ISSUE 6 — SPRING2019

VA BIOREPOSITORY BRAIN BANK NEWS

A YEAR IN REVIEW

Department of Veterans Affairs Biorepository Brain Bank
VABBB
Committed to research on brain disorders that affect Veterans

CELEBRATES 13 YEARS IN SERVICE TO VETERANS!

THE VABBB: 2017-18 SUMMARY

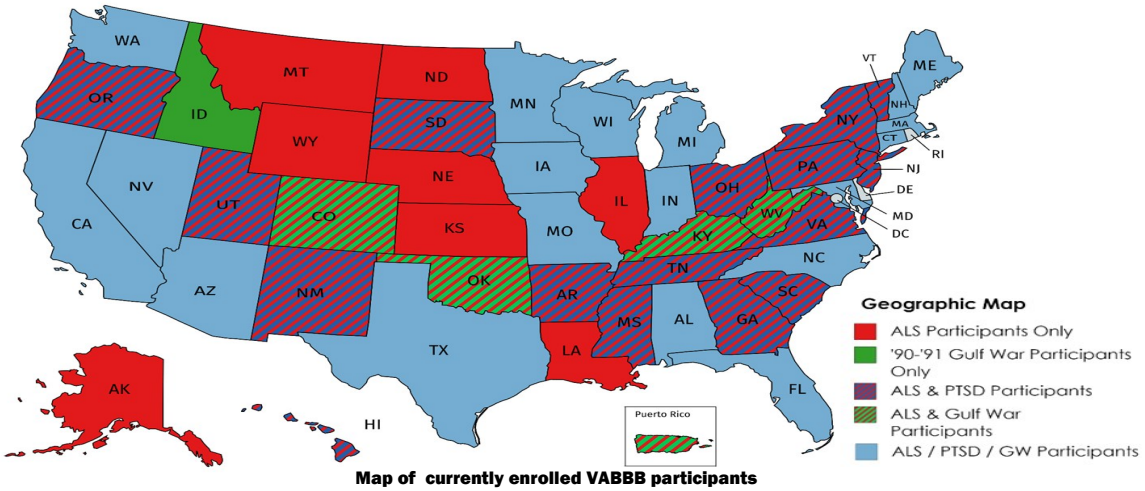
As the VA Biorepository Brain Bank (VABBB) begins its thirteenth year, we would like to bid farewell to Hannah Burris and Gabriel Walt. Both Hannah and Gabriel departed the brain bank team to pursue medical school. We'd like to thank them for their contributions and commitment to Veterans and the Department of Veteran's Affairs. They will be missed, and we wish them the best of luck with their pursuits.

The VABBB Staff (*From left to right*): Nazifa Abdul Rauf, Keith Spencer, Latease Guilderson, Neil Kowall M.D., Tarnjit Singh, Derek Collins, Christopher Brady Ph.D.

With Hannah and Gabriel's departure, staffing at the VABBB was reorganized. Nazifa Abdul-Rauf is now project coordinator of the Amyotrophic Lateral Sclerosis (ALS) Brain Bank, Keith Spencer is project coordinator of the Gulf War Veterans Illness Brain Bank, and Derek Collins is project coordinator of the "Cognition, Behavior, and Caregiver Burden" study and the Head of Recruitment for the VABBB. Tarnjit Singh remains the coordinator of the Post-Traumatic Stress Disorder Brain Bank. This past year was focused heavy on recruitment and outreach for each of the research studies. Members of the VABBB networked with various clinics, doctors and research projects around the VA Healthcare System to increase awareness of our research studies. Members of the team also attended various Veteran stand downs and health fairs across the state while also making some appearances on both television and radio networks. This recruitment effort has more than tripled the number of participants enrolled in the VABBB over the past year.

INSIDE:

VABBB IS CURRENTLY ENROLLING



Map of currently enrolled VABBB participants

Who can join the VABBB?

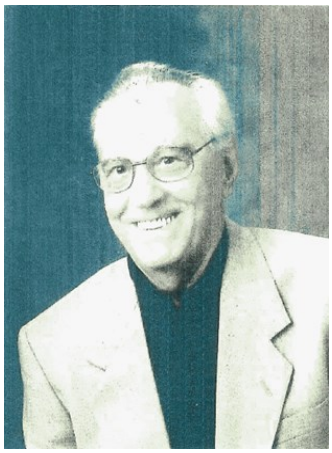
- Veterans with ALS, PTSD, Gulf War Veterans Illnesses (GWVI), or those without neurological disorders.
- Non-Veterans with PTSD may also enroll.

