INNOVATE
EVIDENCE-BASED MENTAL HEALTH RESEARCH

Memory Enhancement through Stimulation

The ability to remember shapes our everyday lives. Remembering a loved one's birthday, what to buy at the grocery store or recognizing a friend on the street are all different types of memory that can dramatically impact day-to-day functioning. Medical disorders including Alzheimer's disease, diabetes, schizophrenia and even healthy aging all have an effect on memory. The importance of understanding how memory works is an integral step toward providing care and improving the quality of life for those suffering with a mental illness as well as helping healthy individuals optimize their ability to remember.

Charan Ranganath, Professor in the Department of Psychology at UC Davis was awarded one of 23 pilot awards for the project, "Individualized Transcranial Direct Current Stimulation (tDCS) to Enhance Oscillatory Activity and Cognition in Healthy Individuals and Patients with Schizophrenia." Ranganath's work draws from basic science, memory disorders, and treatment modalities to better understand how memory works and how it can be improved and enhanced. "Memory is about using experiences to plan for the future, make good decisions, and avoid threats," said Ranganath.

Basic science is used to understand how memory works functionally and to study the patterns of electrical activity that help us learn and remember information. Results from these studies are used to understand how memory goes awry in disorders like schizophrenia and Alzheimer's disease. The collaboration between basic and clinical research is also crucial for accelerating the development of therapeutic approaches to improve and enhance memory. Other contributors to this project include co-PI, Dr. Cameron Carter, and project scientist, Dr. Brooke Roberts.

Measuring Memory

Schizophrenia is most commonly associated with voices and delusions that alter one's sense of reality. In addition to the visions, psychosis has a debilitating effect on memory. A recent study by UC Davis researchers found that the type of memory used for making associations, called relational memory, is most impacted in patients with schizophrenia.[1]

Patients were evaluated using a new memory test called RiSE (relational and item-specific encoding). In the test, patients study pictures of individual objects and pairs of objects. After this learning phase, participants are later tested on their ability to recognize the individual objects and also whether

they can recognize which objects had been paired together. Interestingly, patients with schizophrenia were able to identify if they had seen an object in a previous trial but struggled to identify whether two objects were seen together. This demonstrates a decreased ability to perform relational encoding. Without relational encoding, activities of daily living such as putting together names and faces or recalling directions to a store can become extremely difficult. "We've developed a measure of memory that is fast, is reproducible, and you can give the patient multiple tests and then compare the scores before and after," Ranganath said of the RiSE task.

Theta Waves

The brain is made up of neurons that use electrical activity to communicate with each other. EEG (electroencephalogram) is a technology that is used to monitor the brain waves that are produced by this electrical activity. Different oscillations are associated with different brain states like wakefulness, sleeping, concentrating, dreaming and learning. Ranganath and his team are specifically interested in one type of wave for this project, theta waves. Theta waves are low-frequency waves that are measured when you are alert, focused, concentrating or anticipating something.Ranganath's lab has shown that cognitive control and memory processes are linked to theta oscillations.[1]

Targeted Stimulation

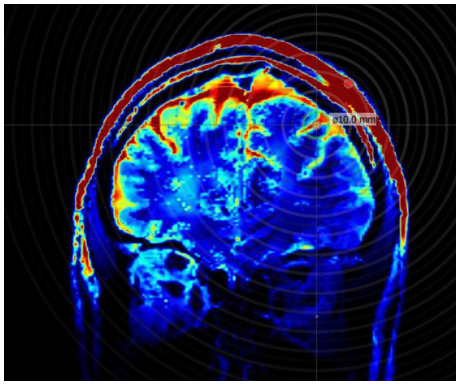
Transcranial direct current stimulation (tDCS) is a burgeoning non-invasive technology used to stimulate patterns of oscillation in the brain. It works by sending currents to specific brain regions through electrodes placed on the scalp. This project is unique because the current will be precisely delivered to a specific region of the brain at a specific frequency based on characteristics of the individual. The team will use a combination of technologies such as MRI and EEG to target the dorsolateral prefrontal cortex (DLPFC) on an individualized basis. Evidence shows that the DLPFC and theta oscillations measured from this area are affected in patients with schizophrenia.[3] Ranganath states, "The project will test whether tDCS can increase theta activity and thereby improve performance on memory and cognitive control tasks."

Studies with the RiSE memory task have shown that prefrontal activity is reduced in patients with schizophrenia.[1] By stimulating the prefrontal cortex using tDCS and then comparing patient performance on the task before and after it will elucidate whether the stimulation enhanced memory or cognitive control.

The aim is to develop targeted approaches to improve and enhance memory. Electrical markers, or biomarkers, are useful to say, "Here is the pattern of brain activity that we see in healthy people, and this is how the activity pattern is altered in patients with schizophrenia," Ranganath explained.

Basic and Clinical Sciences Have Impact

Neuroscience methods developed by basic science researchers in collaboration with clinical scientists have the potential to transform the way care for the severely mentally ill is approached. "Establishment of tDCS as a neurotherapeutic technique could revolutionize clinical psychology and psychiatry, by making neuroscience methods essential to clinical training," stated Ranganath. Specifically, interventions that aim to improve



Brain image highlighting areas of stimulation using tDCS

cognitive control can dramatically improve quality of life and performance outcomes for patients. Ranganath's project represents a targeted approach to treatment aligned with an ever-growing interest in precision medicine and individualized treatment.

1.Ragland JD, et al., Functional and Neuroanatomic Specificity of Episodic Memory Dysfunction in Schizophrenia: A Functional Magnetic Resonance Imaging Study of the Relational and Item-Specific Encoding Task. JAMA Psychiatry. 2015. doi: 10.1001/jamapsychiatry.2015.0276.

2.Backus et al., Hippocampal-Prefrontal Theta Oscillations Support Memory Integration, Current Biology. 2016. http:// dx.doi.org/10.1016/j.cub.2015.12.048

3.Lesh TA, et al., Proactive and reactive cognitive control and dorsolateral prefrontal cortex dysfunction in first episode schizophrenia. Neuroimage Clin. 2013. doi: 10.1016/j.nicl.2013.04.010.

Behavioral Health Center of Excellence at UC Davis

UC Davis launched the Behavioral Health Center of Excellence in October 2014 to advance mental health research and policy with initial funding from the Mental Health Services Act. The Innovate series highlights the Center's $4.3 million Research Pilot Award program.

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