MREDI Quarterly Report: SYNERGISTIC IMPROVEMENT IN THE DIAGNOSIS & TREATMENT OF MENTAL ILLNESS, DEMENTIA, & CHRONIC PAIN
December, 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 nine months 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 are still waiting to receive our head caps, which will allow for combined EEG/fNIRS data collection, to be delivered in order to begin data collection.

We remain partnered with Veridical Research and Design and are nearly ready to pilot the collection of fNIRS data. This has resulted in the installation of grommets to hold fNIRS sensors and training of research assistants in the paradigm to be used during data collection. Veridical Research and Design has tested our task on both systems to assure that data can be collected. The final signals are being integrated this week. As a result of this partnership, a fNIRS study can still be run even if delays continue on the integrated (EEG/fNIRS setup). Combined with previous results from our lab, results will still be of value for understanding how components derived from EEG data overlap with regulatory activity in the brains frontal cortices.

Pilot data collection consistent with the original proposal will begin as soon as caps arrive and hardware setup is complete. Combined EEG/fNIRS data will still be collected to the extent allowed by the grant timeline.

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.

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

Total amount of expenditures by report date:

Salaries:

- Project coordinator salary: $4772.50
- Project coordinator benefits: $199.93

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

Software:

- Software for EEG data processing: $7902.80
- Neurobehavioral Systems software programming for experimental task: $750.00
- 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:

As with Objective 1 that is also using EEG-fNIRS technology, Object 2 remains approximately nine months 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.

We are also currently waiting for the head caps, which will allow for combined EEG/fNIRS data collection, to be delivered in order to begin data collection. As of November 30, 2016, we have received notice from TechEn, Inc. that an initial cap should be finalized and shipped to Western Montana Mental Health Center the first week of December 2016. Once the cap is received, the study coordinator will verify that it is correct, and then TechEn, Inc. will finalize and send out the remaining caps.

Due to the delay in receipt of the head caps, we now expect enrollment of the first study subject to be in late December 2016 or early January 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):

- Practice on the TMS machine, fNIRS system, and EEG system has been ongoing throughout September, October, and November.
- The research coordinator has been collecting sample EEG and fNIRS data and working with project collaborators to ensure the accuracy of data.
- Case report forms for capturing visit data have all been finalized, and subject binders have been created.
- Recruitment for the study is also ongoing. The research coordinator has continued to conduct several information sessions for the Alzheimer's community in Butte and has several interested individuals ready to participate once we are able to begin enrollment.

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
- Payroll of Research Managing Director, Business Manager, and Faculty Consulting: $30,915.06
- Travel expenditures: $14.69
- Western Montana Mental Health Center: $52,384.72
- Consultants: $2778.45

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 ongoing to further validate these compounds as clinical candidates. Our medicinal chemistry team continues to synthesize additional compounds that will be tested in the primate model in 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 ~$135,000
- Site One Therapeutics: $124,920.20
- Payroll of MSU Faculty Consultant: $4,958.33

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. The YAM program lifted off in our first school (Gardiner High School) in September. Since then, we've completed baseline assessments and delivered the YAM intervention in a total of 5 schools. YAM delivery is currently underway at Browning High School and will finish up there in mid-December 2016. Two additional schools are expected to liftoff with their first courses of YAM in January 2017, bringing our total to 8 schools.

Hirings (since previous update):

We have hired 15 YAM Facilitator Assistants since September. We expect to hire approximately 5 more assistants by January 2017.

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 total of 15 YAM Assistants since September 2016.
- We have completed baseline assessments and YAM delivery in Gardiner High School and Pryor High School. Three-month follow-up assessments will occur at both schools in January/February 2017.
- We have completed baseline assessments and the first wave of YAM delivery in Helena High School, Capital High School, and Terry High School. The second wave of YAM delivery will take place in all three schools starting in January 2017. Baseline assessments for both waves will occur in 2017.
- We have completed baseline assessments and are currently in the process of completing the first wave of YAM delivery in Browning High School. The second wave of YAM delivery will start in February 2017. Baseline assessments for both waves will occur in 2017.
- We are currently working with administrators from Custer County District High School (Miles City) and Lodge Grass High School. We expect both schools to begin YAM delivery in January 2017.
- We continue to work on next-step administrative/logistic activities with all of our participating schools.

Total amount of expenditures by report date:

- Contracted Services (YAM Training): $14,526.23
- Travel & School Recruitment Costs: $18,755.68
- Services: $739.15
- Supplies: $13,377.06
- Payroll of YAM Facilitators and Assistants: $30,455.34
- Payroll of Research Managing Director, Research Study Coordinator, & Business Manager: $59,975.09