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Non-Invasive Brain Stimulation to Treat or Cure Disease

NONINVASIVE NEUROMODULATION OF THE CENTRAL NERVOUS SYSTEM

ReachMD would like to wish you a Happy and Healthy New Year and with each New Year comes a fresh start. As we look ahead, ReachMD is proud to present this month's special series Focus on Future Medicine.

So many illnesses are caused by central nervous system damage and a new medicine of noninvasive brain stimulation treat or cure disease. Welcome to the Clinician's Roundtable on reachmd.com, on XM160. I am your host, Dr. Bruce Bloom and joining us to discuss noninvasive neuromodulation of the central nervous system are senior scientists, Kurt Kaczmarek, PhD and Yuri Danilov, PhD, and researcher, Mitchell Tyler, MSTE; all from the Tactile Communication and Neurorehabilitation Laboratory and the Department of Orthopedics and Rehabilitation Medicine and the Department of Biomedical Engineering at the University of Wisconsin-Madison.

DR. BRUCE BLOOM:

Gentlemen, welcome to ReachMD.

MITCHELL TYLER, MSTE:

Thank you. It's our pleasure, Bruce.

DR. BRUCE BLOOM:

So, Mitch what is the acronym CN-NINM stand for and what does it describe?

MITCHELL TYLER, MSTE:

Thanks Bruce. CN-NINM stands for cranial-nerve non-invasive neuromodulation. It is the process of stimulating the afferent nerves of the fifth and seventh cranial nerves via the tongue. It is believed that the stimulation excites the brain structure responsible for movement control and sense integration. There are some results we have from our fMRI studies, which show that we seem to be activating the pons, medulla, cerebellum, and even the thalamus and the very recent pilot data we have from EEG studies also show that multiple

regions of the neocortex were also involved.

DR. BRUCE BLOOM:

So, Kurt who is working on this research in your group and what are all of your backgrounds?

KURT KACZMAREK, PHD:

We have three core area researchers and a network of collaborators. Yuri Danilov is our neuro scientist. He has a PhD from the Russian Academy of Science and he has been in our lab since approximately 2001 with extensive experience in neuro anatomy and senses of vision, taste, hearing, and balance. Mitchell Tyler is a mechanical and biomedical engineer with the degree from UC Berkeley, also registered professional engineer specializing in Human-Machine Interfaces including Sensory Substitution Systems. He has been with our lab since about 1992 and is our director of clinical studies and I am nominally a biomedical and electrical engineer degreed from University of Wisconsin-Madison where we are calling from. My interest is in medical instrumentation design and electrical stimulation of touch for tactile information displays, then more recently in rehabilitation, and I have been with the lab since 1991.

DR. BRUCE BLOOM:

Kurt, who are some of the kinds of collaborators that you do this work with?

KURT KACZMAREK, PHD:

We have a network of collaborators in the basic sciences as well as our clinical collaborates in Biomedical Engineering, Neuroscience, Otolaryngology, Neurology, Rehabilitation Medicine, and Kinesiology.

DR. BRUCE BLOOM:

And is most of the work that you do are restricted to the University of Wisconsin-Madison or some of these collaborators at other institutions?

KURT KACZMAREK, PHD:

We have external collaborators as well.

DR. BRUCE BLOOM:

And Mitch, how did this idea of CN-NINM? How did it start? When did it start? And how has it progressed?

MITCHELL TYLER, MSTE:

The genesis of this idea CN-NINM actually goes back to the mid 1960s with Paul Bach-y-Rita's theory of Brain Plasticity using sensory substitution, the idea of presenting information from 1 sensory modality to another and investigating the case where there is loss of function and you could replace that with an intact functional sense. Paul originally demonstrated vision substitution using carefully controlled electrical stimulation of the tactile sense and it was originally done on the back in the form of a dental chair with a large array of electrodes involved to stimulating the abdomen and then developed and demonstrated for use on the hand and fingertips. Then about 15 years ago, Paul came with the idea of presenting this electrical stimulation out of tongue as an interface for human machine interaction and specifically for vision substitution and in retrospect we realized that this was actually a real brilliant insight and that the tongue is richly innervated and has the low electrical impedance and it is in protected environment. So, it's well suited for electrical stimulation of the sense of touch. Kurt and Paul then demonstrated this was possible and the concept and the technology was patented. Then, after my own case of transient vestibulitis, I came with this idea of using sensory substitution for a balance feedback and began using down the tongue and then most recently Yuri has been the one that made the crucial observations and the clinical trials with their balance patients from a number of studies we had initiated that other senses are improving equally well and we realized this. Yuri's key concept was that this idea of CN-NINM cranial nerve neuromodulation could be used to potentially treat a whole host of neurological disorders that we had not originally envisioned.

DR. BRUCE BLOOM:

Mitch, when you first started out doing this work of when Paul Bach-y-Rita did, tell us a little bit more about this sensory substitution, so how in fact would a blind person learn to see using this?

MITCHELL TYLER, MSTE:

The idea is that you present information from 1 modality to another. So, for example, if an individual is blind, then you can take tactile information from the tip of a cane for example and the individual learns to move the cane to sweep their environment and to obtain information about what the objects are in their environment just as you would with your eye. So, the same concept is being applied here for sensory substitution using modern technologies, so instead of a cane out there, you could use a camera for example that captures 2-dimensional information in space and then presents that as a pattern of intensity mapped information on the skin just as the retina does. All we are using is a high-tech version of simple mapping process. The same concept can be true for balance substitution as well where you are taking information from say accelerometer or information telling where up is and presenting that on the tongue.

