Potential of Receptive Music Intervention on Mild Cognitive Impairment: A Resting-State fMRI Study

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Introduction

Background: Music-Based Interventions (MBIs) have become a widely adopted non-pharmacological intervention among older adults due to their impact on mood and stress reduction (1). Several randomized controlled trials have shown benefits of listening to familiar music, against other interventions on cognition, mood, perceived stress, and quality of life measures in older adults with Mild Cognitive Impairment (MCI) and Alzheimer's Disease (AD) (2-6), but evidence for their effectiveness is not yet well established due to small sample sizes and large intersubject variability. This lack of coherency underscores the demand for a unified mechanistic understanding to motivate music-based interventions. Studying the effect of MBIs at a neural connective level will not only enable scientists to gain a better understanding of MCI and the effectiveness of our proposed therapy, but also to come up with a non-invasive method that could sustainably improve subjects' health and well-being, identifying possible pathways that are affected by musical intervention. Based on our understanding of how music affects the brain and results from the previous literature, we propose the following hypothesis:

Hypothesis: Music based interventions would be effective, non-pharmacological methods of managing and alleviating symptoms of MCI by engaging the heightened intrinsic auditory prediction and reward networks which could sustainably delay its progression to dementia.

Methods

Sample: We used open-source data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) (7). From the available data, we extracted structural MRI and resting-state functional MRI data that were free of artifacts and met the specific scan parameters below. Overall, 105 older adults matched in age and gender were selected, consisting of a healthy control (CN) group (N=47, 27 females), a MCI group (N=47, 27 females), and a AD group (N=11, 3 females).

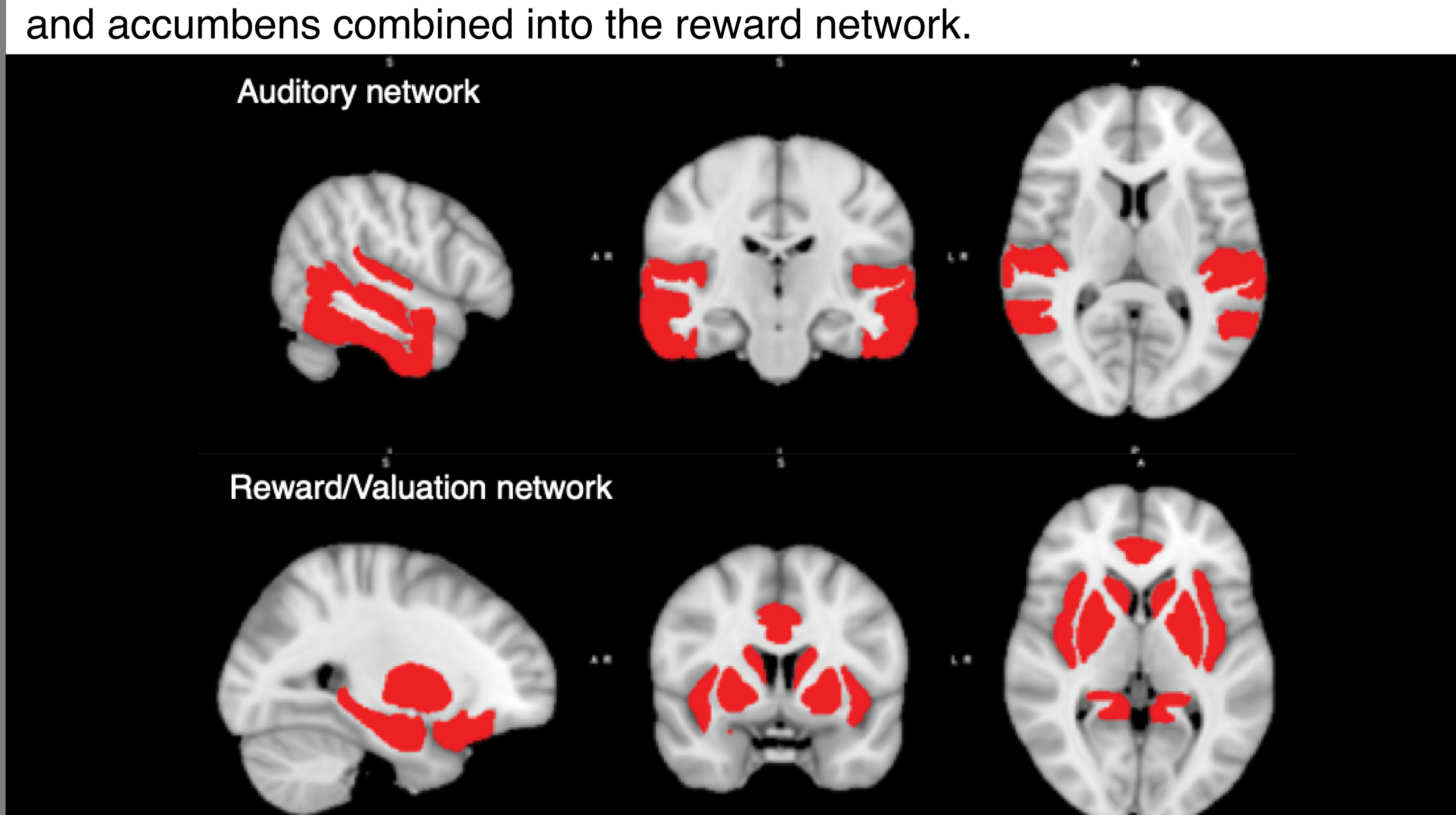
Magnetic Resonance Imaging acquisition and preprocessing: MRI (structural and rsfMRI) data were acquired in a 3T SIEMENS scanner. T1 structural data had a voxel resolution that was 0.8 x 0.8 x 0.8 mm^3. rsfMRI data was acquired as 197 contiguous EPI volumes (TR = 3 s; voxel size= 3.4375 × 3.4375 × 3.4375 mm^3). MRI data were analyzed using the CONN Toolbox (8). T1 and rest data underwent standard preprocessing and denoising steps, including a band pass filter for resting state data from 0.008 to 0.09 Hz.

