

New multiple sclerosis subtypes identified using artificial intelligence

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Scientists at UCL have used artificial intelligence (AI) to identify three new multiple sclerosis (MS) subtypes. Researchers say the groundbreaking findings will help identify those people more likely to have disease progression and help target treatments more effectively.

MS affects over 2.8 million people globally and 130,000 in the UK, and is classified into four 'courses' (groups), which are defined as either relapsing or progressive. Patients are categorized by a mixture of clinical observations, assisted by MRI brain images, and patients' symptoms. These observations guide the timing and choice of treatment.

For this study, published in *Nature Communications*, researchers wanted to find out if there were any—as yet unidentified—patterns in brain images, which would better guide treatment

choice and identify patients who would best respond to a particular therapy.

Explaining the research, lead author Dr. Arman Eshaghi (UCL Queen Square Institute of Neurology) said: "Currently MS is classified broadly into progressive and relapsing groups, which are based on patient symptoms; it does not directly rely on the underlying biology of the disease, and therefore cannot assist doctors in choosing the right treatment for the right patients.

"Here, we used artificial intelligence and asked the question: can AI find MS subtypes that follow a certain pattern on brain images? Our AI has uncovered three data-driven MS subtypes that are defined by pathological abnormalities seen on brain images."

In this study, researchers applied the UCL-developed AI tool, SuStaln (Subtype and Stage Inference), to the MRI brain scans of 6,322 MS patients. The unsupervised SuStaln trained itself and identified three (previously unknown) patterns.

The new MS subtypes were defined as 'cortex-led', 'normal-appearing white matter-led', and 'lesion-led.' These definitions relate to the earliest abnormalities seen on the MRI scans within each pattern.

Once SuStaln had completed its analysis on the training MRI dataset, it was 'locked' and then used to identify the three subtypes in a separate independent cohort of 3,068 patients thereby validating its ability to detect the new MS subtypes.

Dr. Eshaghi added: "We did a further retrospective analysis of patient records to see how people with the newly identified MS subtypes responded to various treatments.

While further [clinical studies](#) are needed, there was a clear difference, by subtype, in patients' response

to different treatments and in accumulation of disability over time. This is an important step towards predicting individual responses to therapies."

NIHR Research Professor Olga Ciccarelli (UCL Queen Square Institute of Neurology), the senior author of the study, said: "The method used to classify MS is currently focused on imaging changes only; we are extending the approach to including other clinical information.

"This exciting field of research will lead to an individual definition of MS course and individual prediction of treatment response in MS using AI, which will be used to select the right treatment for the right patient at the right time."

One of the senior authors, Professor Alan Thompson, Dean of the UCL Faculty of Brain Sciences, said: "We are aware of the limitations of the current descriptors of MS which can be less than clear when applied to prescribing treatment. Now with the help of AI and large datasets, we have made the first step towards a better understanding of the underlying disease mechanisms which may inform our current clinical classification. This is a fantastic achievement and has the potential to be a real game-changer, informing both disease evolution and selection of patients for clinical trials."

Researchers say the findings suggest that MRI-based subtypes predict MS disability progression and response to treatment and can now be used to define groups of patients in interventional trials. Prospective research with clinical trials is required as the next step to confirm these findings.

Dr. Clare Walton, Head of Research at the MS Society, said: "We're delighted to have helped fund this study through our work with the International Progressive MS Alliance. MS is unpredictable and different for everyone, and we know one of our community's main concerns is how their condition might develop. Having an MRI-based model to help predict future progression and tailor your treatment plan accordingly could be hugely reassuring to those affected. These findings also provide valuable insight into what drives progression in MS,

which is crucial to finding new treatments for everyone. We're excited to see what comes next."

MS is a neurological (nerve) condition and is one of the most common causes of disability in young people. It arises when the immune system mistakenly attacks the coating (myelin sheaths) that wrap around nerves in the brain and spinal cord. This results in the electrical signals, which pass messages along the nerves, to be disrupted, travel more slowly, or fail to get through at all.

Most people are diagnosed between the ages of 20 and 50, however the first signs of MS often start years earlier. Common early signs include tingling, numbness, a loss of balance and problems with vision, but because other conditions cause the same symptoms, it can take time to reach a definitive diagnosis.

Many patients have relapsing MS at first, a form of the disease where symptoms come and go as nerves are damaged, repaired and damaged again. But about half have a progressive form of the condition in which nerve damage steadily accumulates and causes ever worsening disability. Patients may experience tremors, speech problems and muscle stiffness or spasms, and may need walking aids or a wheelchair.

More information: Arman Eshaghi et al, Identifying multiple sclerosis subtypes using unsupervised machine learning and MRI data, *Nature Communications* (2021). [DOI: 10.1038/s41467-021-22265-2](https://doi.org/10.1038/s41467-021-22265-2)

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