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様式３

論　文　内　容　の　要　旨

氏　名　（SITI NURUL ZHAHARA）	
論文題名	Reduced functional connectome uniqueness on the whole brain and network levels as a clinically relevant and reproducible neuroimaging marker in major depressive disorder （うつ病における臨床的関連性および再現性を有する神経画像マーカーとしての、全脳およびネットワークレベルでの機能的コネクトーム独自性の低下）

論文内容の要旨

Major Depressive Disorder (MDD) is a debilitating condition that widely affects individuals in their productive age period. Despite numbers of studies in neuroimaging to understand its pathophysiology, MDD lacks reliable neurobiological markers, in part due to methodological heterogeneity across functional neuroimaging studies. Functional connectome (FC) uniqueness, an individual-level metric derived from brain fingerprinting, quantifies the distinctiveness of intrinsic connectivity patterns and offers a standardized, reproducible framework for biomarker discovery. In this study, multi-site resting-state fMRI data from 35 patients with MDD and 42 healthy controls (HC), each scanned twice across months to years, were analyzed using a harmonized preprocessing pipeline incorporating rigorous motion correction, denoising, and ComBat-GAM site harmonization. Individual connectomes were constructed using a 300-ROI atlas spanning 14 networks. FC uniqueness was defined as the ratio of self-similarity (calculated as Pearson correlation between connectomes from the same individual across different time points) to similarity-to-others (calculated as Pearson correlations between an individual's connectome and those of other participants at the next timepoint). FC uniqueness score more than one indicates successful individual identification and termed as fingerprinting accuracy.

Consistent with previous studies, fingerprinting accuracy was found highest at the whole-brain level followed by the default mode and frontoparietal networks in this study. Compared to HC, individuals with MDD showed significantly reduced FC uniqueness at both whole-brain and network levels, with the most pronounced reductions in frontoparietal and sensorimotor networks. Lower FC uniqueness was further associated with higher PHQ-9 and BDI-II scores, linking diminished connectome distinctiveness to greater symptom severity. Exploratory network-level analyses using FDR-controlled thresholds revealed medium-to-large effect sizes, supporting the robustness of these findings despite sample heterogeneity.

These results demonstrate that reduced FC uniqueness reflects altered neurobiological organization in MDD and represents a reproducible, clinically interpretable neuroimaging marker. This study represents an innovative research direction as it is the first to clinically validate FC uniqueness as a standardized, biologically grounded index with potential utility for diagnostic refinement, stratification, and future personalized interventions.

様式７

論文審査の結果の要旨及び担当者

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論文審査の結果の要旨

In this study, multi-site resting-state fMRI data from 35 patients with MDD and 42 healthy controls (HC), each scanned twice across months to years, were analyzed using a harmonized preprocessing pipeline incorporating rigorous motion correction, denoising, and ComBat-GAM site harmonization. Individual connectomes were constructed using a 300-ROI atlas spanning 14 networks. FC uniqueness was defined as the ratio of self-similarity (calculated as Pearson correlation between connectomes from the same individual across different time points) to similarity-to-others (calculated as Pearson correlations between an individual's connectome and those of other participants at the next timepoint). FC uniqueness score more than one indicates successful individual identification and termed as fingerprinting accuracy.

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