RESEARCH HIGHLIGHTS

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IN BRIEF

MOTOR NEURON DISEASE

Detection of glycine-proline repeat protein offers new biomarker in patients with *C9orf72* expansion

The discovery of a G_4C_2 repeat expansion in C9orf72 as the most common known cause of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia prompted investigation into new therapies that target the aberrant RNA and protein molecules synthesized from the repeat. However, biomarkers that enable the efficacy of such treatments to be monitored are lacking. A new study has shown that the glycine-proline (poly(GP)) peptides translated from the repeats can be detected in the cerebrospinal fluid of individuals with the expansion, both before and after symptom onset. Researchers administered antisense oligonucleotides (ASOs) that target and reduce the levels of G_4C_2 RNA to cells from patients with the expansion and to a mouse model of C9orf72 ALS. The ASO treatment was associated with decreased intracellular and extracellular levels of poly(GP) proteins. The results indicate that poly(GP) levels could be used as a biomarker to assess the efficacy of therapies in patients with C9orf72 ALS.

ORIGINAL ARTICLE Gendron, T. F. *et al.* Poly(GP) proteins are a useful pharmacodynamic marker for C9orf72-associated amyotrophic lateral sclerosis. *Sci. Transl. Med.* **9**, eaai7866 (2017)

MULTIPLE SCLEROSIS

Perinatal risk factors for paediatric MS

A new study has revealed novel environmental risk factors for paediatric-onset multiple sclerosis (MS) that seem to act in the perinatal period. The team studied 265 individuals with paediatric MS and 412 healthy controls, and found that illness of the mother during pregnancy was associated with a 2.3-fold increase in the risk of MS in the offspring. By contrast, caesarean delivery was associated with a 60% reduction in MS risk. The researchers also found an association between paediatric-onset MS and pesticide exposure: the offspring of fathers with a gardening-related occupation had a 2.8-fold increase in MS risk, and use of pesticide products in the household yielded a 1.7-fold increase in the risk of MS. The investigators note that more research is required to characterize the part played by these factors in MS pathogenesis.

ORIGINAL ARTICLE Graves, J. S. et al. Maternal and perinatal exposures are associated with risk for pediatric-onset multiple sclerosis. *Pediatrics* <u>http://dx.doi.org/10.1542/</u>peds.2016-2838 (2017)

STROKE

Cortical superficial siderosis absent in CADASIL

Cortical superficial siderosis (cSS) is known to be an imaging feature of cerebral amyloid angiopathy (CAA), and has prognostic relevance in patients with this condition. However, the relevance of this marker in other forms of small vessel disease is unclear. In a recent study, investigators carried out MRI in 364 patients with CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy), 100 patients with CAA, and 372 healthy controls. Most imaging features, including white matter hyperintensities and cerebral microbleeds, were similar in the CADASIL and CAA patients, but cSS was only found in the patients with CAA. This finding suggests that the presence of cSS is strongly indicative of CAA in individuals with other features of small vessel disease.

ORIGINAL ARTICLE Wollenweber, F. A. *et al.* Cortical superficial siderosis in different types of cerebral small vessel disease. Stroke <u>http://dx.doi.org/10.1161/STROKEAHA.</u> <u>117.016833</u> (2017)