

The VOICE of FTD

WINTER 2019

Brain Donations

It takes brains to solve frontotemporal degeneration (FTD)

Your brain is the best gift you can give to help decipher FTD. Donating your brain can help advance the science to find treatments and a cure for these disorders. This includes both healthy and diseased brains.

Only when brain tissue is studied under a microscope can answers be found to questions asked by both researchers and the family of the donor. The two main reasons to make a brain donation are to receive an accurate diagnosis and to support research.

“Some families are primarily interested in a diagnosis, and some primarily want to help others through science,” said Robin Riddle, CEO of the [Brain Support Network](#) (BSN). “But most families donate equally for both reasons.”

Currently, there are no known cures nor treatments to slow the progression of FTD. But brain donations provide researchers tools to investigate the complex genetic and biochemical steps that lead to loss of brain cells. This may provide clues to discovering ways to prevent, treat, or cure these neurological diseases.

The [National Institutes of Health](#) (NIH) describes FTD as a clinical syndrome associated with shrinking of the frontal and temporal lobes of the brain. Symptoms can include changes in behavior, issues with movement, and problems with language. Several specific diseases, as defined by their characteristics under the microscope, cause the various forms of FTD. These include behavioral variant frontotemporal lobar degeneration

(bvFTLD, also called bvFTD), progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), primary progressive aphasia (PPA), and frontotemporal dementia – amyotrophic lateral sclerosis (FTD-ALS). “Pick’s disease” is a set of findings at autopsy that can be associated with any one of several of these outward, clinical pictures.

The FTD syndromes can be difficult for physicians to distinguish from one another and from conditions such as Alzheimer’s disease and Parkinson’s disease (PD). Riddle created Brain Support Network (BSN) in 2004 when her father was diagnosed with PSP. One of his early symptoms, leg rigidity, was misdiagnosed as arthritis in 2000. In 2003, his slurred speech, falls, and cognitive dysfunction led to a misdiagnosis of stroke. Finally, in February 2004, a neurologist correctly diagnosed PSP.

Riddle arranged for the donation of her father’s brain upon his death in October 2007. The autopsy confirmed PSP. In 2011, the brain was included in a landmark study, published in [Nature Genetics](#), in which researchers identified three new genes linked to PSP.

Riddle said of the more than 700 brain donations BSN has coordinated since that first one, about half of the diagnoses made while the person was alive were changed following autopsy.

The most common misdiagnosis for FTD is for Alzheimer’s disease. If it’s not FTD, usually it is hippocam-

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pal-sparing Alzheimer's because unlike most Alzheimer's, in this type the memory is not impaired, Riddle explained.

"FTD is an umbrella for several dementias. It is not unusual to get a clinical diagnosis of PSP or CBD and after death receive a pathological diagnosis of Pick's disease," Riddle said. "Unfortunately, you must have a specific clinical diagnosis before donating, even though an autopsy is needed to obtain a correct diagnosis."

Receiving an accurate diagnosis can be very helpful for the family for several reasons.

"There is a psychological benefit to knowing the diagnosis," said [Lawrence I. Golbe, M.D.](#), [CurePSP's](#) Director of Scientific Affairs and professor at [Rutgers Robert Wood Johnson Medical School](#) in New Brunswick, N.J. "I don't know exactly why, but we like to label our enemies."

However, in theory there also could be a direct benefit to surviving family members, Dr. Golbe said. "If the donation brings a cure, the children of the donor could benefit if the disease is hereditary."

Dr. Golbe speaks from experience. He led a team that discovered a family with autosomal-dominant PD in 1987. Through genealogical and clinical work, they were able to include 61 affected family members. Ten years later, they found a mutation in the gene for alpha-synuclein, which since has been found to be central to the development of all Parkinson's, including the majority that are not hereditary. There is a similar study being conducted for Alzheimer's disease in Colombia, South America, he said. In that family, the causative gene is already known, and the purpose of the project is to discover other factors that influence the development of the illness.

"We can now sequence every gene in an individual's genome, but we can't tell which variants in that person are causing their disease and which are not," Dr. Golbe said. "This is easier when a disease runs in a family because the genes of the members are similar and there isn't a lot of other 'noise' or variations.



"However, finding genes causing non-familial diseases is more difficult and requires hundreds or even thousands of DNA samples from autopsy-confirmed brain donations in order to statistically cancel out all those variants among unrelated individuals.

