PRESS RELEASE

Brain microstructural damage related to cognitive dysfunction and steroid medication in lupus patients – NUS study

Further research hopes to see if adjustment in steroid dosage and reduction of free water in brain white matter would alleviate cognitive dysfunction

Singapore, 16 September 2021 — Systemic lupus erythematosus (SLE) is an autoimmune disease in which the immune system attacks the body's own tissues, causing widespread inflammation and damage in the affected organs. It can affect the joints, skin, brain, lungs, kidneys, and blood vessels. Asian SLE patients suffer from more severe disease and damage compared to patients in western countries.

In Singapore, the prevalence of childhood SLE has been reported to be 14.2 per 100,000 children, while that of adult SLE is 40 per 100,000 adult population. Cognitive dysfunction is common in patients with SLE. Earlier studies have shown that 25% of SLE patients were found to have cognitive dysfunction, compared to 7.3% in age- and gender-matched healthy individuals. Common cognitive dysfunction demonstrated by SLE patients includes impairment of simple reaction time, sustained and selected attention, memory search, working memory, and short-term memory for learnt associations, which result in reduced health-related quality of life and a negative impact on vocational capability.

The neural mechanism leading to cognitive dysfunction in patients with SLE remains unknown. Researchers at the NUS Yong Loo Lin School of Medicine attempted to unravel such mechanisms by adopting non-invasive diffusion magnetic resonance imaging (MRI) to study the brains of SLE patients, particularly the white matter, coupled with computerised neuropsychological assessment. White matter lies beneath the grey matter cortex in the human brain and comprises millions of bundles of nerve fibres that transmit signals to different brain regions.

Led jointly by **Associate Professor Juan Helen Zhou**, from the Centre for Sleep and Cognition and Deputy Director for the Centre for Translational Magnetic Resonance Research at NUS Medicine, and **Associate Professor Anselm Mak**, a clinician scientist with the Division of Rheumatology at the Department of Medicine, the group investigated brain white matter free water changes in SLE. White matter free water refers to water molecules surrounding white matter in the brain that are able to diffuse unhindered

In the paper published in *Rheumatology*, a Tier 1 journal in the field of Rheumatology with the Oxford University Press, they compared the free-water signals in SLE patients without clinically overt neuropsychiatric manifestations with a group of matched healthy participants using the novel free water diffusion MRI technique. They discovered that patients with SLE had significantly higher white matter free water than their healthy counterparts, suggesting possible microvascular degradation and/or inflammation. Such increases in free water were

significantly related to cognitive dysfunction, especially sustained attention, as well as cumulative dosage of medical steroids.

“The clinical implications of the study would indicate to physicians that steroids should be judiciously prescribed, aiming for the lowest possible dose for the shortest possible duration. While systemic use of steroids will continue to be the mainstay of treatment for moderate to severe SLE-related inflammation, there are other therapeutic options that could produce similar results: these should be considered first in order to reduce steroid use or shorten the necessary course,” said Assoc Prof Anselm Mak.

He also added that there are other SLE manifestations that could be symptomatically treated without the prescription of steroids. For example, non-steroidal anti-inflammatory drugs could be used for milder inflammation, topical treatment for hair loss and topical analgesics for oral ulcers.

SLE patients on long-term steroid treatments should also be regularly assessed and monitored for cognitive dysfunction. The researchers noted that the use of the Automated Neuropsychiatric Assessment Matrix (ANAM), which has been validated for use in adult and paediatric SLE patients, is an efficient and effective tool for these regular evaluations.

Further research will have to be conducted to find out if a reduction of steroid dosage would be related to reduction of white matter free water that would lead to an improvement to cognitive function in SLE patients. The team is also keen to further investigate the mechanism of the increase in white matter free water underlying cognitive decline using multimodal imaging, behavioral, and blood assays in SLE patients longitudinally.

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Our multidisciplinary and real-world approach to education, research and entrepreneurship enables us to work closely with industry, governments and academia to address crucial and complex issues relevant to Asia and the world. Researchers in our faculties, 30 university-level research institutes, research centres of excellence and corporate labs focus on themes that include energy; environmental and urban sustainability; treatment and prevention of diseases; active ageing; advanced materials; risk management and resilience of financial systems; Asian studies; and Smart Nation capabilities such as artificial intelligence, data science, operations research and cybersecurity.

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In our pursuit of health for all, our strategic research programmes focus on innovative, cutting-edge biomedical research with collaborators around the world to deliver high impact solutions to benefit human lives.

The School is the oldest institution of higher learning in the National University of Singapore and a founding institutional member of the National University Health System. It is Asia's leading medical school and ranks among the best in the world (Times Higher Education World University Rankings 2020 by subject and the Quacquarelli Symonds (QS) World University Rankings by Subject 2020).

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