How can I sign up?

You can enroll in this study by calling:

866-460-1158

VETERAN'S VIEW
WHY DONATION IS IMPORTANT TO ME
BY: LOUIS SCHAVIE



I served three years with the Army Air Force on B-24 heavy duty bombers. I was drafted in March of 1943 and was sent to Camp Grant in Rockford, Illinois. I was later sent to Biloxi, Mississippi, where I spent eight months in school learning about airplanes and their engines. After graduation, I was sent to Liberal, Kansas where we trained cadets how to fly a B-24 heavy duty bomber. I spent two years at that field. In the early stages of the war, we worked 12 hours a day and 7 days a week. We needed to send tons of pilots and planes overseas to help end the war. I also worked on the C-47 and C-54 cargo planes.

I was on furlough from the U.S. Army Air Force when I met the love of my life. It was 1944, World War II was winding down, and she had just moved in next door.

I was visiting the Artesian Street neighborhood at Grand and Western in Chicago where I was born and raised. There, everyone celebrated the Fourth of July together and young adults gathered on street corners at night.

I went to see some of the old gang, so as I was crossing the street I heard this girl sitting on her porch hollered out, 'Are you too good to say hello?' I stopped and turned back instead of going to the corner. We talked all evening and went for a walk. I was in love before the night was over with the most beautiful girl I'd ever met.

The war ended and I was discharged in March of 1946, but it would take almost another year before we were able to get married. Because both of our parents didn't have the money to do it, we were both working so we pooled our money and on January 18, 1947 we were married at the Holy Rosary church.

I had a beautiful wife, home and a son; Lou, Jr., a 7 chair barber shop in Park Ridge, Illinois and another 5 chair shop in DesPlaines. Two shops employing 12 barbers. Life was good.

Then, in 1967, the trouble started.

I experienced difficulty with my left hand's forefinger and thumb. I saw a doctor and several specialists. They said it was an injury to the motor nerve. Therapy and tests followed. After a year, I couldn't give crew cuts because my arms shook uncontrollably when extended over a client's head for several minutes. Finally, after many months of frustration I realized I had to bite the bullet and change my occupation. I sold the business and took a job on the nightshift at a waste treatment plant in Hanover Park. There, I began taking classes in environmental control technology to become a treatment plant operator.

My wife arranged a visit to the Mayo Clinic in January 1972. There, a team of doctors said that I had Amyotrophic Lateral Sclerosis (A.L.S.) or "Lou Gehrig's disease," an incurable degenerative disease of the motor neurons and muscles that killed baseball legend Lou Gehrig. My life expectancy was three to five years. My wife and I were devastated. Without my faith in God, family and loved ones, I believe my chances to fight this thing would have been slim.

However, I refused to give up. I worked hard to become an expert supervisor of two wastewater treatment plants in Hanover Park, Illinois, and wrote a trade article entitled, "Gravity Fed Mixed Media Filters." I moved around a lot. As I worked and walked around the plant, checking on the filters and pumps, I became aware that if kept my muscles stimulated, it seemed to slow the progress of my illness. I stimulated my muscles with acupuncture treatments from a chiropractor in 1973 and, later, with a neuropathic specialist's massage and expertise. I participated in a study when the University of Chicago opened an ALS research clinic. After my fifth visit, lead doctor Dr. Antel said, "What are you doing to yourself to stay in such shape?" Clearly, my efforts were paying off.

Still, it has been a difficult and mixed journey. I think about all the things this disease took away from me, my hands, arms and legs. It destroys your dignity. I need help getting dressed, taking a shower, opening locks, or taking a (cont. on page 3) wallet out of my pocket. My wife has become my arms and hands. She's the love of my life. I can still shave, eat, drive and operate a computer with the aid of a long pointer. For years, I was not able to write, but with the computer, I am no longer handicapped.

I wrote short stories about my past for my niece, Dawn, while she attended the University of Illinois. When I had a quadruple bypass operation in 1998, she presented me with a bound book of all the stories I sent her.

Inspired by what she did, I wrote a mystery novel set in Wyoming entitled "Big Horn Incidents," that was later published. A sec-

IN THIS SECTION

Each newsletter, we highlight stories from caregivers in *Caregiver Corner* or from participants in *Veteran's View*. In this issue we present the Veteran's View. The piece provides a small window into a Veteran's with ALS donation.

HAVE A STORY TO TELL?

We would like to thank Louis Schavie for sharing his story with us!

