# A setup for real-time fMRI Neurofeedback for Cannabis Craving: A Pilot Study

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## BACKGROUND

- Cannabis use disorder (CUD) is a common addiction characterized by hyperactive brain function during cue-induced craving fMRI tasks (1).
- A key region involved in cannabis craving is the anterior cingulate cortex (ACC).
- Real-time fMRI neurofeedback (NFB) is a novel technique that allows participants to receive immediate feedback from their brain function and consciously regulate it (2). NFB has been explored as an intervention for various psychopathology, including addiction (3).
- Preliminary work suggests that NFB during drug-induced craving can identify the craving neurocircuitry at the individual level and reduce abnormal brain activity in addiction to various substances (e.g., alcohol) and subjective craving (4). Yet, no study has tested NFB to change craving related brain function in CUD.

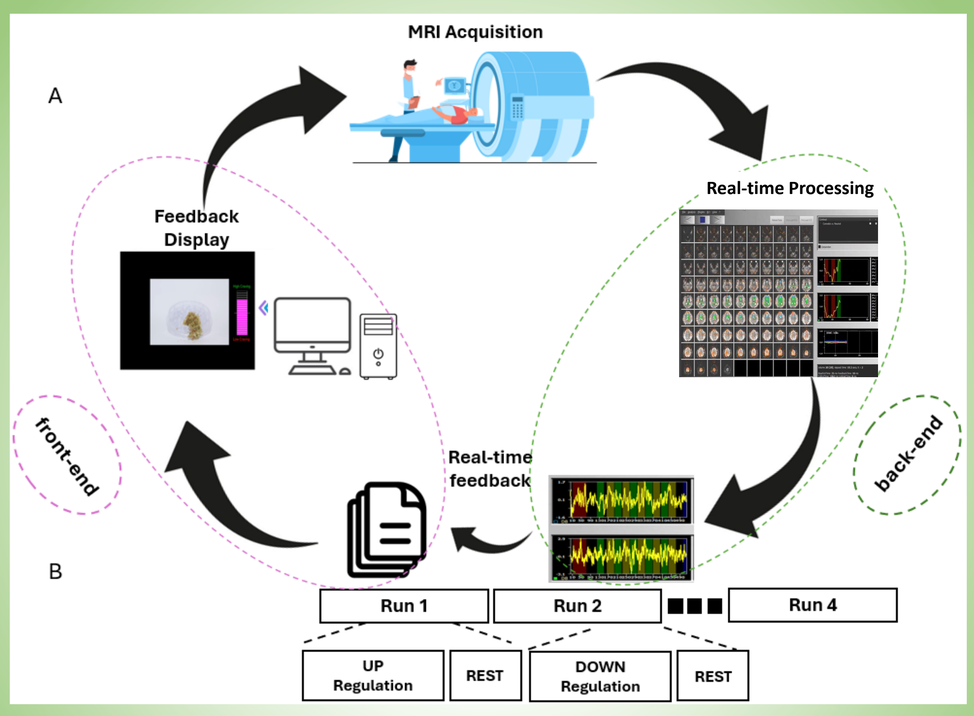


**Figure 1**: **The components of a fMRI-based NFB experiment.** (A) Image acquisition, real-time data reconstruction and processing, feedback calculation & presentation, (B) NFB task design including functional localizer (i.e., Baseline) run and subsequent regulation and control runs, with subjective in-between runs.

## AIMS

- To test the feasibility of a novel real-time fMRI NFB setup to regulate the activity of the ACC during cue-induced craving in CUD. To this end, a high-strength 7 Tesla scanner was used at the Melbourne Brain Centre Imaging Unit, The University of Melbourne.

## METHODS

- Multi-band fMRI data (TE= 22ms, TR= 1000ms, Voxel size = 1.6 x 1.6 x 1.6mm) is acquired and streamed to the data analysis workstation for real-time analysis using Turbo-BrainVoyager software version 4.2 (i.e., **back-end**).
- The target voxel of interest (VOI), which is the 33% most activated voxels located within the ROI (i.e., ACC, 5); was personalized based on a cue-induced craving fMRI task (i.e., functional localizer) to map the craving neurocircuitry individually.
- A confound VOI (red area, Figure 2), used to measure and account for nuisance physiological effects.
- To assess region specificity, the Percent Signal Change (PSC) from the personalized target region (ACC) for each regulation block within each run was used as a separate parametric regressor in a general linear model (GLM) analysis.

