

MREDI Quarterly Report: SYNERGISTIC IMPROVEMENT IN THE DIAGNOSIS & TREATMENT OF MENTAL ILLNESS, DEMENTIA, & CHRONIC PAIN
March, 2017

This progress report is organized “by project” for each of the Center’s four funded projects.

Objective 1: Combine EEG and fNIRS for clinical diagnostic development for anxiety and depressive disorder.

Overview:

Objective 1 remains behind schedule as the result of setbacks associated with the renegotiation of prices of the equipment being purchased with our Montana-based business partner, delays in equipment setup and training, changes in vendor personnel, and continuing delays in the acquisition of the remainder of the hardware from the vendors.

We have received our head caps, but remain engaged in talks with TechEn and Veridical Research and Design to integrate the stimulus presentation software collection of EEG and fNIRS data. Just this week, we received word from engineers at TechEn that additional hardware may be necessary to resolve this issue.

As previously indicated, the fNIRS portion of this study can still be run despite setup delays on the integration of the EEG and fNIRS systems. Pilot data collection for this work is currently underway and is scheduled to be finished March 3rd, 2017.

Recruitment of subjects for the fNIRS only study is set to begin March 6th, 2017.

A project coordinator has assembled all recruitment materials, identified and created digital copies of study measures for computerized administration, and has programmed an online signup option for study participants. An IRB protocol has been submitted and approval has been obtained. Undergraduate research staff has been recruited and trained. Approval has also been obtained for the use of the Psychology subject pool and the recruitment of community participants.

Equipment purchased:

Equipment has been purchased from Neuralynx, Inc. and TechEn, Inc. as described in the research proposal. Software has been ordered, received, and set up to begin processing EEG data as soon as it is collected. Brain Vision Analyzer software has been purchased for EEG data cleaning. Presentation stimulus presentation software has been purchased for the task to be used during data collection. Consumable supplies for the application of the fNIRS optodes have also been purchased.

Progress towards milestones (since previous update):

- Research assistants have collected sample EEG and fNIRS data.
- Integration of EEG and fNIRS systems (stimulus presentation) is nearly complete
- Computer systems have been added to MSU network for data storage
- Configuration to allow system integration is complete
- Integration of Presentation software with systems is complete
- Training cap grommet installation

- Experimental task (child and adult versions) has been programmed
- Grommets have been installed for fNIRS data collection
- Practice data has been sent to TechEn for feedback regarding procedural adjustments
- 2 pilot participants have been run

Total amount of expenditures by report date:

Salaries:

- Project coordinator salary: \$5412.50
- Project coordinator benefits: \$202.23

Contracted Services/Consultation:

- Veridical Research and Design: \$5800.00
- Veridical Research and Design parts reimbursement: \$12.39

Equipment:

- Neuralynx, Inc.: \$65,000 for EEG setup and caps
- TechEn, Inc: \$134,000 for fNIRS setup
- ActiCap for data collection: \$1724.00

Software:

- Software for EEG data processing: \$7902.80
- Neurobehavioral Systems software programming for experimental task: \$150.00
- Presentation software license for stimulus presentation: \$511.65

Other Costs:

- Facilities services charge to move equipment shipped from vendors: \$58.50
- Shipping cost for EEG data processing software: \$30.00
- University charges for purchasing hardware: \$158.88
- Secure safe for storing participant payments: \$16.81
- Wooden sticks to use for optode application: \$12.65
- Human subjects payment advance: \$2,000

Objective 2: Conduct a breakthrough study on the use of Deep TMS for Alzheimer's Disease (AD) in order to improve the lives of Montana families affected by AD and make Western Montana Mental Health Center in Butte a treatment destination for patients from across Montana.

Overview:

Previously reported delays for Object 2 have continued to place the project behind schedule. However, we have addressed all issues related to hardware and enrollment in the Alzheimer's protocol has officially begun. To date, we have screened three study participants. One subject was a screen fail (did not meet all inclusion criteria), one subject is still in the screening process, and one subject successfully completed

screening and is in the treatment phase of the study. We anticipate enrolling 2-3 more study participants before enrollment ends in mid-March 2017.

Hirings (since previous update):

No new hirings have occurred since our last update.

Equipment purchased:

No new equipment has been purchased since our last update.

Progress towards milestones (since previous update):

- Two subjects have completed screening procedures and have successfully enrolled into the protocol.
- One subject has received 5 TMS treatments to date.
- One subject will start TMS treatments on March 9, 2017.
- Practice on the TMS machine, fNIRS system, and EEG system has been ongoing throughout December and January in preparation for the first study subjects.
- The research coordinator has been collecting sample EEG and fNIRS data and working with project collaborators to ensure the accuracy of data.
- Recruitment for the study is also ongoing. The research coordinator has continued to conduct several information sessions for the Alzheimer's community in Butte.