If you would like to contribute to the next installment of Caregiver Corner or Veteran's View, please contact us at *866-460-1158.*

Let us keep looking, in spite of everything. Let us keep searching. It is indeed the best method of finding, and perhaps thanks to our efforts, the verdict we will give such a patient tomorrow will not be the same we must give this man today."

- Charcot (1889)

VETERAN'S VIEW...CONTINUED

ond mystery of mine, "The Hillsdale Incidents" was also published.

"Memories of a Bygone Era," is another novel I authored and is about all the little funny things I experienced growing up during the depression years. We have been living in Streamwood for some 44 years now. We will be celebrating our seventy second wedding anniversary in January. My son takes right after us, he has been married for 44 years and that makes us very proud parents.

The reason I decided to donate my brain to the VA Biorepository Brain Bank is because when I was diagnosed at Mayo clinic with ALS, I was sent home. There was nothing more they could do for me. There were no doctors out there that that would address this ailment. Finally, after all these years the VA has taken a giant step and in the right direction, I believe. That is why I whole heartily gave my consent to donate my brain.

When one is diagnosed with ALS, it is devastating and very frustrating when you have no help. I can recall back in 1972 doctors would not have anything to do with it.

Maybe with the few of us that have this slow crippling disease, a solution can be found from our brain donations.

I want to thank all the dedicated people who are working with the brain bank, may god bless you all.

Learn more about the need for adult participants at:

http://www.research.va.gov/programs/tissue_banking/control/

WHAT HAPPENS TO YOUR TISSUE AND DATA?

VABBB participants and families are rightfully curious about what happens to the tissue and data collected from our generous donors and their families after a brain donation. Brain donations arrive from all over the nation to our brain banks in either Tucson, Arizona or Boston, Massachusetts. Our team works around the clock to assure a smooth delivery process to our sites. After the Veteran has completed the organ donation, the tissue is packed safe and securely by the medical professional and transported to one of our private storage facilities. Our neuropathology team receives the brain donation, weighs the tissue, and photographs each step of the process. The brain is sliced to separate the right and left hemispheres. One hemisphere is frozen and the other is treated in a process called fixation. When tissues are "frozen" this process preserves tissue by cooling them to a very low temperature versus "fixation" which uses a chemical agent to preserve the tissues. These processes are complementary and allow scientists and researchers to explore both the visual and microscopic aspects of brain. One hemisphere is rapidly frozen to minimize damage and preserve the quality of the tissue. The frozen tissue is stored in the freezers until it is needed to conduct scientific experiments by researchers. With frozen tissue, researchers perform various experiments including extraction of DNA and RNA, and genes. Researchers can also conduct genetic studies to identify risk factors of various diseases. With frozen tissue, experiments can be done at the single cell level.

The other hemisphere is soaked in a chemical called formalin as part of the fixation process. Formalin locks the tissue into place permanently. This allows researchers to look at the structures in the brain and examine it for any abnormalities. The VABBB neuropathology team studies the tissue for signs of PTSD, ALS, and other neurodegenerative diseases. From the fixed state, the tissue can be further processed into slides. The tissue is put into paraffin wax and sliced thin using a device called cryostat microtome. The slides are then stained using various dyes with some dyes being able to target specific types of molecules.

Researchers from across the country have sent the VABBB tissue requests and have done groundbreaking work across the years. You can read some of this work in this year's issue on page 5. To read about experiments done in past year's you can read about them in our past year's newsletters on our website.

Top: Dr. Bertrand Huber dissects a brain tissue sample
Bottom: Dr. Huber displays dissected brain regions for Secretary of the VA Robert L Wilkie

PTSD BRAIN BANK HOSTS EDUCATIONAL BRAIN DISSECTIONS

The PTSD Brain Bank has begun educational brain dissections at VA Boston. The goal of the brain dissection is to educate students and faculty at VA and local academic institutions about neuroanatomy and different neuropathological features of various illnesses. These regular dissection meetings enhance the value of brain donations beyond the traditional use in research by also serving a role in educating future clinicians and researchers. No personally identifying information is revealed during these dissections to preserve the confidentiality of those who make these precious donations. No tissue is lost during educational dissections, all tissues continue to be used for research. Displaying tissues does not affect their integrity or quality.

