

AAIC 2020

SARS-CoV-2 and the brain to be studied long-term

An ambitious research study to investigate the long-term impact of exposure to SARS-CoV-2 on the brain was announced at the Alzheimer's Association international conference (AAIC) 2020 (27–31 July 2020, online).

Although SARS-CoV-2 infection predominantly causes respiratory symptoms, an increasing number of reports suggest that the virus can also affect the CNS. The new study, known as the Alzheimer's Association international cohort study of chronic neurological sequelae of SARS-CoV-2, will be led by researchers at the Alzheimer's Association US and the University of Texas Health San Antonio, and will involve >50 centres across >30 countries. The project will also receive technical guidance from the WHO.

"To build a strong foundation for this research, we will align with existing studies — such as the Framingham Heart Study — and clinicians from around the world on how the data is measured and collected," explained Maria Carrillo, the Chief Science Officer at the Alzheimer's Association US. "To better understand the impact of the virus on the brain, we will consider cross-study collaborations."

Further details of the study were given by Gabriel De Erausquin, a Professor at the University of Texas Health San Antonio. Multiple cohorts that include individuals who have been exposed to SARS-CoV-2 and those who have not will be established by sampling three independent data sources — health registries, hospital discharge records and pre-existing research cohorts. A key focus of the study will be to investigate the influence of factors such as genetic variation, cultural differences and health disparities on the neuropsychiatric sequelae of COVID-19.

Enrolled individuals will be assessed within 6 months of recovery from COVID-19 and a follow-up assessment will be carried out after a further 12 months. Carrillo indicated that the researchers hope to present initial results at the AAIC conference in 2021.

Sarah Lemprière

RELATED ARTICLE Wood, H. New insights into the neurological effects of COVID-19. *Nat. Rev. Neurol.* **16**, 403 (2020)

MULTIPLE SCLEROSIS

TREM2 activation promotes remyelination

Activation of the microglial protein TREM2 could represent a novel therapeutic approach for demyelinating diseases such as multiple sclerosis (MS), new research published in *Acta Neuropathologica* suggests. In a mouse model of CNS demyelination, Laura Piccio and colleagues found that a TREM2-activating monoclonal antibody (mAb) increased the clearance of myelin debris and promoted remyelination.

"We previously demonstrated a key role for TREM2 in the activation and proliferation of microglia in an experimental model of CNS demyelination that mimics MS," explains Piccio. "In this model, mice that were genetically deficient for TREM2 showed severely reduced microgliosis and increased accumulation of myelin debris."

In post-mortem brain tissue samples from people with MS, the researchers found high levels of TREM2 expression on myelin-laden phagocytic cells in active demyelinating lesions. *Trem2*-haploinsufficient (*Trem2*^{+/-}) mice showed reduced clearance of myelin debris following treatment with cuprizone (CPZ), which induces demyelination. Taken together, these

findings suggested a role for TREM2 in myelin phagocytosis.

The team tested a newly developed TREM2 agonistic mAb, known as AL002a, in *Trem2*^{+/-} mice that had been treated with CPZ. Intraperitoneal administration of AL002a increased the clearance of myelin debris from demyelinating lesions and also promoted the formation of new myelin and the preservation of axonal integrity.

"The continuation of this study will be to develop a treatment that could activate TREM2 in humans and eventually to test it in clinical trials in people with MS," concludes Piccio. "Currently, we are focusing on studying the mechanisms through which TREM2 exerts its key functions in microglia and identifying the molecules that couple with TREM2 to mediate the effects that we have observed."

Heather Wood

ORIGINAL ARTICLE Cignarella, F. et al. TREM2 activation on microglia promotes myelin debris clearance and remyelination in a model of multiple sclerosis. *Acta Neuropathol.* <https://doi.org/10.1007/s00401-020-02193-z> (2020)

RELATED ARTICLE Ulland, T. K. & Colonna, M. TREM2 — a key player in microglial biology and Alzheimer disease. *Nat. Rev. Neurol.* **14**, 667–675 (2018)

AAIC 2020

Highlights from the first virtual AAIC

New findings reported at the Alzheimer's Association International Conference (AAIC) 2020 (27–31 July 2020, online) suggest that modifiable dementia risk factors are present at multiple life stages. The results were presented as part of the first virtual AAIC, which included more than 3,000 scientific presentations given via an online platform.

New data presented at the conference included the results of two studies that found an association between receiving a flu or a pneumonia vaccine and a lower risk of developing Alzheimer disease (AD). In the first study, Albert Amran and colleagues analysed the health records of 9,066 individuals and found a reduced prevalence of AD among individuals who had received at least one flu vaccination. In the second study, led by Svetlana Ukraintseva, receiving a pneumonia vaccination between 65–75 years of age was associated with a 25–30% reduction in AD risk.

Also presented for the first time at the AAIC were data from two studies that investigated the effects of early adulthood risk factors on prevalence of dementia. In one study, Kristen

George and colleagues found that in a study population of more than 714 individuals, having diabetes, high blood pressure or two or more heart health risk factors in adolescence, young adulthood or midlife was associated with worse cognition in later life.

Adina Zeki Al Hazzouri and colleagues investigated the associations between early-life BMI and dementia risk in 5,104 older adults from multiple cohorts. Compared with individuals who had a healthy BMI in early adulthood, individuals who were obese during this stage of life had a 2.5-fold greater risk of developing dementia.

"These new findings reported at AAIC 2020 make an even stronger case for the potential of behavioural interventions throughout life to reduce risk of AD and other dementias," said Maria Carrillo, the Alzheimer's Association's chief science officer.

Sarah Lemprière

RELATED ARTICLES Itzhaki, R. F. et al. Do infections have a role in the pathogenesis of Alzheimer disease? *Nat. Rev. Neurol.* **16**, 193–197 (2020) | Kivipelto, M. et al. Lifestyle interventions to prevent cognitive impairment, dementia and Alzheimer disease. *Nat. Rev. Neurol.* **14**, 653–666 (2018)