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NEUROANATOMICAL DEVIATIONS IN SCHIZOPHRENIA: A NORMATIVE MODELING APPROACH

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BACKGROUND AND AIM: Schizophrenia is linked to widespread structural brain abnormalities, but individual variability complicates their characterization. Traditional case-control studies show group-level differences but miss personalized deviations. Normative modeling refines this by establishing a reference brain structure distribution in healthy individuals and identifying patient-specific deviations. This approach helps detect neuroanatomical abnormalities at the individual level and reveals schizophrenia subtypes based on structural variation. By comparing patient data to a normative model, we can assess significant changes in volume, cortical thickness, or surface area, offering insights into schizophrenia's pathophysiology.

METHODS: Structural MRI data from 92 schizophrenia patients (mean age: 38.3±9.5 years; 69.6% male) were analyzed using a centile brain-based normative model. MRI preprocessing was performed using FreeSurferv7.4.1, following standard ENIGMA pipeline recommendations. Deviations were classified as either supranormal (increased volume or thickness) or infranormal (reduced volume or thickness), with thresholds set at Z-scores of 1.96(supranormal) and -1.96 (infranormal). The frequency and distribution of these deviations were assessed across multiple brain regions. We utilized the open-access ENIGMA Centile Brain Group's normative model for comparison. The study was approved by Ege University Ethics Committee (approval number: 19-12T/42, approval date: 11.12.2019; additional ethics committee clarification approval: 24-3T/89, approval date: 13.03.2024)

RESULTS: The most pronounced deviations were observed in the pallidum(right), accumbens (left), and frontal pole (left). Specifically, the right pallidum (Rpal) exhibited the highest rate of supranormal deviations (32.6%), indicating increased volume compared to the normative model. Conversely, the left accumbens (Laccumb) showed the highest rate of infranormal deviations (31.5%), reflecting reduced volume. Additionally, the left pallidum (Lpal) and left frontal pole exhibited significant supranormal deviations (25%), while the right thalamus (Rthal) also showed notable supranormal deviations (14.1%).

CONCLUSIONS: These findings highlight distinct neuroanatomical deviations in schizophrenia, particularly in subcortical structures associated with motor and cognitive processing. The observed supranormal increases in the pallidum and thalamus, alongside infranormal reductions in the accumbens, suggest potential alterations in basal ganglia and limbic system function. Further research is needed to explore the clinical implications of these structural changes in schizophrenia.

Keywords: Schizophrenia, normative modeling, structural MRI, basal ganglia, neuroanatomical deviations