

THE **TRIBUNE**

SEPTEMBER 2018

Stimulating Research

TRI Pilot Leads to \$1.1 Million VA Grant for rTMS Dementia Study



Prasad Padala, M.D., demonstrates use of the repetitive Transcranial Magnetic Stimulation coil.

The research participant reclines in what looks like a dentist chair, and suddenly her thumb begins to twitch. The movement is involuntary, controlled by Prasad Padala, M.D., a UAMS/VA researcher who is leading a study of repetitive Transcranial Magnetic Stimulation (rTMS) as a way to delay the onset of dementia.

The thumb movement signals Padala's starting point for mapping the brain with the rTMS coil, which is positioned just above the participant's head. Having calculated his coordinates for pinpointing the reward center, Padala moves the coil anteriorly 5.5 centimeters, away from the motor cortex, reaching the brain region where the device is put to work – the frontal lobe.

Each participant will have 20 sessions over four weeks, and 3,000 stimulations each session. The total 60,000 brain stimulations with the highly focused 3 Tesla magnet – the same strength of an MRI scanner – is key.

(Continued on page 2)

A Call for Pilot Applications and a Call to Action



Dear Colleagues,

Since its inception in 2009, TRI has offered pilot awards to researchers to help expand translational research at UAMS and to secure larger extramural grants. An example highlighted in this issue is Dr. Prasad Padala's promising work to delay the onset of dementia using repetitive transcranial magnetic stimulation. A TRI pilot helped him acquire a \$1.1 million Veterans Affairs award to conduct an expanded study. We're also using pilot awards as part of UAMS' multi-faceted efforts to combat opioid addiction, a public health crisis that killed more than 42,000 Americans in 2016. On Sept. 10, TRI announced a pilot grant opportunity focusing on opioid addiction and optimizing pain management. This new pilot will expand teams of UAMS researchers working in these important areas and provide seed funds that bolster efforts to secure future federal grants. NIH's

new HEAL (Helping to End Addiction Long-term) Initiative seeks to fund research that will address the opioid public health crisis and develop alternative approaches to pain management. This year alone, NIH has nearly doubled its opioid research budget to \$1.1 billion.

Pilot studies are crucial to building the case for large-scale exploration of innovative solutions. With the opioid crisis in full swing, ours isn't just a call for pilot applications, it's a call to action.

Sincerely,

A handwritten signature in black ink, appearing to read "Laura James, M.D." with a stylized flourish at the end.

Laura James, M.D.
Director, UAMS Translational Research Institute
Associate Vice Chancellor for Clinical and
Translational Research, UAMS

Stimulating Research

(Continued from page 1)

“The nerves learn to remain in their modified state by repeated stimulation - that’s how it improves depression,” he said, noting that rTMS has been approved by the Food and Drug Administration for treatment of refractory depression. The same concept applies to the treatment for apathy.

Promising results from a 2013 TRI-supported pilot study helped Padala obtain a \$1.1 million award from the Department of Veterans Affairs to test the benefits of rTMS in patients with pre-dementia and apathy.

Pre-dementia patients who also have apathy are seven times more likely to convert to dementia, said Padala, a professor in the departments of Psychiatry and Geriatrics in the UAMS College of Medicine, and director of the Memory Disorders Consultation Clinic at the Central Arkansas Veterans Healthcare System (CAVHS).

Padala has also studied Ritalin as a treatment for apathy in pre-dementia patients, but he found that many VA patients are not good candidates for Ritalin due primarily to cardiovascular risks. The search for a non-pharmacological treatment option led to rTMS.

“We decided to study rTMS because we knew it was already FDA approved for depression, which would allow us to target the reward circuitry of the brain,” he said.

Padala has been researching apathy in Alzheimer’s for 14 years, and when he was recruited to UAMS and CAVHS in 2012, an rTMS device was purchased as part of the recruitment package. Soon after he arrived, he applied for and was awarded a pilot, a study that involved nine people with pre-dementia. The cross-over study used both a sham coil and a real coil.

“We found significant improvement in motivation using the real treatment compared to sham treatment,” said Padala, whose research participant pool is mostly veterans seen at the Geriatric Research Education and Clinical Center (GRECC) at the Eugene J. Towbin Healthcare Center in North Little Rock. “We also found some improvement in their attention span and executive function.”

The VA grant will allow Padala to test rTMS in 125 participants over the next four years.

