Not many research labs around the world analyze living human brain tissue — and no one is doing it like Seattle’s Allen Institute for Brain Science.

Here’s an offer most people can easily refuse: Donate part of your brain to science — while you’re still alive. But in the Seattle area, about 50 people every year say, “Sure.” Gary Williams is one of them.

The former logger and Army veteran suffers from epilepsy so severe he was forced to give up the job he loved as a tattoo artist. The electrical storms in his brain robbed him of a near-photographic memory. He can’t even ride his mountain bike anymore for fear the exertion will bring on an attack.

So on the morning of his 48th birthday, Williams is lying in a bed at Harborview Medical Center, waiting to be wheeled into the operating room. Bearded and heavily inked with designs that range from Sasquatch and Mount Rainier to a pot-smoking gypsy, he also sports a small checkerboard on his left temple. It confirms the spot where neurosurgeons will soon open his skull and attempt to cut out the part of his brain responsible for seizures that wrack his body and leave...
ABOVE: Williams, of Montesano, shows off some of his ink before brain surgery. Williams hopes the operation will eliminate the hand tremors that forced him to give up his career as a tattoo artist.

RIGHT: A television monitor shows UW Medicine neurosurgeon Dr. Jeffrey G. Ojemann preparing to remove a healthy piece of brain tissue in order to reach the diseased portion of the brain causing Williams’ seizures.

Williams limps and shatters for days at a time. In order to reach that faulty patch of brain, Williams’ surgeon will first have to strip out a marble-sized piece of healthy cerebral cortex — the wrinkled, outermost layer of the brain, where our higher cognitive abilities reside. At most hospitals, the bits of normal tissue excised during surgeries for epilepsy or brain tumors are burned as medical waste. But to scientists in Seattle, they’re a treasure trove — an astonishingly rare opportunity to peer into the workings of the living human brain.

By rushing the tissue from the OR to laboratories in South Lake Union, researchers at the Allen Institute for Brain Science can study the cells while they’re still alive and connected to each other, tracking with the electrical impulses that are the currency of thoughts, memories and perception. Many samples remain viable for three days. With special handling and storage, some of the tiny slices will continue to function for a month or more.

If you’ve watched many horror movies, the notion of scientists zapping human brain tissue in the lab might conjure images of Dr. Frankenstein screaming, “IT’S ALIV!" But these bits of tissue lack anything approaching sentience, and the Seattle work has more noble goals. The loftiest is a better understanding of how billions of neurons collectively give rise to human consciousness. Studying live human brain tissue is the only way to learn how those neurons actually function within the body’s most complicated organ, the researchers say.

And because decades of mouse studies have yet to yield cures for Alzheimer’s, autism, epilepsy and a host of other vexing disorders, many experts argue that live human brain tissue might offer a more effective way to figure out what goes awry in diseases and how to fix it.

"This is very cutting-edge stuff," says neuroscientist Jonathan Ting, a leader of the project. "We don’t even know the limits of what we can do or the questions we can ask with these techniques." No one would be possible without people like Williams, who’s happy to see his surgical leftovers put to good use.

None of it would be possible without people like Williams, who’s happy to see his surgical leftovers put to good use. "Why wouldn’t I want to help other people that have the same problems as me?" he asks, shrugging.

F OR A MAN about to have a 3-inch hole cut in his head, Williams is remarkably calm. He’s a combat veteran,” he says, as machines beep and monitor his vital signs. "I’ve been through worse.

During the operation, UW Medicine neurosurgeon Dr. Jeffrey Ojemann will do his best to avoid critical areas of Williams’ brain. But the procedure carries risks, including memory and speech impairment. Williams is betting on the upside: that he will have fewer seizures and a clearer head.

"I’m being reborn," he says, with a grin. Ninety minutes later, Williams is out cold and covered with blue surgical drapes. Only the left side of his cranium is visible. After bone is cut and the tough, protective dura peeled back, Williams’ brain is exposed, glistening and pulsing. Ojemann slides a strip of electrodes into the area where he suspects the epilepsy originates. EEG...
Research associate Herman Tung uses an instrument called a vibratome to carve fish-scale-sized slices from a chunk of fresh human brain tissue.

After recording the electrical activity of a single, living neuron from human brain tissue, Allen Institute for Brain Science research associate Lindsay Ng extracts the nucleus of the cell and places it in a tube so another team of researchers can determine which genes are switched on and off — information that might be directly relevant to human brain disorders.

