Longitudinal Multimodal Data Fusion Reveals Brain–Symptom Change Patterns in Depression

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Abstract

Understanding how brain structure and psychopathology co-evolve over time is central to unravel individual variability in affective disorders. We applied multiset canonical correlation analysis followed by joint independent component analysis (mCCA + jICA) to longitudinal data from 105 participants (48 healthy controls, 57 with major depressive disorder, MDD), using cortical surface area (SA), cortical thickness (CT), and symptom checklist-90-revised (SCL-90) symptom scores as input modalities. Five joint components were extracted. Two components revealed significant brain–symptom change associations involving depression-dominant SCL-90 profiles. Regions showing progressive reduction in SA and CT overlapped with those reported by ENIGMA studies in adolescent and adult MDD, respectively. Correlations between structural and symptom component loadings were stronger in the MDD subgroup than in controls, highlighting diagnosis-specific change trajectories. Our results support multimodal fusion as a promising approach to identify clinically meaningful brain–symptom change patterns and better understand brain–behavior coupling in affective disorders.

Keywords: mCCA+jICA; multimodal data fusion; major depressive disorder

Introduction

Understanding how brain structure and psychopathological symptoms co-evolve over time is key to advancing our knowledge of major depressive disorder (MDD). While cross-sectional studies have revealed structural alterations in MDD, longitudinal data better capture within-subject dynamics related to disease progression. Psychiatric disorders involve interconnected changes across modalities, making single-modality approaches insufficient. Multimodal data fusion techniques can reveal shared patterns across the brain and symptom data, particularly when applied to longitudinal change. In this study, we applied multiset canonical correlation analysis followed by joint independent component analysis (mCCA + jICA) to identify co-varying change patterns in cortical thickness, surface area, and SCL-90 scores in a mixed sample of MDD and healthy controls.

Method

Participants and data

We used longitudinal data from 105 participants (48 healthy controls, 57 with major depressive disorder) from the FOR2107 cohort (age 18–65, M = 41.4; 26 males). Structural MRI (T1-weighted) and SCL-90 psychopathology scores were acquired at timepoints two years apart. Cortical thickness and surface area were derived from a standard FreeSurfer pipeline (Fischl, 2012). Cortical thickness, surface area, and symptom change scores (Δ =T2–T1) were computed. Data preprocessing followed standardized FOR2107 protocols (Winter et al., 2024).

Multimodal data fusion and analysis

We applied mCCA plus jICA using Fusion ICA Toolbox (FIT) to identify shared change patterns across modalities (Lottman et al., 2018; Saha et al., 2023; Sui et al., 2013). Five joint components were extracted based on the elbow criterion. We examined component maps and performed correlation analyses on subject loadings to assess cross-modal association.

Results

Two components derived from multimodal data fusion revealed meaningful cross-modal associations. Surface area Component 2 (SA2) was significantly correlated with SCL-90 Component 2 ($r = 0.36$, $p = 0.0014$), which was characterized by strongest loadings in the depression subscale. SA2 reflected decreasing patterns in surface area over time in different regions,

notably the left lateral occipital cortex, right inferior parietal cortex, right pericalcarine cortex, left medial orbitofrontal cortex, and left precentral gyrus as shown in Figure 1. These regions overlap with those identified in adolescents with MDD in the ENIGMA study (Schmaal et al., 2017,2020), suggesting alignment between longitudinal decline and known cross-sectional effects.

A similar association was found between cortical thickness Component 1 (CT1) and SCL-90 Component 1 ($r = 0.35$, $p = 0.0023$), where depression again featured prominently as shown in Figure 2. CT1 showed thinning patterns in bilateral insula, bilateral posterior cingulate, left middle temporal gyrus, left fusiform, left rostral anterior cingulate, and right inferior temporal regions—consistent with ENIGMA's findings in adult MDD (Schmaal et al., 2017,2020). Similar to SA1, these regions also carried some of the strongest negative weights, indicating robust structural decline in contributing individuals.

To assess diagnostic specificity, subject loading correlations were computed separately for MDD and HC. Associations were stronger and significant in MDD (SA2–SCL90_2: $r = 0.48$, $p = 0.0022$; CT1–SCL90_1: $r = 0.55$, $p = 0.0002$), whereas no significant associations were observed in the healthy control group, indicating stronger coupling between components in participants with MDD.

