GBA and APOE $\epsilon 4$ associate with sporadic dementia with Lewy bodies in European genome wide association study

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Résumé

Dementia with Lewy Bodies (DLB) is a common neurodegenerative disorder with poor prognosis and mainly unknown pathophysiology. Heritability estimates exceed 30% but few genetic risk variants have been identified. Here we investigated common genetic variants associated with DLB in a large European multisite sample. We performed a genome wide association study in European cohorts of 720 DLB cases and 6490 controls and included 19 top-associated single-nucleotide polymorphisms in an additional cohort of 108 DLB cases and 75545 controls from Iceland. Overall the study included 828 DLB cases and 82035 controls. Variants in the ASH1L/GBA (Chr1q22) and APOE $\epsilon 4$ (Chr19) loci were associated with DLB surpassing the genome-wide significance threshold ($p< 5\times10\text{-}8$). One additional genetic locus previously linked to psychosis in Alzheimer's disease, ZFPM1 (Chr16q24.2), showed suggestive association with DLB at p-value$< 1\times10\text{-}6$. We report two susceptibility loci for DLB at genome-wide significance, providing insight into etiological factors. These findings highlight the complex relationship between the genetic architecture of DLB and other neurodegenerative disorders.

Mots-Clés: Cryo EM, atomic structure, alpha synuclein, Lewy body, human brain

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