



V A B I O R E P O S I T O R Y B R A I N B A N K N E W S

A YEAR IN REVIEW

VABBB CELEBRATES 10 YEARS IN SERVICE TO VETERANS!

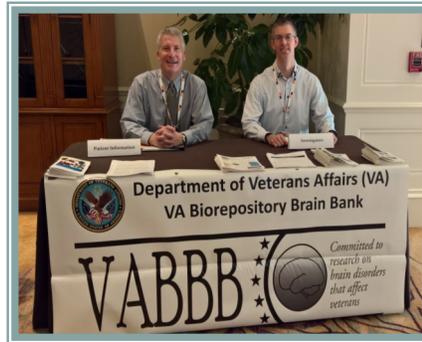
THE VABBB: 2015 SUMMARY

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2015 was an eventful year for the VA Biorepository Brain Bank. We added new staff, and we are currently enrolling participants for our ALS, Gulf War, and PTSD Brain Banks, as well as in our Cognition and Caregiver Burden Study.

- Currently, the ALS Brain Bank is actively following 121 participants (114 persons with ALS and 7 controls) and has successfully collected tissue from 187 participants. We're also happy to report that we continue to have a 100% success rate for tissue recoveries in which we are notified by families who wish to proceed with a donation. This success is due in no small part to the dedication and generosity of the Veterans and their

families in making these donations, as well as the numerous medical professionals and teams • that have assisted us .



[Christopher Brady, Ph.D. and Thor Stein, M.D. Ph.D. attended the Motor Neuron Disease Association Conference]

- The Gulf War Brain Bank is seeking to enroll Veterans of the 1990-1991 Gulf War era. For more information on the this study, please see p. 3.
- The PTSD Brain Bank is recruiting Veterans and non-Veterans

with PTSD. For more information, please see p. 4.

• Christopher (Kit) Brady, and Thor Stein attended the Motor Neuron Disease Association (MND) Conference in November 2015. Dr. Stein noted, "There was a lot of interest in the resources available from the VABBB at the conference...the clinical and pathological data the VA has collected is unique and will be important for unraveling the mechanisms of ALS.

• Finally the Cognition and Caregiver Burden study is recruiting Veterans with ALS and their caregivers nationally and from the ATSDR's National ALS Registry. For more information on this study, please see p.6.

- We continue to send tissue and data to investigators doing cutting-edge ALS research. Please see p. 4

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

VABBB ENROLLING HEALTHY ADULTS

The VABBB is continuing to accept donations from healthy individuals to complement our ongoing studies. Comparing healthy brain tissue to tissue donated by persons affected with brain disorders is an important tool for studying neurological problems. These comparisons help provide unique insights into the causes of brain diseases and disorders. If you are healthy, and have thought about donating after your death, please feel free to contact us.

HELP US SPREAD THE WORD:

Learn more about the need for healthy adult participants at:

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

STAFF CHANGES AT THE VABBB

Several staff members have joined the VABBB team this year. In March, we welcomed Hannah Burris, B.S. to the Cognition and Caregiver Burden study. In April, Max Stewart, B.A. joined the ALS Brain Bank. The previous ALS Coordinator, Latease Guilderson, shifted to working on the growing PTSD Brain Bank. In May, Shannon Murphy, B.S. joined the team and works on several projects. November saw several new staff beginning with Tarnjit (Tannu) Singh, M.A. joining the Gulf War Brain Bank, Nazifa Abdul Rauf, M.P.H.

starting with the Cognition and Caregiver Burden study, and Gabriel Walt, B.A. coming on board to work on several projects.



The VABBB team in Tucson, AZ.

Sean Walker, Health Science Specialist (left); James Averill, Research Specialist (middle); Ian Robey, Ph.D., Technical Director (right).

Unfortunately, the VABBB also said goodbye to four team members in 2015. June saw the departure of Shelley Amberg, former coordinator of the Gulf War Brain Bank, and in July Melissa Weiner, former coordinator of the Cognition and Caregiver burden study, moved on to a new position in Pennsylvania. The end of the year also saw one more departure from the

Boston group, as Data Manager Sally Perkins retired after seven years with the VABBB. For more on Sally's time at the VABBB and her recent retirement, see p. 5.

