AAMTI Project Spotlight: Use of High-Resolution Relational Resonance-Based Electroencephalic Mirroring (HIRREM®): a Closed-loop Neurotechnology for Optimization of Brain Oscillations

There is tremendous interest to develop new technologies that can have transformative impact on human brain functioning. The objectives span the gamut from supporting recovery for the severely injured, to optimizing the skills of elite performers. Researchers from the DoD, universities, and industry, are pioneering and collaborating to achieve breakthroughs for our most complex organ. This article introduces one such potential breakthrough for advancement of brain function, which has involved participation from the U.S. Army Research Office (ARO), Brain State Technologies (BST), Wake Forest School of Medicine (WFSM), Womack Army Medical Center (WAMC), the Defense and Veterans' Brain Injury Center (DVBIC), and the Uniformed Services University of Health Sciences (USUHS).

Through an AMEDD AAMTI Rapid Innovation Fund (RIF) Award, WAMC is evaluating the feasibility of self-use allostatic neurotechnology devices developed by BST in Scottsdale, Arizona. The technology works through noninvasive monitoring of brain electrical activity, high resolution spectral analysis (frequency bins as narrow as 0.01 Hertz), and algorithms to convert selected frequencies into real-time acoustic stimulation – audible tones of variable pitch and timing, delivered through standard earbud headphones (Fig. 1). Allostasis refers to "stability through change," and the allostasis paradigm does not assume that there is any single "normal" form of brain function. Allostasis rather models that all biological function should be changing, adaptive, and anticipatory, for successful engagement with the complex needs of changing environments. The net effect is to support auto-calibration of neural oscillations, or a process whereby the brain itself can make its own unique self-optimizing adjustments, on its own terms. One expression of self-optimization is reduction of hemispheric asymmetries that may be related to chronic or traumatic stress (Fig. 2).

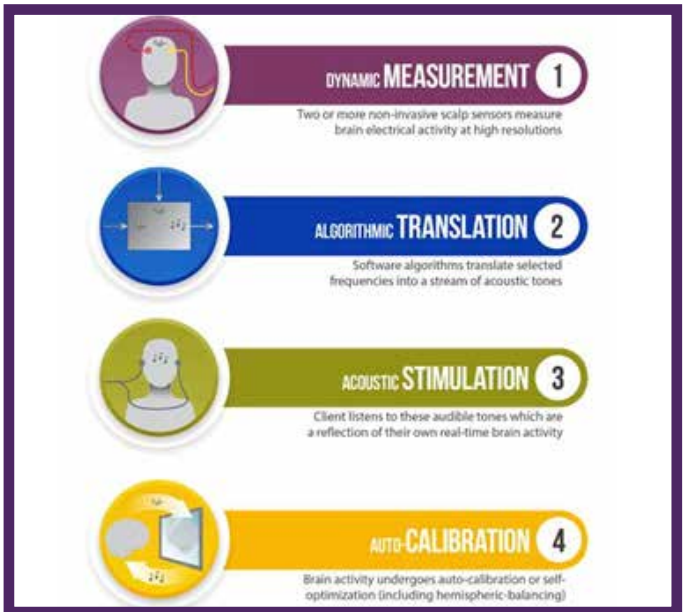

Fig. 1 (top). Sequential steps applied by closed-loop allostatic neurotechnology. Steps iterate to facilitate self-optimization of brain activity. Cables shown for Step 1 are indicative of an office-based intervention (cf., Fig. 3).

The self-use device was adapted from the core technology of HIRREM®, (high-resolution, relational, electroencephalic mirroring, also developed by BST). HIRREM® has been studied as an office-based intervention to treat insomnia and other conditions at WFSM since 2011. In 2014, the ARO made a phase one award to BST to produce devices for regulation of circadian rhythm. To achieve the award objectives, BST engineered their technology to operate in a self-use configuration, for self-directed optimization of brain electrical activity, improved sleep, attenuation of the effects of stress on the brain, and ultimately reduction of circadian misalignment. In March 2015, the company successfully delivered a working self-use prototype, which has since undergone two iterations and is available currently as the B2v2 (Fig. 3).

