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Letter to the Editor

Comments on Callosal Morphometry in Juvenile Myoclonic Epilepsy: Fronto-Thalamocortical Network Dysfunctions and Methodological Insights

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Dear Editor,

I read with great interest the study by Eğilmez and Keskin Güler[1] evaluating regional corpus callosum morphometry in juvenile myoclonic epilepsy (JME). The authors report a selective reduction in callosal genu thickness in JME patients compared with healthy controls, along with secondary morphometric variations associated with biological sex and antiseizure medication regimens.[1]

The finding of isolated thinning of the callosal genu, without significant correlation to disease duration, age at onset, or seizure frequency, aligns compellingly with the paradigm of JME as a neurodevelopmental system disorder driven by aberrations in fronto-thalamocortical networks.[2] Rigorous voxel-wise meta-analyses and quantitative neuroimaging consistently confirm structural gray and white matter alterations within thalamocortical loops interconnecting the anterior thalamus, prefrontal cortex, and supplementary motor area.[3,4] The callosal genu serves as the primary commissural bridge interconnecting homologous prefrontal cortices. Consequently, isolated genu thinning likely represents a primary neurodevelopmental trait—characterized by altered white matter microarchitecture and transcallosal axonal guidance—rather than a secondary degenerative injury resulting from recurrent seizures.[2] Furthermore, cutting-edge translational evidence reveals that regional fronto-cortical gray matter alterations in JME tightly map onto specific neurotransmitter receptor profiles and spatial transcriptomic signatures.[5] This novel molecular framework demonstrates how genetically governed neurodevelopmental network disruption underpins both thalamocortical hyperexcitability and executive cognitive dysfunction in JME.

To rigorously determine whether subtle 2D callosal changes reflect intrinsic fronto-thalamocortical pathology, key methodological factors warrant careful consideration. First, planar measurements of callosal dimensions, particularly the anterior-posterior diameter, scale directly with total intracranial volume (TIV).[1] If linear parameters are not adjusted for TIV or the total midsagittal brain area, observed sex differences cannot be distinguished from physiological cranial dimorphism.[1] Second, analyses of morphometric variations between monotherapy and polytherapy cohorts must account for clinical indication bias.[1] Patients requiring broad-spectrum polytherapy typically present with greater baseline network hyperexcitability or treatment resistance, necessitating multivariable regression models to decouple drug effects from intrinsic disease severity.[1] Finally, complementing 2D manual planar measurements with automated 3D volumetric tractography or diffusion tensor imaging will enhance measurement reproducibility and provide deeper microstructural resolution of prefrontal transcallosal fibers.

Regional callosal morphometry provides valuable structural evidence of fronto-thalamocortical commissural involvement in JME.[1] Incorporating intracranial volume normalization, multivariable risk-adjustment models, and transcriptomic-imaging correlations within prospective cohorts will be critical for determining whether callosal genu metrics can serve as objective structural biomarkers for clinical risk stratification in JME.

Footnotes

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