CS 5970 - Team A Final Project Proposal

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1 Abstract

Many studies indicated that individuals with major depressive disorder MDD prefer to listen to sad music compared to those who don't suffer from MDD. As it is a condition that significantly impacts an individual's quality of life, it is imperative to understand how emotional auditory input affects their mood and its possibilities in alleviating symptoms of MDD. Our objective is to identify the regions of the brain that are activated given musical and non-musical stimuli in subjects with MDD and a never-depressed control group. Additionally, we aim to estimate the connection between those identified brain regions. T-contrast analysis was used to identify activation patterns in the fMRI images. A Functional Connectivity analysis was performed to determine the connectivity between regions of interest that could potentially be used as targets to treat MDD. The results showed that the Auditory Cortex (AC) was the most activated region in the brain. The region with the highest connectivity with that region was identified as the anterior cingulate cortex (ACC). Moreover, this connectivity between these two regions is lower in the MDD subjects than in the control subjects. In conclusion, the ACC is strongly stimulated when emotional auditory paradigms are applied and should be included in targeted auditory treatment for MDD.

2 Introduction

The Diagnostic and Statistical Manual of Mental Disorders describes depression, also known as major depressive disorder (MDD), as a severe mood disorder. MDD leads patients to experience constant negative feelings, sadness, and the loss of activities they once enjoyed [1]. Many studies indicated that individuals with MDD prefer to listen to sad music than those who don't suffer from MDD [3].

An article published by Yucel et al. indicates that the anterior cingulate cortex (ACC) is linked to the impairments in cognition and emotion exhibited in mood disorders. Patients with major depressive disorder have been observed to experience bilateral ACC volume decreases [2]. According to Rudebeck, the subgenual anterior cingulate cortex (ACC) is critical in regulating emotion [4]. Hence, it is a region of interest in exploring how stimuli affect subjects with MDD versus the control group.

The project aims to identify the regions of the brain that are activated given musical and non-musical stimuli in subjects with MDD and a never-depressed control group. Furthermore, the project intends to estimate the connection between the identified regions of the brain. We hypothesize that there should be a correlation between Auditory Cortex (AC) and ACC because the stimuli presented to the subjects are emotional. Our second hypothesis is that the connection between the AC and ACC regions should also be lower in the MDD subjects compared to the never-depressed (ND) subject, given Yucel's findings on the ACC of individuals with MDD.

3 Materials and Methods

3.1 Dataset

The dataset was obtained from OpenNeuro [5]. The data had a total of thirty-nine participants. The dataset had nineteen individuals with MDD and twenty never-depressed (ND) control participants. Participants in the MDD group were all experiencing a current depressive episode at the time of scanning. All the participants listened to positive and negative emotional musical and non-musical auditory stimuli during fMRI scanning [5]. The auditory stimuli were presented in a block manner in 33-second intervals, with pure tones (baseline) lasting for 33 seconds and positive and negative music for 33 seconds. The fMRI scanning was conducted on a 3 Tesla Siemens Skyra scanner with a repetition time of 3 seconds and an echo time of 0.025 seconds [5].

3.2 Data Preprocessing

Data was passed into the FMRIPREP pipeline in Python, where preprocessing performed included brain extraction, motion correction, susceptibility distortion correction, alignment to the T1 image, MNI152 transformation, and confound regression. The data was further cleaned using the confound-regressor obtained from FMRIPREP preprocessing.

3.3 T-Contrast Analysis

A threshold T-map produced by General Linear Model (GLM) gives a compelling summary of activation patterns in functional brain images [6]. A t-contrast brain map was created by constructing a general linear model (GLM) based on the onsets of the fMRI experiment and computing t-values for each voxel in the fMRI images. Once the t-values were computed for each voxel, the t-values were plotted onto the surface of a brain map with a threshold of 90 percent to identify the highly activated regions.

