

**MREDI Quarterly Report: SYNERGISTIC IMPROVEMENT IN THE DIAGNOSIS &
TREATMENT OF MENTAL ILLNESS, DEMENTIA, & CHRONIC PAIN**
June, 2016

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 is approximately 120 days 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 current delays in the acquisition of the remainder of the hardware from the vendors.

Research assistants have undergone training for data collection on the EEG and fNIRS systems. The task to be used for data collection has been programmed and tested on an alternative system. EEG and Neuralynx technicians will work with our laboratory to integrate task presentation with data collection from both sets of hardware. Pilot data collection will begin as soon as caps arrive and hardware setup is complete.

A project coordinator has finished assembling recruitment materials, has 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 have been recruited to allow for data collection during the summer months; these additional personnel are scheduled to begin training as soon as the final pieces of equipment arrive.

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.

Progress towards milestones (since previous update):

- Research assistants have been trained in EEG and fNIRS data collection. Piloting will begin on the combined system as soon as the final hardware arrives.
- Recruitment materials have been prepared.
- IRB approval has been obtained.
- Study materials (e.g., consent forms, questionnaires) are prepped and ready to begin data collection.
- Additional personnel have been hired (as volunteers) to work on the project over the summer.

Total amount of expenditures by report date:

- Neuralynx, Inc.: \$65,000 for EEG setup and caps

- TechEn, Inc: \$134,000 for fNIRS setup
- Facilities services charge to move equipment shipped from vendors: \$58.50
- Project coordinator salary: \$1867.50
- Project coordinator benefits: \$71.90
- Software for EEG data processing: \$7932.80

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:

As with Objective 1 that is also using the EEG-fNIRS technology, Objective 2 remains approximately 120 days behind schedule due to previously described delays in contracting as well as new delays in equipment setup and training, changes in vendor personnel, acquisition of the remainder of the hardware from the vendors. However, substantial progress has been made since the previous update as we now have received most of the necessary equipment.

Training on the EEG system has already begun. Training on the combined EEG-fNIRS system is planned for June 2016. Training for the recently delivered TMS device is planned for July 2016. We plan to complete all staff training by end of July 2016 with enrollment of the first study subject in the first week of August 2016.

Hirings (since previous update):

We have completed contracting for our TMS expert co-investigator (Sambit Mohapatra, Ph.D., University of Montana). We have also completed the hiring of our research study coordinator based at Western Montana Mental Health Center (WMMHC) in Butte.

Equipment purchased:

Purchases have been completed with Neuralynx, Inc. (EEG) and TechEn, Inc. (fNIRS). Contracting has also recently been completed with Brainsway USA Inc. for the TMS device. The equipment for all three purchases has been delivered to WMMHC.

Progress towards milestones (since previous update):

- We received IRB approval on April 13, 2016.
- We received FDA approval of our Investigational Drug Exemption application on April 13, 2016.
- The EEG and fNIRS equipment has been delivered to Western Montana Mental Health Center.
- The TMS machine was delivered to WMMHC on June 3, 2016.
- Western Montana Health Center has successfully hired a study coordinator for the project. She has already begun required trainings for study procedures.
- Recruitment for the study has started and there are already several interested study participants who will be ready to begin screening procedures once the study starts enrollment in August 2016.

Total amount of expenditures by report date:

- Neuralynx, Inc. : \$58,484.70 for EEG setup
- TechEn, Inc.: \$133,650 for fNIRS setup
- Payroll of Research Managing Director & Business Manager: \$13,180.80
- Travel expenditures: \$14.69

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 potentially validate these compounds as clinical candidates – additional in-vitro and in-vivo toxicology and pharmacology testing are currently being completed to further validate these compounds as clinical candidates. Our medicinal chemistry team are synthesizing additional compounds that will be tested in the primate model over the summer.

Hirings:

Potential hires specifically supporting these activities are being evaluated for this calendar.

Equipment purchased:

Cardiac/respiratory monitor at \$3,000.

Progress towards milestones:

- Selection of non-opioid drug candidates for evaluation in IND enabling studies has been successfully completed pending the outcome of additional in-vitro and in-vivo testing.

Total amount of expenditures by report date:

- Total expenditures to date are \$93,000

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 is entirely on track for timelines. Training of YAM Facilitators has been completed and we are on target with beginning the delivery of YAM in 8-10 schools starting in September 2016.

Hirings (since previous update):

A YAM research study coordinator has been hired and began working May 23, 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 obtained official commitment to conduct the study in 8 schools (Helena High School, Capital High School, Gardiner High School, Custer County District High School-Miles City, Browning High School, Heart Butte High School, Ronan High School, and Hays-Lodge Pole High School). We have already begun next-step administrative/logistic activities with each school for liftoff in the Fall 2016-Spring 2017 school year.
- It is possible that we may receive confirmation from additional schools by the end of summer 2016.
- Our YAM facilitator training took place April 4-8 and 12 Montanans completed the training and are now certified to deliver YAM in our committed high schools.

Total amount of expenditures by report date:

- Contracted Services (YAM training): \$16,686.66
- Travel & School Recruitment Costs: \$6,551.58
- Supplies: \$805.35
- Payroll of Research Managing Director & Business Manager: \$27,712.45