Blood-brain barrier transcytosis genes, risk of dementia and stroke - A prospective cohort study of 74,754 individuals

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Background

Nearly 50 million people are affected by dementias worldwide. Clinically, Alzheimer's disease often coexists with cerebral vascular diseases, and the major pathological hallmark of Alzheimer's disease is accumulation of amyloid- β in the brain and in cerebral vessels.

Objective

To test whether genetic variants in *PICALM*, *BIN1*, *CD2AP*, and *RIN3* - suggested to be involved in blood-brain barrier amyloid- β transcytosis pathways - associate with dementia and stroke and whether such associations are independent of the strong $\epsilon 4$ *APOE* risk allele.

Methods

74,754 individuals from the Copenhagen General Population Study and the Copenhagen City Heart Study. Mean follow-up was 10 years.

Conclusion

Genetic variants in *PICALM*, *BIN1*, *CD2AP*, and *RIN3* are associated with increased risk of all-cause dementia, Alzheimer's disease, and vascular dementia independent of the *APOE* $\epsilon 4$ allele, but do not seem to associate with stroke. These findings may suggest that clathrin-mediated endocytosis in clearance of amyloid- β across the blood-brain barrier is important for the integrity of both brain tissue and cerebral vessels.

Results