"This is one of the most important functions of a brain bank for neurodegenerative diseases," Dr. Golbe noted.

BRAIN BANKS & RESEARCH

There are numerous brain banks across the United States and around the world. A list of brain banks that collect central nervous system tissue from various neurodegenerative diseases and normal aging controls is available via a map view along with a search option on the [Alzforum website](#). In addition, the [NIH NeuroBio-Bank](#) has a network of brain and tissue repositories.

Brain banks that focus on neurodegenerative diseases are interested in brain donations from persons with diagnoses such as the FTD disorders, but also Lewy body dementia (LBD), multiple system atrophy (MSA), PD, and others.

Brain banks store both the tissue and clinical information about a patient. Scientists can then investigate what clinical features went along with the pathology findings.

As soon as the brain is removed from the head, it is cut in half, said Dr. Golbe. Half is frozen at minus 70 degrees Celsius (minus 94 degrees Fahrenheit). The other half is preserved in formalin.

"The frozen half is used for chemical analysis, in-

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cluding DNA tests,” he explained. “This half is used for experiments.”

The preserved half is used to make the diagnosis. It is sliced and stained (dyed) and put under a microscope. Researchers then look to see if certain proteins are present in the brain, as identified by their telltale dye. This is not a chemical test; it must be done visually after dyes specific for certain chemicals have been applied.

“Researchers can extract DNA from donated tissue to correlate the DNA with other pathological features or correlate it with clinical features such as disease onset age or speed of the disease progression,” said Dr. Golbe. “If we could find a gene associated with early-adult-onset of a usually late-life disease, then that would be a huge clue to the disease in general.”

How many experiments can one brain be used for? It depends, said Dr. Golbe. If a researcher is interested in one small cluster of brain cells in one specific spot, then only one or two experiments can be performed using that one brain. However, each person’s DNA is generally the same throughout the brain, so one brain can support hundreds of experiments. But for reasons mentioned above, hundreds or even thousands of brains with one disease are needed to tease out genetic information related to that specific disease.

[CurePSP’s brain donation program](#) has enabled the [brain bank at Mayo Clinic](#) in Jacksonville, Florida, to have more than 2,000 brains. “To get that many brains together in one place is great for a rare disease such as PSP,” Dr. Golbe said.

The best place for the family of a patient with FTD to make a brain donation for research is the medical center where the person is being seen, said Riddle of BSN, but only if it has a brain bank and it actively conducts and publishes research for FTD.

Her dad was treated by doctors at the [University of Utah](#), which Riddle said is a great institution, but it did no FTD research. Instead, his brain was donated to the Mayo Clinic in Jacksonville where Dr. Dennis Dickson researches Alzheimer’s disease, dementia, PD, PSP, and



other neurodegenerative disorders. Dr. Dickson is also part of the new [ALLFTD Study](#) as is BSN.

“As part of the new ALLFTD Study, we can handle the brain donation arrangements for centers that don’t have their own neuropathologist or for research participants who have moved outside the geographic area of the participating site,” Riddle explained.

While there are other places around the United States that accept brains and actively do FTD research, most of the BSN brain donations have found their way to the brain bank in Jacksonville. One reason is because it accepts brains from persons not seen at the Mayo Clinic. Some brain banks will only accept brain donations from patients at their facilities or enrolled in a clinical trial, Riddle explained.

Riddle noted that she favors Mayo Clinic’s brain bank because families receive the neuropathology report that indicates the person’s accurate diagnosis within 100 days and she knows that research is being conducted in the area of this diagnosis.

“Some brain banks take a year or even a year and a half,” Riddle noted. “My dad’s report took only two weeks, but that was 12 years ago.”

HOW TO DONATE

Brain donation can seem complicated, but planning ahead reduces stress for family members when death of their loved one is imminent.

Riddle said that about half of the calls to BSN are urgent, meaning the person’s death is near or has already occurred, and half are people making plans in advance.

“We have some who made the arrangements five

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years ago,” Riddle said. “We’ll do occasional check-ins with those families.”

The first step is to learn about brain donation, talk about it as a family, and make the decision whether to do it.

Next, contact the facility to where the donation will go for its instructions. Another option is to work with BSN for assistance with all of these logistics.

Three things are needed to successfully donate a brain, said Riddle: brain tissue; medical records from a specialist such as a neurologist, psychiatrist or psychologist; and a written report from the family. Of course, there is also paperwork to complete, which includes not only basic information about the donor, but also a consent form. The person who may legally sign the consent form varies according to the state you live in, she said.