“We will know immediately at four years whether the treatment with rTMS changes the rates of conversion to dementia,” he said.

“I’m thrilled - I’m thrilled that TRI gave me that initial funding,” he said, adding that Neuronetics, the device’s maker, also provided funds to help make the pilot possible.

He is also excited about the possibilities at the conclusion of the larger study. If magnetic stimulation can keep dementia at bay, it would be a significant advance.

“When you look at the burden of dementia now, there are six million Americans with Alzheimer’s,” he said. “If we can postpone the onset of dementia by five years, we would cut prevalence of dementia by 50 percent.”

Researcher Profile



Prasad R. Padala, M.D., M.S., FACHE

Associate Director, Clinical Programs, Geriatric Research Education and Clinical Center (GRECC), Central Arkansas Veterans Healthcare System
Professor of Psychiatry and Geriatrics, UAMS

What inspired you to become a researcher?

It takes a long time to improve quality of care one patient at a time. Research seemed then as a way to have the most impact on the quality of health care.

What do you like most about your area of research?

It’s very exciting to develop a research protocol to address the problems raised by patients and caregivers. While answering that one question, so many other answers/questions pop up and the thrill of the chase never ends. Many people see geriatrics and dementia as the end of the road. However, I like the challenge and my team is seeking to slow the process and change the outlook.

What career would you have chosen if not research?

Stand-up comedian. It must be an awesome feeling to connect to a room full of people, have them experience what was in your head a few seconds ago and see them rolling on the floor, laughing.

What current or former biomedical researcher (from anywhere) do you admire most? Why?

Yellapragada Subbarao. He made significant contributions to many fields including biochemistry, pharmacology, microbiology, and oncology by his discovery of ATP (adenosine triphosphate) and methotrexate. I admire him the most because he could apply his knowledge to solve a major clinical problem. When his brother died of tropical sprue, he discovered folic acid as a treatment of tropical sprue.

TRI Open House ‘Eye-Opening’ for Researchers



Jonathan Laryea, M.D., (left) visits at the Open House with Trey Spencer, M.S., (Biostatistics), Ahmad Baghal, M.D. (Arkansas Clinical Data Repository), and TRI Executive Director Amy Jo Jenkins, M.S.

Oleg Karaduta, M.D., made the rounds at TRI’s recent Open House, loading his bag with information cards, brochures and flyers from the 26 research services being promoted. While many are relevant to his work, the Mock Study Section/Grant Review program really caught his eye.

“I am planning to submit a grant application in a couple of months, so the Mock Study Section will be really useful for me,” said Karaduta, a post-doctoral fellow, referring to his NIH ROO Pathway to Independence application.

TRI’s Mock Study Section/Grant Review program assembles experienced NIH-funded researchers to review applications at no cost.

The Aug. 28 Open House, held for a second year, this time included representatives from the Central Arkansas Veterans Healthcare System, Arkansas Children’s Research Institute, UAMS IRB and Research Pharmacy.

Among the nearly 100 attendees was Jonathan Laryea, M.D., associate professor in the Department of Surgery.

“I know about some of the services, but having everything together in one place is very helpful,” Laryea said. “I think it’s eye-opening.”

Two breast cancer fellows, Sherry Johnson, D.O., and Michalina (Michelle) Kupsik, M.D., said the timing for the Open House couldn’t have been better. They were due to report on their research project plans the day after the Open House but still needed key information.

Helpful guidance came from the Arkansas Clinical Data Repository table with information about accessing de-identified UAMS clinical data. “We knew our clinical question but we didn’t know how we were going to get the data,” Kupsik said.

“Now we know!” Johnson said.

[Learn more and request services at TRI.uams.edu.](http://TRI.uams.edu)

Research on the Horizon New TRI Study of the Month

- **UAMS Principal Investigator:** Erika Petersen, M.D., Associate Professor, Department of Neurosurgery, College of Medicine
- **Summary:** A post-market, multicenter, randomized clinical trial comparing high-frequency spinal cord stimulation to conventional medical treatments for chronic, intractable neuropathic pain from diabetic peripheral neuropathy
- **Significance:** One of every nine Arkansans has a diagnosis of diabetes, while another 75,000 are unaware they have diabetes. About 25 percent of people with diabetes will develop significant pain from peripheral neuropathy.
- **TRI Services:** Medicare coverage analysis, study budget review and negotiation, IRB submission, completion of sponsor’s



Erika Petersen, M.D., (center) with (left) TRI Research Coordinator Ashley Sides and TRI Project Manager Michael Bailey, and Sub-Investigator Heejung Choi, M.D.

regulatory startup packet, training for study staff/investigators, oversight of enrollment startup, and research nurse coordinator services.

