Multiple sclerosis research links brain activity to sharper cognitive decline

January 10 2012, By Michael C. Purdy

(Medical Xpress) -- When it comes to communication in the brain, more is usually better. But now scientists have linked increased communication in a network of brain regions to more severe mental impairment in patients with early-stage multiple sclerosis (MS).

“Measuring how well this network’s connections are working may provide a way to look beyond the wide-ranging symptoms of MS to help us quantify the disorder’s effects on the brain,” says co-author Maurizio Corbetta, MD, the Norman J. Stupp Professor of Neurology at Washington University School of Medicine in St. Louis. “This assessment could be very useful in diagnosing the disease and tracking the effectiveness of new treatments.”

Scientists at Washington University and the University Medical Center at Hamburg-Eppendorf and the University of Tübingen, both in Germany, published the results in the *Proceedings of the National Academy of Sciences.*

MS damages brain cell branches, impairing the cells’ ability to communicate. The disease is highly unpredictable and produces a hodgepodge of symptoms that vary from patient to patient. These include fatigue, numbness, dizziness, pain, bowel and bladder dysfunction, visual impairments, speech disorders, headache, depression and problems with balance, coordination and walking.

The brain can redirect energy and resources to make it possible for more

signals to flow through damaged circuits. But in MS, the researchers speculate, that redirection may lead to a decrease in the brain's ability to reconfigure itself for different cognitive tasks, such as speaking, processing sensory information, controlling movement, regulating mood and creating and accessing memory.

The current study focused on whether correlations could be made between the structural damage caused by MS, the cognitive problems experienced by patients and changes in brain networking, which refers to the ability of various regions in the brain to work with each other.

The study involved 16 patients who had been diagnosed with MS in the previous four years. For comparison, scientists also included 16 healthy individuals. All participants were given an extensive battery of behavioral and cognitive tests, as well as brain scans to look for structural damage. Researchers also evaluated the connectedness of brain regions that often work together in networks.

The scientists could see damage to brain cell branches on the scans of MS patients. The greater the damage, the more likely patients were to experience difficulties with brain function. These problems affected a range of cognitive domains, including decision-making, memory, attention and other factors. Researchers found that changes in one component of cognitive function that they defined as "cognitive efficiency" correlated with the great majority of symptoms and deficits measured by the battery of cognitive and behavioral tests.

The scientists also showed that patients with lower cognitive efficiency had enhanced connections in the brain's default mode network. This network is one of many that supports brain function; it is only active when the brain is not engaged in a particular mental task. Increases in default mode network connectivity gave a direct index of the degree of impairment in cognitive efficiency.

“This correlation is very surprising because normally we would expect cognitive efficiency to improve with increases in the connectivity of the default mode network,” says lead author David Hawellek, a graduate student at the University Medical Center at Hamburg-Eppendorf. “Prior studies have found that the strength of connections in the default mode network is a direct indicator of how well other networks can interact to support brain function. But that doesn’t seem to be the case here.”

The observation may result from the fact that the MS patients had only been recently diagnosed. Corbetta speculates that if scientists scan the patients’ brains again in a few years, more extensive damage from MS would likely impair connectivity in the default mode network.

“Another possibility is that the brain’s response to structural damage from MS may cause the various brain networks to lose their flexibility to interact with each other to support brain function,” says senior author Andreas K. Engel, MD, PhD, professor of physiology at the University Medical Center at Hamburg-Eppendorf. “The networks might thus have become less variable, more often interacting among themselves instead of with other networks.”

Such a change could register as increased default mode network connectivity on scans, Engel says, but might actually indicate impaired cognitive function in early-stage MS patients.

MS symptoms tend to flare in intensity episodically. These unpredictable flares, known as relapses, involve worsening of symptoms and the development of new problems. None of the patients in the study was having a relapse. Scientists plan to follow up on their findings by gathering data on the same brain characteristics from individuals who are relapsing.

“This may give us additional insights into the relationship between

changes in brain networks and problems in cognition," Engel says. "If we can understand the dynamics that lead to these episodes, that may help us find better ways to predict and prevent them."

More information: Hawellek DJ, Hipp JF, Lewis CM, Corbetta M, Engel AK. Increased functional connectivity indicates the severity of cognitive impairment in multiple sclerosis. *Proceedings of the National Academy of Sciences*, Nov. 22, 2011.

Provided by Washington University School of Medicine in St. Louis