Discussion and conclusion

This study highlights the potential of multimodal data fusion to uncover meaningful brain–symptom associations in major depressive disorder (MDD). Two components revealed co-varying changes between cortical morphometry and depression-dominant symptom profiles. Regions with the most pronounced progressive changes overlapped with those identified in ENIGMA's cross-sectional studies of adolescent and adult MDD. Associations between components were stronger in MDD than in controls, suggesting diagnosis-specific change patterns. However, factors such as symptom severity, treatment status, and illness duration, which may influence structural trajectories, were not considered yet. Overall, our findings support longitudinal multimodal data fusion as a tool for identifying associated structural and symptomatic changes in psychiatric populations.

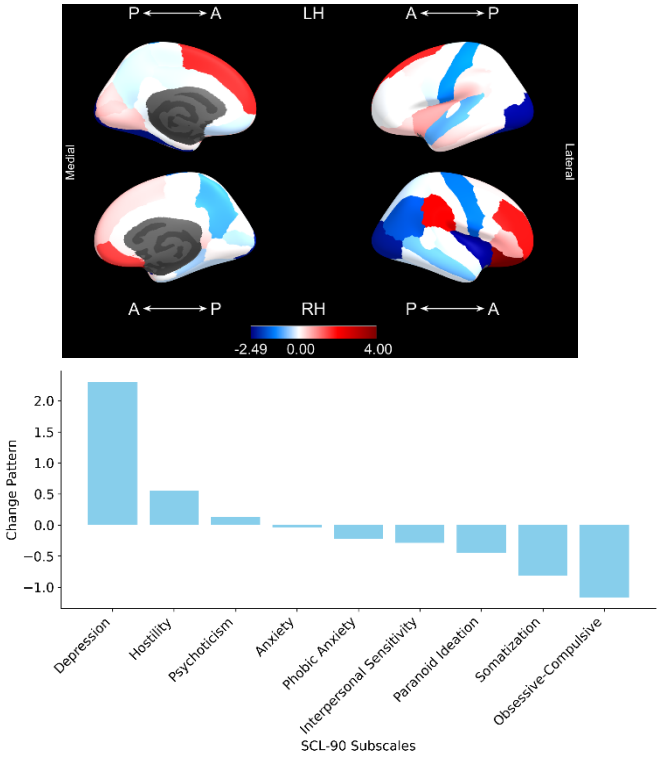

Figure 1: Spatial map of Surface Area Component 2 associated with SCL-90 Component 2.

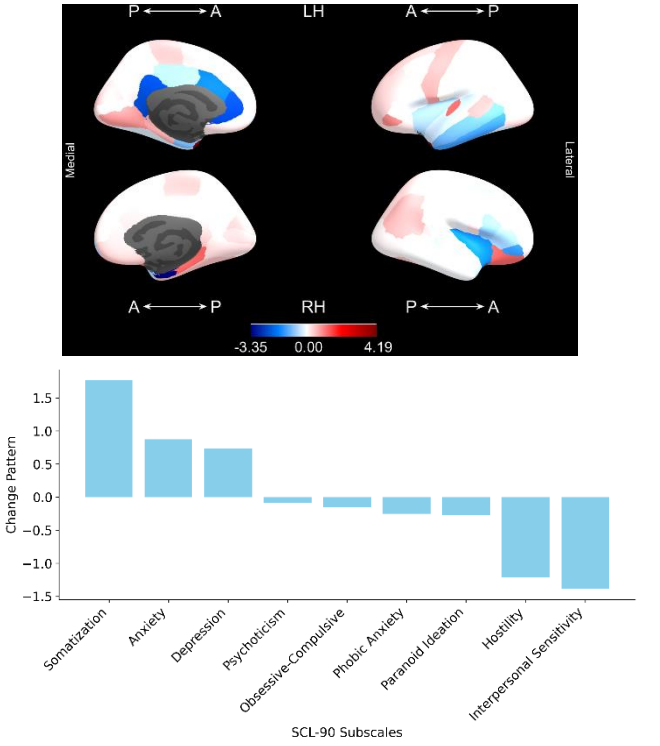

Figure 2: Spatial map of Cortical Thickness Component 1 associated with SCL-90 Component 1.

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