- **Sponsor:** Nevro

TRIBUTES

The following UAMS researchers cited the Translational Research Institute (TRI) in publications after utilizing TRI resources or funding:

Bryant-Moore K, Haynes T, Kuo DZ, Stewart MK, Yeary KHK, Smith J, Turner J, Ounpraseuth ST, Sullivan G, McCoy S, Hudson B and Harris K. "Lessons Learned from Using an Audience Response System in a Community Setting for Research Data Collection." *Public Health Nurs* 2018 Jul 35(4): 353-359.

Chiang D, Chen X, Jones SM, Wood RA, Sicherer SH, Burks AW, Leung DYM, Agashe C, Grishin A, Dawson P, Davidson WF, Newman L, Sebra R, Merad M, Sampson HA, Losic B and Berin MC. "Single-Cell Profiling of Peanut-Responsive T Cells in Patients with Peanut Allergy Reveals Heterogeneous Effector Th2 Subsets." *J Allergy Clin Immunol* 2018 Jun 141(6): 2107-2120.

Dinwiddie DL, Hardin O, Denson JL, Kincaid JC, Schwalm KC, Stoner AN, Abramo TJ, Thompson TM, Putt CM, Young SA, Dehority WN and Kennedy JL. "Complete Genome Sequences of Four Novel Human Coronavirus Oc43 Isolates Associated with Severe Acute Respiratory Infection." *Genome Announc* 2018 May 24 6(21).

Koturbash I. "2017 Michael Fry Award Lecture When DNA Is Actually Not a Target: Radiation Epigenetics as a Tool to Understand and Control Cellular Response to Ionizing Radiation." *Radiat Res* 2018 Jul 190(1): 5-11.

Mock DM, Nalbant D, Kyosseva SV, Schmidt RL, An G, Matthews NI, Vlaar APJ, van Bruggen R, de Korte D, Strauss RG, Cancelas JA, Franco RS, Veng-Pedersen P and Widness JA. "Development, Validation, and Potential Applications of Biotinylated Red Blood Cells for Posttransfusion Kinetics and Other Physiological Studies: Evidenced-Based Analysis and Recommendations." *Transfusion* 2018 May 16.

Ray-Griffith SL, Wendel MP, Stowe ZN and Magann EF. "Chronic Pain During Pregnancy: A Review of the Literature." *Int J Womens Health* 2018 10: 153-164.

Swindle TM, Jarrett D, McKelvey LM, Whiteside-Mansell L, Conners Edge NA and Kraleti S. "Test of a Conceptual Model to Explain Television Exposure of Head Start Children." *Clin Pediatr (Phila)* 2018 Jul 57(8): 970-980.

Tran SM, McGregor KM, James GA, Gopinath K, Krishnamurthy V, Krishnamurthy LC and Crosson B. "Task-Residual Functional Connectivity of Language and Attention Networks." *Brain Cogn* 2018 Apr 122: 52-58.

Xiong J, Almeida M and O'Brien CA. "The Yap/Taz Transcriptional Co-Activators Have Opposing Effects at Different Stages of Osteoblast Differentiation." *Bone* 2018 Jul 112: 1-9.

Thank you for remembering to cite TRI in your publications resulting from studies that receive TRI support. Find the appropriate citation language at tri.uams.edu/about-tri-2/cite-tri.

Pilot Study RFA for Opioid Addiction and Pain Management

UAMS researchers are encouraged to apply for pilot awards being offered for opioid addiction and pain management research. One-year awards of \$25,000 will be available for studies that can produce data to support applications for larger extramural awards. Letters of intent are due Oct. 8 by noon. Multidisciplinary teams will be given priority. Visit TRI.uams.edu to learn more and access the Request for Applications (RFA) document.

The TRIBune is produced by the UAMS Translational Research Institute (TRI).

Website
TRI.uams.edu

Email:
TRI@uams.edu

TRI Main Number
(501) 614-2287

Editor
David Robinson

Designer
Mindy Stout

TRI Director
Laura James, M.D.

UAMS | Translational
Research Institute