The RIF to WAMC will permit feasibility testing of BST's self-use device in 30 U.S. Army Special Forces Soldiers. The purpose of the device is explained as well as its possible benefits. Soldiers are asked to use it for 10-20 minutes per session, at a minimum of two to three times weekly, up to twice per day, for 4-6 weeks. At the end of the period, service members are asked whether they did or did not use the device and why, what they experienced, and any changes they may

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have noticed since using it. Preliminary data show that Soldiers embrace the use of the device during travel or in the privacy of their homes. The only suggestion for improvement was to modify the headband so that it was easier to achieve adequate sensor contact. BST has already modified the headband allowing for much improved operations. There have not been any adverse effects reported.

These results will inform an upcoming research protocol this fall to BST to lead a controlled clinical trial (2018-19) that evaluates office-based HIRREM® as a way to remediate persisting symptomatology after mild traumatic brain injury. A second trial (2020-21) will examine whether integration of the self-use device with HIRREM® can support even more scalability and cost effectiveness of an allostatic brain optimization strategy. Overall partners for the trials are Principal Investigator Dr. Sung Lee, BST; Dr. Wes Cole, Senior Scientist at DVBIC, Fort Bragg, NC; Dr. Y. Sammy Choi, WAMC, and Dr. Michael Roy (COL, RET), Center for Neuroscience and Regenerative Medicine, USUHS.

The burdens of suffering from traumatic stress and Traumatic Brain Injury are enormous. Military service members and their loved ones are affected disproportionately. Medications have modest benefit at best, and entail non-trivial risk. Many standard behavioral treatments have limitations including low uptake and minimal impact on sleep disturbance. There is still no FDA-approved treatment for pain and sensory disturbances attributable to TBI. "Every brain is different – and always changing – and it may be critical for strategies to approach and respect the brain accordingly. As researchers, we are excited to see what this technology can do," said Dr. Y. Sammy Choi, a driving axiom of the researchers introduced in this article. "When the brain is viewed as the organ of central command, multiple benefits are predicted from the use of interventions that can genuinely advance its functionality." U.S. Army medical research divisions to include TATRC, are playing a critical role to support the testing of the far-reaching technologies and ideas associated with this axiom.

Fig. 3 (bottom). B2v2®, self-use device for closed-loop self-optimization of brain activity (photo courtesy of Brain State Technologies, Scottsdale, Arizona).

Some of the information regarding this feasibility project was presented at the Military Health System Research Symposium, Kissimmee, FL, 27-30 August 2017.

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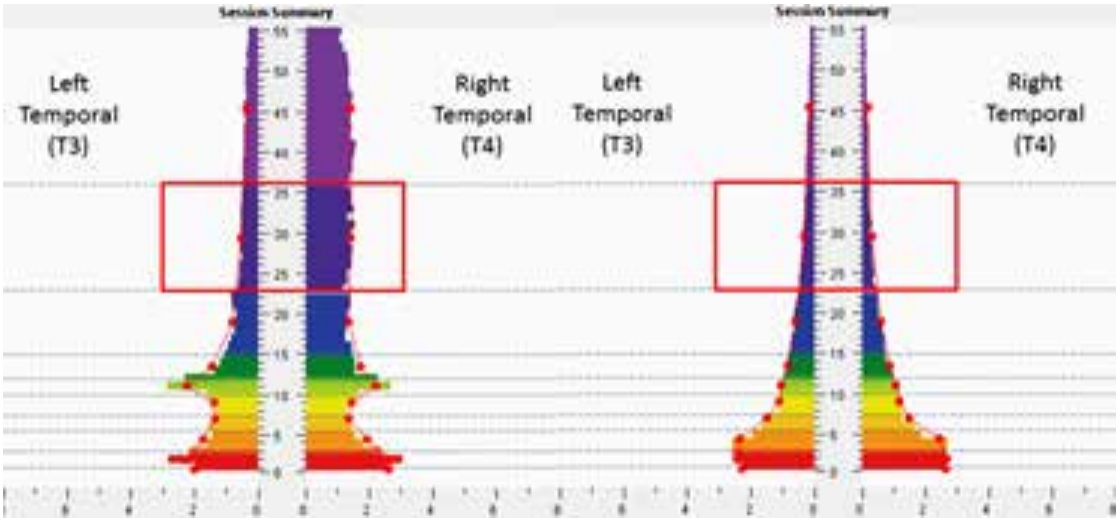

Fig. 2 (middle). Spectrographs of bilateral temporal lobe activity, before and after use of closed-loop allostatic neurotechnology (HIRREM). Left and right sides of each panel show averaged activity (one minute) for left and right temporal lobes, respectively. Amplitudes (microvolts) and frequencies (Hz) are shown on horizontal and vertical axes, respectively.