The Product: **Bodhi** [bō·dee] – *awakening, enlightenment and understanding*

Our product is a **Bi****O**feedback and brain stimulation **DE**vic**E** (**Bodhi**) that enables the dynamic control of mental states through real-time recording and entrainment of oscillating brain waves. Bodhi will further our understanding of the neurobiology of substance use disorders by demonstrating the controllability of two mental states that predict relapse: (1) increased stress and (2) impaired cognitive control. Bodhi is a science-based tool for enhancing self-control in motivated individuals seeking treatment for their drug use.

Drug abuse is estimated to cost the US more than $700 billion annually[1]. In 2013, estimates indicated that about 58.5 million Americans 18 or older had a problem with drug abuse, and 22.7 million Americans needed drug abuse treatment[2]. At the heart of this epidemic are people who report a lack of control of their thoughts and feelings; especially in the presence of relapse triggers that promote continued drug use. The most common relapse triggers are stress, cues linked to previous drug use (e.g., people, places, things and moods), and exposure to drugs[3]. Understandably, current behavioral and pharmacological treatment approaches emphasize the need for enhancing self-control[4] and managing relapse triggers[5]. A critical barrier, however, is that relapse triggers are often an unpredictable and unavoidable part of daily life, so individuals who do not have effective self-control and relapse-trigger management strategies remain trapped in the drug abuse cycle. **Bodhi** is an accessible and portable relapse prevention tool, which uses state-of-the-art technology that lets individuals recognize and manipulate their own brain waves to induce mental states of calm and cognitive control.

In the brain, relapse triggers are realized as electrochemical events that increase stress[6] and impair decision-making[7]. The prefrontal cortex (PFC) of the brain underlies higher-order processes, including cognitive control[8] and self-awareness of calm vs. stress states. Research has shown that PFC functionality is impaired in drug abusers[9] and that effective treatments for drug abuse enhance PFC functionality[10]. **Bodhi** permits the identification and entrainment of PFC brain waves (frequencies) scientifically linked to mental states of *calm* (alpha frequencies: 8-13 Hz) and cognitive *control* (gamma frequencies: 30-40 Hz)[11]. **Bodhi** relies on four main components to operate: (1) Electroencephalogram (EEG) to decode and categorize brain frequencies of *calm* and *control*; (2) Sensory feedback for the product user to identify and track these brain waves, (3) Entrainment and strengthening of these brain wave frequencies via transcranial alternating current stimulation (tACS), which has been shown to evoke these frequencies and enhance weakened synchrony in the PFC[12]; and (4) A motivated individual seeking treatment for their drug use problems who wants to learn a personal strategy for controlling them. Computer and smart device applications provide online support and training modules, and enable confidential data collection (e.g., demographic information, device use parameters, and drug use/psychosocial functioning outcomes). These data will grow our scientific knowledge about using innovative, cutting-edge neuroscience technologies in the natural environment to control mental states associated with problematic drug use.

Portable EEG has been developed and marketed to record and classify brain waves for various applications, including the control of physical and virtual devices. Others are using portable electrical stimulation devices to induce desired mental states. **To date, no company has combined EEG with brain stimulation in a single biofeedback device to enable the recognition and control of an individual's brain waves. Bodhi** represents a significant innovation that is consistent with the recent NIH emphasis on precision medicine. **Bodhi** is affordable, with a price point comparable to other commercially available brain-computer interfaces. The market for this product consists of individuals with drug use disorder, education/research institutions and treatment facilities. Importantly, **Bodhi** could be applied to other mental conditions characterized by impaired volitional control of feelings and thoughts, such as eating, depression, and anxiety disorders[13].

