

Computational Modeling of Neural Networks Underlying Emotional Music Processing in Major Depressive Disorder

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Abstract

Major Depressive Disorder (MDD) is associated with disruptions in affective processing and altered neural connectivity within emotion-related networks. This study used computational modeling to examine neural activation during emotional music perception in individuals with and without MDD. Open-source fMRI data from Lepping et al. (2016) were analyzed using NeuroElf and SPM12, incorporating preprocessing, voxel-wise modeling, and contrast mapping for positive, negative, and neutral auditory stimuli. Regions of interest (ROIs) included the anterior cingulate cortex (ACC), Brodmann Area 6 (BA6), and Brodmann Area 31 (BA31). Through custom Python and MATLAB scripts, group-level contrasts and beta estimates were modeled to assess emotional valence effects. While results revealed no statistically significant group differences, patterns of activation suggested altered emotion appraisal pathways in MDD, characterized by reduced differentiation between positive and negative stimuli. This project underscores the value of computational approaches in cognitive neuroscience, highlighting the potential of open-source modeling pipelines to explore emotion, music, and mental health.

Introduction

Depression is one of the most prevalent and disabling mental health conditions worldwide. It affects an estimated 280 million people globally and is characterized by altered emotional regulation, blunted reward sensitivity, and persistent low mood. Previous neuroimaging research has shown that individuals with Major Depressive Disorder (MDD) exhibit differences in brain activity in regions related to emotion processing, particularly within the anterior cingulate cortex (ACC) and prefrontal regions.

Music is a powerful stimulus for evoking emotion, and its neural processing overlaps with regions involved in affect regulation. The current study uses computational modeling to explore the neural correlates of emotional music perception in MDD. Specifically, we used fMRI data from Lepping et al. (2016) to examine differences in activation patterns between individuals with MDD and healthy controls while listening to positive, negative, and neutral musical stimuli. The purpose of this analysis was to determine whether individuals with MDD exhibit distinct activation patterns in emotion-related neural circuits during the perception of emotionally valenced music. We focused on three regions of interest (ROIs): the ACC, Brodmann Area 6 (BA6), and Brodmann Area 31 (BA31), which are implicated in emotional regulation and cognitive control.

Methods

Dataset and Participants

The dataset used for this project was obtained from the OpenNeuro repository, originally published by Lepping et al. (2016). Participants included individuals diagnosed with Major Depressive Disorder (MDD) and healthy controls (HC). Exclusion criteria included the use of antidepressant medication and comorbid psychiatric conditions.

Controls	mdd
1 - F	1 - F
2 - M	2 - F
3 - F	3 - F
4 - M	4 - M
5 - M	7 - F
6 - M	8 - F ☐
7 - F	10 - F
11 - F	14 - F
15 - M	16 - M
16 - F	17 - F
17 - F	
18 - M	
19 - F	
20 - M	

Table 1

Subject Inclusion and Demographic Data - M indicates Male, and F indicates Female.

Stimuli and Task Design

Participants were presented with auditory stimuli consisting of emotionally positive, negative, and neutral (tone) music. Each stimulus was played in blocks, with resting intervals interleaved between trials.

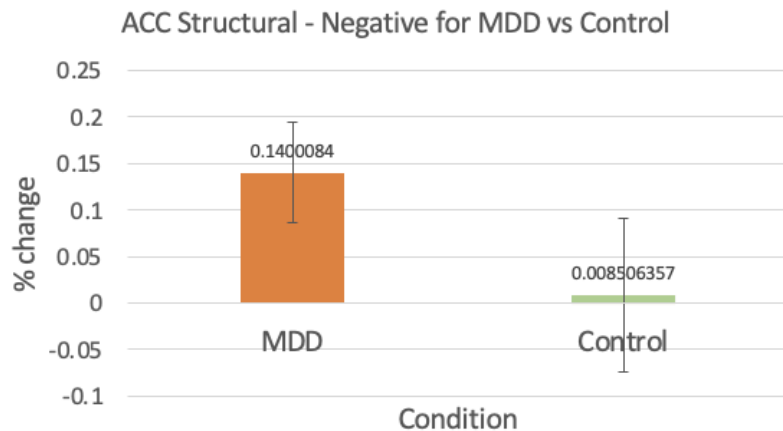


Figure 1

Negative Stimulus for Anterior Cingulate Cortex comparing MDD to Control.