Regions of Interest (ROIs) Definition

All ROIs are from the CONN default atlas (containing 185 ROIs and 32 networks) to avoid overlap among the seed regions of the below networks.

Auditory Network (18 ROIs): all bilateral ROIs in the superior, middle, and inferior temporal lobes (anterior, posterior, and temporooccipital) and the bilateral Heschl's Gyrus combined into the auditory network.

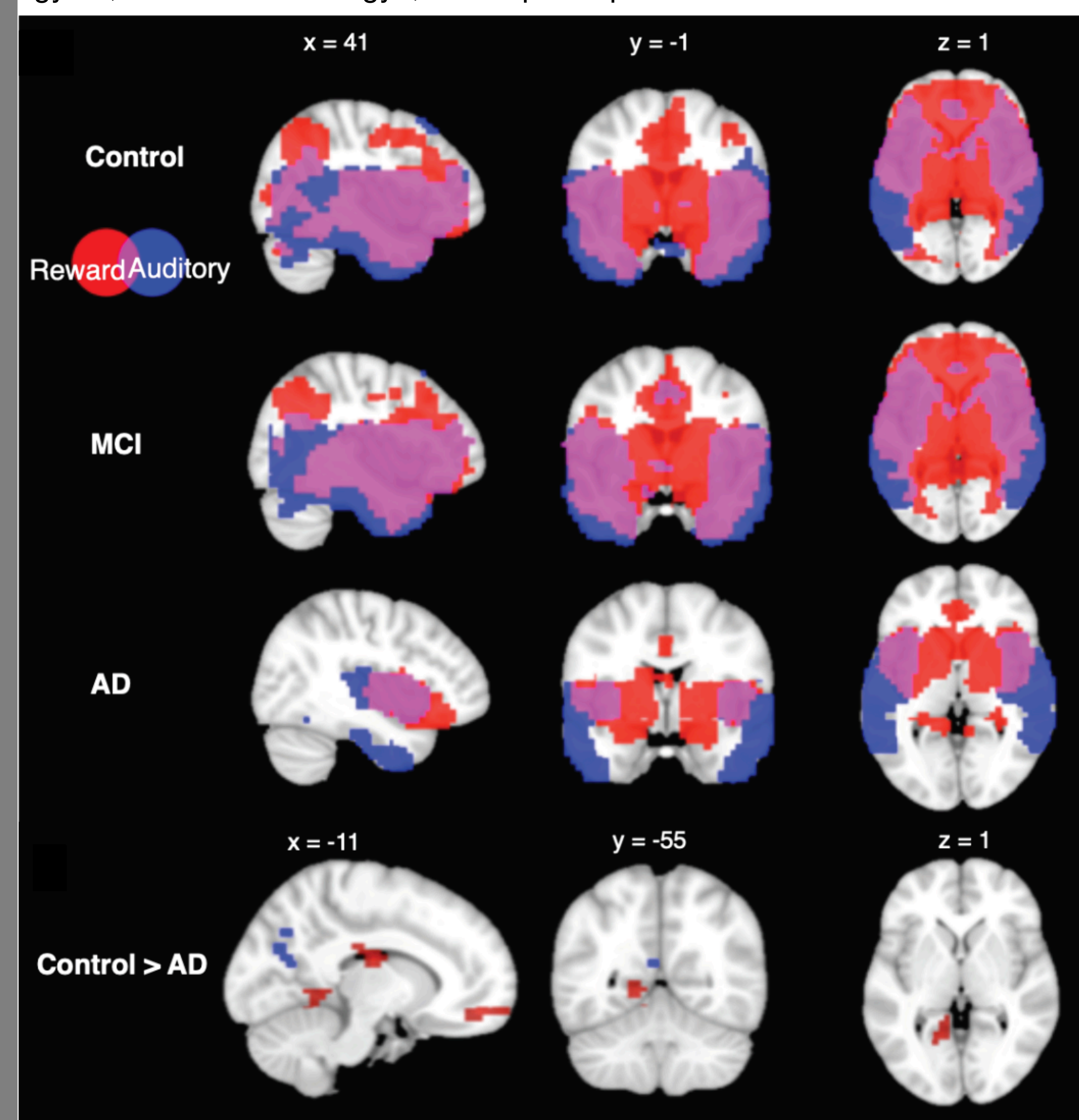
Reward Network (18 ROIs) (9): bilateral insular cortex, cingulate gyrus, frontal orbital cortex, caudate, putamen, pallidum, hippocampus, amygdala, and accumbens combined into the reward network.



Seed-Based Connectivity

Method: For whole-brain connectivity patterns and between-group comparisons, we extracted all voxels that were significantly functionally connected (using bivariate correlation) to the seed ROIs at the p<0.05, p-FWE corrected level and at the p<0.05, p-FDR cluster-size corrected level. Slices were chosen at the peak cluster for all three groups.

Results: *Auditory Network Seed:* all groups showed highly significant connectivity to auditory areas. CN and MCI group showed significant connectivity in the parietal, occipital, and frontal lobes. Between-group comparisons showered higher functional connectivity in the precuneus for CN>AD. *Reward Network Seed:* all groups showed highly significant connectivity to reward areas. CN and MCI groups both have significant connectivity to auditory network ROIs and significant overlap in areas functionally connected to auditory and reward ROIs in the frontal, parietal, and occipital lobes. Between-group comparisons showed higher functional connectivity in the cingulate cortex, medial prefrontal cortex, left lingual gyrus, bilateral fusiform gyri, and superior parietal lobule for CN>AD.