Tracings race across a screen, some jumbled and staccato. "That's really abnormal," Ojemann says, pointing to a pattern of frenetic peaks. "It's like a mini-seizure."

Ojemann was born to the brain business. His father and brother are neurosurgeons, as was his late uncle; his mother is a neurologist who specializes in epilepsy. When he's not operating, Ojemann analyzes brainwave recordings to find better treatments for stroke and epilepsy. He was eager to collaborate when the Allen Institute started its human brain tissue initiative five years ago.

"I hope this helps us treat epilepsy and helps us develop new therapies," he says. "I think the sky's the limit on what they can learn."

Once he's pinpointed the troublesome portion of Williams' brain, Ojemann is ready to begin cutting. Peering through a surgical microscope, he trims away a disc of tissue from the outermost layer of the temporal lobe, a part of the cerebral cortex involved in memory, speech and comprehension. He places the pinkish blob in a beaker filled with a frozen slurry of artificial cerebrospinal fluid.

It's just the beginning of Williams' surgery, which will continue for another two hours. But the race is on to get that morsel of brain into the lab.

Amara Casper, a research associate at the Allen Institute, is waiting in the hall with a wheeled cart and a small blue cooler. She hooks the beaker to an oxygen tank, tucks it in the cooler and rolls the cart into the back of a white van for the 1.8-mile trip through some of Seattle's worst traffic.

About 15 minutes later, the blob is the center of attention in a narrow lab where half a dozen people swarm purposefully. Some examine the chunk and separate it into smaller bits. A technician uses an instrument called a Vibratome to slice the brain pieces into paper-thin slices the size of fish scales.

"Literally, it's like slicing through a hot dog," Ting says. The brightly lit room has only one thing in common with the dungeons where Hollywood's mad scientists cackle over brains in jars: lots of bubbling fluid. Keeping the tissue alive requires constant oxygenation and perfusion with a cold broth of nutrients, chemicals and buffers, Ting explains.

It's an unusually busy day. Another human specimen arrived earlier, from an emergency brain surgery at Swedish Neuroscience Institute. "It's always boom or bust," Ting says. Sometimes the researchers pull all-nighters when tissue arrives in the evening. "There's a lot of pressure, because you're feeling like this is the most precious material you can possibly handle."

Eight Seattle neurosurgeons participate in the program, and roughly 50 patients a year donate tissue. That's nearly a fourfold increase since Ting joined the institute to help launch the human tissue work after several frustrating years in university labs. 
BRAIN POWER
trying to understand mental illness by study­ing mice. "It’s hard to convince yourself alone anyone else in the academic community, that these things are relevant for human use," he says. But the new project was so risky, even the institute’s chief scientist wasn’t sure it would pan out. "He thought it was the craziest idea ever," Ting recalls.

The institute’s industrial-scale approach is on display in the electrophysiology lab, where a controlled microsurgery is underway with the goal of identifying cells with the proper spatiotemporal pattern to generate electrical signals that could be directly relevant to human disease. "Most research doesn’t treat people with diseases," says Mansvelder, "they’re game. It’s a world where you’re working with data that includes genetic analyses of 2.5 million living human brain cells and clinical measurements from more than 13,000 patients. Williams is still grappling with the trauma of today’s blunt-force approach to brain disorders like epilepsy. He has a hard time carrying on conversations and will start speech therapy soon. It could take months for his energy to come back and even longer before he sees improvements from the operation. Ojemann estimates the surgery has a 50 to 70 percent chance of eliminating Williams’ seizures. Williams’ greatest hope is that it will stop the tremors in his right hand so he can get back to the tattoo business. If that happens, he’s promised Ojemann and his staff free ink work — if they’ve gotten it.

Two weeks after Williams’ surgery, the tissue he donated to the Allen Institute has been used — every bit of information from the cells and added to a database that includes genetic analyses of 2.5 million living human brain cells and clinical measurements from more than 13,000 patients. Williams is still grappling with the trauma of today’s blunt-force approach to brain disorders like epilepsy. He has a hard time carrying on conversations and will start speech therapy soon. It could take months for his energy to come back and even longer before he sees improvements from the operation. Ojemann estimates the surgery has a 50 to 70 percent chance of eliminating Williams’ seizures. Williams’ greatest hope is that it will stop the tremors in his right hand so he can get back to the tattoo business. If that happens, he’s promised Ojemann and his staff free ink work — if they’ve gotten it.