Mini project 1:

Neural Processing of Emotional Musical and Nonmusical Stimuli

Neural Signal and Signal Processing

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7th November 2024

1 Introduction

The project aims to study the neural processing of emotionally provocative auditory stimuli. We will conduct a single-subject analysis using Control Subject 1 from the public dataset openneuro. More specifically, we aim to assess differences in the processing of music based on its emotional content. The subject's brain activity was recorded while listening to successive blocks of positive and negative music, interleaved with pure tones.

This report is divided into two parts: a description of the combined pipeline and answers to theoretical questions. The pipeline includes preprocessing of the functional data and statistical analysis using a General Linear Model to identify significant differences in activation between positive and negative auditory stimuli. Finally, a dimensionality reduction (PCA) is conducted as a confirmatory analysis.

2 Practical Pipeline

2.1 Preprocessing

We will conduct the preprocessing of the functional data using the following steps:

1. Standardization: we normalized each of the runs to a consistent intensity scale for concatenation and comparison across the runs.
2. Concatenation: we combined all standardized runs into a single file to be used in further analyses.
3. Motion correction: this step corrects for head movements in the scanner. This first volume was used as a reference volume as in the article [1]. The frame-wise displacement (FD) was computed to check whether there was aberrant motion between successive TRs. A maximum FD of 1 mm was used as in the article so no volume was censored as they are all below 0.8 mm of displacement.
4. Spatial smoothing: we applied Gaussian smoothing with a 4 mm kernel to reduce high-frequency noise and improve the signal-to-noise ratio.

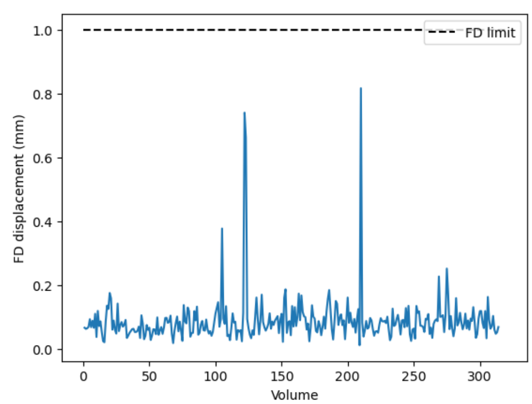


Figure 1: Frame-wise displacement between successive TRs

Signal artifacts were checked as part of quality control. DVARS was used as a metric to identify signal artifacts. Since DVARS remained fairly constant around 30 with no outliers, no censoring was applied based on signal artifacts. Additionally, no high-pass filter was applied, as most of the relevant frequencies were in the low-frequency range.

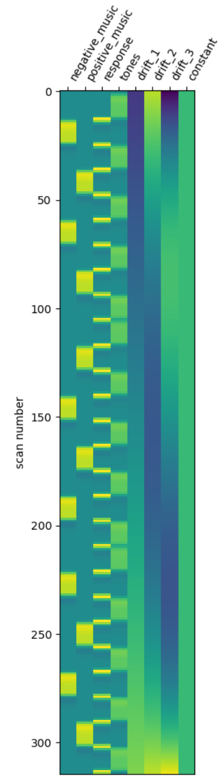
2.2 General Linear Model

The general linear model uses multiple linear regression to fit the fMRI data and explain the effects of different conditions or variables represented by the regressors. To build the model, we first need to download and define the experimental design. This information can be found in the event files associated with the fMRI data.

We have three runs of listening sessions, each followed by a response period. The type of sound the subject listens to in each session varies: it can be a pure tone, positive music, or negative music. To build our experimental matrix we concatenated the events from the three runs. The repetition time (TR) can be found in the JSON file for the experiment, where it is specified as 3 seconds.

We will create a regressor for each type of sound and add polynomial drift with three regressors, as the experiment duration is extended due to the number of sessions and runs. The drift regressors aim to capture signal variation due to gradual polynomial changes in the setup. Additionally, we include a regressor to capture signal variation during the response time, ensuring it does not interfere with the auditory and emotional signals.

