

Study unlocks mystery of dystonia with advanced imaging

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An estimated 300,000 people in North America are afflicted with dystonia, a disorder characterized by a progressive loss of motor control. Patients with generalized dystonia grapple with involuntary muscle spasms that lead to uncontrolled twisting and turning in awkward, sometimes painful postures. Although cognition, intelligence and life span are often normal, the disorder can have a devastating impact on quality of life, as its victims frequently struggle to perform simple activities of daily living.

At University Hospitals (UH) Case Medical Center's Neurological Institute, a research team is using advanced imaging technology to explore the complex network of brain activity relating to movement in healthy subjects and in patients with dystonia. "Normally, MRI is used to provide an image of the structure of the brain," says Benjamin L. Walter, MD, Medical Director, Deep Brain Stimulation Program, UH Case Medical Center, and Assistant Professor of Neurology, Case Western Reserve University School of Medicine. "Functional MRI [fMRI] takes advantage of the artifact that's created by blood flow and the oxygenation of blood. The level of oxygenation is highly correlated with neural activity in the same regions, so we can see which parts of the brain are being used."

Dr. Walter's current research explores two key areas: the nature of brain activity in patients with dystonia, and how that differs from activity in normal subjects; and understanding how <u>deep brain stimulation</u> (DBS), a leading-edge treatment for selected dystonia patients, works to quiet the



involuntary spasms. Treating dystonia with DBS involves the placement of electrodes in the internal segment of the globus pallidus, a subcortical structure also targeted in the DBS treatment of Parkinson's disease, essential tremor and obsessive compulsive disorder. "In disorders such as Parkinson's and essential tremor, when you turn the stimulator on there's a pretty quick benefit," Dr. Walter explains. "That's not the case with dystonia – it slowly improves over a long period of time, six months or longer. So there's more of a neuroplastic effect that's probably involved in the mechanism of DBS."

The initial stage of Dr. Walter's research involves using fMRI to observe brain activity in healthy subjects and in patients with dystonia who have not received DBS implants.

"We're looking to examine how sensory and motor information is handled in the brain in patients with dystonia. Dystonia is obviously a movement disorder, but there's a lot of evidence that the integration of sensorimotor information is dysfunctional."

The research team chose to study their subjects' proprioception – the sense of how their own limbs are oriented in space – "because that's very close to movement, and you get direct feedback about joint position when you move a limb."

Using a small device that vibrates over a wrist tendon, the researchers induce a movement illusion (the false perception that the subject's wrist is flexing) and examine the resulting fMRI images.

"In our normal patients, we're seeing that the motor cortex and the motor portion of the basal ganglia and the posterior striatum are involved," Dr. Walter notes. "In our dystonic patients, we'll look for changes in how the proprioceptive input is being handled. We're hoping to discover where the signal is becoming abnormal in these patients, whether there are



different anatomical structures involved, and whether there's a different place we could put the DBS wire and get a more robust effect."

The next stage of the research will include fMRI imaging of patients who have received DBS treatment. "DBS is not really well understood," Dr. Walter says "In part you need to know where to look, and this type of neuroimaging can tell us where there are abnormal hot nodes that are involved in our proprioception paradigm and may be worth investigating using other methods. Essentially, we're defining the differences between dystonia and normal patients, and in the dystonia patients who get DBS, we'll be looking for changes in their brain activity over time, as the dystonia melts away."

Provided by University Hospitals Case Medical Center

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