École Polytechnique Fédérale de Lausanne

Report

Neural signals and signal processing

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Mini Project 1

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1 Part 1

1.1 Practicals 1: Preprocessing

By inspection of the mean voxel intensities for each run, no high contrast was observed at the beginning of the runs with respect to the rest of the run. Thus, there were no problematic volumes to be removed.

Skull stripping: We applied skull stripping to both anatomical and functional images to remove non-brain tissue. This step helps improve the accuracy of subsequent analyses by focusing only on brain structures and reducing potential artifacts from surrounding tissues. Skull stripping on the functional was performed volume per volume.

Standardization and concatenation: To address the difference in voxel intensity ranges across runs and increase in voxel intensity within runs, we applied two-fold standardization. First, each run was standardized by subtracting the run's mean intensity and dividing by its standard deviation. Second, each volume within the run was standardized by subtracting its mean. This ensured that both the runs and individual volumes were centered around 0 and spanned a similar intensity range. Finally, the runs were concatenated in numerical order.

Motion correction: Motion correction was performed on the concatenation of all the runs using the MCFLIRT tool. This step helps to stabilize the position of the brain across volumes. To detect problematic motion, the Framewise Displacement (FD) between volumes was computed and plotted. FD exceeding the threshold of 0.3 mm was detected for volumes 105, and 210 in the concatenated data, corresponding to the transition between runs 1 and 2 and runs 2 and 3, respectively. These high FD volumes were dealt with by adding columns in the design matrix instead of eliminating them from the data. This way, there was no adjustment to apply to the duration of the events.

Smoothing: For the smoothing, a common rule is to use a Full width at half maximum (FWHM) value approximately 2 times the voxel size, this balances signal enhancement with spatial detail retention. The voxel size here is 2.9 x 2.9 x 3 mm^3. This gives us a FWHM of 5.8 mm. So we first tried with a FWHM of 6 mm. We wanted to preserve fine spatial detail so we decided to lower the FWHM to 4 mm. This moderate level of smoothing helps enhance signal-to-noise ratio without excessively blurring localized neural activations, allowing for more precise localization of activity in targeted regions.

Coregistration: We opted not to implement coregistration, as our analysis did not require perfect alignment. Visual inspection confirmed that the functional and anatomical images were already well-aligned, allowing us to streamline the preprocessing pipeline without compromising result quality.

1.2 Practicals 1: Experimental design matrix

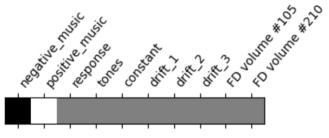

Figure 1: Contrast for testing positive against negative music

For the construction of the design matrix, the three .tsv files containing the event information for each run were first concatenated, similarly to the fMRI runs. Then the `nilearn.glm.first_level` tool was used to extract the regressors from the concatenated .tsv files. The regressors included initially are "negative music", "positive music", "response", "tones" and "constant". To improve our model, nuisance regressors of no-interest were added in the form of polynomial drifts of degree 3 to mitigate the effect of increase or decrease of signal throughout time. Two additional regressors were added to censor the frame displacement (FD) outliers: volumes 105 and 210. These columns are filled with 0 and 1 is only at the position of the FD outlier volume. The final design matrix obtained is shown in figure 2.

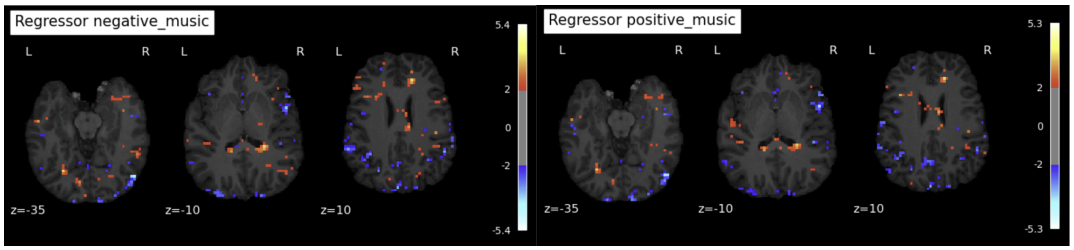

Figure 3: Statistical maps for regressors positive music and negative music

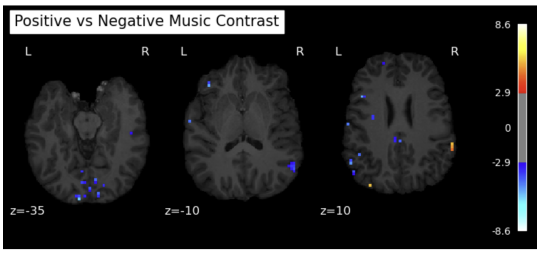

Figure 4: Statistical map for contrast positive against negative

1.3 Practicals 1: GLM

The model was fitted to the data using the defined design matrix, which allows us to estimate beta coefficients. From these estimates, we calculate z-scores for each voxel. Given that we are performing a mass univariate analysis, each voxel has its own z-score based on the null hypothesis being tested, defined by a contrast. Simple contrasts like [1,0,0,0,0,0,0,0,0,0] are used to extract the beta estimates for individual regressors. While the contrast used for comparing positive against negative music is shown in figure 1.