From the VABBB Tucson team, Katrina Trevor, Ph.D. retired near the end of 2015, with Ian Robey, Ph.D. taking her place as the new technical director.

We bid sad good byes to past staff and happy hellos to our new members. See page 8 for the full list of VABBB staff.

CAREGIVER CORNER SIX MONTHS TO FOREVER

BY: SEAN HALL

It's been a long road since my father was diagnosed with ALS over thirty five years ago. He is seventy now and at times I think he will outlive me. We are very fortunate for the care he receives at the VA hospital. I visit him three to four evenings per week, attend school full-time, and work part-time. Since he has been afflicted with this disease for so long, I can hardly remember the man he used to be. My two half-brothers have rarely seen him outside of a wheelchair or hospital bed, nor have they ever heard him speak as normally as you or I would. He has had *no voice* for the past fifteen years.

My role as caregiver has changed over time. As a teenager, when my father first started to deteriorate, I would assist him getting in and out of his wheelchair, and help him stand with his walker. At that time, his hands became less efficient and his speech heavily slurred.

When I graduated high school, I moved to Los Angeles leaving my father, stepmother, and my half brothers. I kept in touch and would visit now and then, seeing how my half-brothers were coming along. For primarily medical benefit reasons, my father divorced and then had roommates and daily health care, living close

to and seeing his two young sons frequently. As the internet became more accessible, emails became his new tool for communication. In 2000, he sent an email explaining he was having a very difficult time getting a roommate; he asked if I would consider living with him as a partial caregiver. I agreed.

Things were fairly easy as I settled into my new life. I quickly got a job and we had in-home caregivers on a daily



(Continued on page 3)

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 Caregiver Corner. The piece provides a small window into the experience of a caregiver.

CAREGIVER CORNER...CONTINUED

SIX MONTHS TO FOREVER

BY: SEAN HALL



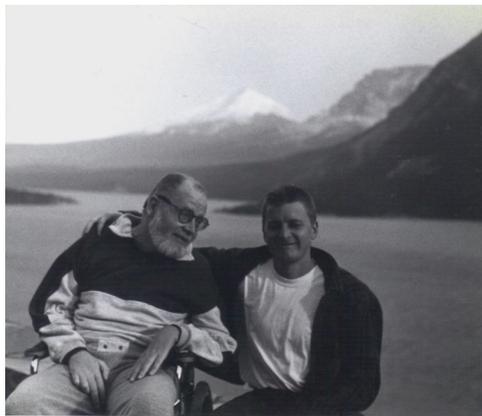
basis, so I didn't have to do much direct care other than maintaining the house and helping him with finances and communications. He was active in his electric wheelchair and I would assist in taking him places by van. Gradually things became more challenging once our primary long-term caregiver was no longer

with us. Regular outside care became less consistent and I ended up doing more and more as my father is completely dependent upon others for his care. I was responsible for putting him in and out of bed, dressing, bathing, feeding him, and maintaining an external catheter along with other necessary bathroom duties.

As part of the progression of ALS, his breathing difficulties and emergency room trips resulted in him having a tracheotomy. Full-time care for him at home was insufficient for his medical needs, so he was moved permanently into the VA Spinal Cord Injury Unit. My role as a caregiver now consists of frequent visits. I bring him things he needs and wants, and despite being on ventilator and having a feeding tube inserted in his abdomen, he still eats food by

mouth and I bring him outside food every Friday night. He is able to communicate with a single electronic button that he touches with his head, and through a long process of elimination (EZ Keys program), he is able to write and speak messages, operate the computer to compose emails, Facebook, and surf the web. Patience and time has been the biggest frustration in my interactions with him, and some things go unsaid, for both of us. I suppose this is true for most of us and our fathers.

I have heard many people comment, "I don't know how he does it, hanging in there all this time." It is a hard thing to imagine: becoming



a prisoner in your own body, yet your mind still functions. I don't think there is one ultimate secret as why he has persevered, but rather a combination of professional health workers, advances in science and technology, support of friends and family, and "luck". Although it seems one could hardly say there is luck involved in this case, it is a matter of personal perspective. As Lou Gehrig once said when faced with his affliction, "Today...I am the luckiest man alive."

