Predicting Affective Cognitions in the Resting Adult Brain

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Abstract:

Patterns of estimated neural activity derived from resting state functional magnetic resonance imaging (rs-fMRI) have been shown to predict a wide range of cognitive and behavioral outcomes in both normative and clinical populations. Yet, without links to established cognitive processes, the functional brain states associated with the resting brain will remain unexplained, and potentially confounded, markers of individual differences. In this work we demonstrate the application of multivoxel pattern classifiers (MVPCs) to predict the valence and arousal properties of spontaneous affect processing in the task-non-engaged resting state. rs-fMRI data were acquired from subjects that were held out from a subject set that underwent image-based affect induction concurrent with fMRI to train the MVPCs. We also validated these affective predictions against a well-established, independent measure of autonomic arousal, skin conductance response. These findings suggest a new neuroimaging methodology for resting state analysis in which models, trained on cognition-specific task-based fMRI acquired from well-matched cohorts, capably predict hidden cognitive processes operating within the resting brain.

Keywords: resting state; emotion; fMRI; MVPA; SCR

Introduction

Measures of resting state fMRI (rs-fMRI) brain activations have been shown to predict diverse cognitive and behavioral outcomes in both normative and clinical populations (Lee et al., 2013). While predictive, rs-fMRI measures often lack theoretical mechanistic explanations of why and how variation in resting brain function explains individual and group variation. Due to a lack of "ground truth" as to the identity of the spontaneous cognitions underlying the temporal fluctuations of resting state neural activations, rs-fMRI is largely characterized by its functional or effective connectivities. In this work, we consider an alternative exploration of resting state brain activations by applying highly accurate, reproducible, and physiologically validated whole-brain multivariate pattern classification models (MVPCs) of the valence and arousal properties of dimensional emotion (Bush et al., 2017; Bush et al., 2018a; Bush et al., 2018b) to label a specific cognitive process (affect) as it spontaneously evolves through time. We show that emotion labeling of rs-fMRI data can be accomplished on out-of-sample datasets and that the neural pattern classifier prediction of at least one affective property, arousal, significantly agrees with the temporal course of an independent measurement of autonomic arousal captured via skin conductance response (SCR).

Methods

Overview: We conducted analyses of data acquired from two separate fMRI studies that shared a common design structure up to and including the resting state "task" of the neuroimaging session. All study procedures were conducted in the Brain Imaging Research Center (BIRC) at the University of Arkansas for Medical Sciences (UAMS). All subjects provided written informed consent and all procedures were conducted with approval and oversight by the UAMS Institutional Review Board. Study participation involved two sessions on separate days. Session 1 included obtaining written informed consent, determining if subjects met clinical exclusionary criteria via structured clinical interview (SCID-I/NP), and administering behavioral surveys and questionnaires. Session 2 included the neuroimaging session, lasting approximately 1 hour and comprised of three sequential task conditions: Emotion Identification, Resting State, and Intrinsic Neuromodulation. This data analysis focused on the Emotion Identification and Resting State Task conditions.

Subjects: The participant sample (n=38) used for this analysis had the following demographic characteristics: age [mean(s.d.)]: 32.1(13.6), range 18–63; sex: 22 (57.9%) female; race/ethnicity: 31 (81.6%) self-reporting as White or Caucasian, 6 (15.8%) as Black or African-American, 1 (2.6%) as Hispanic or Latino; education [mean(s.d.)]: 16.5 (2.6) years, range 12–23; IQ [mean(s.d.)]: 106.1(14.3), range 74–137. All subjects were right-handed, native-born United States citizens (to comport with the

affective stimulus normative scores), medically healthy, with no current psychopathology, no current usage of psychotropic medication, and produced a negative urine screen for drugs of abuse immediately prior to the MRI scan. Additionally, subjects' vision was corrected to 20/20 during the MRI scan and color-blindness was exclusionary.

MR and SCR Acquisition and Preprocessing: Imaging data was acquired using a Philips 3T Achieva X-series MRI scanner (TR=2s). We recorded psychophysiological response measures using a BIOPAC MP150 Data Acquisition System using the AcqKnowledge software platform for simultaneous recording of skin conductance via the EDA100C-MRI module (sampling frequency was 2000 Hz). fMRI signals were preprocessed to remove noise and motion artifacts and segmented to remove all voxels except gray matter (GM) according to the methods in Bush et al. (2017); 2) SCR signals were preprocessed to remove noise and tonic signal components as described in Bush et al. (2018b).

