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IN BRIEF

HEADACHE

Norwegian study identifies headache as a risk factor for vascular dementia

A prospective, population-based study involving a cohort of 51,383 individuals from Norway has provided evidence that headache is a risk factor for vascular dementia (VaD) and mixed dementia, but not for Alzheimer disease (AD). The study examined the relationship between headache status (headache-free, any headache, migraine, or nonmigrainous headache) and later development of dementia in participants enrolled in the Nord-Trøndelag Health Study. The researchers found that compared with headache-free individuals, those with any headache at baseline demonstrated a twofold or greater risk of developing VaD or mixed dementia. By contrast, no association was observed between any headache and the risk of developing AD.

Original article Hagen, K. *et al.* Headache as a risk factor for dementia: a prospective population-based study. *Cephalalgia* doi:10.1177/0333102413513181

NEURODEGENERATIVE DISEASE

Histone deacetylase 4 promotes cytoplasmic huntingtin aggregation in mouse models of Huntington disease

In the brains of mice with Huntington disease (HD), the transcriptional repressor histone deacetylase 4 (HDAC4) colocalizes with mutant huntingtin to form cytoplasmic inclusions, according to research reported in *PLoS Biology*. Mielcarek *et al.* found that an HDAC4 knock-down in these animals delayed the formation of these inclusions without affecting global transcriptional regulation or nuclear huntingtin aggregation. The knock-down also restored neuronal and synaptic function, ameliorated neurological impairments, and increased survival times. The researchers conclude that HDAC4 could represent a new target for small-molecule therapeutics in HD.

Original article Mielcarek, M. *et al.* HDAC4 reduction: a novel therapeutic strategy to target cytoplasmic huntingtin and ameliorate neurodegeneration. *PLoS Biol.* **11**, e1001717 (2013)

ALZHEIMER DISEASE

Primate study deals a fresh blow to the peripheral sink hypothesis

The peripheral sink hypothesis—the idea that levels of soluble amyloid- β (A β) in the brain and the periphery are in equilibrium, such that peripheral depletion of A β should lead to removal of A β from the brain—has prompted preclinical trials of A β -degrading agents. The results to date, however, have been disappointing: one study reported in early 2013 showed that brain levels of A β remained unchanged in a mouse model of AD after treatment with the A β -degrading protease neprilysin. A new study has extended these findings to rats and monkeys. After 1 month of treatment with neprilysin in these animals, peripheral A β levels were substantially decreased, but brain and cerebrospinal fluid levels were unaffected. The authors suggest that these findings invalidate the peripheral sink hypothesis.

Original article Henderson, S. J. *et al.* Sustained peripheral depletion of amyloid- β with a novel form of neprilysin does not affect central levels of amyloid- β . *Brain* doi:10.1093/brain/awt308

Further reading Walker, J. R. *et al.* Enhanced proteolytic clearance of plasma A β by peripherally administered neprilysin does not result in reduced levels of brain A β in mice. *J. Neurosci.* **33**, 2457–2464 (2013)