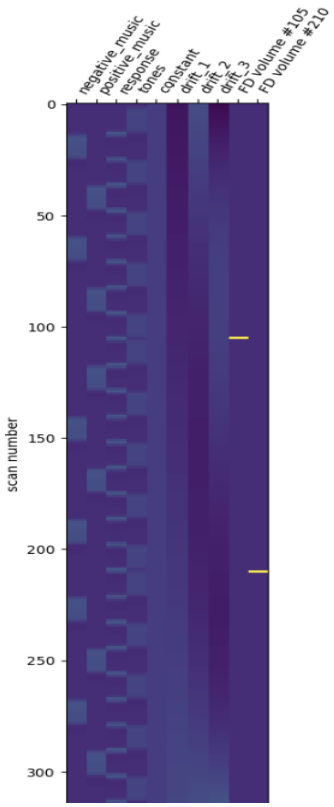

Figure 2: Design matrix of the GLM

Furthermore, we applied FDR (False Discovery Rate) correction to control false positives hence avoiding false detections to be taken into account. Setting the false positive rate to 0.1, which describes the ratio of accepted false positives among all positives, resulted in a reduced overall activation pattern, as expected. The general result differs from the one without FDR but the region of the voxel with maximum activation remained the same.

1.4 Practicals 1: Statistical Activation maps

Figure 3 shows the statistical maps for contrasts extracting the beta coefficients corresponding to the of interest regressors positive music and negative music. The statistical maps show z-scaled t-values calculated using a two-sided t-test. The activation is expressed with the values which are above the defined threshold in red, while the blue dots represent ”deactivated” voxels. The threshold used in these figures was arbitrarily picked at 2. We can see that for regressors positive and negative music there is activation in similar regions, like the auditory cortex and frontal cortex with slight differences.
Figure 4 is the statistical map where the z-scores are calculated based on the contrast shown in figure 1 for testing positive music against negative music. The plot uses a threshold of 2.92 which was calculated based on the FDR parameters described in the section above. Now we can interpret the red dots as the voxels where the difference between positive and negative music activation is the most prominent. The region with the maximal contrast is Precentral-L, with a maximum activation z-score of 1.7370. After applying FDR correction, the maximum contrast z-score is 0.4533, also observed in the region Precentral-L.

1.5 Theoreticals 1: Question 1

A second level analysis could be attempted on the provided dataset. This analysis would allow us to generalize findings about brain response to emotional stimuli across subjects, rather than limiting to individual responses. The dataset used in this project contains two groups of subjects, namely never depressed (ND), i.e. control subjects and major depressive disorder (MDD) subjects. Knowing this, the second level analysis could be setup to compare the contrast maps obtained for each subject at the end of the first level analysis between the two aformentioned types of subjects.

1.6 Theoreticals 1: Question 2

The model for this analysis could be a one-sample t-test on the MDD subjects, a one-sample t-test on the ND subjects or a two sample t-test comparing MDD to ND subjects. A one-sample t-test can be used to determine if the mean of these contrast images across subjects of the same group is significantly different from zero, which would indicate a consistent difference in brain activation between positive and negative music at the group level.Suppose that the first level analysis contrast maps compared positive music against negative music. If the second level design matrix is constructed using two regressors, the first one containing ones for the ND subjects and zeros for the MDD subjects, and the second regressor containing ones for the MDD subjects and zeros for the ND subjects. The contrast for one sample t-test would be either [1 0] or [0 1]. For two-sample t-test contrast vector to be used should be [1 -1]. The latter example would allow to answer the following experimental question: "is the difference in neural response to positive versus negative music between ND subjects and MDD subjects statistically significant?". Mathematically, the null hypothesis of the test performed could be written as $H_0 : \mu_1 = \mu_2$, with μ_1 being the average contrast map of ND subjects and μ_2 the average contrast map of MDD subjects.

2 Part 2

2.1 Practicals 2: K-means clustering

We applied temporal K-means clustering to the 315 volumes from the concatenated fMRI data, treating each volume as a sample and flattening it into a 1D array of voxel intensities. The volume at each timepoint was then assigned to a cluster based on its spatial activation pattern. The aim was to identify clusters that correspond to the brain's responses to different stimuli, such as positive and negative music, response times, tones, and any additional tasks, as well as default network activity and noise artifacts. Ideally, the clustering would reveal distinct patterns for positive and negative music.

