Sameer Sheth, MD, PhD

Associate Professor of Neurosurgery, Psychiatry & Behavioral Sciences, and Neuroscience
Cullen Foundation Endowed Chair
Vice-Chair, Research
McNair Scholar
Surgical Director, Comprehensive Epilepsy Center
Director, Psychiatric Neurosurgery

Deep Brain Stimulation for Depression using Directional Current Steering and Individualized Network Targeting

Dr. Sameer Sheth is currently Associate Professor, Cullen Foundation Endowed Chair, Vice-Chair of Research, and McNair Scholar in the Department of Neurosurgery, Baylor College of Medicine, Houston, TX. He also holds joint appointments in the Department of Neuroscience and Department of Psychiatry & Behavioral Sciences at Baylor, and is an Adjunct Associate Professor in the Department of Electrical and Computer Engineering at Rice University.

Dr. Sheth received his bachelor's degree in Physics and Astronomy at Harvard University summa cum laude before earning his MD and PhD from the University of California Los Angeles. Dr. Sheth completed his residency and a fellowship in stereotactic and functional neurosurgery at the Massachusetts General Hospital and Harvard Medical School.

Clinically, Dr. Sheth specializes in stereotactic/functional neurosurgery, including the surgical treatment of movement disorders, epilepsy, and psychiatric disorders. He employs a combination of stereotactic and traditional open surgical techniques, including deep brain stimulation (DBS), neuromodulation, laser ablation, radiosurgery, and microsurgery.

Dr. Sheth's research focuses on cognitive neurophysiology, often using opportunities derived from his clinical work. He studies higher order human cognitive processes, including decision-making and emotional regulation, using intracranial electrophysiological recordings and advanced imaging techniques. His lab also strives to improve neuromodulatory treatments for neurological and psychiatric disorders, including depression and dementias, using innovative surgical techniques.

Abstract: Background. Deep brain stimulation (DBS) for treatment-resistant depression (TRD) is investigational, with previous heterogeneous results. This inconsistency is

largely driven by incomplete understanding of the brain networks regulating mood, especially on an individual basis. We focused on gaining this crucial understanding and using it to optimally engage and treat symptomatic networks. We report results from the first subject treated with DBS for TRD using this approach.
Methods. The subject underwent implantation of DBS leads targeting two brain regions considered to be hubs of depression networks, and implantation of several temporary intracerebral recording electrodes in key implicated network regions. Recordings obtained while varying mood with behavioral tasks allowed us to identify network states – patterns of neural activity – associated with a range of emotions. We also recorded while delivering DBS to measure the network's response to stimulation across a wide parameter space. These data enabled us to choose a desired network state and calculate the combination of stimulation parameters most likely to achieve it. Following these inpatient recordings, the subject underwent an outpatient trial testing the efficacy of these data-derived DBS parameters.
Findings. Open-label stimulation with these customized parameters produced symptom remission. The subject then entered the double-blind, randomized discontinuation phase to distinguish true from sham response. As DBS therapy was withdrawn, he reported steadily worsening mood and anxiety, and symptom scores increased until he met rescue criteria. Resumption of stimulation again produced remission.
Interpretation. Conventional DBS involves trying various stimulation parameters until an effective combination is found. This trial-and-error process is often cumbersome and time-consuming and may not produce an optimal result. The novel approach described here inverts the typical process, using individualized recordings to identify healthy brain states and derive bespoke parameter combinations. Our initial results demonstrate the feasibility of this platform, which may be used to improve surgical neuromodulation for a vast array of neurological and psychiatric disorders.