There may be one element to his longevity that I find keeps him and myself looking ahead to the future: long-term goals. After seeing that he would outlive the original pre-

dicted diagnosis, and with the birth of my second half-brother, he set in his mind that he would try and live to see them both graduate high school. When they graduated high school, he decided that he would keep going to see them graduate college- they did. Through his many years living with ALS, he continues to try new things, remain connected to others, and offer kindness as he can. He has his daily ups and downs, just as we all do, but I have noticed overall, when he is focused on long-term projects he seems happier, more alert and alive.

HAVE A STORY TO TELL?

We would like to thank Sean Hall 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)

NEW RESEARCH PROJECTS USING THE VABBB

The primary mission of the VABBB is to support ALS research in pursuit of a cure and better diagnosis, therapies, and treatments for ALS. Below we've highlighted four projects utilizing tissue donated to the VABBB by the Veterans enrolled in the study.

Endogenous Retrovirus Activity in ALS Neurodegeneration

Endogenous retroviruses are a natural part of the human genome and normally dormant. We all have them, but endogenous retroviruses generally do not cause disease. Some inflammatory diseases, however, are linked to the activation of endogenous retroviruses. The human endogenous retrovirus-K (ERV-K) has been observed in the neurons of patients with ALS. Researchers are trying to determine if ERVK activity plays a role in ALS. It is possible that ERVK is not eliminated by the immune system because of defects in normal anti-viral immunity and inflammatory reactions. This

project seeks to identify which inflammatory immune signals enhance or limit ERVK activity in ALS brain and spinal cord tissue. The findings will be applied to the development of new therapies that will inhibit ERVK activity.

RNA Binding Proteins in ALS

RNA is the genetic material used to make proteins. RNA produced in the cell nucleus undergoes a complex series of processes before being translated into protein. When RNA is processed improperly in neurons, it can lead to neuron damage or death (neurotoxicity). Several RNA Binding Proteins (RBPs) involved in RNA processing have been associated with ALS. This study focuses on

RBP genes called ELAVs. Different ELAV RBP genes are expressed within the nervous system. The primary aim of this project is to determine if ELAVs (particularly ELAV4) are altered in ALS tissues. Research on the role of ELAVs will provide new perspectives on the mechanisms of ALS and novel targets for diagnosis and treatment.

TAR-DNA-binding protein-43 (TDP-43) in ALS DNA Damage

TAR-DNA binding protein of 43kDa (TDP-43) is a DNA binding protein that normally resides in the cell nucleus. In ALS, TDP-43 accumulates, or aggregates abnormally in the cytoplasm of neuronal cells (see Figure 1). TDP-43 cytoplasmic aggregation

is also associated with frontotemporal lobar dementia (FTLD) and approximately 40% of other neurodegenerative diseases. Previous studies have identified a key DNA repair protein called Ku in TDP-43 aggregates, suggesting that TDP-43 is involved in DNA repair. The aim of this project is to determine if the shift of TDP-43 from the nucleus to the cytoplasm of neurons results in deficient DNA repair. This lack of DNA repair may prove to be a new factor in the cause of ALS. Continuing research will lead to new models of ALS disease mechanisms and promising avenues for drug therapy.

ALS-related Tau Tubulin Kinases

Cellular proteins are often modified by a process called phosphorylation. Phosphorylation is when a protein known as a kinase adds a phosphate to another protein to alter its structure slightly and manipulate its function. The aggregation accumulation of phosphorylated TAR-DNA binding protein of 43kDa (TDP-43) in neurons is a hallmark of ALS (see Figure X(1)). Kinases called Tau Tubulin 1 and 2 (TTBK1/2), have been found to directly phosphorylate TDP-43. This leads to the alteration and change in function of TDP-43. Elevated TTBK1/2 kinases have been observed in ALS nervous system tissue in ALS. This study seeks to discover if disease-related versions of TTBK1/2 occur in ALS, and if these kinases can be targeted for the treatment of both early and late stage ALS.