P-value: 0.194428372 and T-statistic: 1.338420531

Preprocessing and Computational Modeling

Data were preprocessed using NeuroElf and SPM12, including slice-timing correction, realignment, normalization to MNI space, and motion correction (<2 mm threshold). A design matrix was generated using Python and MATLAB scripts to model hemodynamic response functions (HRF) for each stimulus type.

Voxel-wise general linear models (GLMs) were computed to estimate beta coefficients representing neural activation. Contrasts were generated for negative > tones, positive > tones, and positive > negative conditions. Group-level analyses compared MDD and control participants across ROIs.

Results

The ROI-based analysis revealed that activation differences between MDD and control groups did not reach statistical significance. However, qualitative assessment indicated variability in activation patterns, particularly within BA31.

T-test MDD VS CONTROL - Brodmann 6			
	tones	negative	positive
pvalue	0.659438	0.656909	0.343323
t-statistic	0.446728	0.450288	0.968498

T-test MDD VS CONTROL - Anterior Cingulate Cortex			
	tones	negative	positive
p-value	0.335344156	0.984978305	0.10469953
t-statistic	0.984978305	1.338420531	1.6923308

T-test MDD VS CONTROL - Broadman Area 31			
	tones	negative	positive
pvalue	0.120971	0.919997	0.341407
t-statistic	1.613124	0.101597	0.972431

Table 2

Statistical Summary of ROI Activation Values - T-tests differentiated by anatomical structure, comparing MDD to Control.

Visual inspection of contrast maps revealed consistent engagement of the ACC and BA6 during both positive and negative music conditions. MDD participants demonstrated reduced differentiation between emotional valences compared to controls, suggesting blunted emotional reactivity.

Discussion

The results of this computational analysis align with previous literature suggesting attenuated emotional processing in MDD. Although no significant group-level differences were observed, the observed trends in neural activation across emotional stimuli may reflect reduced sensitivity to affective valence in depression.

The anterior cingulate cortex and Brodmann Area 6 showed consistent activation across conditions, supporting their roles in cognitive and emotional regulation. Reduced differentiation in the posterior cingulate (BA31) among MDD participants may indicate altered integration of emotion and memory during music processing.

Methodological limitations include the small sample size, heterogeneity of depression severity, and potential noise introduced by varying head motion or scanner drift. Future analyses could benefit from machine learning approaches, such as convolutional neural networks (CNNs), to model complex non-linear relationships between neural activation and emotional perception.

Conclusion

This project demonstrates the use of computational modeling to analyze neural activation during emotional music processing in Major Depressive Disorder. While findings were not statistically significant, observed activation patterns suggest potential disruptions in emotional appraisal networks. Future research should expand on these methods using larger datasets and more advanced modeling frameworks to explore the intersection of affective neuroscience, computational modeling, and mental health.

Appendix

Appendix I - Preprocessing 24 subjects, 120 runs

NeuroElf - configure (SPM based) preprocessing

1. select a subject folder (or pattern; last part=subject ID); 2. configure the subfolder and filename patterns; 3. hit search (and remove subjects not to be processed); 4. configure the required settings; 5. run the preprocessing

Subject folder pattern:

Anatomical subfolder pattern: Image filename pattern:

Functional subfolder pattern: Image filename pattern:

Optional DTI subfolder pattern: Image filename pattern:

Display advanced options: ☐ Deselect subjects with VTCs already imported: ☒

Force data to single precision: ☒ Brain-extract anatomical: ☒ Register to T1 template: ☒ cleanup: ☐

Subjects found: (24 valid subjects/120 runs found) Skip volumes per run: cleanup: ☒

Slice-Timing settings: Perform slice-timing: ☒ cleanup: ☒

Slice acquisition order: Edit order:

TR: TA: auto-TA: ☒ Ref-slice: MUX:

Realignment settings: Coregister mean (+ other) functional(s) to anatomical

Quality (accuracy trade-off): Sampling grid (mm): To-mean (2-pass): ☒

Spline interpolation degree: (estimation) (reslicing) Reslice: ☒ cleanup: ☒

Normalization settings: Segment anatomical and apply determined parameters to all data

T1 anatomical template:

Normalization bounding box: Resolution (mm):

Write normalized anatomical: ☒ Normalize each of the EPI runs separately: ☐ cleanup: ☒

Smoothing kernel (mm): Perform smoothing: ☒ cleanup: ☐

Run fmriquality (pre/post): ☒ ☒ create VTCs after realignment: ☐ after preprocessing: ☒

VTC filename pattern: first index:

Appendix 2 - GLM set-up

Correction: sub* in front of each file pattern and take it out of the base folder

