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Neurite-Localized mRNA Transport Genetics Shapes Clinical and Brain Features in Schizophrenia

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Introduction: Advances in psychiatric genetics link synaptic plasticity to schizophrenia (SZ), though specific mechanisms remain unclear. This process depends on rapid molecular regulation, where mRNA transport from soma to synapses via neurites plays a key role. Studying mRNAs localized in neurites may provide new insights into the involvement of mRNA transport and availability regulation processes in SZ.
Objectives: We aimed: i) to calculate the SZ polygenic risk score based on neurite-localized transcripts and compare it between healthy controls and SZ patients; and, ii) to test its association with clinical variables and brain structure.
Methods: We selected 70 neurite-localized transcripts, consistently identified in more than 15 transcriptomic studies comparing soma and neurite content (von Kügelgen et al., 2020). In a sample of 115 controls and 169 patients with SZ, we calculated the polygenic risk score (PRS) using PRSet, grouping SNPs near these transcripts (±10 kb). The resulting PRS (nPRS) was evaluated in relation to diagnosis, clinical variables (age at onset and PANSS scores), and brain structural measures (cortical surface area and thickness).
Results: The nPRS did not differ between patients and controls, but it was associated with age at onset (β=5158.09, SE=2518.78, p=0.04) and showed a trend with the positive PANSS dimension scores (β=–4110.00, SE=2303.00, p=0.08). Additionally, an association was also observed between the nPRS and the surface area of the left frontal pole (β=39,800; SE=9,373; t=4.243; p<0.001) in patients.
Conclusions: Our data suggest that the genetic load associated with neurite-localized mRNAs is related to clinical and brain features of SZ, supporting the hypothesis that transcript transport and regulation mechanisms play a relevant role in its pathophysiology.
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Geriatric depression and white matter hyperintensities in Alzheimer's disease

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Introduction: White matter hyperintensities (WMHs) in magnetic resonance imaging (MRI) scans are age related but appear to be more prevalent in depressed patients.
Objectives: We aimed to assess whether WMHs are associated with depressive symptoms and physical performance in Alzheimer`s disease(AD)
Methods: One hundred twenty one
AD who visited the Psychiatriy department of Jeju National University Hospital underwent MRI scans. The volume of WMHs was quantified using Lesion Segmentation Toolbox (LST) which allows the performance of accurate brain tissue volume measurements without any kind of manual intervention. After then, for the volume of WMHs, we used a logarithmic transformation to produce normally distributed data. Subjects were assessed for depressive symptoms (GDS-15), cognitive (CERAD-K) and physical (muscle mass index, grip strength, gait speed and timed up and go test) functions. Korean Frailty Index (K-FI) also performed.
Results: WMHs of presumed vascular origin, also referred to as leukoaraiosis, are a very common finding on brain MRI or computed tomography (CT) in older subjects. Most recent studies have shown that WMHs are associated with a host of poor outcomes, including cognitive impairment, depression, gait disturbance and increased risk of death. Thus, it is important to determine the impact of WMHs on mood, physical and cognitive function in AD. In 121 subjects, the mean age was 80.6±7.7.
After analysis, we found that the degree of WMHs was associated with higher depression scores after controlling for age, sex, sum of box and estimated total intracranial volume(p=0.023). Gait speed(p<0.001), timed up and go test(p=0.02), and FI(p=0.002) were significantly associated with the degree of WMHs, though not cognitive function assessed by CERAD-K.
Conclusions: In AD, the degree of WMHs was associated with depressive symptoms as well as gait and balance impairment, though not cognitive function. However, there were further study is required to identify the association between WMHs and other variables.

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