A Rapid Whole-Brain Classifier for Real-Time Functional MRI Feedback

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Introduction: Advances in online image reconstruction and real-time processing of functional MRI data in recent years have opened new possibilities for providing patients with real-time information on their brain state as they participate in functional MRI experiments [1,2]. Recent studies have demonstrated that subjects can learn to control activity in localized regions of the brain through a series of training exercises in which they are instructed to try to periodically increase or decrease the level of a real-time feedback marker. Typically, the marker is designed to target a localized region of the brain. In a pioneering study of this type, deCharms et al. [3] demonstrated that real-time fMRI feedback from the pain-control region of anterior cingulate was effective in teaching both chronic pain patients and healthy subjects to control their pain. These studies offer hope for applying real-time fMRI feedback in other disorders where enhanced control over a brain state, e.g., increasing control of craving in addicted individuals, is the therapeutic goal. However, unlike the well-characterized "pain control" region of the anterior cingulate, the "craving control" circuits in addiction are just beginning to be characterized, and – adding to the challenge – may vary considerably across individuals. To address these challenges, we have pursued the use of whole-brain classifiers (i.e. classifiers computed on the basis of activity throughout the entire brain).

In this study, we have implemented software to provide cocaine-addicted patients with real-time information on their brain state(s) occurring during cue-induced cocaine craving vs. a neutral comparison condition (e.g., watching a non-drug video). As a prelude to the formal training experiment, the software was tested retrospectively on data acquired from a group of MRI-eligible treatment-seeking cocaine patients during their stay in a residential treatment facility.

Methods: All imaging was performed on a 3T Siemens scanner (Siemens, Erlangen, Germany) using a T2*-weighted Blood Oxygen-Level-Dependent (BOLD) imaging sequence (single shot EPI), with the following imaging parameters: 3x3 mm^2 in-plane resolution; 3.4 mm slice thickness; 33 slices; 192x192 mm^2 field of view; TE = 30 ms; TR = 2 s; total scan time = 16 minutes.
fMRI tasks: Subjects (n=5, ongoing) were shown a series of 30 second videos (each preceded by 10 seconds of instructions) alternating between videos containing cocaine-related content (simulated buying, selling and smoking of "crack" cocaine), and neutral (non-drug) videos. Each 80 second interval was considered a *task cycle* (comprising a neutral video and a cocaine video).
Real-time software: By using BOLD data acquired during the first few task cycles of the session, the software computes a linear classifier on the basis of voxels throughout the brain, and then begins feeding back a visual representation of the whole-brain state (cursor moving along a color bar, directly underneath the video) to the patient in real time. As additional data is acquired, the classifier is continually re-optimized. The classifier is computed using partial least-squares (PLS) regression [4], in which each image voxel is considered a predictor variable and the dependent variable is defined as +1 for cocaine-video frames and -1 for all other frames. In order to minimize BOLD drift and other confounding effects, the mean signal intensity at each voxel is subtracted out over each task cycle.
Data analysis: As mentioned above, the software was tested retrospectively on data collected from a group of cocaine addicts. The data were analyzed using two modes: *retrospective* and *prospective*. In *retrospective* mode, cycles were excluded one at a time, and the remaining data were used to compute the classifier, which was then used to predict the level of craving throughout the excluded cycle. In *prospective* mode, the analysis was the same, except that only previously acquired cycles were used to predict the data of a given cycle.

Results: Fig. 1 shows the results of the retrospective analysis for one of the five subject datasets analyzed. In retrospective mode, the classifier was able to distinguish between the neutral and craving states in almost every cycle (for all 5 subjects). In prospective mode, the classifier began to closely match the retrospective data after around five minutes of training (or around three task cycles). Computation of the real-time classifier took less than one second on a standard workstation (Intel Core 2 Duo CPU 2.53GHz) for 480 frames and 22,000 voxels.

Conclusion: These initial data demonstrate that a whole-brain classifier based on PLS regression can rapidly distinguish between the brain states associated with viewing a cocaine video vs. a neutral (non-drug) video, and that relevant visual feedback based on this distinction can be fed back to the patient in near real-time (1-2 sec lag). Rapid and accurate classification was evidenced for each cocaine patient's dataset, with minor variation in the time needed to train the classifier. This technical success sets the stage for clinical application in the target population, where the classifier and feedback will be focused on successful inhibition of cocaine craving.

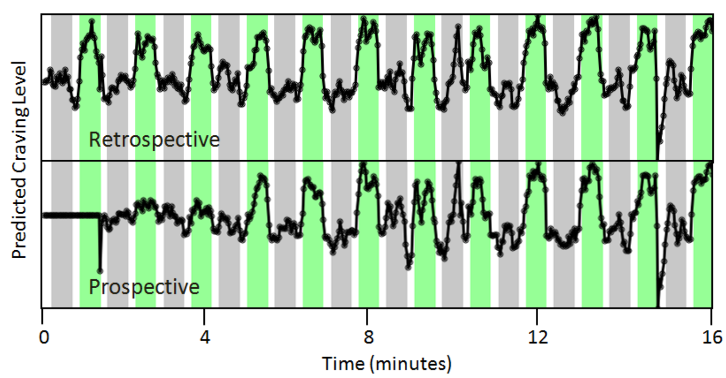

Fig. 1. Whole-brain real-time craving classification for a single cocaine patient, analyzed retrospectively and prospectively. Green and gray regions represent cocaine and neutral videos respectively. The prospective data begin to match the retrospective after around 5 minutes of training.

References: [1] deCharms et al, Trends Cogn Sci. 11(11):473-81 (2007); [2] Posse et al, Neuroimage 18(3):760-8 (2003); [3] deCharms et al, PNAS 102(51):18626-31 (2005); [4] McIntosh et al, Neuroim age 3(3 Pt 1):143-57 (1996).
Acknowledgement: NIH: NIDA R21/R33-DA026114, NIBIB K25 EB007646.