NeuroElf GUI - run a multi-study RFX GLM

Base folder:

VTC file pattern: SDM/PRT file pattern:

Motion parameter files: ☒ + diff ☐ + squared ☐

List of VTC files to be regressed:

List of design files:

List of motion parameter files:

Transformation: ☐ none ☒ PSC ☐ z Intensity threshold: Mask file:

Regression type: ☒ Ordinary Least Squares (OLS) ☐ Robust regression Deconvolution / ☐ Number of lags:

Temp. filter: ☐ none ☐ DCT ☒ Fourier Cut-off (sec): Global sigs:

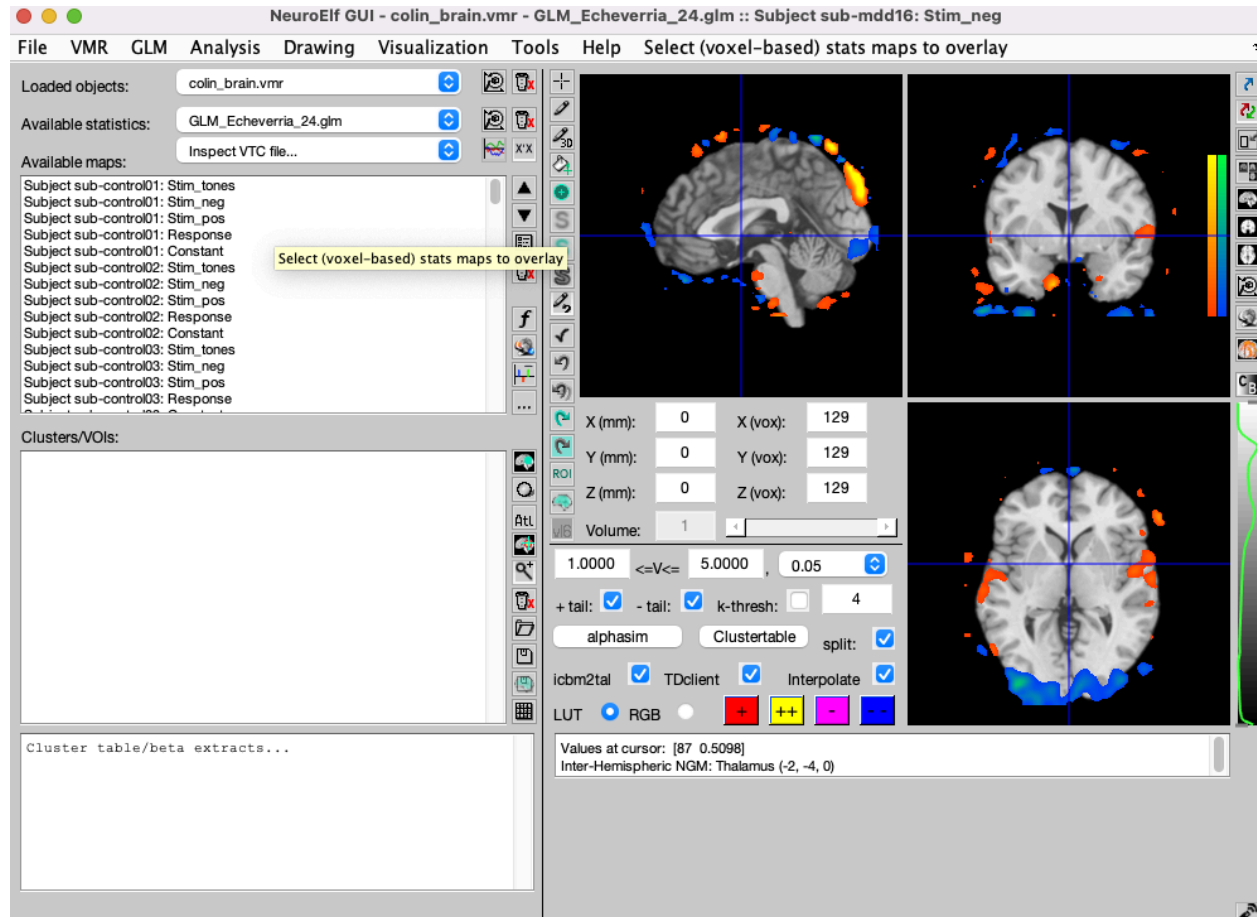
Modeling type: ☐ fixed effects (no separation) ☐ separate by subjects ☐ separate by studies ☒ random effects

