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Directing neural plasticity to understand and treat neurological disease

Neurological disorders are characterized by dysfunction across multiple brain networks. Effective treatments will require tools capable of modifying activity across these networks. During normal learning the timing of neuromodulator release regulates network plasticity. Brief bursts of vagus nerve stimulation can safely trigger release of these same plasticity-promoting neuromodulators in patients to repair damaged networks. We have shown that pairing VNS with specific experiences causes highly-specific and long-lasting changes in sensory, motor, or emotional networks. Pairing VNS with a specific movement reorganizes motor cortex. Pairing VNS with a specific tone frequency reorganizes auditory cortex. Pairing VNS with speech selectively enhances the cortical response to specific words. Pairing VNS with emotionally salient cues directs plasticity in the amygdala. Animal models of chronic stroke, traumatic brain injury, spinal cord injury, nerve damage, PTSD, and tinnitus all make substantially greater gains when VNS is timed to coincide with specific rehabilitation events compared to identical rehabilitation without VNS. The four clinical trials of this approach have all been successful. Pairing VNS with physical therapy in chronic stroke patients tripled the functional gains compared to controls who received identical physical therapy without VNS. Pairing VNS with tones in chronic tinnitus patients reduced tinnitus severity and decreased hypersynchronous gamma activity in auditory cortex, as in earlier animal studies. These results demonstrate that pairing VNS with rehabilitation generates highly specific network changes that treat the underlying problem. Targeted Plasticity Therapy will be an important addition to the growing toolbox of technology to facilitate study and repair of the human brain. Millions of lives were saved once scientists developed effective adjuvants (aluminum salts) that made it possible to direct plasticity in the immune system. Like vaccine technology, Targeted Plasticity Therapy is a platform technology that can be applied to many conditions.

Speaker Biography

Michael Paul kilgard has his training in Biochemistry and Genetics at UC Berkely and in Neuroscience at UC San Francisco. He is the Margaret Fonde Jonnson Professor and the Associate Director of the Texas Biomedical Device Center. He has published more than 90 papers in peer reviewed journals, including *Nature, Science, Neuron*, and *Stroke*. He holds 23 US patents and regularly reviews for the NIH. His work is currently supported by DARPA, NINDS, NIDCD, Wings for Life Spinal Cord Research Foundation, and the W W Caruth, Jr. Foundation Fund at Communities Foundation of Texas.

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