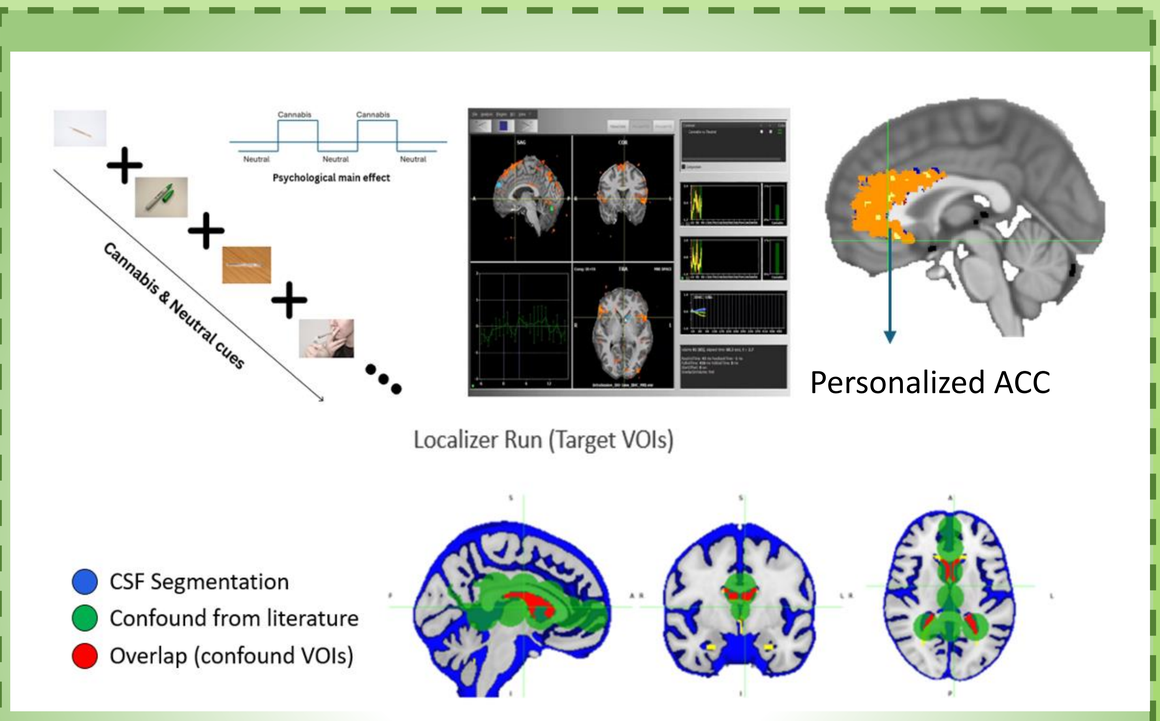


**Figure 2: Target ROI (yellow) and confound ROI (red).**
**Top:** (top left) shows a sample of the event-related cue-induced craving fMRI task presenting neutral and cannabis related cues; (top middle) the contrast cannabis > neutral; (top right) the most active voxels of the ACC (blue region) will be used as target VOI in the NFB experiment.
**Below:** The confound VOI was determined by overlapping CSF and white matter masks from the literature (6) and atlases, to regress out the physiological effects from the signal of the target VOI.

- The **front-end** refers to a NFB task script, developed using Psychtoolbox 3.0.19 in MATLAB 2023a, which runs on the STIM-PC, linking the task screen to the scanner display.
- This **front-end** concurrently presents: (i) cannabis-related cues to induce craving, (ii) 1-to-10 visual analogue scale (VAS) to rate subjective craving experienced in real-time, (iii) feedback calculation in real-time using GLM model with signal from the target & confound VOIs.
- Subsequently, the NFB feedback values representing change in brain function, will be converted to **brain computer interface** (craving bar in Figure 3) and will be presented to the participant as a thermometer that reflects BOLD signal changes, and will be updated every TR.