Model options: single-trial (only PRT): ☐ combine RFX-GLM from FFX: ☐ Weigh betas by variance across runs: ☒

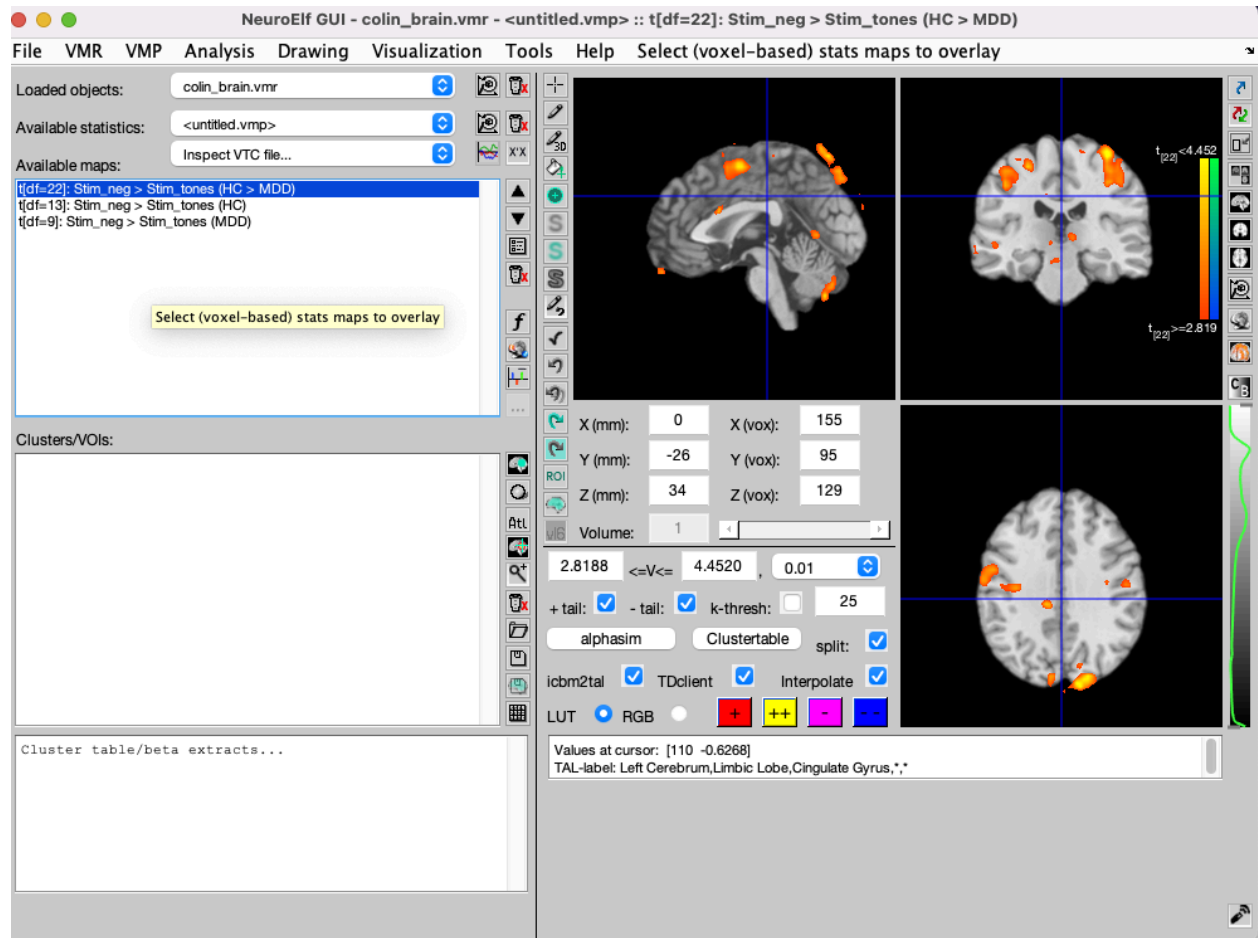
Target GLM file: Redo subjects: ☐