“Medical records show the person’s medical history and what treatments were done,” Riddle said. “The written report from the family does not have to be long, but family members are better with providing examples of symptoms, behavior changes, or language problems.”

When death is imminent (hours or days away), calls are made to confirm the donation, discuss costs, and alert necessary parties that a brain recovery may occur soon.

“Donating a brain is very easy,” Riddle said. “The hard part for some families is the time ordering medical records from doctors’ offices. If the loved one has seen ten, maybe more neurologists, it can be hard to remember those names and order those records, especially if doctors were visited only once.”

When the decision is made and plans arranged in advance, copies of the completed paperwork should be provided to family members and other necessary parties. At the time of death, the process is simple because the family only has to follow the instructions provided.



Brain Support Network

COSTS

The average cost in the United States to recover a brain for research is \$1,000, said Riddle. It can range from \$500 to \$1,500, and will vary by state and locale. In addition, sometimes the funeral home or cremation company charges for work that is performed at their site. Removing the brain does not disfigure the body and should not delay or complicate funeral plans.

Fees are paid directly to the pathology specialist and funeral home (or cremation organization). BSN does not charge a fee.

Each brain bank has different practices for recovering a brain. Some, like Mayo Clinic, does not pay anything to recover a brain, and they provide the autopsy report to the family at no charge.

For families unable to afford the costs, CurePSP offers brain donation grants of up to \$750 for persons diagnosed during life with FTD, PSP, CBD, or MSA. BSN also offers grants for some disorders, including LBD, Pick’s, PPA, PD, early onset Alzheimer’s, etc. for people who cannot afford the cost.

“We don’t want families to not donate because of cost,” Riddle said. “Nonprofit funding can make it happen.”

When possible, BSN requests that families donate \$500. Riddle said about half of the families donate the amount themselves, and about half request donations to BSN in lieu of flowers.

“It is a ‘pay-it-forward’ contribution,” Riddle said. “Past contributors help your family, and your donation helps the next family.”

Brain donation is not for everyone and is not always feasible. Sometimes a person’s religious beliefs or prac-

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tices may preclude brain donation. In addition, brain recovery must occur within 24 hours of death. Beyond that time, the brain is much less useful for research, noted Golbe.

The FTD Disorders Registry (FTDDR) is not directly involved in facilitating brain donations. Nor does the Registry currently receive or record brain autopsy results. However, participants can contact FTDDR to update their loved one's diagnosis. To do this, contact the Registry Director Dianna Wheaton, M.S., Ph.D., at 888-840-9980 or director@ftdregistry.org.

"In time, we hope to increase the clinical information the Registry is collecting," Dr. Wheaton said. "The autopsy results specifically would be highly desirable in order to have the definitive diagnosis."

Positive things can come from making a brain donation, Riddle said.

"Psychologically, it is challenging for most people to accept that we will die or that our loved one will die, even when the loved one is on hospice. Being on hospice is a good indicator of the right time to finalize end-of-life arrangements such as brain donation," she said. "Just because those arrangements are finalized doesn't mean that the person is going to die right away."

Donating a brain, whether diseased or healthy, for research is an important decision. It needs to be made after careful consideration and with the support of the whole family.

If you feel you would like to contribute to FTD research through brain donation, please consider learning more by following the links under the RESOURCES heading on the right.

**Join the Registry.
Tell Your Story.
Advance the Science.**

"Together, we can make a difference!"

RESOURCES

More information:

- ◆ [AFTD Brain Donation Info](#)
- ◆ [Brain Support Network Brain Donation Info](#)
- ◆ [CurePSP Brain Donation Info](#)
- ◆ [NIH Brain Donation FAQs](#)

Handouts:

- ◆ [CurePSP Brain Donation Pamphlet](#)
- ◆ [Brain Support Network Brain Donation Infographic](#)
- ◆ [Brain Support Network Brochure for Alzheimer's, FTD, Lewy body degeneration](#)
- ◆ [Brain Support Network Brochure for Parkinson's disease and parkinsonian disorders \(PSP, MSA, CBD, LBD\)](#)



Brain Banks:



- ◆ [AlzForum List of Worldwide Brain Banks](#)
- ◆ [NIH NeuroBioBank](#)

Brain Donations Overview Video:

- ◆ <https://youtu.be/Y4s4u5AE6AA>

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