PUBLICATIONS AND NEW STUDIES UTILIZING VABBB TISSUES

ALS is a progressive neurodegenerative disease of motor neurons in the brain and spinal cord. Over time, progressive degeneration of motor neurons leads to their death. The causes of ALS disease progressions remain unknown. Research studies are working towards identifying various cellular and molecular processes that lead to cell death in ALS. The three major categories of these processes in ALS are: 1.) Motor neuron damage/death due to buildup of proteins associated with ALS such as SOD1, TDP-43 and FUS (i.e., neurotoxicity), 2.) Mutations of ALS genes such as the C9ORF72 that interfere with proper expression of genes and the proteins they code for, and 3.) Problems in the support structures of cells or the cytoskeletal elements that keep cells stable and prevent them from dying. The studies described have made groundbreaking publications utilizing VABBB tissues or strive to understand some of these mechanisms utilizing VABBB tissues in in pursuit of a cure and better treatment and therapies.

PUBLICATIONS:

Chronic Traumatic Encephalopathy Within an Amyotrophic Lateral Sclerosis Brain Bank Cohort . Walt et al. (2018), Journal of Neuropathology & Experimental Neurology, VA Boston Healthcare System, Boston, MA.

Chronic traumatic encephalopathy (CTE) is a neurodegenerative disorder linked to repetitive head impacts and has been associated with amyotrophic lateral sclerosis (ALS), a fatal, degenerative neuromuscular disorder. The Department of Veterans Affairs Biorepository Brain Bank (VABBB) is a tissue repository that collects disease progression data prior to death and postmortem central nervous system tissues from veterans with ALS. We set out to determine the prevalence of ALS+CTE diagnoses in cases from the VABBB. We characterized the clinical, genetic, and pathological distinctions between participants with ALS only and those with both ALS and CTE (ALS+CTE). 5.8% (n=9) of these cases had ALS+CTE. These participants with ALS+CTE were more likely to have a history of traumatic brain injury. Most of them served during the first Persian Gulf War. Their pathological condition was marked by increased protein expression known as tau protein in the brain and spinal cord. The most common head injuries included contact sports and military service. In these ALS+CTE participants, ALS manifested as problems with speech and swallowing. They also had marked changes in mood and behavior. These findings suggest that repeated blows to the head may be one of many risk factors for developing ALS and/or CTE. More research will be needed to understand why people develop the different conditions.

Mutant FUS causes DNA ligation defects to inhibit oxidative damage repair in Amyotrophic Lateral Sclerosis. Wang et al. (2017), Nature Communications, Houston Methodist Research Institute, Houston, TX

Damage to the genetic material in the genome (a person's complete set of DNA, including all genes) and errors in DNA repair are linked to neurodegeneration, but the cause is unknown. This study evaluated a subset of persons with ALS with mutations in a protein called FUS, which interacts with DNA. The authors identified the nature of DNA defects caused by the mutation in FUS protein in this group of PALS. In healthy neurons, FUS protects the genome inside the cell nucleus. The FUS mutation in ALS causes the FUS protein to move outside the nucleus rather than inside where it should be doing its job. The study found that when FUS does not function properly, a protein known as a ligase does not receive the signal to repair DNA when it is damaged. The damaged DNA remains unrepaired, which may contribute to impaired neuronal function and cell death seen in ALS.

Genome-wide Analyses Identify KIF5A as a Novel ALS Gene . Nicolas et al. 2018, Neuron, National Institute of Health (NIH) and University of Massachusetts Medical School

To identify new genes that might be involved in ALS, the authors studied the genomes of 20,806 ALS cases and 59,804 control cases. The study also evaluated 1,138 cases of ALS that were passed down from family members, known as familial ALS. The authors identified a gene known as KIF5A to be associated with ALS. The protein produced from this gene helps to move cellular components inside the cells to keep them functioning properly. In general, those with the KIF5A mutation developed ALS at a younger age than those without the mutation. Additionally, mutations in KIF5A were different between PALS. Interestingly, in PALS where the KIF5A is not working at all (loss-of-function), survival was longer relative to typical ALS cases. The reasons for the longer survival in these cases is unknown.

Endocytosis regulates TDP-43 toxicity and turnover Liu et al. 2017, Nature Communications, University of Arizona, Tucson, AZ

Motor neurons in ALS show the aggregation of a protein called TDP-43 in a different region of the cell than where it should normally reside. This is thought to contribute to motor neuron disease, but the mechanisms are unclear. The authors demonstrated that TDP-43 toxicity is linked to a cell function known as endocytosis. Endocytosis is a process which allows a cell to take in material from the fluid surrounding the cell. TDP-43 build up inhibits endocytosis. This further increases TDP-43 toxicity and aggregation. Alternatively, enhancing endocytosis reverses TDP-43 toxicity and build up. These observations were confirmed in a TDP-43 ALS fly model. Thus, endocytosis dysfunction may be an underlying cause of ALS pathology.