☐

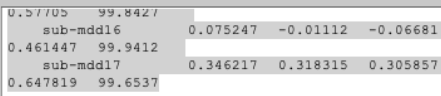
Appendix 3 - GLM for Subject MDD 16



Appendix 4 - Contrast example for comparing MDD vs Control, for Negative > Tones

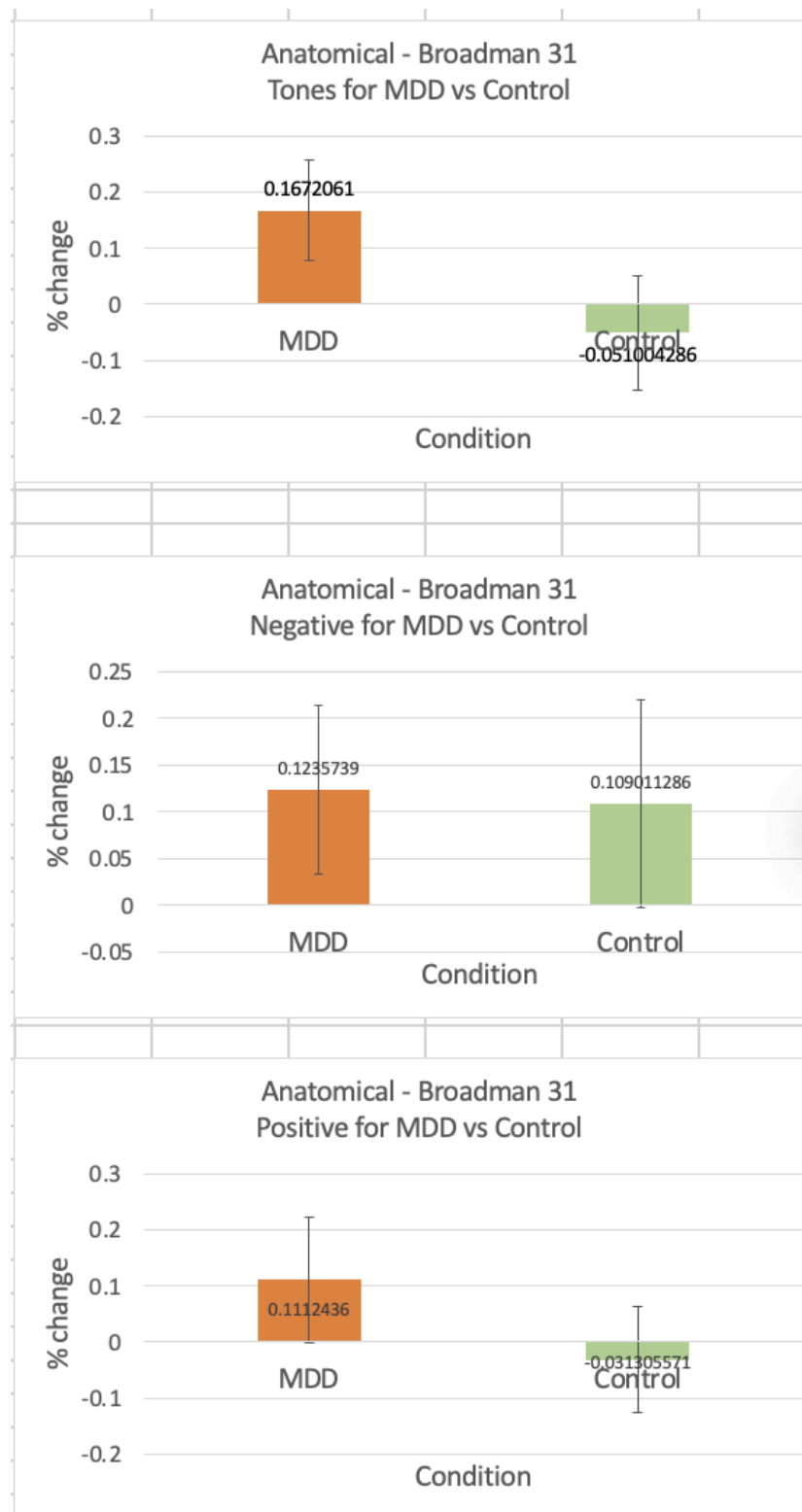


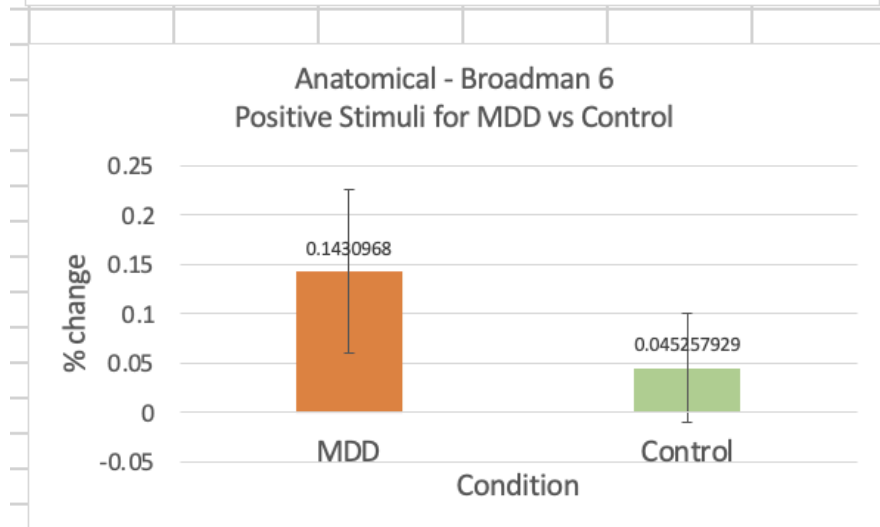
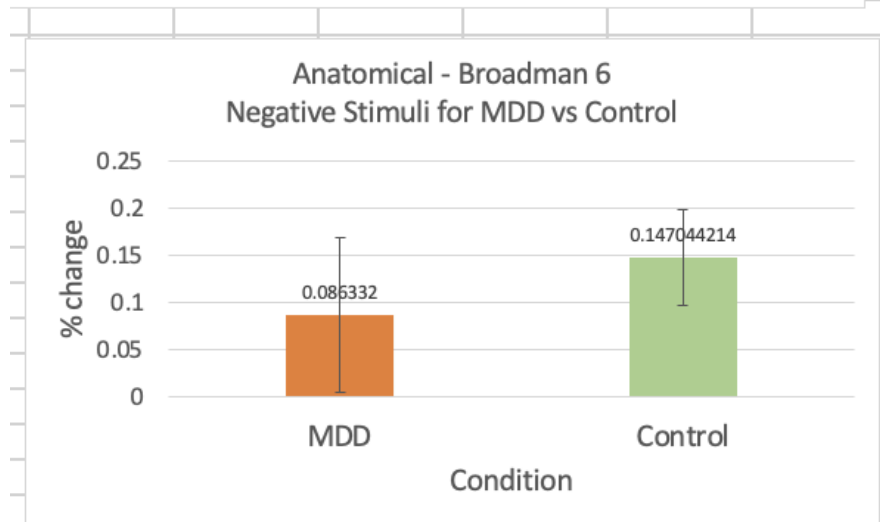
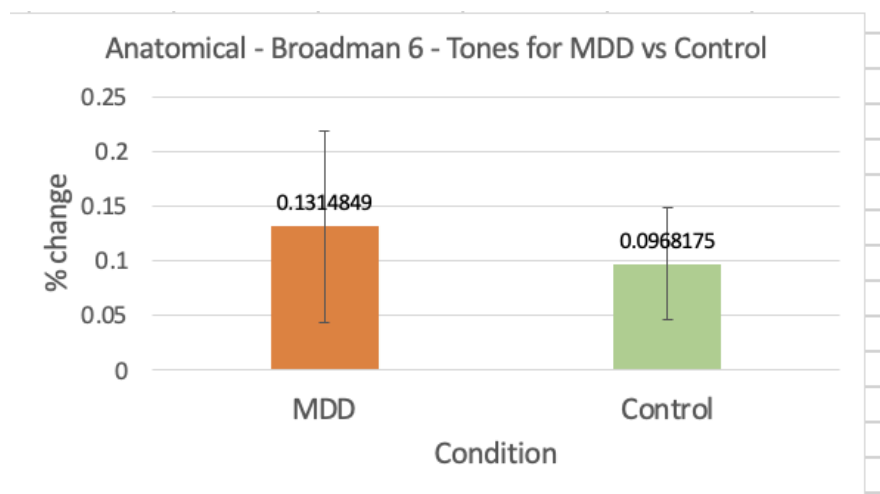
(green/blue)