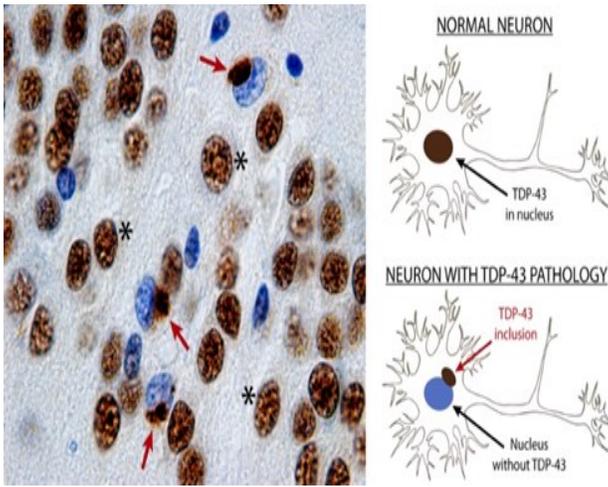


Figure 1

Ongoing Studies :

The VABBB is pleased to support several ongoing research projects using VABBB tissue donated by Veterans. Such studies are vital to .

Ongoing projects include:

- ◆ Understanding Defects in Vulnerable Brain Motor Cortex Neurons
- ◆ Genetic Studies of Familial and Sporadic ALS
- ◆ Promoting the Protection of Motor Neurons in ALS
- ◆ Role of Cell-Cell Communication in ALS
- ◆ RNA (ribonucleic acid)-based Causes of ALS
- ◆ MicroRNA in ALS

GULF WAR BRAIN BANK UPDATE

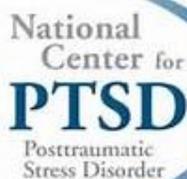
The Gulf War Veterans' Illnesses Biorepository (GWVIB) brain bank is seeking veterans of the 1990-1991 Gulf War era who would like to participate in research and conditions affecting Gulf War veterans. Veterans enrolled in the GWVIB will complete surveys about their health every six months or so, and upon their death donate their brain and other body tissue for future Gulf War Veterans' Illnesses research.

Veterans can begin helping now by enrolling even though the tissue donation may occur years from now. All veterans of the 1990-1991 Gulf War era, regardless of whether they served in the Gulf War region or are experiencing symptoms are eligible to participate in the GWVIB brain bank.

Contact Tarnjit Singh, M.A. at 855-561-7827 for more information.

Learn more about the Gulf War Veterans' Illnesses Brain Bank at:
http://www.research.va.gov/programs/tissue_banking/GWVIB/

PTSD BRAIN BANK ADVANCES THE FIGHT AGAINST PTSD



National
Center for
PTSD
Posttraumatic
Stress Disorder

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

The PTSD Brain Bank (PTSD BB) began recruiting Veterans with PTSD and those without during the summer of 2015 to increase awareness about PTSD. Non-Veterans are also eligible to participate. Led by Dr. Matthew Friedman, the former Executive Director of the US

Department of Veterans Affairs National Center for Posttraumatic Stress Disorder (PTSD), the PTSD BB is the first repository uniquely devoted to the study of PTSD. There are participating sites across the country, with the Boston VABBB offices serving as the primary site for coordinating activities and receiving brain tissue.

The National PTSD Brain Bank's findings should help pave the way for new approaches to diagnosis and treatment of individuals with PTSD." For more information on enrolling in the PTSD Brain Bank, visit us on the web at http://www.research.va.gov/programs/tissue_banking/PTSD/ or contact Latease Guilderson, MSW at 800-762-6609.

Learn more about the PTSD Brain Bank at:

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

June is National PTSD Awareness Month!



FAREWELL TO SALLY PERKINS, M.S., P.T.

Sally Perkins was with the VABBB from 2008 until the end of 2015

On December 17, 2015 we congratulated Sally Perkins on her 7 years of service and commitment to the Department of Veterans Affairs. She was honored with a retirement party and a plaque from the VABBB.

Sally Perkins has played an integral role in the administration and data management of the brain bank.

During her time at VABBB she improved the groups' data technology by building databases, monitoring usage, and troubleshooting.

However, most of our participants knew her to be a nurturing soul who developed mean-

ingful relationships with them and their spouses.

She, along with her husband, are experienced botanists and active members of the American Rhododendron Society with her home garden being devoted primarily to the study and growth of rhododendrons.

As a retiree, she looks forward to devoting her newly deserved free time to tending to her plants, volunteering with her church, and travelling. She will be missed.



Left: Sally is presented with a plaque for her time at the VABBB by P.I. Neil Kowall, M.D.

Bottom Right: Sally and her husband John alongside the members of the VABBB.