3.4 Functional Connectivity Analysis

After getting some ideas about regions where most activation occurred, more analysis can be done on a region of interest (ROI) using functional connectivity analysis. Based on the method provided by Jeyachandra, the data was parcellated into different brain regions based on the Yeo_2011 thick_7 atlas [7]. A relabeled atlas was created using the Yeo_2011 thick_7 atlas as a base, and spatial separation of the network was done to have an atlas related to relabeling the atlas based on the connectivity of the voxels that belong to the same network. For each subject, the time series of the fMRI image was then extracted according to the parcellation. Then, a correlation matrix was constructed for each subject group (ND and MDD). The correlation between the regions shows the connectivity between the brain regions. Further investigation was done on specific ROI to see the connectivity between the Anterior cingulate cortex (ACC) and the Auditory Cortex (AC).

4 Results and Analysis

4.1 T-Contrast Analysis

T-contrast brain maps for musical and non-musical tasks constructed from our GLM is displayed in Figure 1. It can be seen in all four cases that the brain region that has the highest brain activation is the region within the temporal lobe. This area can be the auditory cortex. The high activation in the temporal lobe should be expected, as the experiment is about hearing audio. Since the t-values here are only plotted on the surface, it is hard to see if the region inside the brain is also highly activated, especially for our region of interest of the ACC. Another observation from the t-maps is that the brain activation in the MDD group is visibly less than the never-depressed control group. This can be something to investigate further into.

4.2 Functional Connectivity Analysis

The correlation matrix for music and the non-music task can be seen in Figure 5 and Figure 6, respectively. The correlation matrix showed the connectivity between each brain region according to the earlier parcellation. The parcellation resulted in 50 different regions. Since we were interested in seeing if there is a connection between the ACC and the AC, the ROIs related to those brain regions are ROI numbers 44, 41, and 49 for the ACC, right AC, and left AC, respectively. The correlation matrixes showed that the highest connectivity to ROI 44 is from ROI 41 and 49, as seen by the higher brightness of the green color blocks. Furthermore, a box plot of connectivity between the ACC and the AC was created using connectivity from each subject. Specific connectivity between the two regions can be seen in Figure 7. It can be seen that the connectivity stayed relatively similar in musical and non-musical tasks. However, one key observation was that the connectivity between ACC and AC differed in ND and MDD groups. The connectivity in the MDD group was lower than in the ND group.

5 Discussions and Conclusion

5.1 Interpretation of results

The results of the t-maps showed that the brain region active the most during the experiment period was the AC This is reasonable since the experiment was based on listening to musical and non-musical audios. It was not clear if the ACC was also highly activated, but since the ACC was hypothesized to implicate MDD, the connectivity between these two regions should also be investigated. A correlation matrix from our functional connectivity analysis showed that when looking at the correlation between the AC and any other regions of the brain, the AC has the highest correlation with the ACC. This confirmed our first hypothesis about the connectivity between these two regions of interest. Furthermore, when looking deeper at the difference between the connectivity in MDD and the control group, the results showed that the connectivity between the AC and ACC in MDD subjects is lower than in control subjects. This supported our second hypothesis as well.

5.2 Robustness of solutions and how results could be used in the real world

Since our research confirmed that the connectivity between AC and ACC is significant when listening to emotional audio, and the connectivity is lower in the MDD group, it can be further researched why that happened. This could further the development of a model to diagnose or treat patients with MDD. The outcomes of this project can be used to develop a model for targeted musical therapy on patients with MDD to alleviate and treat symptoms of depression.

5.3 Limitations and Potential Future Works

One of this report's main limitations is the data preprocessing. Since the preprocessing must be done using python, FMRIPREP is the best fMRI preprocessing pipeline. However, this pipeline requires a heavy amount of computer resources and time. Preprocessing fMRI data for each subject took more than 7 hours. And therefore, not all of the subject's data were preprocessed. This also led to a lower volume of data to be analyzed. Thus, in the future, the research can be improved by preprocessing all the data. Another limitation is the accuracy of our GLM. The GLM can be improved for better-computed t-values; this can improve the brain map to identify activation regions more accurately. Lastly, a potential future work would be to investigate how positive and negative stimuli impact the activation areas and connection between brain regions in MDD subject group.

