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Genome-Wide Architecture of East Asian Patients With Migraine: A Genome-Wide Association Study Based on Familial History

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The demand for genetic research into neurological disorders is increasing as personalized medicine becomes more important. A genome-wide association study (GWAS), one of the most common tools used in genetic research, facilitates both the elucidation of genetic pathogenesis and the development of novel treatments. As migraine is often hereditary (heritability of 30%−60%), genetics is considered vital in its pathogenesis.[1] The authors of this article conducted a GWAS in patients with migraine disorder based on their clinical and familial history.[2] The study population comprised 1,561 individuals with migraine and 473 without from a Taiwanese tertiary institution. This was the largest GWAS conducted in East Asia.

The authors especially focused on the association between single-nucleotide polymorphisms and the familial history of migraine, which has been investigated in few previous studies. Mendelian migraine disorders, typically known as familial hemiplegic migraine, are primarily monogenic and rare, and caused by mutations in genes such as *CACNA1A*, *ATP1A2*, and *SCN1A*.[1] However, non-Mendelian migraine is more common, and exhibits a polygenic architecture with multiple gene variations that contribute to susceptibility.[1] GWASs have recently contributed to delineating the polygenic architecture of several diseases. Two large-scale GWAS meta-analyses in 2022 and 2023 revealed more than 100 loci associated with migraine disorder; however, a subgroup analysis was not conducted on familial history.[3] The authors discovered two novel loci, adjacent to *DDX1* and *ELMO1*, associated with familial history in all patients with migraine.[2] Subgroup analysis of migraine groups revealed several novel loci related to environmental stress responses, neurodegenerative disease, inflammation, and neoplasms. In particular, rs117958200, located downstream of *MESP2*, significantly affected episodic migraine and migraine-without-aura groups, but its biological implications should be investigated further.

The population composition was notable in that there was considerable genetic discrepancy between ethnicities. The 1000 Genomes Project demonstrated the difference in genetic composition between ancestries by presenting the discordance of novel variants across them.[4] However, since most of the GWAS data were from European ancestry, the prediction accuracy of polygenic risk score was highly imprecise for East Asians compared with Europeans.[5] Two Taiwanese GWASs in 2018 and 2021 revealed novel loci related to migraine disorders that did not overlap those from the European population.[6] Given that GWAS data are the source of the polygenic risk score in disease prediction and Mendelian randomization for causal inference, this study was noteworthy as it included a larger East Asian population than in previous studies.

The authors performed a GWAS based on familial history of migraine by collecting familial information and performed subgroup analyses according to migraine disorder subtypes. Moreover, the study included the largest East Asian population, allowing for the elucidation

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of polygenic architecture and further post-GWAS analysis specific to this ancestry. Given the significant burden on modern society caused by migraine, this study was essential to advancing our understanding and treatment of migraine disorders.[7]

Availability of Data and Material

Data sharing not applicable to this article as no datasets were generated or analyzed during the study.

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Conflicts of Interest

Chu MK was the site investigator for a multicenter trial sponsored by Biohaven Pharmaceuticals, Allergan Korea, and the Ildong Pharmaceutical Company. Additionally, Chu MK has received lecture honoraria from Eli Lilly and Company, Handok-Teva, and the Ildong Pharmaceutical Company over the past 24 months; grants from the Yonsei University College of Medicine (6-2021-0229) and the Korea Health Industry Development Institute (KHIDI) (HV22C0106); and an NRF grant from the Korean government (MSIT) (2022R1A2C1091767). The other authors have no conflicts of interest to declare.

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