CURRENT STUDIES USING VABBB TISSUES:

(Liachko -) Investigating calcineurin regulation of pathological TDP43 phosphorylation in ALS

Changes in the gene coding for TDP-43 cause some cases of ALS, indicating that TDP-43 functions are critical for brain health. In ALS, the TDP-43 protein undergoes a modification process known as phosphorylation, which helps pathologists identify disease-related TDP-43 structures. Phosphorylation of TDP-43 increases its build up and increases harmfulness in motor neurons. The enzyme responsible for reversing TDP-43 phosphorylation is a phosphatase known as calcineurin. Calcineurin reduces levels of neurotoxic TDP-43 and protects motor neurons. This study is evaluating whether impaired calcineurin function is a potential mechanism involved in ALS pathology.

(Bingol -) Investigation of necroptosis cell death pathways in ALS

ALS is a neurodegenerative disorder characterized by death of motor neurons in motor cortex and spinal cord. Motor neurons primarily die though apoptosis, or programmed cell death, but recent studies indicate the neuron associated glial cells die by, necroptosis, or programmed inflammatory cell death. Necroptosis is mediated by cell receptor interacting enzymes called RIPK1 and RIPK3. RIPK1 may drive inflammation in glial cells, and further damage motor neurons. Thus, prevention of necroptosis pathways by RIPK1 inhibition, should be beneficial for ALS patients by preventing both breakdown and inflammation in glial cells, and promoting the overall health of motor neurons. The purpose of the study is to understand what cell types die through necroptosis in ALS.

(Shewmaker -) Detecting post-translational protein modifications present within FUS-positive neuronal inclusions in post-mortem tissue

FUS is a protein involved in RNA regulation and cellular stress pathways. Mutations in FUS cause familial ALS. In such cases, FUS is found in the cytoplasm of neuronal and glial cells. Accumulated FUS protein causes toxici-

PUBLICATIONS AND NEW STUDIES UTILIZING VABBB TISSUES… CONTINUED

ty to cells. It has been shown that modification of FUS by adding a molecular phosphate (phosphorylation) is able to prevent toxic accumulation in cells. This project uses custom made anti-phospho FUS antibodies to identify patterns of protein build up in cells of patients with FUS-linked ALS pathology. The anti -phospho FUS antibodies will help to confirm the presence of FUS-positive buildup in human neural tissue and determine if phosphorylated and non-phosphorylated FUS populations are different in how they aggregate in neural tissues. This work is important in demonstrating the value of phosphorylation in delaying pathological aggregation in FUS-associated ALS .

(Scearce-Leavie/Huang -) Investigating RIPK pathway activation and inflammatory biomarkers in ALS

RIPK1 may play a role in inflammation in glia cells and astrocytes that are linked to motor neuron death in ALS. This project seeks to confirm that RIPK is increased in the central nervous system of patients with ALS. Additionally, this project will compare expression of RIPK with inflammatory cytokines. Cytokines are proteins involved in cell signaling. The results from the studies with ALS tissues will provide valuable information on the relationship between RIPK1 activity, neuroinflammatory markers, and disease stage to enhance the potential for future clinical trials using RIPK1 inhibitors.

(Zarnescu –) Identifying translational targets of TDP-43 in ALS tissues

A hallmark of ALS is the aggregation of TDP-43 in motor neurons and glial cells. TDP-43 mutations have been identified in patients with familial and sporadic ALS. TDP-43 is an RNA binding protein that aids RNA transport and RNA translation, the process that makes proteins in cells. TDP-43 associates with RNA stress granules as well as factors involved in translation. This suggests there is a link between TDP-43, RNA stress granules, translation and ALS pathology. Current knowledge of TDP-43's role in translation and its contribution to ALS remain poorly understood. TDP-43 is thought to interact with stress granules and translation factors, which regulates its harmfulness to the cell. This project will evaluate the physical and functional interactions between TDP-43 and RNA translation. This will help determine how errors in RNA translation lead to the pathology of ALS.