6 References

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7 Supplemental Materials

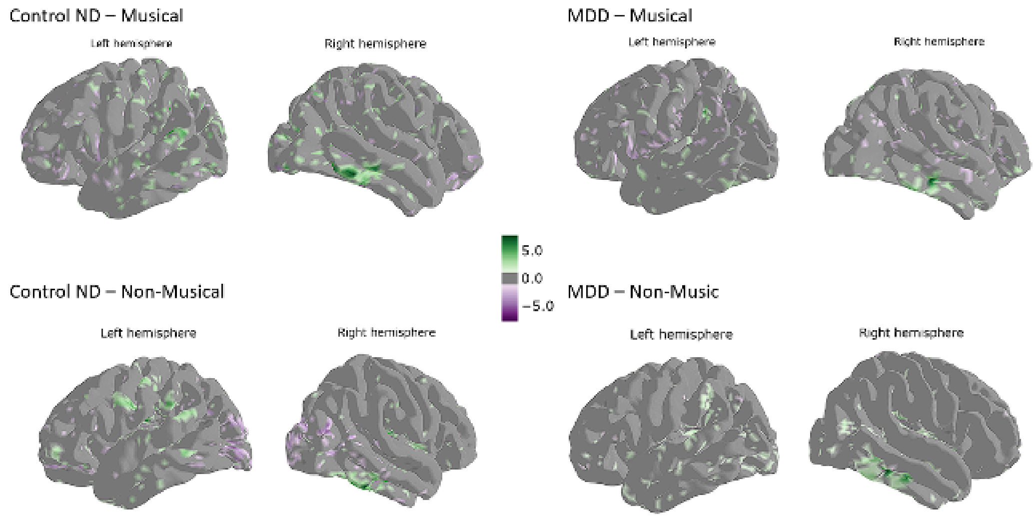


Figure 1: T-contrast Brain Maps for Each Task and Group

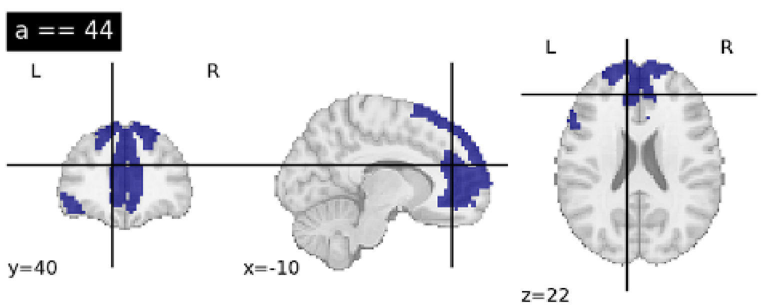


