Biological Affect Modulation (BAM) Lab
University of Pittsburgh School of Medicine

Amygdala Neurofeedback Treatment and Protocol Manual

Background and Purpose

Rationale and Motivation

This manual describes the implementation and design decisions associated with the BAM lab neurofeedback protocol for amygdala neurofeedback. The rationale is that reduced amygdala activity to positive stimuli (including positive autobiographical memories) is a potential causal mechanism underlying major depressive disorder (MDD). Using fMRI neurofeedback is one way to change activity in this region so that activity in this region can be normalized which may lead to improvements in depressive symptoms.

Basic Protocol, Design decisions, and Availability

The basic protocol involves using neurofeedback to change amygdala reactivity to positive autobiographical memories. To maximize implementability and disseminability, we use off-the-shelf neurofeedback software, standard processing, and tasks, consistent with those in the literature, written in Matlab, which can be compiled and executed for free by any team. We are making the software, regions, and this protocol, available with the request that we (Young and Siegle) be authors on publications using it.

Protocol Implementation

Neurofeedback Software Platform

We use the commercially available software Turbo Brain-Voyager (Brain Innovation, the Netherlands) to provide rtfMRI-nf. This platform provides the functionality that as functional images are downloaded off the scanner, they are submitted immediately to statistical processing (smoothing using a 6mm kernel and motion correction), the result of which is displayed to participants in the form of a thermometer.

Task Description

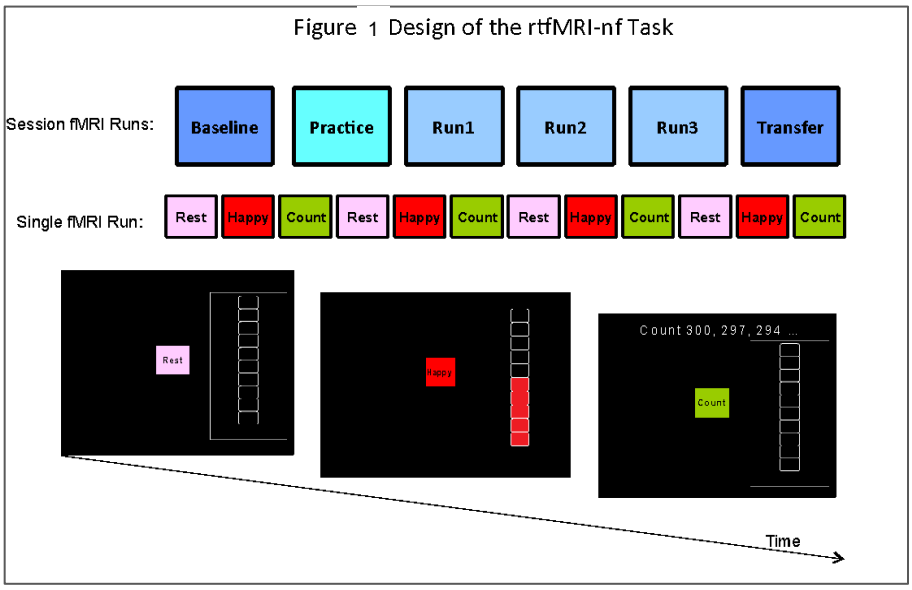
Composition

The neurofeedback task is the same every day it is presented. The rtfMRI-nf procedure consists of five fMRI runs each lasting 8 minutes and 40 seconds: a baseline run in which no neurofeedback information is provided, three training runs, and a final transfer run in which no neurofeedback information is provided. The Baseline run serves as a measure of amygdala ROI activity prior to rtfMRI-nf training and is used to determine neurofeedback success, defined as the difference between the initial baseline run and final transfer run. Participants are instructed simply to recall positive autobiographical memories. No feedback will be presented. During the subsequent three Training runs participants will be encouraged to use various positive autobiographical memories to increase the level of the thermometer. During the Transfer Run, participants will be instructed to perform the same task as during neurofeedback training, but rtfMRI-nf information will not be provided. The transfer run is performed to assess the transfer of the learned control and to check whether the training effect generalizes to situations where no neurofeedback is available.

Task Blocks and Participant Instructions

The task consists of 5 runs which, in turn, are composed of alternating 40sec blocks of Rest, Regulate, and Count conditions (see Figure 1). For each of the blocks within a run, cues are presented on the screen using both text and color icons to indicate each condition, as well as with a beep to indicate changing conditions.

Figure 1 Design of the rtfMRI-nf Task



The **Rest** condition is used to establish a baseline for the regulate neurofeedback block. During the Rest condition, participants are presented with the cue “Rest” and are asked to relax and breathe regularly while looking at the display screen. An empty thermometer is displayed.