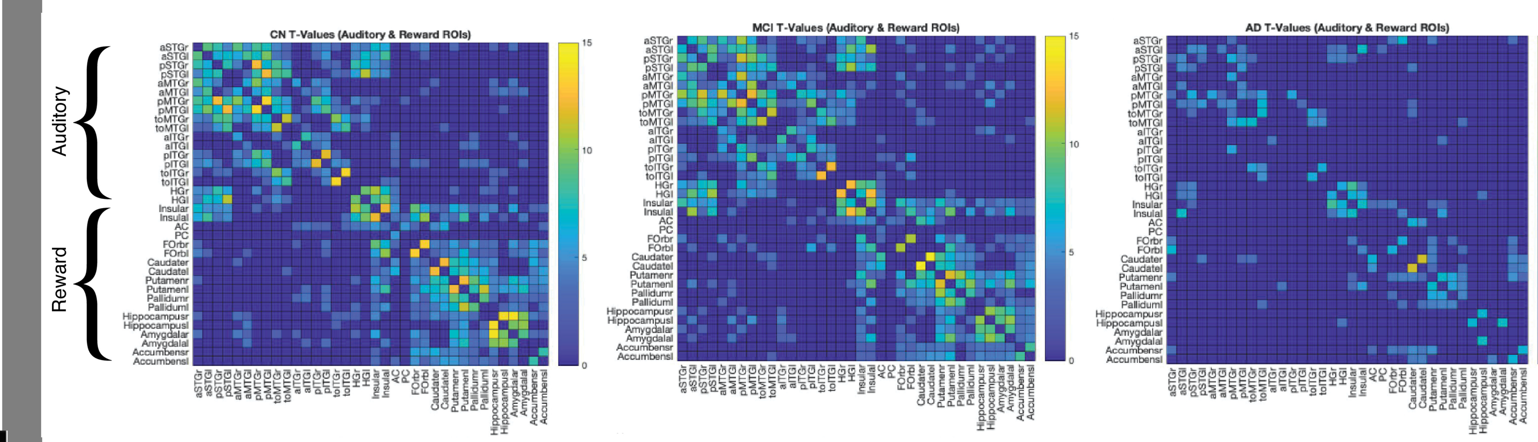
Conclusion & Discussion

- Using the past literature, including seminal research by Belfi & Loui (2019), we have identified an anatomical model of auditory and reward systems, and characterized their intrinsic functional connectivity using resting state fMRI from a large sample of age and gender matched AD, MCI, and CN individuals.
- We observe an overlap between seed-based connectivity patterns from the auditory and reward networks, centering around the anterior insula, support previous work surrounding a neuroanatomical model for the reward of music listening (9) and in lesion mapping studies.
- The pattern of graph theory results show that MCI individuals have consistently high between-network connections as well as within-network clustering within the reward network relative to controls and AD individuals. AD individuals have decreased functional connectivity within and between the two systems with disruptions that affect degrees, strengths, and betweenness centrality of the overall network.

ROI-to-ROI Comparisons

Method: *r*-correlation values for each of the 36 ROIs were extracted for every participant and averaged across each group into correlation matrices.

