Altered structure-function coupling along with functional hierarchy in major depressive disorder

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Introduction

- Altered structural and functional networks have been extensively investigated in major depressive disorder (MDD). However, the results of relationships between structure and function were heterogeneous and unclear [1].
- Emerging evidence indicated that the structure-function relationship was not uniform in the brain.:
- Structure and function were closely aligned in the unimodal cortex (i.e. primary sensory and motor regions), while diverged in transmodal cortex (i.e. default mode networks) [2-3].
- **Aim:** exploring altered structure-function coupling from a hierarchical perspective along with the macroscale gradient.
- **Hypothesis**: the abnormality of structure-function coupling in MDD exhibited multiple patterns from low-level sensory networks to high-level transmodal networks.

Methods

Functional hierarchy:
Measurements: regional principal gradients

-Sample:
Resting-state fMRI of healthy populations from the Human Connectome Project (N=217, 56.22% female, mean+sd age = 28.5 ± 3.7).

-Parcellation: Schaefer seven-network atlas with 400 parcels and 18 subcortical regions from AAL.

-Diffusion map embedding:
- A group-averaged functional connectivity matrix was constructed, then thresholded, normalized, and decomposed.
- The first gradient component was the principal gradient.
- The gradient scores are used to rank the different networks across whole-brain.

Structure-Function Coupling:
-Sample:
Diffusion tensor imaging (DTI) and resting-state fMRI were obtained from 258 MDD participants and 99 healthy controls.

-Methods:
We assessed the structure-function coupling at the region level using the Spearman rank correlation between regional connectivity profiles of structural and functional networks.

We compared regional coupling between healthy controls and patients with MDD using the independent two-sample t-test or the Mann-Whitney test depending on data normality.

The normal distribution of structure-function coupling was measured by the Shapiro–Wilk test. False discovery rate (FDR) correction was applied for multiple comparison corrections.