The **Happy** condition is used for primary regulation of amygdala activity. During this Condition, the cue "Happy" and a thermometer is displayed on the screen. The thermometer represents the actual neurofeedback signal, which is updated continuously by changing the height of the bar either upwards or downward based on the corresponding level of BOLD activity. Participants are instructed to recall positive memories from their life while increasing the level of the thermometer. Participants are told to focus on the positive/rewarding aspects of their memory, how it affected them, and how it is related to who they are today. They are told they can use any positive memory and as many positive memories as they need in order to raise the level of the thermometer

During the Baseline runs participants are told simply to recall positive memories from their lives. During the Practice run, for the first three Happy blocks, participants are instructed to recall and contemplate AMs prepared pre-scan, and for the last block to use the one memory that they felt was most successful in regulating their brain activity. During the transfer runs they are told to use what they learned during training to recall positive memories from their lives.

The **Count** condition is used to return brain activity to baseline. Because the Regulate condition may induce rumination that could potentially not be stopped quickly, the count condition is necessary to distract participants' attention from ruminative thoughts and to allow ROI activity to return to baseline. During the Count condition, the participants are shown the cue "Count" with the specific instruction to count backwards from 300 by subtracting a specified integer (9, 3, 4, 6, 7 for Baseline, Run 1, Run 2, Run 3, and the Transfer run, respectively). An empty thermometer is displayed.

fMRI data acquisition parameters

We use a standard 64-channel receive-only head coil array for fMRI data collection. A single-shot gradient-recalled EPI sequence with GRAPPA acceleration (factor R=2) will be employed for fMRI. The following EPI imaging parameters will be used: field-of-view/slice=220/3mm, axial slices per volume=38, acquisition matrix=96x96, repetition/echo time=2010/27.8 ms, posterior to anterior phase encoding, flip angle=73°, sampling bandwidth=250 kHz, number of volumes=263. A T1-weighted magnetization-prepared rapid gradient-echo (MPRAGE) sequence with GRAPPA acceleration (factor R=2) is used to provide an anatomical reference for the fMRI analysis. It has the following parameters: field-of-view=240mm, axial slices per slab=128, slice thickness=1.2 mm, image matrix=256x256, repetition/echo time=5/1.9ms, flip angle=10°, delay/inversion time=1400/725 ms, sampling bandwidth=31.2 kHz.

fMRI region definitions

Method for amygdala region selection

Our primary neurofeedback target is the left amygdala region. This is defined as a 7 mm sphere centered at Talairach coordinates, -21, -5, -16. Figure 2 shows the resulting amygdala ROI template we use for the intervention. This template will be provided to researchers upon request.

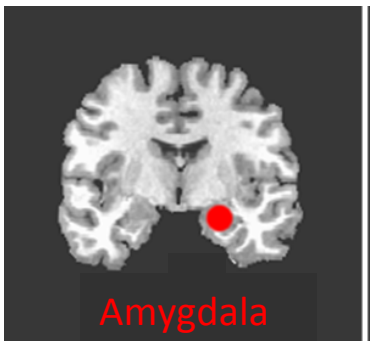


Figure 2: Left Amygdala Target Region

On-line analysis and calculation of feedback signal

On-line Analysis

We use the commercially available software Turbo Brain Voyager (Brain Innovation, the Netherlands) to provide rtfMRI-nf. As functional images are downloaded off the scanner, they are submitted immediately to statistical processing (smoothing using a 6mm kernel and motion correction), the result of which is displayed to participants in the form of a thermometer. Physiological noise correction is not used, as recent evidence suggests that correction for physiological noise does not affect the neurofeedback signal (Hellrung et al., 2019). The region-of-interest, defined as described above, is transformed to the EPI image space using each subject's high-resolution MPRAGE structural data. We perform a visual inspection of the region-of-interest prior to the start of neurofeedback.

Feedback Signal

The neurofeedback signal for each Regulate condition is computed as the fMRI percent signal change relative to the average fMRI signal for the preceding Rest block, updated every 2 seconds and displayed as a thermometer. To reduce bar fluctuations due to noise in the fMRI signal, the thermometer level is computed at every TR as a moving average of the current and two preceding values. These percent signal change values are averaged over each run and used as a performance measure. Neurofeedback success is defined as the mean percent signal change in the region-of-interest from the Baseline Run at Visit 2 to the final Transfer run. Higher scores indicate more activity following training relative to baseline and lower scores less activity following training relative to baseline.