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## MIND OVER MATTER

By Ron Cassie

Photography by Christopher Myers

POST-MORTEM BRAIN TISSUE STORED AT THE UNIVERSITY OF MARYLAND MAY HOLD THE KEY TO UNDERSTANDING DISORDERS FROM AUTISM TO ALS.

**Preparing in Hawaii** to compete in the 2005 Ironman World Championships, neural scientist Robert Vigorito, then at the University of Maryland's Brain and Tissue Bank, overheard athletes talking throughout the week about a certain competitor. Jon Blais hadn't qualified for the event based on his season's best finish, but instead received a waiver to enter the brutal triathlon, a 2.4-mile ocean swim, 112-mile bike, and 26.2-mile run. As Vigorito soon learned—and race officials already knew—the curtain was closing fast on Blais's lifelong dream of racing on the Big Island. ¶ Several months earlier, doctors had told the 33-year-old that he was suffering

Ronald H. Zielke, Ph.D., professor at the University of Maryland School of Medicine, created the Brain and Tissue Bank two decades ago.

from symptoms of amyotrophic lateral sclerosis, also known as Lou Gehrig's disease.

"Of course, I knew very well what ALS was and that no one with that diagnosis could do this race," says Vigorito. "I was at the finish line when Jon, in the joy of the moment, 'log-rolled' [on his stomach] across in 16 hours and 48 minutes—11.5 minutes before the 17-hour cutoff. It was emotional, obviously, and I congratulated him afterwards. We decided to keep in touch, and then I got to know his family, too."

The following year, Blais, who had become an advocate for ALS research in the short period following his diagnosis, returned to Kona in a wheelchair, meeting Vigorito again. A month later, after Vigorito competed in another triathlon in Florida, where Blais lived but was quickly deteriorating, the neural scientist addressed the elephant in the room. "I finally said, 'Jon, you know where I work, and you know what I do [harvesting brain tissue for research]. We need to have a talk.'"

Blais had expressed interest in donating his brain to science previously, but nothing firm had been set. Both men knew tissue donation, enabling future research, at least offered the potential of something good coming from Blais's heartbreaking circumstances. Vigorito promised Blais that when the moment came, he would remove his friend's brain himself, as well as necessary spinal-cord tissue and periphery nerves, taking every care that the job would be done properly. Six months later, the brain-and-spinal-nerve-cell disease that reduced Blais to a blind quadriplegic, unable to talk or swallow, killed him. At home on a Sunday night, Vigorito took a brief call from Blais's mother, who broke the news. With a 24-hour window for most tissue recovery, Vigorito flew to Florida the next morning. Arrangements

were already in place with a local funeral parlor for Vigorito to do his work. Afterwards, as he returned to Howard County, FedEx delivered Blais's tissue, sealed and packed into dry ice and in a Styrofoam cooler, to the Brain and Tissue Bank on West Baltimore Street for freezer storage.

"The thing Jon often pointed out to people was that in the 75 years since Lou Gehrig, the Yankee slugger, had received his diagnosis, the treatment essentially remains the same—there isn't one," says Robert Blais, Jon's father. "It's a death sentence. And in terms of being an advocate for research, Jon always wanted to 'walk the talk,' which meant, to him, making the donation."

This summer, the National Institute of Child Health and Human Development (NICHD) Brain and Tissue Bank

## BREAKTHROUGHS IN SEVERAL DEVELOPMENTAL DISORDERS ARE ON THE HORIZON, SAYS MELISSA PARISI OF NICHD.

at the University of Maryland School of Medicine marked 20 years of providing needed tissue to researchers studying hundreds of disorders, with a strong emphasis on childhood issues, such as Down Syndrome, autism, cerebral palsy, and sudden infant death syndrome (SIDS). The bank also collects a much smaller percentage of tissue for adult degenerative disorders, including ALS, Parkinson's disease, sickle-cell disease, and Alzheimer's. The Blazeman Foundation, founded by Jon Blais's family, reached an agreement earlier this year with the University of Maryland bank for ALS patients to donate their tissue there post-mortem.