We fit the GLM to the preprocessed data and define four contrasts (positive vs. pure tone, negative vs. pure tone, drifts, and positive vs. negative). The most important contrast is positive vs. negative music, which will help address the project question. We will then analyze the GLM output using statistical methods. We use the z-score threshold that defines the statistical significance of individual voxel activations (p-value¡ 0.001 for threshold set at 3) and explore the area activate 3. We can notice multiple areas of significative activation and if we look for the Anterior cingulate cortex as mentioned [1] we can find a small but significant activity. 5



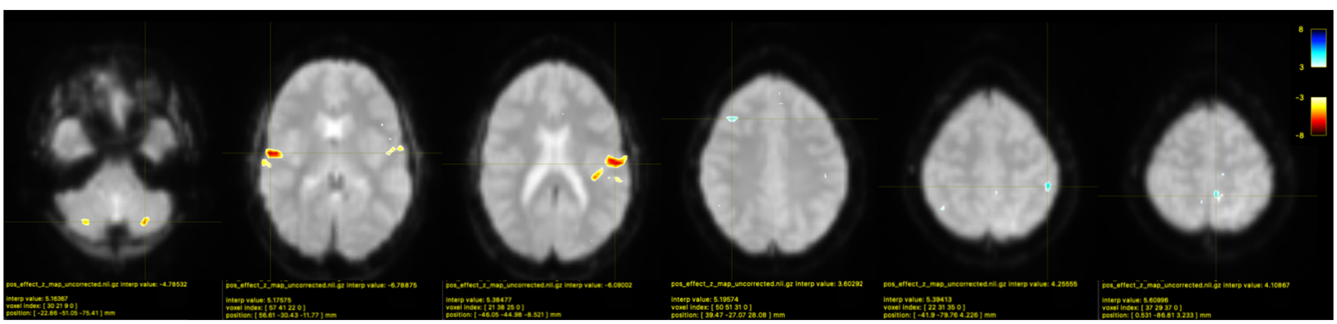


Figure 3: Stat map uncorrected by FDR positive vs. negative music activation, threshold = 3

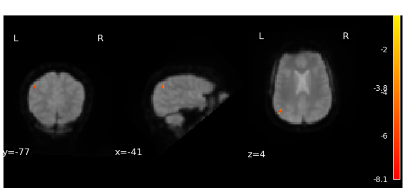


Figure 4: Positive vs Negative music contrast. *Stat map correct fdr = 0.05, cluster threshold = 10*

Due to the multiple statistical analyses conducted across each voxel, we need to apply a correction to our statistics. We chose to control the False Discovery Rate (FDR), which is an alternative to the often too strict Bonferroni correction for detecting changes in activity. The FDR rate represents the maximum proportion of false positives accepted among all significant results (e.g., the percentage of detected activations that may be false positives). We tried with FDR=0.01 but all the signals were removed so for visualization we set FDR=0.05 4. We use as well a cluster threshold that controls for the spatial extent of the activation, ensuring that observed results are not due to random noise. minimizing false positives but potentially missing weaker activations. The cluster threshold is set to 10 contiguous voxels, reflecting the assumption that genuine neural activity tends to activate multiple adjacent voxels, and balancing sensitivity and specificity while accounting for the potential influence of spatial autocorrelation. After this step only a cluster located at the post-parietal left cortex remains. 4 All along we used the visual comparison to the MNI T1 1mm template and its associated parcellation AAL3. [5]

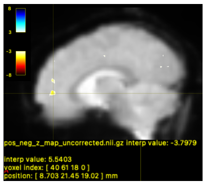


Figure 5: AAC activation on uncorrected z-map, Positive vs Negative music contrast.

We should have used registration to MNI space on our functional data or run a parcellation algorithm such as free surfer to be sure and more precise about the label assignments.

2.3 Principal component analysis

The entire fMRI signal can be viewed as a multivariate mixed signal that we aim to decompose into its dominant and most significant components to highlight those responsible for the majority of variations. Our focus is on spatial components, which capture the primary interactions between voxels. Principal Component Analysis (PCA) extracts these components by optimizing the covariance between voxel signals (Spatial PCA).

To apply PCA, we first normalize the data across space by subtracting the spatial mean. Then we reshape our data to feed the PCA (number samples, number features). The samples are the volumes and the features of all the voxels. To determine the number of components needed, we plot the explained variance and set the optimal number of components to 80. This ensures that at least 90 percents of the variance is explained

3 Questions and analysis

3.1 Can you do the second-level analysis on this dataset (all subjects)?

To advance to the second-level analysis, we first need to ensure that registration to the MNI template was performed during preprocessing. Registration to a common template space, such as MNI, is essential for comparing activity across subjects in comparable brain areas. Secondly, in terms of statistics, we can move from a single-subject GLM to a group-level analysis by comparing the beta coefficients of the regressors using standard statistical tests. The values tested in the t-test or ANOVA will represent estimates of activation levels rather than individual activation values. A second-level analysis thus enables us to generalize activation patterns beyond individual differences.

