Topological data analysis as a novel approach to explore changes in the resting-state functional connectome of individuals with Major Depressive Disorder.

Presentation summary by Javier Fco. Castilla-Jiménez

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Introduction

Major Depressive Disorder (MDD) is a leading cause of disability worldwide, affecting over 322 million people. Recent research suggests that MDD is a network-based disorder, with abnormal functional connectivity across several large-scale brain networks, including the Default Mode Network (DMN), Frontoparietal Network (FPN), and Salience Network (SAL). However, inconsistencies in findings have raised questions about the robustness of traditional graph theory approaches. In this study, we apply Topological Data Analysis (TDA) to a large dataset from the REST-meta-MDD Project to explore alterations in whole-brain functional connectivity in individuals with MDD with emphasis on studying the effect of chronicity of MDD, aiming to provide a more stable framework for understanding these complex interactions.

Objectives

The main objective of this study is to explore alterations in functional brain connectivity in individuals with major depressive disorder (MDD) using Topological Data Analysis (TDA) applied to resting-state fMRI data. We aim to examine differences in whole-brain connectivity patterns, and subnetworks focusing on the Default Mode Network (DMN), Frontoparietal Network (FPN), and Salience Network (SAL), and quantify these differences through Betti curves and their area under the curve (AUC).

Methods

We utilized imaging and phenotypic data from 1,601 participants (830 with MDD and 771 controls) obtained from the REST-meta-MDD Project. Functional connectivity matrices were computed using Pearson cross-correlation between regions of interest for Power's 264 brain atlas. Topological Data Analysis (TDA) was applied to assess the topology of the network as a function of a connectivity threshold, and characterized through the area under the Betti curves. Linear mixed models (LMM) were used to assess the impact of MDD condition and clinical subtypes (associated with chronicity and medication) on connectivity while control for site-related confounding factors.

Results

Significant alterations were identified in the brain network topology of individuals with recurrent major depressive disorder (RMDD). The Betti AUCs (b0, b1, and b2), which quantify the evolution of topological invariant features associated with functional connectivity, were significantly higher in RMDD patients compared to both controls and first-episode MDD (FEMDD) patients (Figure 1). These increases were consistent across medicated (RMDDT) and unmedicated (RMDDnT) subgroups. These findings suggest that RMDD, irrespective of treatment status, leads to more severe disruptions in functional brain connectivity compared to first-episode depression.

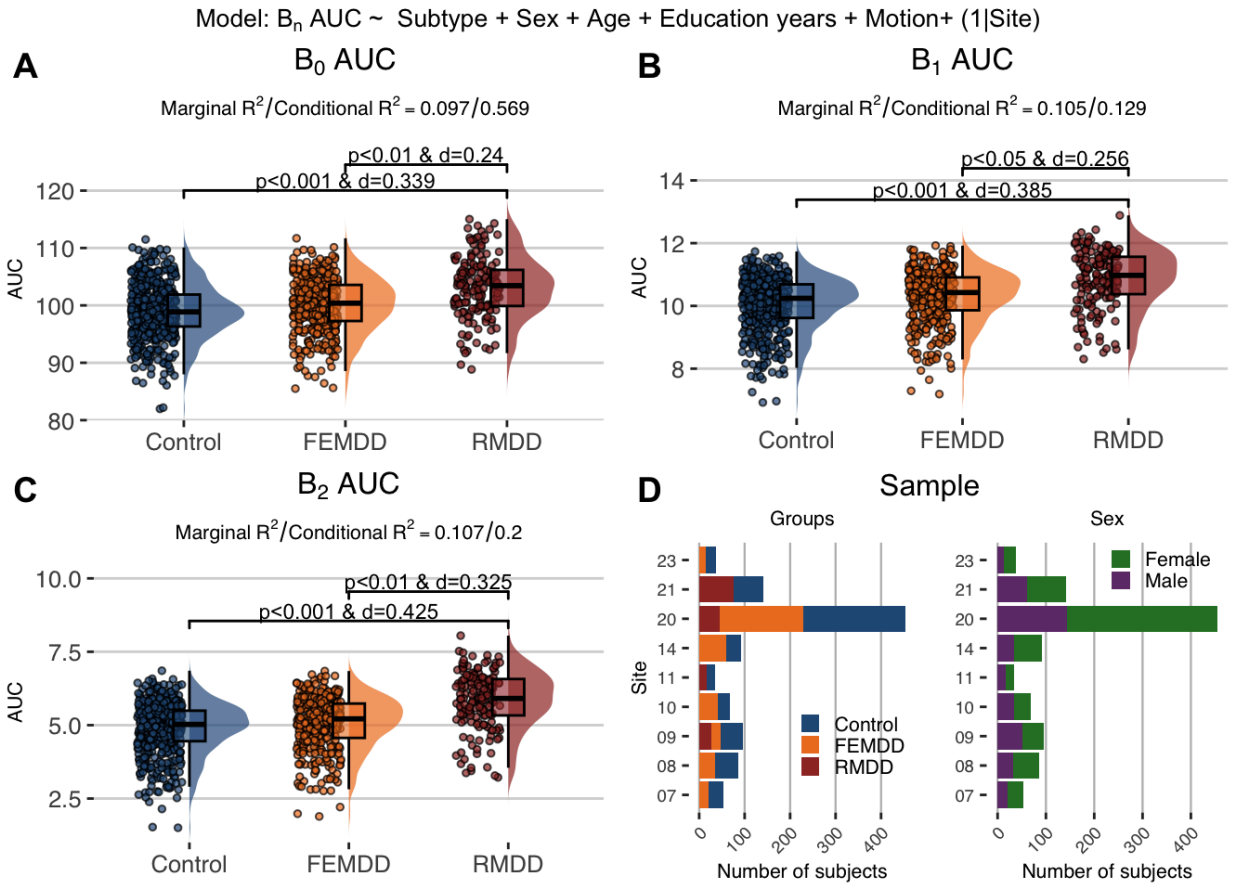

Figure 1. LMM site-detrend predicted values by subtype for $Betti_{1,2,3}$ AUC at whole brain level (panel A, B and C). Sample composition (panel D).

Conclusions

The study demonstrates that recurrent major depressive disorder (RMDD) is associated with more robust and widespread disruptions in brain network topology than first-episode depression. The significant alterations in Betti AUCs highlight the potential of TDA as a tool for identifying complex changes in brain connectivity in psychiatric conditions. These results suggest that topological measures of functional connectivity could be markers of the chronicity and severity of depression, offering insights into the cumulative effects of recurrent depressive episodes on brain network dynamics.