

US space program researchers develop potential nano-tools for deep brain stimulation

June 9 2015

Applying nanotechniques developed in the U.S. space program may help to better understand the electrochemical dynamics of deep brain stimulation in order to fine-tune the therapy, according to a presentation by NASA Ames Research Center scientist Russell J. Andrews, M.D., at the International Neuromodulation Society's 12th World Congress.

"Can we realize truly neuroregenerative neuromodulation through nanotechnology?" asks Andrews.

In a collaboration since 2011 with the Mayo Clinic, NASA Ames researchers have applied their expertise in growing and coating new carbon nanofiber materials for more sensitive, selective, and specific means to efficiently stimulate and detect activity of neural circuits.

Using carbon nanofiber pads that are just tens of microns across and coated with the standard biomedical polymer polypyrrole, the team demonstrated bench-top success in detecting changes in concentration of both dopamine and serotonin in a mixture simulating chemical conditions in the brain. A proof-of-principle device was patterned with nine sensing pads that can each be individually addressed with the intent of detecting different analytes.

Andrews, a neurosurgeon, has collaborated with Kendall Lee, M.D., Ph.D., a Mayo Clinic neurosurgeon who, with Prof. Kevin Bennet, chair

of the Mayo Division of Engineering, is developing analytical tools that have been used intraoperatively during [deep brain stimulation](#) surgery to detect neurotransmitter release.

The ultimate vision is to be able to wed chemical and electrical analysis to get a better picture of what occurs during deep brain stimulation, whose therapeutic effect is known, but mechanisms are not fully understood.

Animal studies indicate that deep brain stimulation to the subthalamic nucleus is linked to release of the neurotransmitter dopamine. In the neurodegenerative disorder Parkinson's disease, the loss of dopamine-producing cells leads to motor symptoms of stiffness and slow movement.

In addition, the neurotransmitter adenosine is thought to halt pathological synchrony in epileptic seizures.

If these neurotransmitter releases could be monitored in real time and with high spatial resolution while functional magnetic resonance imaging tracks metabolic activity during deep brain stimulation, clinical investigators would have a much better sense of how [electrical stimulation](#) and the chemical communication of neural circuits are interconnected.

Such understanding could assist with programming stimulation systems and limit the iterative process that is currently used. Also, it is hoped that nanosensor feedback about neurotransmitter activity could aid development of deep brain stimulation for refractory disorders such as treatment-resistant epilepsy or severe depression.

These systems would use on-board computational analysis to deliver therapeutic stimulation to persuade errant cells to resume normal

relations with their neighbors, Andrews said.

In the long term, he envisions a day when neurosurgeons might say they have restored a damaged nervous system to its full potential through use of such a "smart" neuroprosthetic system.

One of the first steps to getting there, he believes, is to operate at the same scale as biological systems – the micron or submicron level, about one-tenth or less the size of current therapeutic neurostimulation leads. At that level, he hopes, the pathological basis of a condition might actually be corrected rather than focusing on limiting the symptomatic effects.

Carbon nanotubes, which were first described in 1991, have attracted interest as biosensors due to their favorable biological and bioelectrical properties. The structure of carbon nanotubes has been compared to the structure of bamboo and that of the very similar carbon nanofibers to a stack of Dixie cups nested together.

While the biocompatibility of carbon nanofiber over the long term remains to be determined, Andrews said the polymer coating is biocompatible and larger carbon microfiber electrodes have been shown to function up to four months in laboratory animals before the electrode surface becomes fouled by adsorption of biological compounds.

The sensing capabilities demonstrated by NASA in a 20-micron-by-80-micron "nanotrode" and the electrochemical analysis development by the Mayo Clinic are in their early stages.

At the 11th World Congress of the International Neuromodulation Society in 2013, Lee, the principal investigator on the collaboration, presented his research into creation of analytical tools that send up to 100,000 neurochemical readings per second via an optical/wireless link

to a nearby laptop computer where the signals are analyzed with custom software and displayed in near-real time. The system, Harmoni, detected dopamine release in a rat evoked by brain stimulation using a carbon fiber microelectrode.

Meanwhile, potential neural interface materials have been under development at NASA Ames for about a decade by researchers in its Smart Systems group and Center for Nanotechnology. The center formed in the 1990s when the space program redirected its efforts toward "faster, better, cheaper" technological approaches to such missions as exploring the origins of life through astrobiology or developing autonomous networked planetary probes.

The carbon nanofibers are grown through vapor deposition on lithographically patterned catalysts and coated with the conductive polymer through electrochemical deposition. That combination of materials has less impedance and greater capacitance at several orders of magnitude beyond the charge-transfer performance of conventional deep brain stimulation leads – properties that enhance performance.

Beyond deep [brain stimulation](#), this and related technologies are being considered for retinal, cochlear and cardiac implants as well as guided drug delivery systems.

Provided by International Neuromodulation Society

Citation: US space program researchers develop potential nano-tools for deep brain stimulation (2015, June 9) retrieved 27 April 2024 from <https://medicalxpress.com/news/2015-06-space-potential-nano-tools-deep-brain.html>

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