Many of the 3,500 brain donations on hand belong to children and adults with extremely rare conditions; however, "con-

trol" samples from healthy individuals are also gathered. To date, scientists from 23 countries have received tissue from the brain bank, one of the world's largest such facilities, publishing 540 research papers.

"The Brain and Tissue Bank is a unique resource, in that they collect tissue from predominately in the U.S., but distribute it, meeting Institutional Review Board protocol requirements, to researchers all over the world," says Melissa Parisi, chief of the Intellectual and Developmental Disabilities Branch at the NICHD. Parisi points out that animal brain tissue, while valuable for some research, inevitably falls short in meeting the needs of scientists working on genetic and other disorders. A mouse's brain, she notes, obviously does not replicate the size, organizational structure, and complexity of the human brain.

Parisi believes because of progress in genetic science, neurophysiology, and insights from studying brain specimens, breakthroughs in several childhood disorders, including autism, Down Syndrome, and Rett Syndrome (a genetic disorder, which affects development in girls), are on the horizon. Significant progress in brain research, she says, has aided in the understanding of all three disorders. She also notes that important advances in the treatment of adrenoleukodystrophy, or ALD, a disorder profiled in the film *Lorenzo's Oil*, were made by researchers at Johns Hopkins and the Kennedy Krieger Institute with support and tissue from the NICHD Brain and Tissue Bank.

"I'm constantly amazed by many families' response to the idea of tissue donation," Parisi says. "For some families, it's too difficult. To them, it's the essence of their child. But for other families, it's a way to make sure that their children's illness can have a longer, lasting impact. They don't want children and their families in the future to suffer the same way."

H. Ronald Zielke, a University of Maryland professor of pediatrics with a

Ph.D. in biochemistry, who still serves as director of the Brain and Tissue Bank, was the driving force behind the project's creation two decades ago. Vigorito, who recently retired and is also the founder of the Columbia Triathlon Association, was his first hire. Among other duties, Zielke oversees the legal donation procedures, storage protocols, and research applications. Walking between 33 chest and upright freezers in the basement laboratory, which keep tissue frozen at minus-80 degrees Celsius, Zielke notes that some genetic disorders are so rare that there is not yet sufficient tissue collected to warrant full-on research projects.

When the cantaloupe-sized brains arrive at the bank, technicians carefully split them into two hemispheres in the facility's small lab, then further slice the gray matter into quarter-inch sections. Ultimately, sections from one hemisphere are placed into heat-sealed, heavy plastic bags—identified and catalogued by diagnosis—and placed into the freezers. Sections from the other hemisphere, however, are preserved using a formaldehyde chemical process, also identified and catalogued by diagnosis, of course, and kept in Tupperware-like containers on long shelves behind a locked door.

"This is a safe place to store tissue," he says, gesturing to the freezers' alarms, alternative power system, and backup liquid carbon dioxide tanks. "Twenty years from now, the tissue will be good, and people will be able to use it." Zielke is patient and grandfatherly in his manner, but also serious and direct. "So, yes, it may not be within a year when research begins if you have a very rare disease, but, down the road, when research questions arise—and the number of samples grow—it will be available." (Zielke also maintains a dry sense of humor about what some may consider a morbid occupation in a morgue-like environment: "We're going to the basement, of course," he quips, leading a visitor down an elevator from his office to



the facility where brain-tissue donations are stored. "Why is it always these things are in the basement? There's no reason.")

Currently, Zielke notes, 20 percent of all requests from the brain bank come from researchers studying autism—a diagnosis now reported in one in 88 children. This past June, the University of Maryland's collection of autism brain samples became ever more critical when an unfortunate freezer malfunction at Harvard-affiliated McLean Hospital in Boston compromised much of that facility's autism-tissue collection, the world's

largest at the time. Dr. Francine Benes, director of the Harvard Brain Tissue Resource Center, where the brains were housed, described the loss to the *Boston Globe* as a "priceless collection." "You can't express its value in dollar amounts," she says in the story.