STUDY HIGHLIGHT: COGNITION, BEHAVIOR, AND CAREGIVER BURDEN IN ALS

This study is investigating whether there are risk factors for the development of problems with thinking, behavior and mood in **P**ersons with **A**myotrophic **L**ateral **S**clerosis (PALS), and whether these problems affect their caregivers (e.g., spouse, adult child, professional caregiver). Any Veteran or non-Veteran PALS and their caregiver may participate in this study, including those currently enrolled in the VABBB.

Questions We Want to Answer:

- ◆ How does ALS affect changes in thinking, behavior and mood?
- ◆ Are there risk factors for the development of these changes?

- ◆ How do these changes affect PALS' caregivers?
- ◆ Do caregivers have special needs that healthcare providers should be aware of?

What can I expect if I take part in this study?

In order to take part in this study, PALS and their caregivers will both need to participate. After enrollment, PALS and caregivers complete some assessments by telephone and by mail. This may take about an hour of your time for each of you. About 6 months after the initial assessment, we will ask caregivers to answer some questions over the phone and complete some brief questionnaires.

**Interested in participating?
Call us toll-free at
866-460-1158 for more information**

The caregivers will answer questions regarding their observations of PALS thinking, behavior, and mood, as well as whether they are experiencing any challenges or burdens as a result of caregiving. A year after enrollment, PALS and caregivers will have another telephone interview and be mailed questionnaires similar to the initial assessment. These annual and 6-month follow-ups

(caregivers only) will continue for up to 3 years.

What are the potential benefits of taking part?

PALS and their caregivers will be compensated \$20 jointly at the start of the study and at each follow-up visit. In addition, the results of this research may lead to a better understanding of changes that take place in thinking and behavior in PALS, and may help doctors and researchers understand how to better help caregivers and prevent unnecessary stress.

VABBB WALKS TO DEFEAT ALS

VA researchers take action to help raise ALS awareness

For the second year in a row, the VA ALS Brain Bank Team at the VA Boston Healthcare System promoted awareness by raising money for and participating in the ALS Association's Massachusetts Chapter Boston Walk to Defeat ALS® held at Carson Beach on October 24, 2015.

The annual three mile walk raises money that helps fund care services provided by the local ALS Association chapter, as well as supporting ALS re-

search for the following year.

Accompanied by family and friends, members of the team walked in honor of the Veterans living with ALS who are enrolled in the VABBB ALS Study. They also walked as a tribute to the deceased Veteran participants who donated their brain and spinal cord to the VABBB to support ALS research.



Right and Bottom left: The VABBB group walks to defeat ALS with ALSA Massachusetts

Top Right: The VABBB Team and family. From the right is Max Stewart, Shannon Murphy, Hannah Burris, Sally Perkins, and Latease Guilderson

(photo credit to Jarvis Chen, <http://jarvischen.zenfolio.com/>)

The VABBB team raised \$1360 through their efforts and the **ALSA Massachusetts chapter raised \$394,414.91 for research.**



ASK A NEUROLOGIST



Dr. Manisha Thakore-James is a neurologist at the VA Boston Healthcare System and Boston University. She is also the head of the multidisciplinary ALS clinic at the Boston VA.

Are there any new treatments (drugs, diaphragm pacing) being tested?

There are many new trials going on researching different aspects of ALS. Clinical trials offer hope for many people and an opportunity to help researchers find better ways to safely detect, treat, or prevent disease. Clinicaltrials.gov and the ALS Association website are excellent resources for identifying clinical trials that are going on in your area.

One topic that was the center of attention in ALS research is diaphragm pacing. There were several studies going on in Europe and in the US investigating the utility of diaphragm pacing. Currently the information that is coming from these studies is conflicting. A study in the UK was stopped because the risk of mortality was higher in patients that were implanted with the pacer. However, studies in the US are continuing to investigate if there may be a subgroup of patients that might benefit from this technology.

What treatment benefits do Veterans receive through VA compared with the private sector?

Veterans who develop ALS may be eligible for benefits through the VA. These benefits can provide resources to veterans that can sometimes be more difficult in the private sector.

Service connected veterans can be eligible for grants that will allow adaptations to their homes or vehicles that will enable to remain at home. A vehicle can be adapted so that the patient can remain driving as long as it is safe to do so or be adapted so that when the patient can travel safely by wheelchair, if they are unable to walk or transfer to a seat.