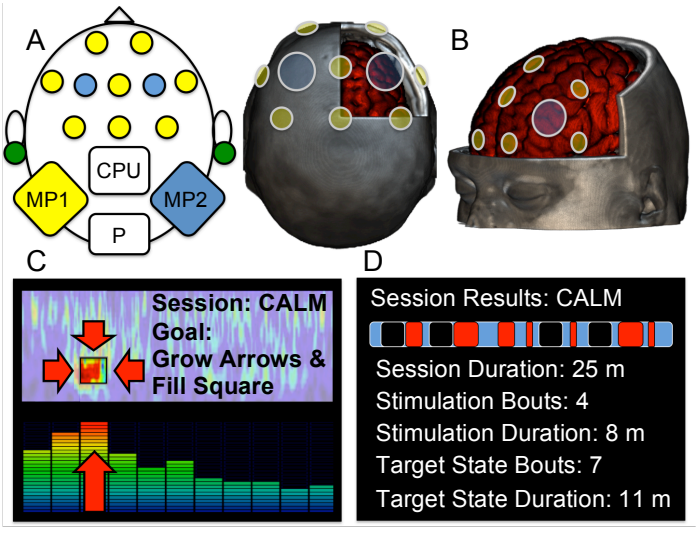
The Founding Team

We are a four-member team of scientists, engineers, thinkers and tinkerers from Lexington, KY. We are a well-rounded group of technical wizards with keen visionary insight. Drs. Michael Wesley and Josh Lile are faculty members in the University of Kentucky (UK) College of Medicine. Michael is an expert in computational neuroscience with over 10 years of experience in neuroimaging the PFC of drug abusers. He is currently the principal investigator on a study examining interactions between drug use and noninvasive electrical brain stimulation. Josh is a multiple award-winning tenured associate professor that has been NIDA funded for approximately 15 years. Josh conducts preclinical, human laboratory and treatment research on drug use disorders. Arit Harvanko is a doctoral candidate at UK with a Master's degree in Behavioral Neuroscience and Psychopharmacology. Arit is also a member of Kre8now Makerspace – a community workshop where individuals collaborate on various projects to learn and share knowledge while promoting community and economic development. David Hempy is a graduate of the UK College of Engineering and a Board Member of Kre8now Makerspace. David is a software developer with 20 years of experience in web development, embedded controllers, application architecture, programming and system integration. Michael, Josh and Arit have collaborated on research projects at UK, and Arit and David have collaborated on projects at the Kre8now Makerspace. Our core competencies include good clinical practice, including human subjects protection, strategic planning, grantsmanship, project implementation and management, human physiology, pharmacology and neuroscience, machine learning mathematics, hardware and software development, application program interface, and data dissemination. Our skills, knowledge and resources, combined with our desire to gain a better understanding of the neurobiology of substance use disorders, thereby empowering individuals to manage their drug use, ensure our success.

Our team has begun early development of a Bodhi prototype using personal funds and open source hardware and software, but further development is cost-prohibitive. NIDA Challenge funds will allow us to develop a minimum viable proof (MVP) version of Bodhi and obtain user feedback in order to determine viability. If viable, we will formally establish our startup and apply for Small Business Technology Transfer Research funding.

What's In the Box

Bodhi is supported on the head by a 3D-printed lightweight skeletal polymer frame. The 10-20 international standard EEG navigation system is used for mapping electrode placement to the PFC (Figure, Panels A & B; skull cutout image reveals cortical targets). Eight EEG recording electrodes (yellow) are situated around two larger tACS stimulation electrodes (blue). EEG electrode tips are disposable and reusable (1.0 cm diameter) with smooth surfaces for areas without hair and spiny surfaces for areas with hair. tACS electrodes are disposable and reusable pads made of a flexible and nonstick conductive gel matrix (4.4 cm diameter). Reference and ground electrodes are clipped to the earlobes (green). The centers of the two stimulation electrodes target the left and right dorsal lateral prefrontal cortex (DLPFC). Our previous research has demonstrated that the DLPFC is



engaged by drug abusers when making healthier future-based choices instead of immediate drug choices[14]. The rear sides of the device contain two microprocessors, one for processing EEG data (MP1) and one for processing tACS data (MP2). The upper rear center of the device contains a central processing unit (CPU) for integrating and controlling the two microprocessors and transmitting/receiving high-speed wireless Bluetooth signals. The lower rear of the device contains a rechargeable power supply (P). Three forms of sensory feedback are available for tracking and training mental states. Visual: a visual interface is displayed on a Bohdi remote control, computer or smart device via customizable application software to select training session modules/parameters and permit real-time monitoring of session goals and post-session results. To accomplish this, real-time EEG data are filtered and transformed into frequencies, which are then displayed in an updating spectrogram with a window over the target frequency range (Figure, top half of Panel C). Intensities are also displayed in easy-to-understand bars positioned below the spectrogram, with an arrow pointing to the target signal (Figure, bottom half of Panel C). Auditory: device speakers relay tones corresponding to targeted mental states. Tactile: a transducer at the base of the rear of the device provides vibrations corresponding to targeted mental states. Auditory and tactile feedback is particularly important when training without visual stimuli, such as when initially training low frequency alpha waves that correspond to mental states of calm that can be induced by closing the eyes. Bodhi is programmed to receive raw EEG data, and then transform and process those data, in order to determine the appropriate visual, auditory and tactile output. In this way, the sensory devices provide feedback to the user when brain waves enter and exit the targeted frequency ranges. All care and usage instructions are provided as a hardcopy and via interactive software. Bhodi comes in small, medium and large sizes with user-adjustable electrode arms for a custom fit.