(Schnellmann -) Mitochondria and drug targets in spinal cord

Mitochondria are organelles that provide energy for cells. Mitochondrial dysfunction is a characteristic of ALS and traumatic spinal cord injury. While several studies have investigated mitochondria as targets for such conditions, enhancement of mitochondrial biogenesis (MB) remains an underexplored strategy. Enhancing MB using drugs called formoterol and LY344864 improves functional recovery of mitochondria in a mouse model of spinal cord injury. The purpose of this study is to assess and compare mitochondrial regulation in ALS and non-diseased human spinal cord tissue. ALS may decrease mitochondrial proteins and mitochondrial DNA. These studies will aid in the future development of drugs for stimulation of spinal cord repair in humans.

VABBB STUDY UPDATES

POST-TRAUMATIC STRESS DISORDER BRAIN BANK

Anyone living with PTSD in the United States may enroll in the PTSD Brain Bank

Learn more about the PTSD Brain Bank at:

http://www.research.va.gov/programs/tissue_banking/PTSD/default.cfm

The PTSD Brain Bank (PTSDBB) has experienced rapid growth in enrollment over the past year. The PTSDBB began a collaboration with PINKConcussions to increase the number of female Veteran and non-Veteran participants. PINKConcussions, is a non-profit organization with a mission to "improve the pre-injury education and post-injury medical care for women and girls challenged by brain injury including concussion incurred from sport, violence, accidents or military service. Additionally, the PTSDBB will begin recruitment collaborations with researchers at the Uniformed Services University of the Health Sciences and the Seattle VA Medical Center in the upcoming year. Please call the PTSDBB Coordinator, Tannu Singh, at 857-364-4198, with any questions or updates regarding the PTSDSBB.

COGNITION, BEHAVIOR, AND CAREGIVER BURDEN IN ALS

The "Cognition, Behavior, and Caregiver Burden in ALS" (CBCB -ALS) is examining whether Veterans with ALS experience changes in attention, thinking, and behavior, and how these changes affect their caregivers. As our study enters its fifth year, we are continuing to recruit and enroll Veterans living with ALS and their caregivers. Participating in this research study may help gain a better understanding of the cognitive and behavioral changes that can occur in people living with ALS and it may provide insight with how to prevent unnecessary burden and stressors for the caregiver. If you are a Veteran living with ALS and you have a caregiver who is not a medical professional, you might be eligible to participate in this research study and receive monetary compensation for your participation. Enrollment is ongoing. Please call the CBCB Coordinator, Derek Collins at (857) 364 -2136, with any questions or updates regarding the CBCB study.

CBCB - ALS
Cognition, Behavior and Caregiver Burden in ALS

Department of Veterans Affairs Biorepository Brain Bank
VABBB
Committed to research on brain disorders that affect Veterans

GULF WAR VETERAN'S ILLNESSES BRAIN BANK

The Gulf War Veterans' Illnesses Biorepository (GWVIB) has made an extensive effort to expand participation and awareness of the research project over the past two years. Beginning in January 2018, the GWVIB began working with representatives of the VA Informatics and Computing Infrastructure (VINCI) to obtain contact information for Veterans who served in the military during the 1990-1991 Persian Gulf War. This request for contact information was reviewed and approved by a VA Institutional Review Board whose role is to protect Veterans' privacy and safety. In a further attempt to increase awareness of the GWVIB to both researchers and Veterans, Derek Collins participated in a radio show airing on WVBF Taunton hosted by a local Veteran Service Officer. Derek provided an overview of the brain bank and how Veterans and researchers can be involved. The radio interview was made available to the public over many different social media platforms. [Please call the GWVIB Coordinator, Keith Spencer, at 857-364-2144, with any questions or updates regarding the GWVIB.

CURRENT VABBB PARTICIPANTS

- Do you have a new phone number?
- Are you moving?
- Have a major health change?

PLEASE LET US KNOW!
Call toll free at
866-460-1158

ALS BRAIN BANK UPDATE

The ALS Brain Bank is excited to share that it has been funded for an additional four years as it enters its thirteenth year since the study began. In the last year, the program has seen much progress and development that will help accelerate our research and understanding of the disease. For example, samples from our generous donors were used to identify a novel gene, KIF5A, associated with ALS by our collaborators at the National Institutes of Health and other institutions. Additionally, our team of neuropathologists uncovered a potential link between ALS and chronic traumatic encephalopathy (CTE) using the valuable tissues and data from our donors. Additional current research is examining factors related to survival in ALS. We are excited at the opportunity to continue working with the generous Veterans who are currently enrolled in our study, as well as with the families of those who have donated. Research into the causes, treatment, and eventual cure for ALS is greatly enhanced by donations made by Veterans and their families to the VABBB. Please call the ALS Brain Bank Coordinator, Nazifa Abdul Rauf, at 857-364-6748, with any questions or updates regarding the ALS Brain Bank.