Emotion Perception Modeling

Emotion Identification Task: Ninety image stimuli were selected from the International Affective Picture System (IAPS) such that the image subset represented the full range of the continuously-valued component properties, valence (V) and arousal (A), as described in Bush et al. (2018a). Concurrently with fMRI and SCR acquisition, the images were passively viewed for 2 s interleaved with random inter-trial intervals [2–6] s. The total task time covered two scans, each 9.25 min. in duration.

Brain and Psychophysiological State Estimation: For each IAPS stimulus, neural activation patterns and skin conductance response patterns were extracted via the beta-series method (Rissman et al., 2004) using either the canonical hemodynamic response function (BOLD beta-series) or the canonical skin conductance response function (SCR beta-series) (Bach et al., 2009).

Classification of Affective Signals: The individual patterns of affective image related neural activation, each matched to the normed labels of the stimulus from which they were derived, were used to conduct intra-subject leave-one-out-cross-validated (LOOCV) linear support vector machine (SVM) classification (Vapnik, 1995). Separate intra-subject valence, $\boldsymbol{\beta}^{V}(i)$, and arousal, $\boldsymbol{\beta}^{A}(i)$, models were fit for each subject i, as described in Bush et al. (2018a).

Resting State Emotion Prediction

Resting State Task: Subjects were instructed to stare at a central fixation cross and allow their minds to freely wander while fMRI and SCR data were concurrently recorded. The task duration was 7.5 min (225 volumes).

Brain and Psychophysiological State Estimation: In the resting state, neural activations and SCR response patterns were extracted according to the following algorithm. We defined a set of theoretical "self-task" stimuli that occur at 2 s intervals on the range of 12–430 s (210 unique stimuli). For 30 independent iterations we: 1) uniformly randomly sampled 100 self-task stimulus times, and 2) extracted the neural and SCR activation patterns according to the beta-series method. Over the course of the iterations, all neural activations extracted for the same stimulus time were separately predicted (see below).

The purpose of this iterative process is to simultaneously estimate the neural and physiological state over the entire resting state task while allowing each general linear model (GLM) to be sufficiently constrained; we also sought to capture variance arising from correlations between the sampled beta-series regressors.

Emotion Prediction of Resting Brain States: We then applied the learned emotion models, $\boldsymbol{\beta}^{V}(i)$ and $\boldsymbol{\beta}^{A}(i)$, of each subject to each brain state extracted from the resting state task, yielding predictions V(i,j,k) and A(i,j,k), which are the valence and arousal estimates of state j predicted by the respective models of subject i for the k^{th} sampling of state j ($k \leq 30$). Predictions are averaged over k for each subject, i. Distributions of affect are computed over all subjects, i, for each state, j. An example prediction outcome for a single subject is depicted in Figure 1 (panel A).

Experiments

Cross-Validation of Valence and Arousal Predictions: The purpose of this test is to validate the accuracy of group-level emotion predictions to hold-out rs-fMRI data. In this test, we use the mean valence and arousal predictions of n=37 subjects models applied to one hold-out subject's rs-fMRI. We then measure the Pearson's correlation (R) of these predictions of emotion to the hold-out predictions of this rs-fMRI made by the subject's own models, i.e. R_V and R_A. We repeated this process for each of the 38 subjects.

