

VA Biorepository Brain Bank News

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Current Status of VA Biorepository Brain Bank ALS Study

The VA Biorepository Brain Bank (VABBB) ALS study was established at the VA Boston Healthcare System to promote and support research in Amyotrophic Lateral Sclerosis (ALS) by collecting brain and spinal cord tissues essential in ALS research. Donors of these tissues are Veterans with ALS or its closely related disorder, Primary Lateral Sclerosis (PLS), who generously volunteered to donate their neurologic organs after death. In this brief newsletter, we would like to describe the major events that have taken place in the past several years.

Veterans with ALS who were interested in participating in ALS research were originally referred to us by the VA's ALS Registry at the Durham VA Medical Center. Although the Registry is now closed, we have continued to enroll interested Veterans who have ALS or closely related neurologic disorders, and have maintained contact with approximately 240 Veterans. In addition to the Veterans referred to us by the Registry, we have also enrolled other Veterans who contacted us on their own after learning of the VABBB.

Study participants come from 47 states including Alaska and Hawaii. Idaho, Delaware and Rhode Island are the only states as yet unrepresented. The Veterans in our study include women as well as men, and differ in terms of race, age and time since onset of ALS. We have re-contacted study participants every six months and have obtained information on current symptoms and health status.

A table summarizing the characteristics of the Veterans in our study is below. As might be expected in a study of Veterans, males outnumber females by about 20 to 1. While it is true that ALS is more common among males, the large

gender imbalance in this study results from the preponderance of males in a Veteran population. Racially, the Veterans enrolled in this study are not as diverse as might be expected since African-Americans as well as other racial groups are far more represented in the military than appear in this group. However, the racial composition of the Veterans who participated in this study closely reflects the racial composition of those who enrolled in the VA's ALS Registry, our referral source. The age at ALS diagnosis of members of this group is slightly older than the age at diagnosis for persons with ALS in the general population.

Characteristics of Veterans Enrolled in the VABBB

Characteristic	
Average age at diagnosis and age range	55.9, 21-83
Average age at study enrollment and age range	65.7, 33-87
Number of men/women	226 / 11
Racial/ethnic group, Number and (%)	
Caucasian	226 (95.3)
African American	8 (3.5)
Other or missing information	3 (1.3)
Diagnosis, Number and (%)	
Amyotrophic Lateral Sclerosis	155 (65.3)
Primary Lateral Sclerosis	32 (13.4)
Muscular atrophy	38 (16.0)
Other	13 (5.4%)
Use of mechanical breathing assistance (%)	48.1
Use of Feeding Tube (%)	24.5



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VABBB

neuropathologist,
Dr. Ann McKee

This research suggests that of the many genetic and environmental risk factors for ALS, trauma to the central nervous system emerges as a strong influence for molecular changes that eventually result in the symptoms of ALS.

Do ALS and Traumatic Brain Injury Have Anything in Common?

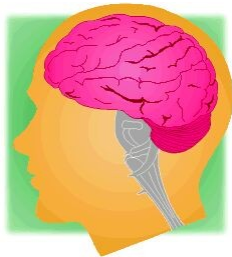
The similarity in symptoms among persons who have experienced repeated head injuries and persons with ALS has been noted for years. Many boxers eventually exhibit signs of motor neuron changes and among professional soccer players in Italy, the occurrence of what has been diagnosed as ALS is six times what it is in the general population. Soccer players, unlike football players, do not use helmets. The high occurrence of ALS, or a disease process very similar to ALS, among soccer players might be explained in part by the use of the head to ram the soccer ball, and in part by the frequent head-on collisions among players.

Dr. Ann McKee, neuropathologist on our staff and an expert on traumatic brain injuries, has studied the potential connection of head injuries and motor neuron disease on a molecular level. She was able to document that frequent head injuries result in a dementia-like disease known as chronic traumatic encephalopathy or CTE. The disease is characterized by specific protein changes in the brain. In some athletes, she found that prior to death, they had developed severe weakness, muscle wasting, and other symptoms that are also present in ALS. After death, the brains and spinal cords of these athletes also displayed physical changes

seen in motor neuron disease.

This research suggests that of the many genetic and environmental risk factors for ALS, trauma to the central nervous system emerges as a strong influence for molecular changes that eventually result in the symptoms of ALS. Dr. McKee is now continuing her work in this area focusing attention on how those molecular changes occur. Since the time span between head injuries and onset of motor neuron disease is often quite long, a clear understanding of the molecular progression may offer the opportunity for intervention and treatment.

How Tissue Donation Assists ALS Research



It is known that the primary and immediate cause of ALS is the destruction of nerve cells. What is not known however, is what triggers cell destruction, and what factors are responsible for nerve cell damage. There is now increasing evidence that the cause of ALS is not a single fac-

tor but rather a combination of factors interacting in very specific patterns. For example, work on mouse models of ALS has suggested that there are complex inter-related molecular and genetic factors that together result in the death of motor neuron cells common in ALS. While studies on

mouse models have yielded important findings, it now becomes necessary to learn whether the results from mouse studies can apply to humans. The neurologic organs donated by Veteran participants are used to support diverse areas of ALS research.

Selection of Investigators to Receive Tissue Samples

We wanted to make sure that all scientists doing research on ALS would be aware of the availability of neurologic tissues. We contacted major departments of neurology throughout the nation. We also reviewed the medical literature to identify investigators currently involved in ALS research, and asked professors of neurology to indicate scientists who needed neurologic samples to further their ALS work. Researchers who requested tissue samples submitted an application describing their current research, explaining why their work required tissues, stating how their investigations would further knowledge of ALS,

and documenting their past scientific productivity.

Approved Applications

The ultimate goal of the approved applications is to provide a clearer understanding of the basic biology of ALS. This information could then lead to the development of better treatment options and life improvement. Research using tissue samples from the VABBB will study the following areas:

- How are growth factor proteins able to establish and maintain the health of motor neuron cells?

- What are the factors that assist motor neuron cells to respond to the stresses caused by inflammation and chemical toxins?

- What is the action of non neuronal cells, such as glial cells, that can impair the health of motor neurons?

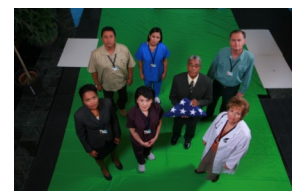
- What is the role that antioxidants play in repairing motor neuron damage?



Providing high-quality tissue and related health data to qualified investigators is the primary mission of the VABBB

Review criteria for submitting tissue requests to the VABBB

A committee of established experts in ALS research reviewed the applications of the tissue requestors. In deciding which investigators would receive tissue samples, the committee carefully considered the scientific importance of the proposed research, the new medical knowledge likely to be derived from the research, as well as the past productiveness of the investigator and the staffing and funding resources available to the applicant to carry out the research.



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Thank you.

Department of Veterans Affairs Biorepository Brain Bank



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.