Interested in participating?

Call us toll-free at 866-460-1158 for more information

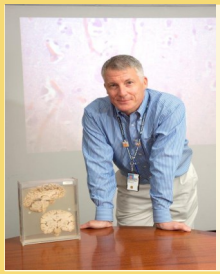
VABBB Team Participates n the "Walk to Defeat ALS"

Top Right: Derek Collins of the VABBB approaches the finish line

The "Walk to Defeat ALS" first began in 2000 and since then has raised over $276 million dollars to aid people living with ALS as well as their families. Each year in October, members of the VABBB research team at the VA Boston Healthcare System participate in the Walk hosted by the Boston ALS Association. Last year's walk marked the fifth year of continuous participation on behalf of the VABBB. Joined by family and friends, our team walked to commemorate Veterans enrolled in our research studies and in memoriam of deceased Veterans who made tissue donations to make our research efforts possible.

The walk, which takes place at Carson Beach, is a 3-mile walk that is open to the general public. People choose to walk for various reasons. They walk "For the Fight" to motivate and educate others about ALS while being hopeful to find a cure. People choose to walk "For Care Services" to connect with others for social support and to ensure that families of patients with ALS have access to loaner equipment and supplies to better accommodate them. Lastly, People walk "For Public Policy" to raise awareness and to garner support from legislators in our nation's capital to introduce and pass bills that will increase funding for ALS research. The 2017 and 2018 "Walk to Defeat ALS" fundraising events raised $503,000 and $455,000 respectively, which are both in the 90th percentile of the goal proposed by the ALS Association.

ASK A NEUROPSYCHOLOGIST



Christopher (Kit) Brady, PhD is a neuropsychologist at the VA Boston Healthcare System and an Assistant Professor of Boston University. He is also the Co-Principal Investigator of the VA Biorepository Brain Bank (VABBB).

Can you tell us about your role in the care of Veterans at the VA?

I am a neuropsychologist. A neuropsychologist is a doctor who assesses persons' thinking and behavior to determine if there is a problem with these abilities. Neuropsychologists also do research on the effects of brain changes on thinking and behavior. I do clinical assessments and research, and also supervise student trainees to help them learn to be neuropsychologists.

What led to your interest in working with Veterans with neurological conditions such as ALS, PTSD and Gulf War Illnesses (GWI)?

Ever since my days as an undergraduate in college, I found myself interested in brain changes that occur in aging. When I graduated college, I worked on research projects studying Alzheimer's and Parkinson's Diseases. That interest translated to my pursuing my doctoral and postdoctoral training in the effects of aging and on cognition. My VA career has provided me the opportunity to assess and study cognition in aging Veterans with ALS, PTSD, GWI, and other conditions. Working with these Veterans in the VA offers many great opportunities to provide a comprehensive continuum of care to the Veterans and their families.

Can you tell us about how ALS impacts thinking and behavior of persons diagnosed with ALS?

For decades, most persons assumed that ALS did not affect the mind. Furthering this idea was that one of the most famous persons to suffer from ALS was Stephen Hawking, who possessed an unparalleled intellect. More recently, we've come to know that some, but not all, persons with ALS (PALS) do experience cognitive and behavioral changes that range from mild in some PALS to more severe in others. When behavioral changes are seen in PALS, they are usually an increase in apathy and/or disinhibited behavior. Cognitive changes can affect attention, the ability to remember certain words (such as people's names or the name of objects), and mental flexibility. Some evidence also suggests that ALS affects social cognition, which is how people process, store and apply information about other people or social situations. If the changes in these behaviors and cognitive abilities progress to become so severe that it impairs the ability to function (beyond the functional movement impairments due to ALS) and make informed decisions, then a more serious condition such as frontotemporal dementia may be present.

Are there any similarities between the cognitive and behavioral changes seen in patients with ALS and those with PTSD and Gulf War Illnesses?

There are differences in the pattern of changes both across and within these disorders. Also, the age of the person with these conditions will influence the pattern of changes seen in individuals. In general, persons with cognitive and behavioral changes associated with these conditions experience impairments in attention and in the ability to block out distracting stimuli (i.e., distractibility). They may also experience changes in language, with problems in word finding ability that are greater than one would expect for their age. In many cases, persons with these conditions may be more prone to become irritable or have trouble controlling how they feel. One condition that is not associated with these conditions is an "amnestic" dementia such as Alzheimer's disease. An amnestic dementia affects the ability to store memories; memories are either never laid down in the brain or are "lost" via memory decay over time. Instead, many times the memory problems experienced by those with ALS, PTSD and Gulf War Illnesses are problems with retrieving previously stored memories. In these cases, a prompt or reminder frequently triggers the memory being recalled. We all experience these types of memory failures as we age, but they may occur more frequently in those with these disorders, beyond what would be expected for a given age.