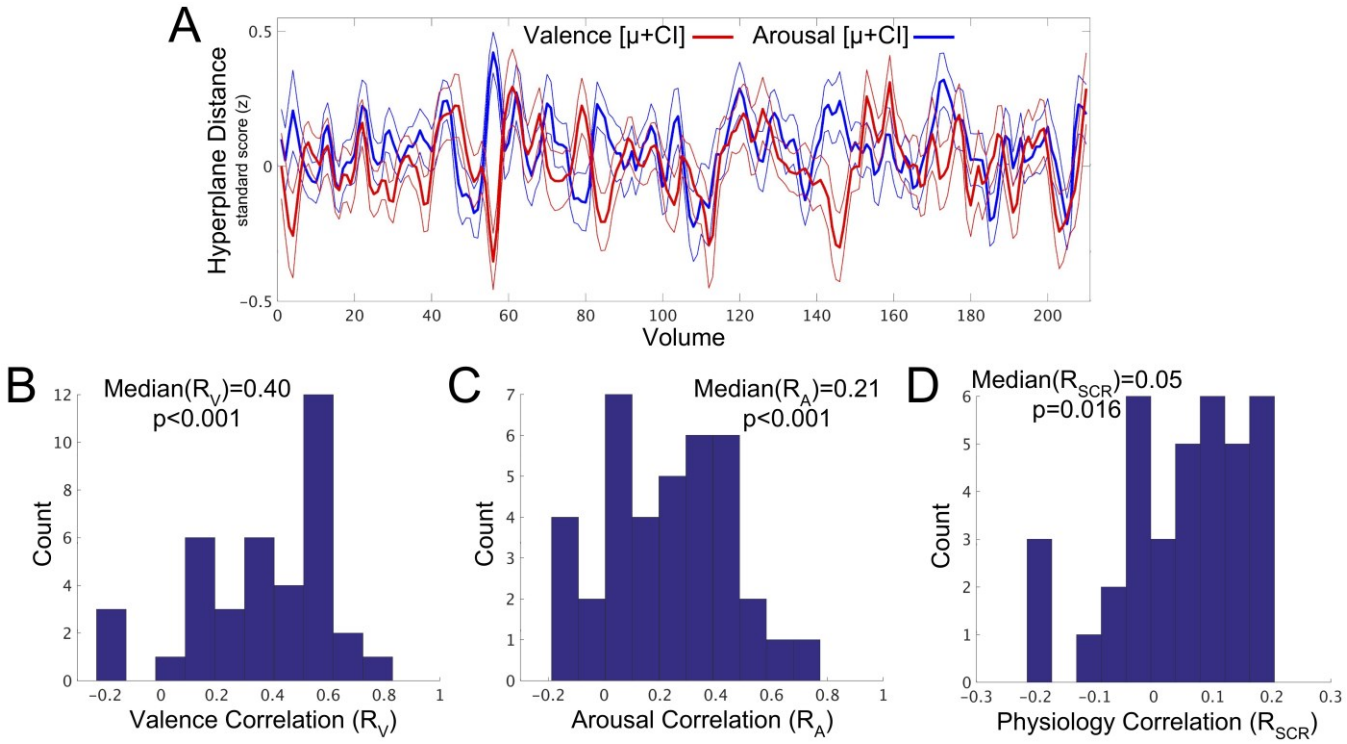

Figure 1. **Example prediction outcome and summary of experimental results.** (A) Example predicted emotion trajectories for a single subject's rs-fMRI. Thick line denotes mean group prediction, μ, and thin lines denote the 95% confidence interval of the mean, CI. (B) Distribution of LOOCV correlations, R_V, between group and hold-out subject predictions of valence, and (C) arousal, R_A. (D) Distribution of LOOCV correlations, R_{SCR}, between group predictions of arousal and hold-out subject autonomic arousal, measured as skin conductance response. Correlations are reported as Pearson's R.

Physiological Validation of Predicted Arousal: The purpose of this test is to validate the MVPA predictions of affective arousal against a well-validated independent measure of physiological arousal, the skin conductance response (Bach et al., 2010). In this test, we use the mean arousal predictions of n=37 subjects' models applied to one hold-out subject's rs-fMRI. We then measured the Pearson's correlation of these predictions against the subject's true physiological state estimates, R_{scr}. We repeated this process for each of the 38 subjects.

Results

Our experimental results are summarized in Figure 1 (panels B–D). We found that our group-level prediction of emotion perception was highly significant using non-parametric testing of the cross-validated correlation result. Median correlation of valence group predictions to hold-out subject predictions (see Fig. 1, panel B) was R_V=0.40 ($p<0.001$, signrank test, null: median(R_V)=0). Median correlation of arousal group predictions to the hold-out subject predictions (see Fig. 1, panel C) was R_A=0.21 ($p<0.001$, signrank test, null: median(R_A)=0). These findings suggest that indeed, pre-built emotion models can effectively estimate the emotion fluctuations in an out-of-sample rs-fMRI signal.

We also found that our group prediction of emotional arousal was significantly correlated with SCR (see Fig. 1, panel D), an independent measurement of autonomic arousal, R_{SCR}=0.05 ($p=0.016$, signrank test, null: median(R_{SCR})=0). This finding suggests that, in agreement with numerous validations of our emotion perception models, resting state MVPA-based emotion state prediction is convergently valid across multiple measurements of affect processing.

Discussion

We have demonstrated that accurate emotion state prediction can be extracted from rs-fMRI data of subjects for which we do not have a subject-fitted prediction model. We have also validated these predictions against a well-established measure of emotion-related arousal. Our technique paves the way for defining the functional structure of the human brain at rest (potentially for any cognitive process for which

MVPC-based models may be constructed and independently validated via concurrent physiological measurement). This approach is particularly relevant to large, openly available datasets for which rs-fMRI data exist. Within these datasets, we foresee highly powered studies of functional brain structure in the absence of task labels to explore the population-level clinical, developmental, and environmental determinants of brain organization.

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