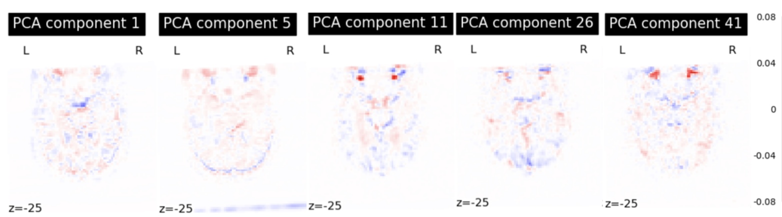


Figure 7: PCA results: examples of components

3.2 For this second-level analysis, what contrast could you consider, and to which experimental question does it answer?

For the second-level analysis, we could consider a contrast of [1 -1], comparing positive music vs. negative music. This allows us to identify areas that are more activated in one condition compared to the other, or areas with consistently different activation patterns across subjects that are not due to randomness. This helps answer the question of how emotional content influences the neural processing of auditory stimuli.

3.3 Do some components match with relevant functional brain networks?

PCA allows to decompose uncorrelated data, by linearly separating components and ranking them by explained variance. In this work, we apply PCA on spatial components, the voxels, to see if spatial networks can be linearly separated, in a task that is set to activate different spatial networks. In the original study [1], Anterior cingulate cortex (ACC) and the striatum are investigated. For control patients (like our study case), Ventral and subgenual regions were more activated for positive than for negative stimuli, and Rostral ACC was more activated for musical stimuli than for pure tone. For nonmusical task, the caudate region was more activated. The reference paper [2] highlighted different separations into functional networks of the brain, like a 7-areas parcellation. Networks can correspond to the following : Visual, Somatomotor, Dorsal Attention, Ventral Attention, Limbic or Frontoparietal network. We would expect our components to match with the attention networks (active listening) and the limbic network (emotions).

The resulting components do not seem to match with a relevant functional brain network. Further preprocessing steps could have helped, such as EPI-coregistration, ICA and high pass filter to remove artifact sources, low pass filter for drift or field map correction.

3.4 What about components that are NOT relevant networks (e.g. noise) ? How could one identify them (see bibliographical reference [3, 4]) ? [Bonus]

Networks that are not relevant can bring spatial variance to the results, so we expect some components to extract this noise. The PCA results showed identifiable unrelevant networks, and we could observe: slow drifts, strong magnetic field inhomogeneity and eyes artifacts.

To identify these components, in fMRI data, different component-based methods exist. CompCor Method [4] is a noise correction technique that identifies noise components by selecting regions of interest (ROIs) likely dominated by physiological noise, such as white matter and CSF. By performing PCA on these ROIs, CompCor isolates noise components, which can be added as nuisance regressors in a GLM to remove it. ICA-AROMA is a method designed to automatically identify and remove motion-related noise from fMRI data. ICA extracts components and uses a decision tree classifier to categorize them based on four key features associated with motion artifacts: high-frequency content, edge fraction, CSF fraction, and correlation with realignment parameters.

3.5 Compare the results obtained from GLM and PCA analysis method. Which method would you perform to figure out what regions of the brain are activated? When would you apply one and when would you apply the other?

The GLM approach outperformed PCA in highlighting activation differences between positive and negative music conditions. GLM successfully isolated relevant activity by using regressors that accounted for various noise sources, such as slow drift (captured by a polynomial regressor) and physiological artifacts (removed with high-pass filtering at a 0.01 cutoff frequency). Additionally, GLM's direct condition-based contrast analysis further helped eliminate irrelevant signals.

PCA, in contrast, mainly extracted mixed noise sources. This was partly due to an excessive number of components (80 instead of a more optimal 30, chosen to reach 90% explained variance), which did not allow to separate meaningful signals. However, PCA proved useful for evaluating data quality and guiding preprocessing improvements. Through PCA, we identified artifacts such as eye movements, drift, and physiological noise, which can be addressed in future preprocessing to improve component separation.

References

[1] Lepping, Rebecca J., Atchley, Ruth Ann, Chrysikou, Evangelia, Martin, Laura E., Clair, Alicia A., Ingram, Rick E., Simmons, W. Kyle, and Savage, Cary R. (2016). Neural Processing of Emotional Musical and Nonmusical Stimuli in Depression. *PLOS ONE*, 11(6): e0156859. `https://doi.org/10.1371/journal.pone.0156859`.

[2] The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of Neurophysiology*. Accessed: 2024-11-05. `https://journals.physiology.org/doi/full/10.1152/jn.00338.2011`.

[3] ICA-AROMA: A robust ICA-based strategy for removing motion artifacts from fMRI data. *ScienceDirect*. Accessed: 2024-11-05. https://www.sciencedirect.com/science/article/pii/S1053811915001822?via%3Dihub.

[4] A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. *ScienceDirect*. Accessed: 2024-11-05. https://www.sciencedirect.com/science/article/pii/S1053811907003837?via%3Dihub.

[5] https://www.gin.cnrs.fr/en/tools/aal/