Higher genetic risk for multiple sclerosis means earlier onset of the disease

December 15 2021, by Todd Hollingshead

Professor Mary Davis and student Will Brugger looked at data for 3,495 multiple sclerosis patients to find the connection between genetic risk and early onset. Credit: Jaren Wilkey/BYU Photo

Anyone who has multiple sclerosis—or has a close friend with the

disease—knows an MS diagnosis is the beginning of a very uncertain future. The degenerative disease is so complex that patients may be fully quadriplegic seven years after onset, or they may be well into their 60s and live a relatively normal life.

Scientists at BYU are now zeroing in on one potential clue to unravel how severe a patient's MS prognosis might look: genetic risk. A new study from BYU professor Mary Davis, students Will Brugger and Jeremy Beales, and their colleagues finds people who have a higher genetic risk for the disease are likely to have accelerated onset of multiple sclerosis.

The finding is critical because people who get MS earlier in life tend to face more extreme symptoms of the disease throughout their life. If a person knows they are at a higher risk for early onset, they and their clinicians can be more aggressive with treatment.

"The earlier the treatment is started for MS, the less disease burden a patient will have and the better their quality of life will be," Davis said. "Prevention is key. If we can find out how many genetic variants a person has for potential onset, we can get them quicker treatment."

The study, published in *Multiple Sclerosis Journal*, looked at data from 3,495 MS patients and found the mean age of onset was 32 years, with 71% of the sample population female. (According to the National Multiple Sclerosis Society, three times as many women get MS as men.) The researchers carried out a comprehensive investigation of the risk variants with a statistical analysis of the data and found those with the greatest genetic risk burden were five years younger at onset than those with the lowest genetics risk burden.

The researchers suggest that since MS genetic risk is associated with age at onset of the disease and age of onset is a strong predictor of long-term

outcomes for patients, genetics risk has a direct effect on patient outcomes.

"Multiple sclerosis is so complex that we haven't ever confirmed before that the variants that are associated with getting the disease are associated with how early you get MS," Davis said. "It wasn't an unexpected finding, but this the first time it has been confirmed."

Frontline treatments, such as weekly injectables, can cause flu-like symptoms and may only be 30–50% effective. While these treatments are generally safe, they are not pleasant and "you don't want to be on them if you don't need to," Davis says. Some people even stop treatments because their quality of life is so low that they don't want to continue, even though those treatments are helping with MS.

According to Davis, some treatments for MS have major risks, including extreme suppression of the immune system. While more effective, the patient is very susceptible to life-threatening conditions and the patient and clinician have to balance prediction of MS severity with the risks of the treatments.

The following are some of the risk factors for developing multiple sclerosis:

- Having a family member with the disease
- Living in temperate climates; the further from the equator the higher the risk
- Having low levels of vitamin D and low exposure to sunlight
- Being of Northern European descent

For those at high risk, the goal for clinicians is to delay full onset of the disease as much as possible. Davis believes that her research will lead to people getting more personalized treatment based on their genetic

variant profile.

"Typically by the time someone is diagnosed, those patients will realize there was a time when they were teenagers or they were in college where they had an event signaling future onset of the disease," Davis said. "We want to help people to be more aware of those events before onset hits so they can take action and have a greater potential for long, healthy lives."

More information: Frances M Wang et al, Predicting self-reported depression after the onset of multiple sclerosis using genetic and non-genetic factors, *Multiple Sclerosis Journal* (2020). DOI: 10.1177/1352458520921073

Provided by Brigham Young University