2
0
Pre
Post
VAS Rating of Anxiety
10
8
6
4
2
0


P = 0 .019
2.000
1.500
1.000
.500
.000
-.500
-1.000
Δ Craving
(Post-Pre Run 1)
-1.500
-1.000
-.500
.000
.500
Mean PSC of VOIs

Prof. Valentina Lorenzetti
Australian Catholic University
University College London



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Saampras Ganesan
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Australian Catholic University

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Thank you!

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