Results

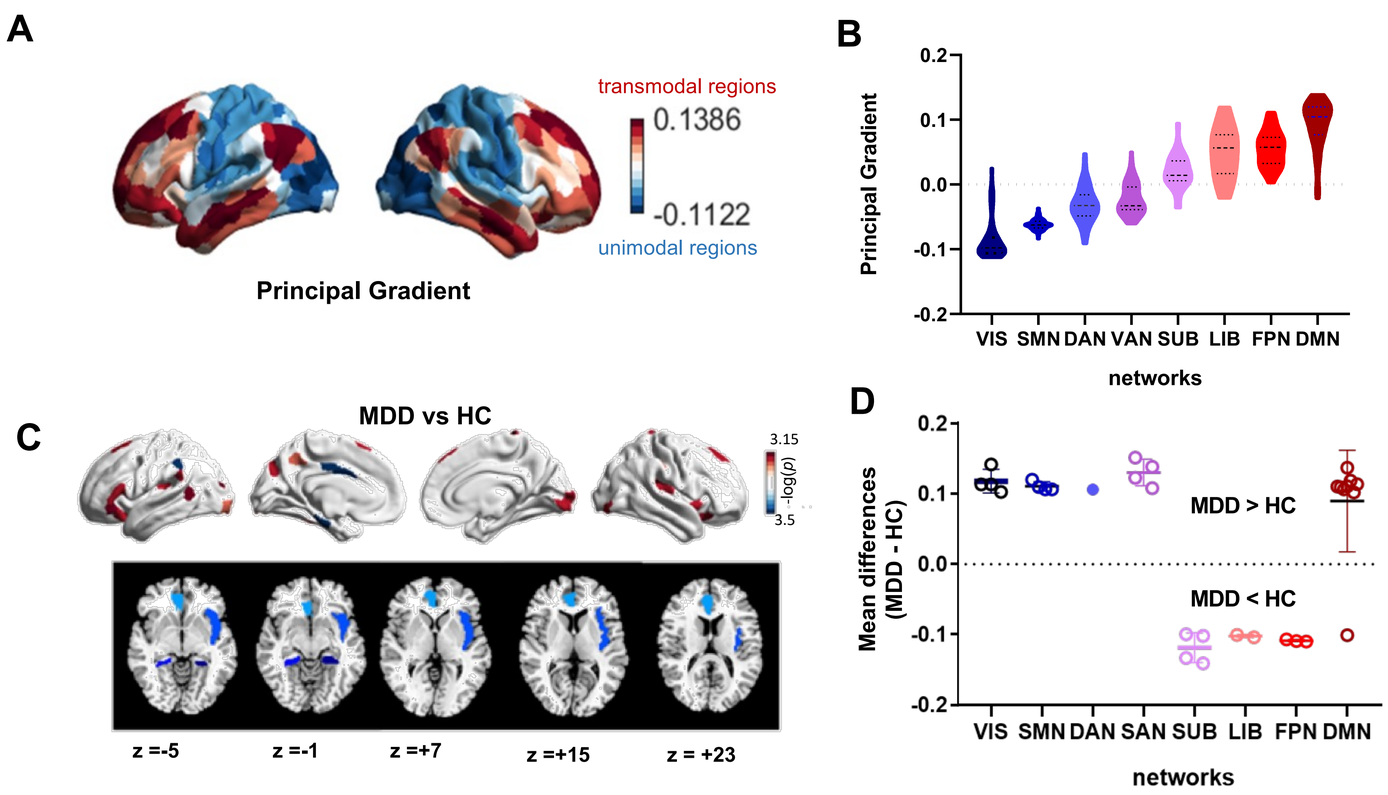

Figure 1. Principal gradients and regions with significant differences in structure-function coupling for MDD disruptions. (A) The principal gradient spans the whole brain. (B) Violin plot of the principal gradients across eight functional networks. (C) Cortical surface rendering and subcortical axial slices show regional significant differences between patients with MDD and healthy controls. The color bar is –log10 transformed *p*-value, where red indicates the higher coupling and blue indicates the lower coupling in MDD patients. (D) Scatter dot plot of mean differences (MDD minus HC) for abnormal patterns between patients with MDD and healthy controls among eight functional networks. Each dot indicates a significant region. The error bar is the standard deviation

Functional hierarchy:
- The first gradient accounted for 27.59% of variances and showed functional differentiation from visual and sensorimotor networks to default mode networks.
- The eight functional networks were ranked according to the increase of gradient values as follows (Figure B): visual network (VIS), sensorimotor network (SMN), dorsal attention network (DAN), ventral attention network (VAN), subcortical network (SUB), limbic network (LIB), front-parietal network (FPN), default mode network (DMN).

Structure-function coupling:
- There were 31 regions spanned eight networks showing significant differences between MDD and HC (Figure C). Above 31 significant regions were divided into their corresponding networks and then ranked these eight functional networks in ascending order of the principal gradient (Figure D).
- Two abnormal patterns across the whole brain: the increased patterns in low-level unimodal networks and the decreased patterns in high-level transmodal networks.
- DMN was a unique network with both increased and decreased abnormality.

Conclusions and discussion

Conclusions:
- Our results replicate the findings of functional gradient from unimodal to transmodal regions. We detected the MDD-induced impairments in structure-function coupling across the observed functional hierarchy (principal gradient).
- Our findings suggested that MDD-induced impairments in structure-function coupling exhibited diverge patterns along with the functional hierarchical axis.
- The increased couplings were found in low-level unimodal regions, while the decreased couplings were found in high-level transmodal regions.

Discussion:
In primary and sensory and visual areas:
- The higher consistency between structure and function suggested functional communication in these regions was more likely to rely on the status of local white-matter pathways in MDD.
- That may result from conserved structural configurations in unimodal sensory and motor areas. The primary visual and sensory regions have highly myelinated associations and stronger laminar differentiation [4].
- It is speculated that conserved regional structural profiles promote more rigid structural network configurations after being attacked, resulting in stronger statistical structure-function correlations.

In transmodal regions:
- Decreased correspondence between structural pathways and functional was also found in psychiatric disorders, such as bipolar disorders [5], and schizophrenia [6].
- The decreased coupling also suggested that functional communication was untethered by structural constraints in limbic systems and frontoparietal regions.
- Given the important role of these regions in emotional regulations and cognition, we speculate that less constrained functional communications in transmodal regions may represent the reduced structural capacity to integrate information, leading to the observed emotional symptoms and cognitive deficits.

References: [1] Scheepens, Dominique S., et al. "The link between structural and functional brain abnormalities in depression: a systematic review of Multimodal Neuroimaging Studies." Frontiers in psychiatry 11 (2020): 485. [2] Baum, Graham L., et al. "Development of structure–function coupling in human brain networks during youth." Proceedings of the National Academy of Sciences 117.1 (2020): 771-778. [3] Vázquez-Rodríguez, Bertha, et al. "Gradients of structure–function tethering across neocortex." Proceedings of the National Academy of Sciences 116.42 (2019): 21219-21227. [4] Paquola, Casey, et al. "Microstructural and functional gradients are increasingly dissociated in transmodal cortices." PLoS biology 17.5 (2019): e3000284. [5] Jiang, Haiteng, et al. "Structural–functional decoupling predicts suicide attempts in bipolar disorder patients with a current major depressive episode." Neuropsychopharmacology 45.10 (2020): 1735-1742. [6] Cocchi, Luca, et al. "Disruption of structure–function coupling in the schizophrenia connectome." NeuroImage: Clinical 4 (2014): 779-787.

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