DR. BRUCE BLOOM:

So, Yuri, what results have you seen in different patients based on this insight that you could affect other kinds of diseases using this sensory stimulation?

YURI DANILOV, PHD:

We were working in the last eight years mainly with patients, who have a balance, posture, or gait disorders. So, the majority of symptoms and parameters that we are measuring on the patients is the result of therapy. It is also related to balance. So, mainly we have seen the patients that we selected for our study, the balance improvement, the stability of the body, alignment of the body segment when they are standing or walking, gait improvement, and general mental and physical relaxation. That’s the package of symptoms that we are observing almost on every patient that we are working with, but at the same time we have improvement in the behavior of the patients. So we see reduction of the falls, reduction of the tension, stiffness, rigidity, and improvement of fatigue. The patients have the energy boost, tactile therapy, and pretty often we see the improvement that will <_____> symptoms. People who have a vestibular

disorder usually have the abnormal eye movement control. At the same time, in many patients, who receive this so called unexpected improvement that never was in our list originally, but now we are carefully watching on that, and to these patients to the symptoms we can mention the sleep improvement, migraines, decreases of the headache, the tinnitus or ringing in the ear, and even we are showing sometimes pretty completely unexpected results, for example the sudden recovery of the taste that was lost and an occurrence had been few years before or improvement of the fingertip sensitivity and some tingling then.

DR. BRUCE BLOOM:

If you have just tuned in, you are listening to the Clinician's Roundtable on reachmd.com on XM 160, The Channel for Medical Professionals. I am your host, Dr. Bruce Bloom and joining us to discuss noninvasive neuromodulation of the central nervous system are senior scientists, Kurt Kaczmarek, Yuri Danilov, and Mitchell Tyler from the Tactile Communication Neuro rehabilitation Laboratory at the University of Wisconsin-Madison.

So, Yuri, what types of diseases might be affected or treated by CN-NINM?

YURI DANILOV, PHD:

Bruce, honestly, we didn't explore our limits yet. So, with every year we are trying to move forward and still see the new and new area almost every month working with the patients, we are discovering something unexpected and pretty beneficial for patients. So, we started eight years ago with peripheral balance disorder, then we came to the central balance disorder, and now we are working in the area of movement disorder that include a wide variety of patients and in the recent years we came from the traumatic injury of the brain like traumatic brain injury and stroke patients and we are planning to go in the field of neurodegeneration and we are probably aware about all these issues in the multiple sclerosis patient and Parkinson's disease patient. We also discovered that in some patients we see the significant improvement in cognitive function like memory and attention. So, its natural development here will be dementia and Alzheimer and we are also trying to move forward the long awaiting project with neuro development like autistic kids. So, you can see the circle of the potential patient is unlimited right now.

DR. BRUCE BLOOM:

Yuri, why do you think you get these effects and how we will try and improve that through the research that you are doing?

YURI DANILOV, PHD:

Well, it is an excellent question. We are asking ourselves for eight years in the past and probably another eight in the future. The mechanisms of the fact is have to be discovered, but for simplicity let’s say we are stimulating the dorsal surface of the tongue and that the projection of two cranial nerve as Mitch mentioned before, the trigeminal nerve and the facial nerve, physically will stimulate in the nerve endings massive spike trends that’s going through the natural pathway of the neural fibers from the tongue to the brainstem, and they ending up in the middle of the brainstem and the two major or largest nuclei in the brainstem is trigeminal nuclear complex and nuclear <_____>. So, practically, during 20 minutes of our stimulation and 20 minutes we empirically discover the optimal way for this kind of stimulation, reproducing massive activation of the trigeminal nuclei and vestibular <_____>. It is a matter of fact during this summer, we get excellent fMRI evidence that prove our concept. That’s the really first time we have got to hard prove that a few days of our therapy producing the long-lasting changes and activity of the dorsal part of the pons, medulla, cerebellum, its all major components that are involved in the movement control. So, what's happening next that is have to be discovered and we are suggesting that there are three possible ways. So, the one way the direct neuro connection between trigeminal nuclear complex with neighbors can change activity and such structures like vestibular nuclear complex, that’s what we are observing first, the dramatic improvement of vestibular

control and balance control. There is another option that during 20 minutes of activity, the nuclei start to produce some chemical compounds that have to be discovered. We don't know whether it is peptides, endorphins or some other compound that physically diffusing the path predicted as a non synaptic transmission, signal that also can activate neighbors and produce long-lasting synaptical changes like also phenomenon of the <_____> beginning of 70s, it is LTP and LTI, long-term potentiation and long-term inhibition.

DR. BRUCE BLOOM:

I would like to thank our guests, senior scientists, Kurt Kaczmarek, PhD and Yuri Danilov, PhD, and the researcher, Mitchell Tyler, MSTE; all from the Tactile Communication and Neurorehabilitation Laboratory and the Department of Orthopedics and Rehabilitation Medicine and the Department of Biomedical Engineering at the University of Wisconsin-Madison joining us to discuss noninvasive neuromodulation of the central nervous system. I am your host, Dr. Bruce Bloom. You have been listening to the Clinician's Roundtable on reachmd.com. on XM160, The Channel for Medical Professionals. For complete program guide and podcast, visit www.reachmd.com, for comments or questions, call us toll free at 888-639-6157 and thank you for listening.

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