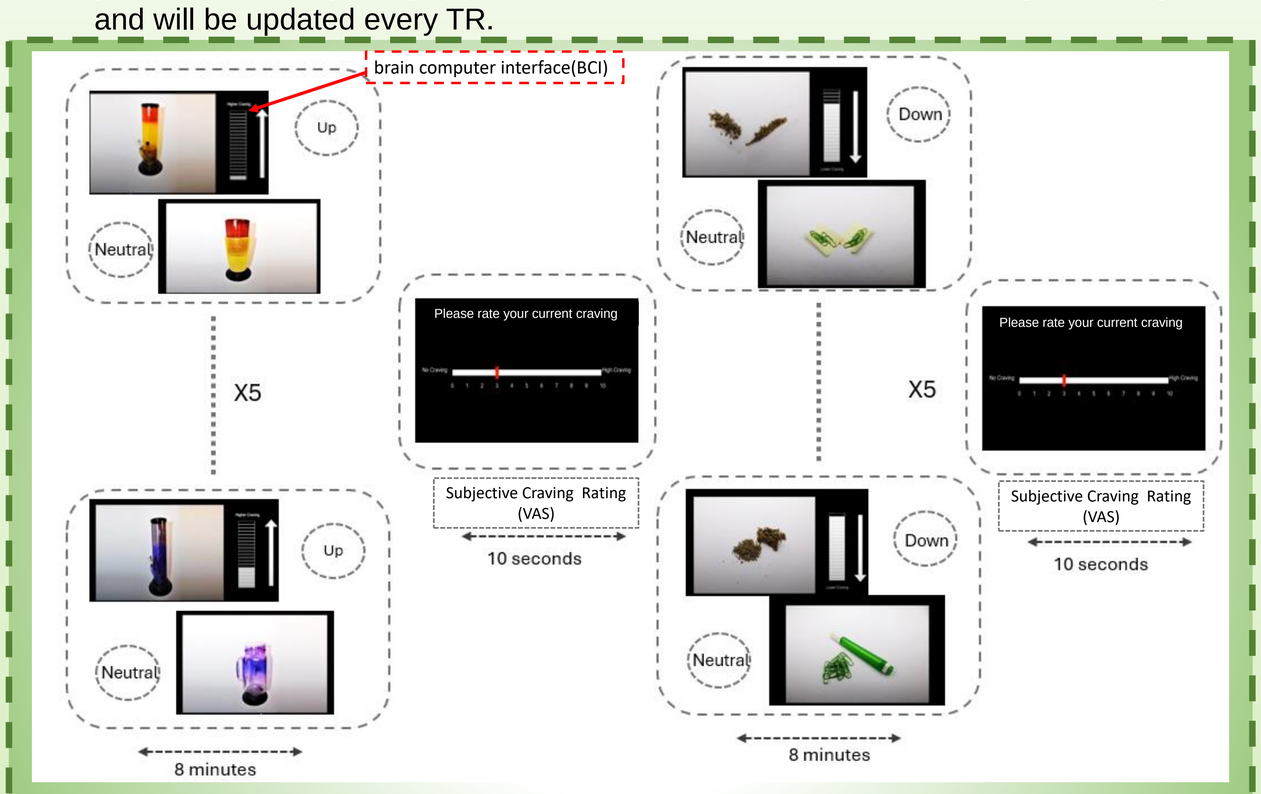


**Figure 3: NFB task presentation.** Participants were asked to focus on regulating their brain activity during craving during the NFB regulation blocks. During NFB regulation blocks, cannabis-related cues were presented to participants (left of screen) alongside a **thermometer**, which shows the level of the participant' craving-related brain function (right of screen).
After each NFB regulation block, a neutral block including neutral images matched in content with the cannabis images of the previous NFB regulation block was presented

## RESULTS

- This pilot study (N=7) validated the technical setup and quality control of our real-time fMRI neurofeedback paradigm.
- Parametric modulation analysis, using individualized ACC PSC as the regressor, revealed significant positive mean beta coefficient within the target ACC (Figure 4).
- For the craving up-regulation runs, Run 1 showed a noisier and less consistent positive beta coefficient with the ACC PSC. This signal significantly improved by Run 3, reflected in a substantially higher positive mean beta coefficient in the individualized ACC.
- Similarly, for down-regulation runs, Run 2 exhibited a lower positive beta in the ACC. This increased by Run 4, demonstrating a stronger, more consistent linear relationship with the ACC PSC.

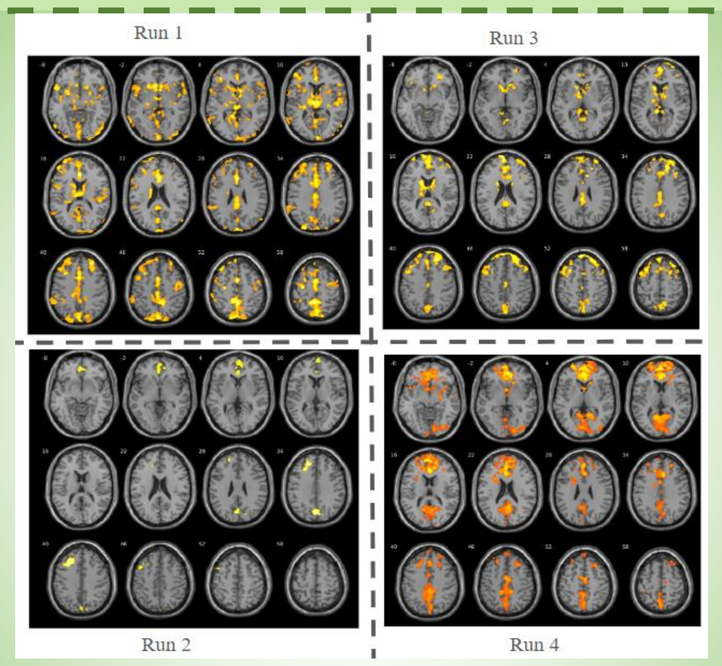


**Figure 4: Parametric Modulation Analysis Map**
ACC mean beta values increased across runs, with improved up-regulation by Run 3 and stronger down-regulation by Run 4.

## CONCLUSIONS

- This technical setup and quality control of seven pilot sessions, was successful in providing a region-specific feedback. This innovative setup may advance NFB as a tool for regulating craving-related brain activity in addiction and support the development of personalized interventions for addiction.

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