Figure 2: ROI of ACC

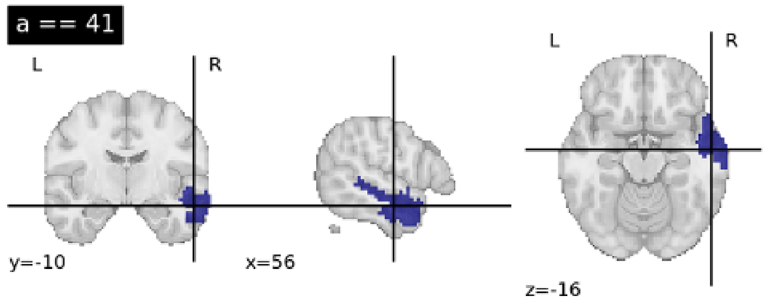


Figure 3: ROI of AC

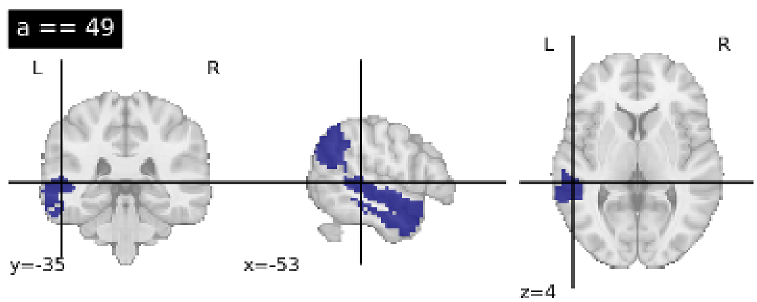
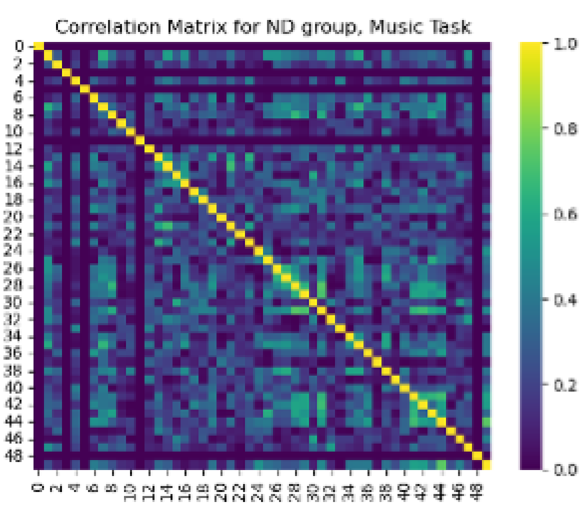
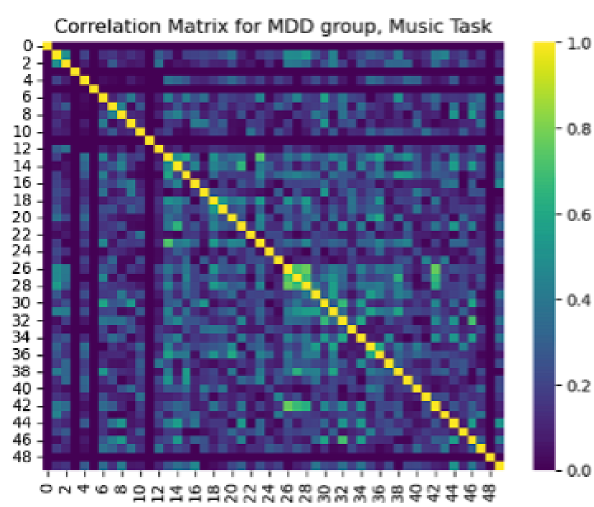