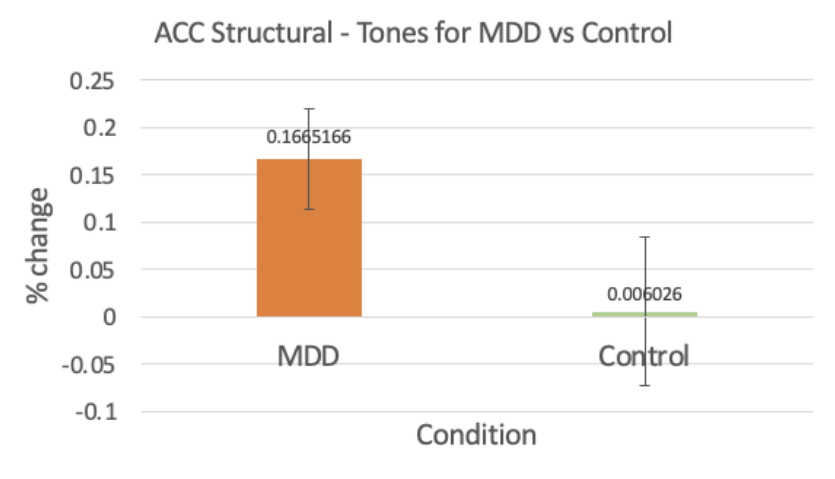
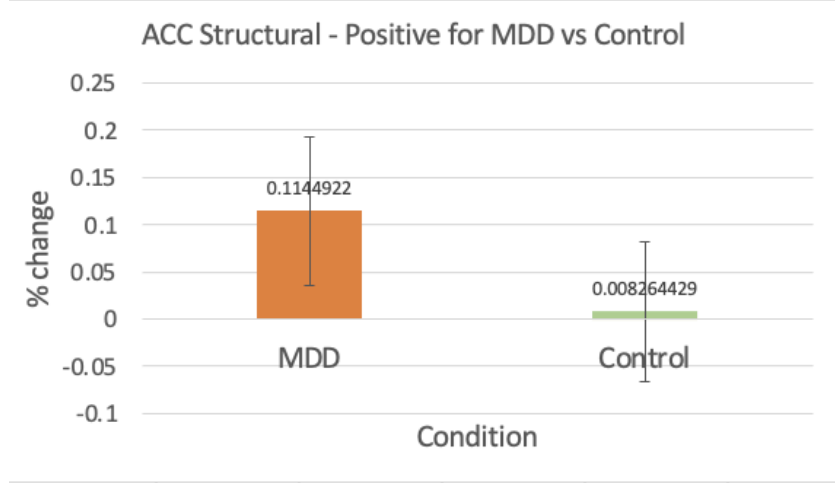
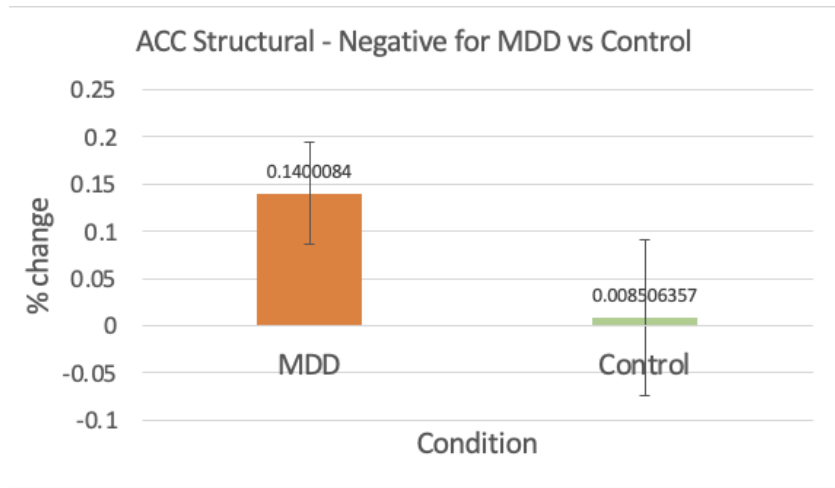


Values at cursor: [240 4.839]
TAL-label: Right Cerebrum,Limbic Lobe,Posterior Cingulate,Gray Matter,Brodmann area 30