How To Use

Users are instructed to use Bodhi in a comfortable and non-distracting environment. To begin a session, users verify the correct placement of the numbered and color-coded electrodes, turn on the device and place it on the head. Electrode contact quality diagnostics are automatically conducted, and electrodes can be adjusted to ensure optimal contact. Next, users provide input parameters for the desired training session (i.e., Stress Control or Cognitive Control) via Bodhi application software. Users determine session duration (e.g., up to one hour); however, the hardware and software work in unison to limit the intensity and duration of brain stimulation that can occur based on published human use and safety guidelines (e.g., 2mA of current up to a total delivery time of 20 minutes for one session).

The goal of using Bodhi is to develop a strategy for attaining and controlling the desired mental states that can then be used in the presence of relapse triggers in the natural environment. During initial Bodhi use sessions, users are instructed to stimulate the PFC at the target frequencies (i.e., PFC alpha waves [8-13 Hz] for Stress Control or PFC gamma waves [30-40 Hz] for Cognitive Control) so that they can experience those mental states and the associated sensory feedback from the device. Then users are instructed to use the device to learn a mental strategy for evoking and maintaining target brain frequency ranges in the absence of external tACS stimulation. When users fail to engage desired frequency ranges, they are prompted with a suggestion to stimulate the PFC at the target frequency for a short duration (e.g., two minutes) in real time. This supplemental stimulation is used to strengthen and entrain weakened neural circuits at the desired range as users are developing individualized mental strategies for calm or cognitive control. Once a short stimulation bout is over, users resume attempts to access desired frequency ranges. Single training sessions may contain several alternating bouts of recording and stimulating as users learn to control desired mental states. Results are recorded during the session and displayed to the user once the session is over (Figure D). These data are used to monitor safety, provide user feedback on training

progress, and will be combined with user demographic and ongoing drug use data (collected via questionnaires embedded into the remote/computer/smart device interface) to determine the relationship between device use, the ability to control mental states and the abuse of drugs.

Space limitations prohibit a comprehensive consideration of all of the innovative applications of Bodhi. One extension includes using Bodhi to learn to control mental states in the presence of personal relapse triggers. Another variation is inducing mental states of cognitive control while performing learning and decision-making tasks. Online support will be available to set guidelines and provide science-based strategies and examples for how to use Bodhi safely and effectively to achieve user goals.

Need and Willingness to Pay

The primary market for Bodhi includes individuals with drug use disorders, research/educational institutions, and treatment facilities. A secondary market includes individuals with other mental conditions characterized by impaired volitional control of feelings and thoughts. For those markets, Bodhi also represents a complimentary or alternative approach to current behavioral and pharmacological treatments of mental dysfunction. A tertiary market is individuals without mental dysfunction who want to learn to control their own brain waves to induce mental states, which may be useful in normal life. We will use online and offline resources to gather data from individuals, institutions and organizations to market parameters for Bodhi.

To collect information of the potential for individuals to use Bodhi, we will use the Amazon Mechanical Turk (mTurk) on-demand workforce. mTurk questionnaires will be used to probe demand and quantify the amount that would be paid for Bodhi in each market. We have successfully used mTurk as crowdsourcing tool to conduct research in drug abusing individuals. Importantly, outcomes from that study were similar in cocaine users who participated in person and via mTurk[15]. That study obtained data from 1763 individuals in the US across 4 weeks, and those individuals reported rates of drug use that were reflective of national estimates.

We expect that individuals serving in professional research investigator and care provider roles would not be well represented within the mTurk workforce. Therefore, in addition to the online data collection methods described above, we will also personally contact local and national research/educational institutions and treatment facilities to determine the market demand and price point of Bodhi. As internationally known and successful scientists, Michael and Josh have extensive social networks of contacts engaged in researching and treating drug use and other mental health disorders.

Timeline and Commercialization

Data collection regarding the demand and price points for Bodhi in each targeted market will be initiated immediately after the prize is awarded and last for 3 months. A working prototype will be developed within 6 months. If viable, we will establish our startup and apply for NIH small business funding. Worth mentioning is that we have university resources (e.g., the UK Advanced Science & Technology Commercialization Center) and personal resources (David and Arit have created startups, and we have many friends and colleagues who have developed successful companies) to help guide the commercialization of Bodhi.

References

https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/41745546

Proposal Video

https://youtu.be/pp8V2K-fdYo