Figure 4: ROI of left AC

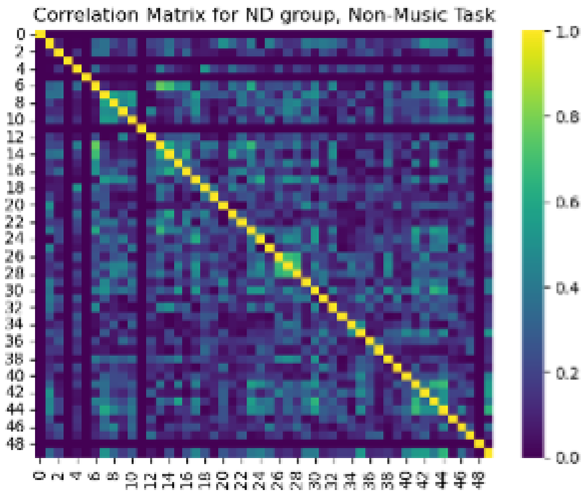


(a) ND group

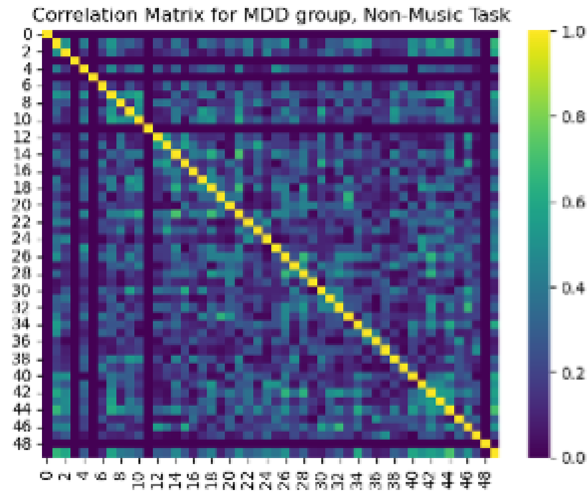


(b) MDD group

Figure 5: Correlation Matrix for Music Task



(a) ND group



(b) MDD group

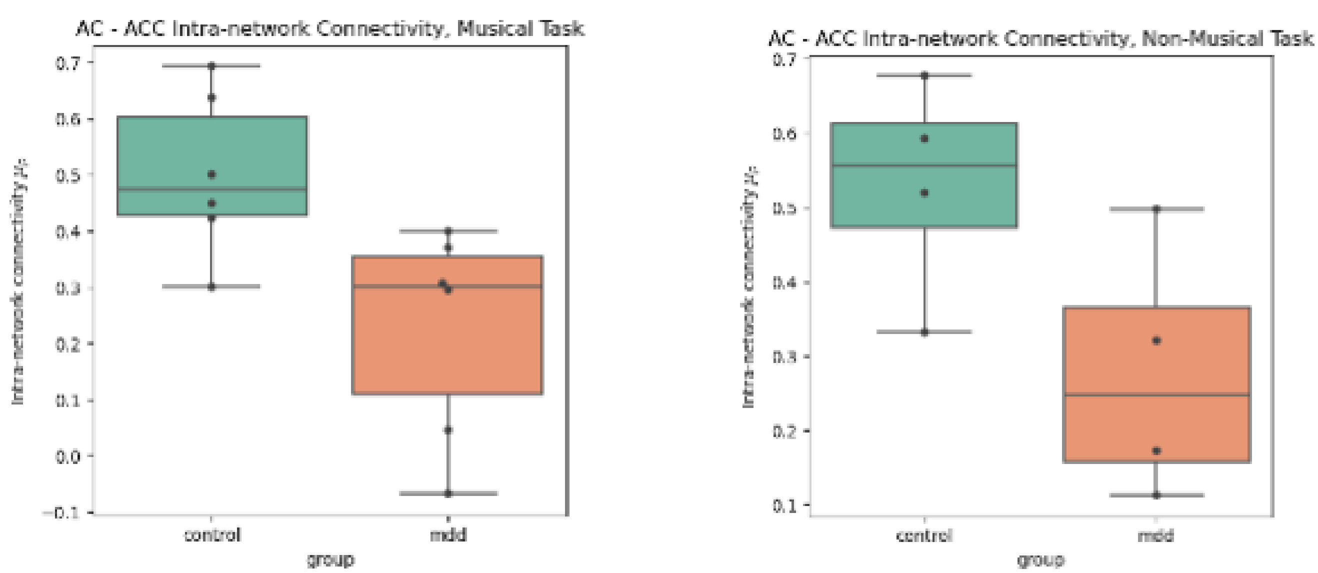
Figure 6: Correlation Matrix for Non-Music Task

	AC_ACC_corr	group
0	0.745819	control
1	0.550316	control
2	0.676431	control
3	0.454386	control
4	0.400613	control
5	0.589507	control
6	0.512664	mdd
7	0.758968	mdd
8	0.516627	mdd
9	0.694276	mdd
10	0.707918	mdd
11	0.770246	mdd

Table 1: Connectivity between AC and ACC in each subject, Music Task

	AC_ACC_corr	group
0	0.676406	control
1	0.591649	control
2	0.331425	control
3	0.518895	control
4	0.320510	mdd
5	0.112568	mdd
6	0.172342	mdd
7	0.496927	mdd

Table 2: Connectivity between AC and ACC in each subject, Non-Music Task



(a) Musical Task

(b) Non-Musical Task

Figure 7: Connectivity Between ACC and AC in Music and Non-Music Task