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EXTRAPYRAMIDAL SYMPTOM SEVERITY ACROSS NEUROANATOMICAL SUBTYPES OF SCHIZOPHRENIA IDENTIFIED BY MACHINE LEARNING

Ibrahim Sungur, Simay Selek, Gozde Bildircin, Ali Saffet Gonul

SoCAT Lab, Psychiatry, Ege University, Izmir, Türkiye

BACKGROUND AND AIM: Machine-learning approaches have identified distinct neuroanatomical subtypes of schizophrenia. However, the clinical relevance of these subtypes for extrapyramidal symptoms (EPS) has received limited attention. Given the role of basal ganglia circuits in EPS, examining EPS across neuroanatomical subtypes may provide translational insight. Based on schizophrenia subtypes derived using the HYDRA (Heterogeneity Through Discriminative Analysis) algorithm, we compared EPS across two neuroanatomical subtypes.

METHODS: (Ethics Committee Approval must be obtained and the number should be specified). Structural MRI data from 222 participants (136 schizophrenia; 86 healthy controls) were analysed. Two HYDRA-defined schizophrenia subtypes were examined: Subtype 1 with cortical atrophy (n=75) and Subtype 2 with preserved cortical morphology and enlarged subcortical volumes (n=61). EPS were assessed using the Extrapyramidal Symptom Rating Scale (ESRS). Demographic, clinical, and ESRS scores were compared using the Mann–Whitney U test. EPS severity was analysed using linear regression models with log-transformed ESRS scores, adjusting for age, sex, chlorpromazine-equivalent dose, and subtype. Additional region-of-interest analyses examined bilateral volumes of the putamen, pallidum, caudate, and nucleus accumbens in separate models adjusted for age, sex, chlorpromazine-equivalent dose, total intracranial volume, and subtype. Ege University Ethics Committee approval number: 19–12T/42.

RESULTS: ESRS scores were available for 108 of 136 patients (79.4%), and availability did not differ between subtypes (Subtype 1 vs 2: 84.0% vs 73.8%; p=0.142). Subtypes were comparable in demographic and clinical characteristics. ESRS total scores were significantly higher in Subtype 1 than Subtype 2 (median: 8 vs 5; U=1000.5, p=0.009).

EPS prevalence did not differ significantly between Subtype 1 and Subtype 2 (93.7% vs 82.2%; p=0.062). In linear regression analyses, subtype remained independently associated with ESRS severity (Subtype 2 vs 1: β=-0.41, p=0.019), and age showed a positive association with ESRS severity (β=0.01, p=0.037). No basal ganglia structures were associated with ESRS (p>0.05).

CONCLUSIONS: Neuroanatomical subtypes of schizophrenia differed in EPS severity. This difference, independent of antipsychotic dose and basal ganglia volumes, suggests subtype-specific vulnerability of motor circuits.

Keywords: Extrapyramidal system, machine learning, neuroimaging, schizophrenia, structural magnetic resonance imaging, subtypes