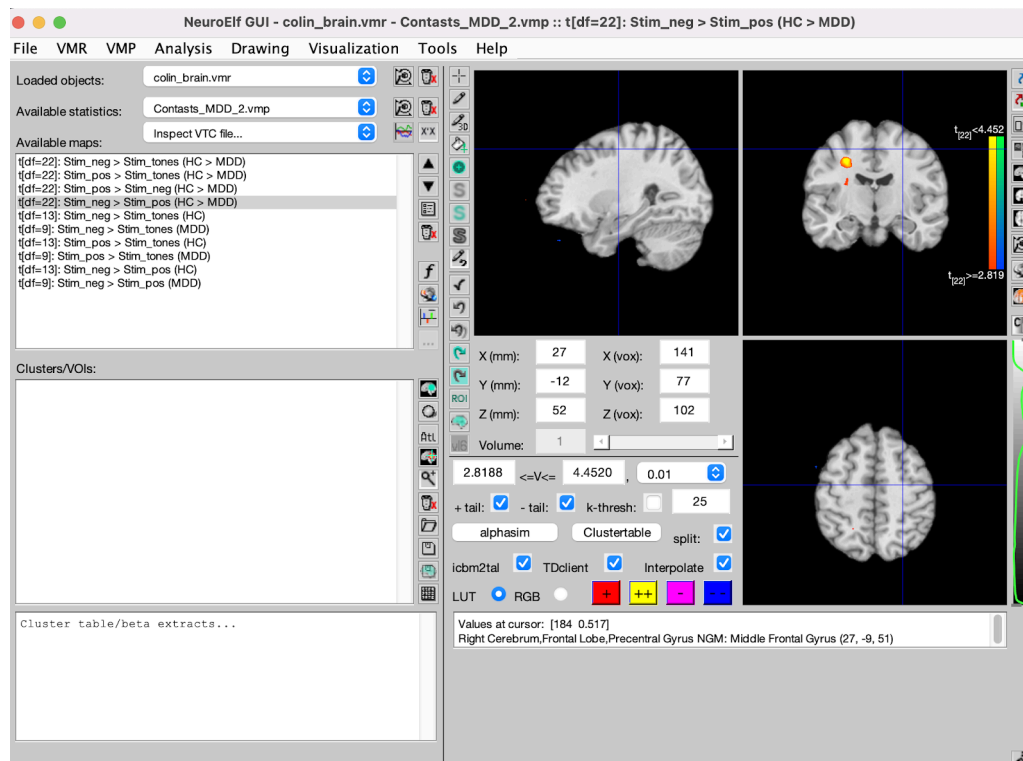
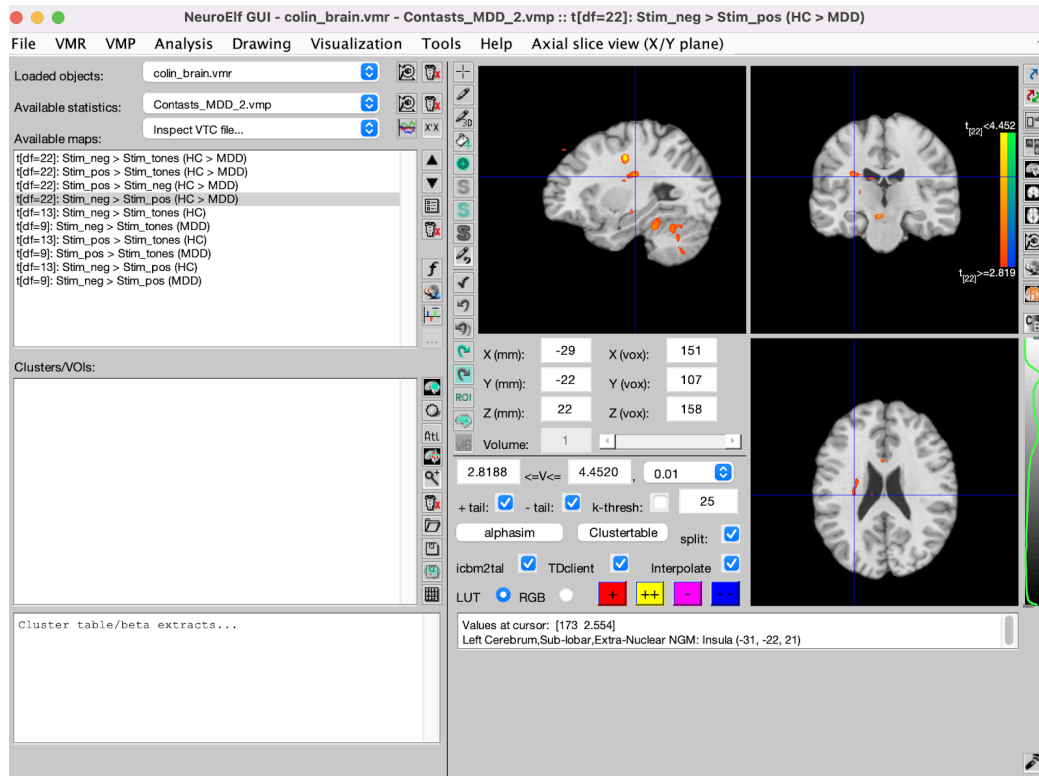
Appendix 6 - Averages and standard error for for different anatomical regions







Appendix 7 - Montage of Scans



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