How do you diagnose patients with cognitive and behavioral impairments? And when should a patient be screened for such impairments?

A clinical diagnosis is arrived at via a clinical interview and a series of neuropsychological tests. Sometimes neuroimaging is helpful in determining the causes of the cognitive change. Also, repeat testing over time can determine if the cognitive impairments are stable or are progressing, as seen in a progressive dementia. Persons should be screened when they complain about problems with thinking and memory. Many times, a screening will calm a person's fears because testing reveals normal performance.

Continued on Page 8

ASK A NEUROPSYCHOLOGIST *CONT. FROM PAGE 7*

Regular screenings may also reveal a more serious cognitive problem early in the course when better treatment options are available.

How do these behavioral and cognitive changes impact PALS' caregivers?

Caring for those with ALS places an extraordinary burden on caregivers. Studies in ALS caregivers show that patient factors such as decreasing functional abilities, increases in problematic behavior and patient depressive symptoms are related to increases in caregiver burden. Alternatively, a strong protective factor in reducing caregiver burden is having a strong social support network of family and friends.

What are some ways clinicians can address these challenges faced by caregivers to improve disease progression in PALS and reduce burden for caregivers?

VA has been a leader in recognizing the important role that family caregivers play in providing care to Veterans with various disorders. However, the demands of daily caregiving frequently make it difficult for caregivers to get respite to care for their needs. Fortunately, the VA Caregiver Center at the Memphis VA has developed a telephone-based caregiver support program, "Resources for Enhancing All Caregivers Health in the VA" (REACH VA), to assist caregivers in building skills in stress and mood management, and problem-solving. REACH helps caregivers manage patient behavioral concerns and their own stress. More information about this program and other caregiver resources may be found at

https://www.caregiver.va.gov/

Can you tell us how brain donations have led to a better understanding of cognitive deficits seen in patients with ALS, PTSD and Gulf War Illnesses?

Although several mouse models have been developed to study conditions such as these affecting Veterans, these models are limited and the need for research quality human central nervous tissue (CNS; brain and spinal cord) tissue for genetic research is critical. Furthermore, the information that Veterans provide while living by completing our regular assessments is invaluable in understanding relations among cognitive abilities and neuropathology seen when conducting postmortem brain examinations. This "clinicopathological" research is essential to understanding the pathology causing brain changes in these disorders. The VABBB is presently the only national prospective cohort study and CNS tissue bank in the U.S. that is enrolling and conducting ongoing follow-up on Veterans with these conditions to conduct this clinicopathological research.

Special thanks to the ALS Clinic Team at the Boston VA for their hard work for the clinic!

- Manisha Thakore-James, MD
- Naomi Turbidy, LICSW (Social Work)
- Elizabeth Bowers, RNP (Palliative Care)
- Michelle Becker, (Licensed Dietician)
- Bernadette Cummings, (Licensed Occupational Therapist)
- Anne Lambergs, (Major Medical Committee)
- Dawn Medeiros, (Clinical Nurse Coordinator)
- Caitlan E. Keane, (Licensed Speech & Language Pathologist)
- Denise Hayes, (Nurse Practitioner)

Call Us Toll Free!

If you're interested in participating in any of our studies, please call any of these numbers toll free. Participants can enroll in more than one study .

ALS Brain Bank

(866) - 460 - 1158

PTSD Brain Bank

(800) - 762 - 6609

Gulf War Brain Bank

(855) - 561 - 7827

Caregiver Study

(857)- 364-2136

THANK YOU!

We are deeply grateful to all the Veterans who have decided to make this generous after-death organ donation supporting the VA's commitment to ALS research. While no one can say when ongoing scientific investigations will discover the magical key that unlocks the secret of this destructive disease, it is certain that without the very precious gift of neurologic tissues, progress would be much slower. We are also deeply grateful to Veterans' families and caretakers who have done everything in their power to fulfill the Veterans' wishes of organ donation.

DEPARTMENT OF VETERANS AFFAIRS BIOREPOSITORY BRAIN BANK

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The VABBB is funded by the Biological Laboratory of Research and Development Service of the Department of Veterans Affairs and the National Center for PTSD.