Decoding of phobic content with multivoxel pattern analysis in patiens with spider phobia

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Introduction: Specific phobias have the highest prevalence of the anxiety disorders,[1] and spider phobia is one of the most common forms.[2] Phobic related brain regions have been investigated in fMRI studies that demonstrated that phobics exhibited greater haemodynamic response to spider images in the insula, anterior cingulate gyrus (ACC), and left dorsomedial prefrontal cortex. However, studies that implemented advanced analysis techniques such as multivoxel pattern analysis (MVPA) to study decoding accuracies in brain areas related of phobic content are sparse. Thus, the present study implemented MVPA to find sensitive brain areas predicting phobic content.

Methods: Data of nine patients with spider phobia in an event-related fMRI experiment were analyzed (seven female, one male; mean age 23.6±3.8 years). We had to exclude nine participants from the analysis (two did not complete the experiment, seven exhibited head movements larger than one degree of translation or rotation). Diagnosis of spider phobia was made according to DSM-IV, using a computer-based structured clinical interview (DIA-X), which is based on the Composite International Diagnostic Interview (CIDI). Exclusion criteria were neurological diseases, psychiatric conditions other than spider phobia, and psychoactive medication. The study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the ethics committee (Bern, Switzerland; No. 161/07). During the event-related experiment, participants looked at 80 randomized pictures (International Affective Picture System, ISAP) of four categories (20 trials each): spiders (phobic), animals (non-phobic, positive), averse, and neutral pictures (objects). The presentation time was five seconds with interstimulus intervals (ISI) between 10.1-13.7s. Data were acquired with a 3T Siemens Magnetom Trio, using an interleaved EPI sequence (579 volumes, 37 slices, 3.6 x 3.6 x 3 mm^3, gap thickness 0 mm, matrix size 64 x 64, FOV 230 x 230 mm^2, TR/TE 2500ms/30ms. Prepocessing was performed in SPM8 and included slice-time correction, realignment, coregistration to anatomy, and normalization; no smoothing was applied. For each trial, we run a GLM including a regressor coding the single trial and another regressor coding all remaining trials.[3] We also included six movement parameter regressors and their first derivative into the model. The resulting beta estimate maps of the individual trials were subjected to a MVPA using the searchlight approach,[4] and a Gaussian Naive Bayes classifier with leave-one-sample-out cross-validation (Searchmight Toolbox).[5] The classifier was trained to classify phobic spider pictures (20 examples) vs. the other picture categories (60 examples). For each subject, the classification accuracy map was shifted by -0.5 for the subsequent statistical testing against a mean of zero, and spatially smoothed (8 mm FWHM). We tested the null hypothesis of chance level accuracy across the subjects (non-parametric t-test; SnPM13). Using the FWE corrected t-maps (voxel-level) we extracted classification accuracies of five clusters from the peak voxel and subjected these to binomial tests.

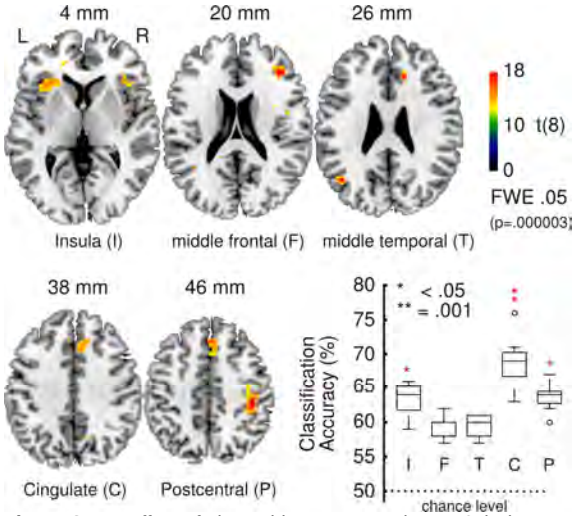

Fig. 1: Group effect of nine subjects. t-Maps (FWR .05) show consistent positive accuracies in five brain regions: insula, middle frontal, middle temporal, cingulate, and postcentral gyrus. Cingulate gyrus has the highest classification accuracy for the phobic images.

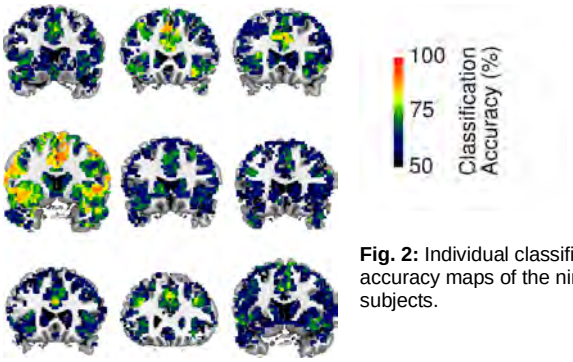

Fig. 2: Individual classifier accuracy maps of the nine subjects.

Results: We found significant positive classification accuracy across subjects in five regions (Fig. 1). Three regions passed above chance (> 0.63, binomial test) categorization accuracies (Fig. 1). A region in the middle cingulate gyrus demonstrated the highest mean classification accuracy of 0.69 across subjects (p = .001, binomial test). Single subject accuracy maps demonstrate increased accuracies in the cingulate gyrus for most of the subjects (Fig. 2). We performed data simulation to investigate the effect of unbalanced designs (20/60 examples) and found increased accuracies in the true positive target area, but also increased accuracies outside of the target area (Fig. 3).

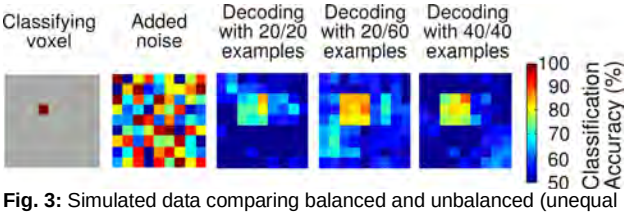

Fig. 3: Simulated data comparing balanced and unbalanced (unequal number of examples per category) training sets. Using a set of 20 phobic pictures and 60 other pictures (20/60) increases the accuracies at the region of interest (position 4,4), and adds noise to the surrounding area of non-interest.

Discussion: The present study showed that the cingulate gyrus can decode phobic vs. non-phobic content with an accuracy of 69%, the insula with 63%, respectively. The results are consistent with previous studies showing that the cingulate gyrus and the insula are key areas in the processing of phobic content. However, the significance of the postcentral gyrus (64%) is to some degree unexpected. A limitation of our approach is that unbalanced design can affect classification accuracies, also shown by our simulations, or that the classifier by coincidence classifies phobic/negative vs. animal/neutral images. Potential solutions to address these problems are to use permutation test for significance and to investigate per-class classification accuracies, or to randomly resample examples from the larger class in multiple balanced classification analyses. Thus, the present study shows that MVPA seems to be a sensitive approach to find brain areas predicting phobic content.

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