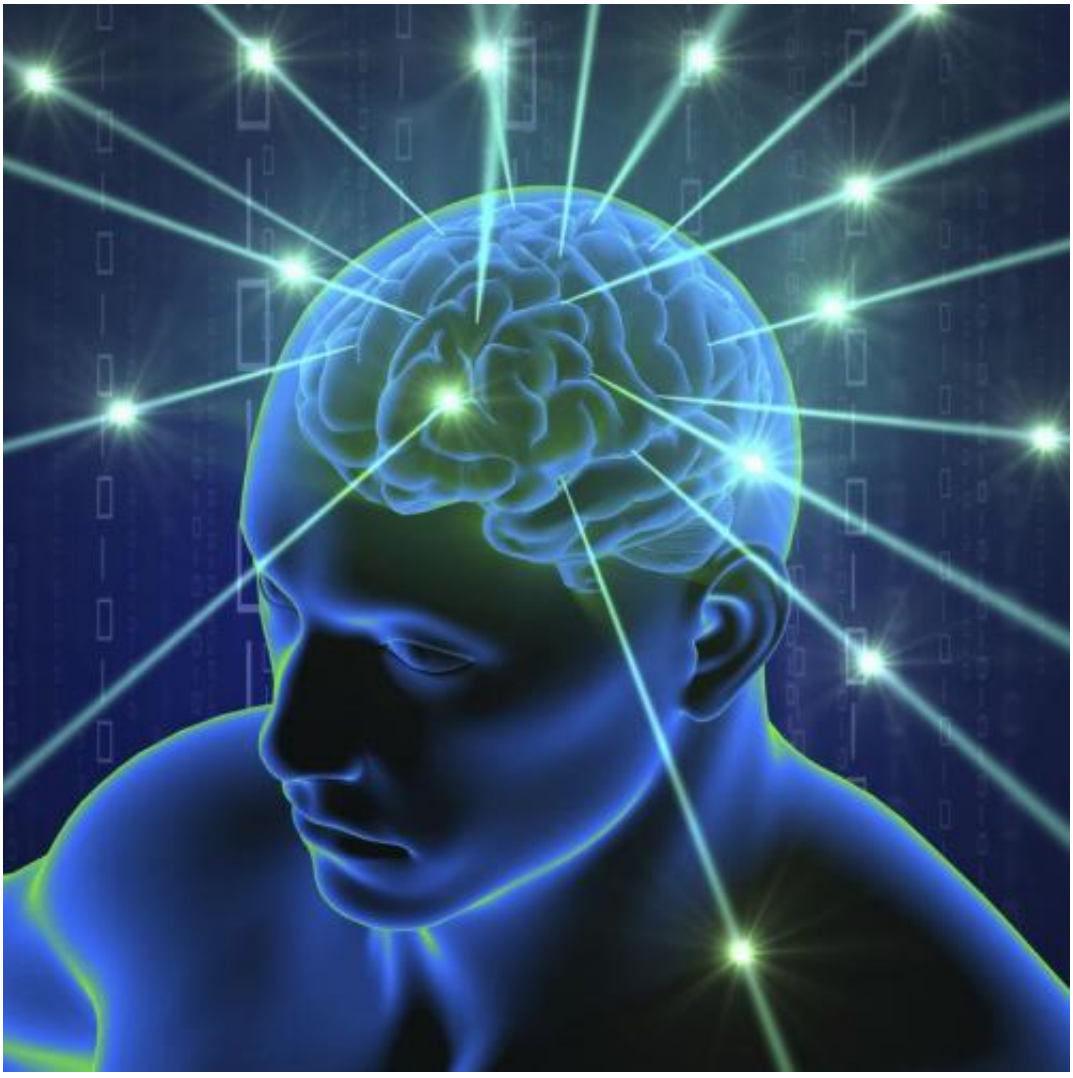
Sweet-spot brain stimulation may halt Parkinson's progression

August 2 2023



Credit: Rice University

Vanderbilt University Medical Center (VUMC) neurologists and scientists, along with colleagues from Charité-Berlin University of Medicine, are reporting that the use of Deep Brain Stimulation (DBS) in a very specific location with a very specific way to deliver the stimulation could slow or stop the progression of Parkinson's disease in very early-stage patients.

The *Annals of Neurology* study led by Mallory Hacker, Ph.D., MSCI, assistant professor of Neurology, with senior author David Charles, MD, professor and vice-chair of Neurology, may offer new hope to the nearly 100,000 new cases of Parkinson's diagnosed each year.

"Parkinson's disease is a devastating condition that is relentlessly progressive, but the new finding is that Dr. Hacker may have finally uncovered why the therapy is slowing or even stopping the progression of the motor symptoms in some of the patients," said Charles, who has been studying DBS for early-stage Parkinson's for more than two decades at Vanderbilt.

"With this finding we may be able to target or plan better where to put the lead, but then, after the lead is in, have very precise stimulation to capture some areas and avoid some areas of stimulation."

When Charles started his early research, all treatments for Parkinson's only temporarily helped the symptoms but did not slow or stop the disease progression, and this is still true today.

In 1997 the U.S. Food and Drug Administration approved DBS for certain symptoms of advanced Parkinson's, and in 2002 expanded its approval for additional symptoms.

"Deep brain stimulation—the treatment—is kind of unique because in the operating room the patient is awake, and we are testing the patient on

the fly to get the electrode in exactly the right location," Charles said. "You may have seen examples of where we have had a person here play a musical instrument, play the banjo, in the operating room as we are testing and finding just the right location for the electrodes."

A new analysis of Vanderbilt data collected from a pilot study of research participants with early-stage Parkinson's more than 15 years ago sought to determine why some (one out of three) patients randomized to DBS surgery experienced a halting of underlying disease progression as measured by motor symptoms.

The pilot was designed to test the safety of DBS in early-stage Parkinson's and was not sized to demonstrate efficacy or influence clinical practice. Of the 15 patients randomized to DBS, five had exceptional responses—no progression of their motor symptoms after two years.

"We'd been searching for a shared patient characteristic that might explain these exceptional responses to DBS, and we'd never really been able to find one," Charles said.

The breakthrough came when Hacker spent a month in Berlin learning how to use lead-DBS at the lab of one of its developers, Andreas Horn, MD, Ph.D., who joins Charles as co-senior author of the new study. (Horn is now at Harvard University).

"Dr. Hacker went to Berlin to collaborate with Dr. Horn's laboratory, and it turned out that patients with electrodes nearer to the sweet spot were able to manage symptoms with less drugs and with lower stimulation settings on their implants," Charles said.

Hacker said that while these same positive network connections show up in studies in more advanced Parkinson's patients, this is the only study to

have looked at the underlying progression of motor symptoms.

"We consider the results of this study hypothesis-generating," she said. "We can't take this result as indication that we should change clinical practice or change the way DBS is done today. But it does provide us with a great foundation to further explore if DBS applied in early-stage Parkinson's may slow motor progression."

The FDA has approved the Vanderbilt team to lead a pivotal multicenter study to determine if DBS applied in early-stage Parkinson's will slow or stop disease progression.

More information: Mallory L. Hacker et al, Connectivity Profile for Subthalamic Nucleus Deep Brain Stimulation in Early Stage Parkinson Disease, *Annals of Neurology* (2023). DOI: 10.1002/ana.26674

Provided by Vanderbilt University Medical Center