Bilevel positive airway pressure (BIPAP) can be very useful for patients to treat the breathing problems that can be associated with ALS. In the private sector, insurance companies will not pay for this until the ALS patients breathing tests have reached a certain threshold. At the VA, these services can be available to the patient as soon as his doctors deem it is necessary. This is very useful since this equipment can take some time to learn to use.

What is "voice banking"?

ALS (Amyotrophic Lateral Sclerosis) can cause problems with speaking, including changes to your speech and voice. Many people with ALS lose their ability to speak and may choose to get a speech generating device (SGD). Some people with ALS like the idea of using their own voice when it becomes necessary to use a SGD to communicate. Voice banking is the recording of one's speech/voice for future use in a SGD. There are two methods of voice banking: playback of recorded messages and synthesized speech.

Playback of recorded messages : Recorded messages can be programmed into a SGD and used when needed for communication. With this method, only recorded messages will use the person's natural voice.

Synthesized Speech: This method of voice banking allows for both recorded messages and newly created messages, using spelling, to be spoken using the person's natural voice. It requires the potential user to record a large sample of words and phrases using a specific software program.

You are strongly encouraged to discuss voice banking with the Speech- Language Pathologist (SLP) associated with the ALS Clinic where you receive services. Each clinic may have a different format for collecting, organizing and providing messages to be used for creating communication displays, and for recording and saving messages.

"I've heard about a drug called GM6 that slows down ALS progression. What is this drug and can I get it?"

GM6 is a drug that works to slow down disease progression by modifying several different pathways in the development of ALS. So far, the drug has been testing in mice with genetically induced ALS, and was found to extend life in these mouse models. It also was found to delay onset of ALS symptoms. This is an exciting new drug that may provide options for disease prevention in families with genetic ALS and may work to slow down progression in many different types of ALS . We would like to note that the drug not being available for public use yet, and that the company is not giving out the drug to people with ALS at this time, as it's still undergoing testing and additional stages of approval for human use.

What can family members of a relative with ALS do to help their relative and themselves cope with the disease?

Every person who is battling ALS has their own background, their own coping styles and ultimately their own perspective on their ALS journey. This is also true of their loved ones and caregivers who are equally as devastated by this disease.

Relationships will be challenged and roles changed to accommodate the loss of functional abilities of the patient. Couples that may have struggled in their marriages or relationships before the diagnosis of ALS may stay in the relationship out of guilt, fear, not wanting to hurt the person, lack of support, or financial reasons.

Not only does the patient have to cope with the initial diagnosis and continued loss of functional abilities but their caregiver too has to adjust to these changes. Family and friends may avoid their loved one with ALS as they do not know what to say or do to help them. Caregivers may take on a protective buffering of their loved one, that could make things worse if the patient is not allowed to work through their own grieving and learning to cope.

In becoming a caregiver, some people experience a loss of the roles and relationships they had with their loved one before the illness. Identify ways to keep your personal and family roles and relationships alive. Talk about family events and news about children and grandchildren. Look at family photos together. Making the effort to retain the relationship you have had with your loved one - aside from your role as caregiver will help you in coping with the multitude of changes family caregiving poses.

Potential Resource : Care Connection

The Care Connection program is simple: it's a network of volunteers from the community - friends, neighbors, members of community organizations like your church, or other service groups - that provide help for the person with ALS and his or her family, and often give the caregiver a break from their day-to-day responsibilities. Visit <http://www.alsa.org/als-care/caregivers/care-connection.html>.

Special thanks to the ALS Clinic Team at the Boston VA for their contributions to the "Ask a Neurologist" article in addition to their hard work for the clinic!

- Naomi Turbidy, LICSW (Social Work)
- Elizabeth Bowers, RNP (Palliative Care)
- Melissa Moore-Boyle (Licensed Dietician)
- Deanna Allen (Licensed Speech and Language Pathologist)
- Kara Valtour (Occupational Therapist)
- Anne Lamberg (Major Medical Committee)
- Jacqueline Deppen, RNP

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
(855) - 561 - 7827

Gulf War Brain Bank
(800)- 762 - 6609

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.

The views expressed in this newsletter are those of the authors and do not necessarily represent the views of the Department of

Department of Veterans Affairs Biorepository Brain Bank