Total amount of expenditures by report date:

- Neuralynx, Inc.: \$58,484.70 for EEG setup
- TechEn, Inc.: \$133,650 for fNIRS setup
- Brainsway, Inc: \$88,000
- BrainVision: \$10,618
- Payroll of Research Managing Director, Business Manager, and Faculty Consulting: \$37,401.18
- Travel expenditures: \$543.42
- Shipping and Communication expenditures: \$67.84
- Western Montana Mental Health Center: \$69,343.93
- Consultants: \$6,371.32

Objective 3: Establish efficacy and safety in a non-human primate model to facilitate clinical candidate selection of non-opioid therapeutic agents for acute and chronic pain, common correlates of anxiety, depression and neurodegeneration.

Overview:

We have successfully tested 2 SiteOne clinical candidates in the primate model, demonstrating strong analgesia with no notable off-target toxicology signals. ST-2257 and ST-2262 have both demonstrated a dose-dependent analgesic response with a complete block of pain at the higher doses. These findings provide important validation of our technology and we are further characterizing these compounds and others as

potential clinical candidates. In December 2016, SiteOne closed a \$15M Series B financing and strategic collaboration with Amgen which provides the resources to accelerate the development of our compounds and complete an initial clinical trial within the next 3 years. We continue to expand our medicinal chemistry team and plan test additional clinical candidates in the primate model throughout 2017.

Hirings:

Potential hires specifically supporting these activities are being evaluated for 2017.

Equipment purchased:

Cardiac/respiratory monitor at \$3,000.

Progress towards milestones:

- Screening of ST-2262, a novel, non-opioid drug candidate, has been successfully completed in this primate efficacy and safety model. Additional in-vitro and in-vivo characterization of this potential clinical candidate are ongoing. Several additional related new compounds have been synthesized and are undergoing initial pre-clinical evaluation for testing in the primate model in 2017.

Total amount of expenditures by report date:

- Total expenditures to date are ~\$145,000
- Site One Therapeutics: \$124,920.20
- Payroll of MSU Faculty Consultant: \$4,999.83

Objective 4: Investigate the ability of the Youth Aware of Mental Health Program (YAM) to prevent suicidal behaviors and improve mental health in freshmen high school students in Montana.

Overview:

Objective 4 continues to be on track for timelines. Since December, we've completed baseline assessments in all 8 schools and completed delivery of the YAM intervention in a total of 6 schools. YAM delivery is currently ongoing at Custer County District High School (Miles City) and Lodge Grass High School and will finish up on March 7, 2017. YAM follow-up assessments have been completed at 2 schools, with the remaining 6 schools having their follow-up assessments completed by end of May 2017.

Hirings (since previous update):

We have hired 4 additional YAM Facilitator Assistants since December 2016.

Equipment purchased:

None.

Progress towards milestones (since previous update):

- We continue to have the support of the Office of Public Instruction and DPHHS

for the proposed study.

- We have hired and trained a 4 additional YAM Assistants since December 2016.
- We have completed baseline assessments, YAM delivery, and 3 Month follow-up assessments in Gardiner High School and Pryor High School.
- We have completed baseline assessments, the first wave of YAM delivery, and 3 Month follow-up assessments in Helena High School, Capital High School, and Terry High School.
- We have completed baseline assessments and the second wave of YAM delivery in Helena High School, Capital High School, and Terry High School. 3 Month follow-up assessments for the second wave of these three schools will occur in May 2017.
- We have completed baseline assessments and first and second waves of YAM delivery in Browning High School. 3 Month follow-up assessments will occur in mid-March 2017 for the first wave and mid-May 2017 for the second wave.
- We have completed baseline assessments at Custer Country District High School (Miles City) and Lodge Grass High School. YAM delivery finishes on March 7 at Custer County District and on March 2 at Lodge Grass. 3 Month follow-up assessments for these two schools will occur in May 2017.
- We have started entering baseline and follow-up survey data into MS Excel.

Total amount of expenditures by report date:

- Contracted Services (YAM Training): \$14,526.23
- Travel & School Recruitment Costs: \$24,375.92
- Services: \$1,597.85
- Supplies: \$15,540.94
- Payroll of YAM Facilitators and Assistants: \$50,489.71
- Payroll of Research Managing Director, Research Study Coordinator, & Business Manager: \$82,316.89