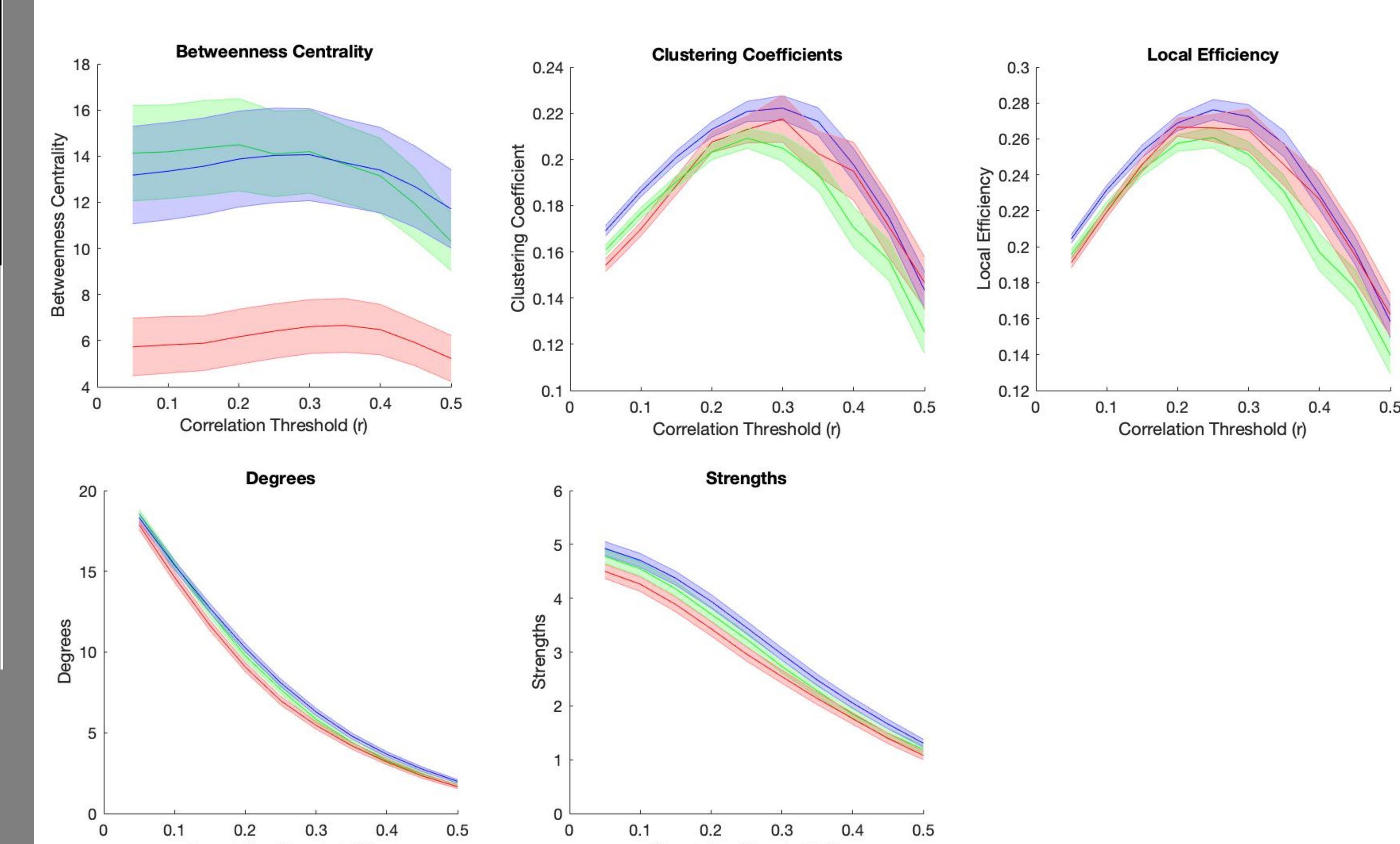
Results: All three groups show higher connectivity within each network – auditory-auditory, reward-reward – shown by higher T values within the diagonal quadrants than in the off-diagonal quadrants – auditory-reward. The T-values are generally similar between CN and MCI groups. In contrast, the AD group has lower connectivity overall, possibly due to fewer valid scans in the AD group associated with head motion during scanning.



Graph Theory Analyses

Method: Using the Brain Connectivity Toolbox (10), network statistics betweenness centrality, clustering, local efficiency, degrees, and strengths were computed at a range of correlation thresholds from r=0.05 to r=0.5 for each individuals' ROIs and averaged across groups. Group averages were compared using one-way ANOVAs, correcting for p<0.05, p-FDR corrected.

Results: Betweenness centrality, the number of shortest paths from one node to another that contains a given node, showed highest levels in the CN group, followed by MCI and then by AD (F(2,105)=6.64, p=0.0019). On the other hand, degrees, the number of nodes significantly correlated to a given node, and strengths, the sum of the correlation coefficients for a given node, now showed highest levels in MCI individuals, followed by the CN group, and trailed by the AD group (F(2,105)=4.75, p=0.0106 and F(2,105)=3.88, p=0.0237).



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