Stephen M. Edelson, Ph.D., director of the Autism Research Institute (ARI), which has a formal partnership with the Brain and Tissue Bank at the University of

Maryland, says that despite the recent explosion in research, autism remains a very mysterious condition. He says brain tissue remains crucial for researchers hoping to develop treatments, and possibly, find a cure at some point. "There is a genetic component and an environmental component," says Edelson, who has been in the field for 30 years. "If we know where the abnormalities are in the brain, for example, that could give us a road map to what the causes are and, potentially, deal with the symptoms."

On their website, ARI encourages donations as well as pre-registration. Tissue donation, they highlight, is accepted by most major religions and the procedure to recover tissue does not interfere with a traditional funeral service. The

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brain bank covers any costs incurred by the donation.

But while many people obviously donate money to various advocacy organizations, participating in fundraising walks and other events, not enough think about tissue donations required for research. "We can't fill a significant number of the requests we get for autism research because of a lack of brain tissue," Zielke says. Those with autism often (thankfully) live long lives, and one challenge in collecting post-mortem tissue arises because the cause of death for those afflicted with autism often comes unexpectedly due to accidents. With that, among many other examples in mind, Zielke and his team have developed relationships with pathologists and medical examiner's offices across the country, maintaining a 24-hour hotline.

About half of the donations, however, arrive via the Maryland medical ex-

aminer's office on nearby West Preston Street, where Anthony Weldon, research program coordinator at the Brain and Tissue Bank, keeps in daily contact. Weldon says about 50 percent of donations begin with an inquiry from the medical examiner's office to a family. The other half of donations typically begin with the family of a loved one contacting the Brain and Tissue Bank on their own. "There's a range of emotions from families, and we don't ever want to say the words 'brain tissue' or 'death,'" says Weldon, a thoughtful, mature young man in his late-20s. "Some are so intimately involved in the care of a loved one that they knew it was coming and are not surprised. They tend to understand it's time-sensitive and are willing to take the necessary steps."

The most difficult cases, unsurprisingly, arise in the death of a child, Weldon says. Particularly, the death of a "normal" child, whose tissue is valuable as a control sample. "Overall, about 60-70 percent of people eligible to be contacted by us say yes," Weldon says. "We never push anyone. It's a personal decision and whatever they decide is fine, of course, and we respectfully accept their decision."

Most major religions support organ donation, including post-mortem tissue donation for research, Zielke says. He adds that Americans are generally open to the concept of brain-tissue donation. "It's cultural," he says. "We are scientifically oriented and forward-looking, and Americans like to help each other—and that extends to organ and tissue donation." A lower rate of organ and tissue donation in Japan, for example, has been reported in the past.

Not long after Linda Long learned that her oldest son, Georgie, who was diagnosed with a severe form of autism as a child, passed away on June 22, she received a call from the coroner's office in Baltimore. The medical examiner's office, she recalls, asked if she would be open

to receiving a phone call from someone at the University of Maryland School of Medicine's Brain and Tissue Bank. Zielke called her personally a few minutes later.

"I found him extremely compassionate," Long says. "He explained why he was asking for this donation and why it was needed, but didn't linger, which I appreciated. I was ready to start grieving. But I knew it was the right place, the right thing to do."

Long says her son, 35 years old when he died, and his surviving brother, Willie, 26, who has a different form of autism, had participated in numerous research studies through the years. "When Georgie was born, it was right in the period after the 'refrigerator mother' (emotionally frigid mother) theory was put to rest," says the retired nurse, who now lives in Charles Village. "I know from my own experience with him that they have done so little research on actual brains, and they are not going to get anywhere otherwise."

At the same time, Long also says that she can appreciate that others may feel a loved one's mind resided, so to speak, in their brain, and may feel differently about donation.

**"I CAN UNDERSTAND** why it's harder to convince people to approve the donation of a loved one's brain tissue, compared to other organs," Long says. "But to me, I saw that as sort of Georgie's computer—and it was broken down. All the neurons didn't fire right.

"I always thought Georgie was very soulful," she continues, "and that part of him was different than just the computer. My greatest hope is that something in research can be found through Georgie's contributions to help other people." ■

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