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MRI research demonstrates ALS attacks multiple parts of the brain

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Recently published studies by a researcher in the Faculty of Medicine & Dentistry demonstrate that ALS – known as Lou Gehrig's disease – damages neurons in parts of the brain responsible for cognition and behaviour.

ALS, which stands for amyotrophic lateral sclerosis, is a fatal neurodegenerative disease that eventually leaves patients unable to move, breathe or swallow. Previous research has shown about 50 per cent of patients with ALS also have mild cognitive and behavioural changes, but between five and 15 per cent of patients can have severe changes resulting in dementia. In Canada, between 2,500 and 3,000 people live with the disease. Most die within two to five years of diagnosis.

Sanjay Kalra, a researcher in the faculty's Division of Neurology and a practising neurologist, has published two papers this year in the *American Journal of Neuroradiology* providing evidence that ALS affects more than just the motor cortex, the part of the brain responsible for motor function.

"ALS was previously thought to be a disease restricted to the motor system causing only weakness," says Kalra, the principal investigator in both peer-reviewed papers.

"But a significant proportion of people with ALS also have cognitive and behavioural changes. We wanted to know how ALS was impacting other parts of the brain to cause these symptoms.

"There is increasing evidence from pathological studies of ALS patients post-mortem that not just the motor system is involved. Our research supports this and demonstrates in those living with ALS, that the disease is indeed attacking other parts of the brain. The cognitive and behavioural changes we are seeing in patients are not reactive," he says. "They are not happening because someone is depressed or doesn't have initiative because he is weak. Those changes are happening because there are biological and chemical changes in parts of the brain that are responsible for behaviour and cognition."

Kalra uses magnetic resonance imaging (MRI) not to just look at pictures of the brain, but also as a means of measuring the levels of various chemicals in the brain. In his most recently published paper, he looked at two different chemicals called NAA and mIns. NAA is known as a neural marker, which means it is only found in neurons, while levels of mIns increase when there is abnormal scarring in the brain.

"If NAA is decreased, it means neurons have died or they are not working. Many papers have shown NAA to be decreased in regions where you expect it to be decreased with ALS – the motor cortex. But our recent study shows that these levels are also decreasing in areas of the brain responsible for cognition and behaviour," says Kalra.

His paper published in early 2011 looked at decreasing levels of NAA in the cingulate cortex – the first time MRI had been used to measure chemicals in this region of the brain in ALS. And his most recently published paper, which came out late this summer, was the first to demonstrate that NAA was decreasing and mIns was increasing in the frontal lobe, even when there weren't signs of cognitive or behavioural issues in patients. The frontal lobe is considered the hub for cognition and behaviour in the brain.

Kalra would like to continue his research using MRI to track the changes

in the brain of those who have ALS, and to evaluate new drugs. Kalra is the leading researcher in Canada to use MRI to study ALS. In November 2010, he was invited to give a presentation at Oxford University, and earlier this year he collaborated with a number of international researchers to write a commentary piece in *Lancet Neurology* about this growing area of research.

He first became interested in studying ALS when he was a neurology resident looking for a research project using MRI. He has continued studying the disease ever since.

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