2.2 Practicals 2: Cluster selection and centroids plotting

To determine the optimal cluster count, we used the elbow method and silhouette score. The elbow method identifies where adding clusters offers minimal variance reduction, while the silhouette score assesses how well data points fit within clusters (higher scores indicate better clustering).
Both methods initially suggested 2 clusters, but we aimed for finer granularity to represent each condition (positive music, negative music, tones, and response), considering some natural overlap.
After evaluating the results, we selected 8 clusters, which emerged as the fourth-best choice in the elbow method and showed a local peak in the silhouette score. This decision achieves a balanced compromise, capturing nuanced distinctions across conditions while ensuring that the analysis remains interpretable and meaningful.
The centroid of the most meaningful clusters are shown in Figure 5.

2.3 Theoreticals 2: Question 1

Based on the activity patterns observed across the 8 clusters we selected, we identified matches with several functional brain networks mentioned in (1). The results can be seen in Figure 5.
Cluster A aligns closely with the frontoparietal network, which is linked to cognitive processes and sustained attention, suggesting that the subject maintained focus throughout the task. Clusters E and F show

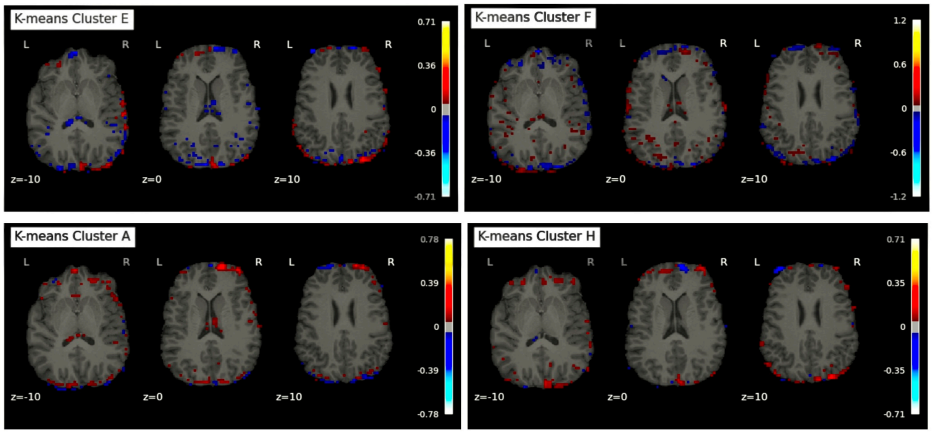

Figure 5: To focus on significant activations and reduce noise, we created these images applying a threshold of 0.05.

activation within the somatomotor and ventral attention networks. Notably, the ventral attention network, which is typically triggered by sudden environmental changes, is part of the brain's broader attention system. Given that these activations are located near the auditory cortex, it is plausible that one cluster reflects responses to positive music while the other corresponds to negative music. Cluster H exhibits activation in the visual network, which, like the frontoparietal network, shows consistent involvement across clusters, indicating its sustained engagement throughout the task.
So, we haven't found separated regions, but regions that are likely to work together during particular tasks. K-means clustering, in our approach, groups together timepoints with most similar activation based on euclidean distance. Therefore, it does not separate distinct anatomical regions but instead highlights areas that are functionally interconnected.
Additionally, due to the lack of further masking post-skull stripping, some activation appears in the cerebrospinal fluid (CSF). This motivated our choice of more than 4 clusters, as extra clusters could capture subtle, task-related distinctions across regions.

2.4 Theoreticals 2: Question 2

According to Pruim et al. (2015) (2) and Behzadi et al. (2007) (3), several factors help distinguish signal from noise: Noise clusters often align with areas like the ventricles, edges of the brain, or regions affected by motion artifacts, which typically do not correspond to recognized functional networks. Noise components often exhibit high-frequency fluctuations or are highly correlated with motion parameters.
Techniques like ICA-AROMA (by Pruim et al.) use spatial and temporal features to classify and remove motion-related components, while CompCor (by Behzadi et al.) uses principal components from noise regions like white matter and CSF for noise correction.

2.5 Theoreticals 2: Question 3

GLM analysis, corrected for FDR, identified the Precentral_L (part of the motor cortex) as having the voxel with the highest activation, this method isolates discrete, statistically significant voxels associated with specific conditions and contrasts. In contrast, MVPA identifies spatial patterns across clusters that correlate with known functional networks, providing a more comprehensive view of collective brain region responses and revealing distributed activity patterns that GLM alone might overlook. With our K-means clustering method we identified clusters of timepoints with similar activation but we don't have a precise relation to the task "negative vs. positive music". For this specific task, we believe that GLM is especially suitable, as it enables precise contrasts that can isolate distinct brain responses to each condition. Alternatively, applying k-means clustering exclusively to timepoints associated with positive and negative music events (while excluding tones and responses) could be valuable; however, this approach may require a follow-up comparison after clustering to effectively highlight the contrast between conditions.
Combining both approaches could yield more comprehensive results: GLM identifies prominent activation regions, while MVPA complements this by revealing broader network patterns, leveraging each method's strengths.

References

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