



Extreme measures

By Erin Graham

Melodie's treatment had been a roller coaster of short-lived successes and backslides into failure. The usual battery of antiepileptic medications, which control seizures in two-thirds of children, helped for a few months at a time, but the convulsions always returned. At times, they'd be so strong that Melodie would be knocked off her feet, often hurting herself during the falls. When she was 3, she became a candidate for brain surgery to remove the epilepsy "hot spots" that caused uncontrolled electrical activity in the brain that resulted in her seizures. Since this kind of surgery has so many risks, Children's only considers it for patients who don't respond to medication. Even in that group, only 5 percent end up having surgery.

So Melodie was admitted for imaging tests and continuous electroencephalogram (EEG) monitoring, during which electrodes attached to her scalp recorded her brain's seizure activity. The equipment is so sensitive that it even picks up the small seizures that don't lead to physical convulsions. This allowed Melodie's doctors to see where the seizures originated, how they traveled and where her normal, epilepsy-free brain functions were based. "Ideally, these tests identify the source of the epilepsy so we can remove it," says Scott Pomeroy, MD, PhD, neurologist-in-chief. "But of course you can't just remove any part of the brain because you don't want to create disability. So extensive testing is crucial."

In order to paint a full picture of the brain's activities with the necessary level of detail, it's often necessary to take an additional step and record directly from the brain's surface through a cutting-edge, high-tech procedure called cortical mapping. To map Melodie's brain, neurosurgeon Joseph Madsen, MD, opened her skull and placed plastic strips embedded with platinum electrodes directly on top of her brain. When she woke up, doctors stimulated each electrode while having her answer questions and remember words to determine

NEUROSURGEON JOSEPH MADSEN (left) and colleagues tried everything they could to calm the seizures overtaking Melodie Mclean's life, but nothing worked. So they turned to the most dramatic option—removing half of her brain—as a last resort.

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which functions were carried by areas underneath, mapping her motor skills, language center, sensation and memory.

“Mapping is like designing a military campaign,” says Madsen. “You want to know where the potential enemies (epilepsy) are and hope they’re separate from the people you want to protect (healthy brain). It’s easier to take out the enemies if they’re alone than if they’re all mixed up together.” Unfortunately, in Melodie’s case, the areas causing the epilepsy and those that housed her crucial language functions were close together, making extensive brain surgery too risky. Also, since Melodie didn’t have many physical limitations



and the operation was likely to cause a fair amount of disability, she wasn’t an ideal candidate for a hemispherectomy. “The decision to perform this surgery on a patient who does not already have significant weakness on one side is an agonizing one for patients, parents and caregivers,” says Madsen. So he performed a smaller surgery, removing some of her epilepsy-tainted frontal lobe. He also cut the corpus callosum, the fibers connecting the two sides of the brain, to protect against the possibility of the epilepsy spreading to her brain’s right side.

Both Melodie’s convulsions and verbal abilities drastically improved: Within six weeks after the operation, she’d gained a year’s worth of vocabulary. But the success, and that of another operation a few years later, didn’t last. “It’s an insidious disease,” Learned says. “You think you’ve finally found the solution and it starts creeping back.” Soon, Melodie lost all control over her behavior. She got kicked out of two after-school programs due to violent behavior and she became more withdrawn, having little interaction with other children. “She was simply miserable,” says Learned.

Last spring, Melodie became a candidate for a complete hemispherectomy, the most drastic neurosurgery that exists; surgeons remove the entire half of the brain causing the epilepsy. Because hemispherectomies are so complex and are guaranteed to affect a patient for the rest of her life, it’s only performed at a few major pediatric epilepsy centers (they’ve been performed at Children’s for 40 years and the hospital is a national referral center for this procedure). Again, her case was scrutinized by a team of neurologists, neurosurgeons and neuropsychologists, who meet weekly to discuss their patients’ progress and treatments. “Every decision must be reasonable to the entire team,” says Madsen. “We consider every option together; the depth of the collaboration is unusual.”

Melodie’s team agreed that a hemispherectomy was the best decision, despite the risk of accidentally removing her brain’s language center, which would leave her unable to speak. “I felt we were losing her,” says Learned. “There wasn’t any other answer.” So, last summer, Madsen and his team gathered Melodie’s mapping information and performed the long, painstaking operation, taking care to navigate the fine lines between her functional and epilepsy-infused brain tissue. After they were done, they filled the empty part of her brain cavity with sterile water to keep the other half in place.

Certainly, it seems incredible—if not impossible—that surgeons can remove half of someone’s brain without rendering them senseless and immobile. Surgeons don’t fully understand it themselves. It could be that the parts of the brain causing the epilepsy aren’t functional anyway because the epilepsy has taken over, displacing functions like language to healthier regions on the other side of the brain. Or, it could be that those functions never grew in the

epilepsy-infected parts to begin with, but still get interrupted by the epilepsy activity.

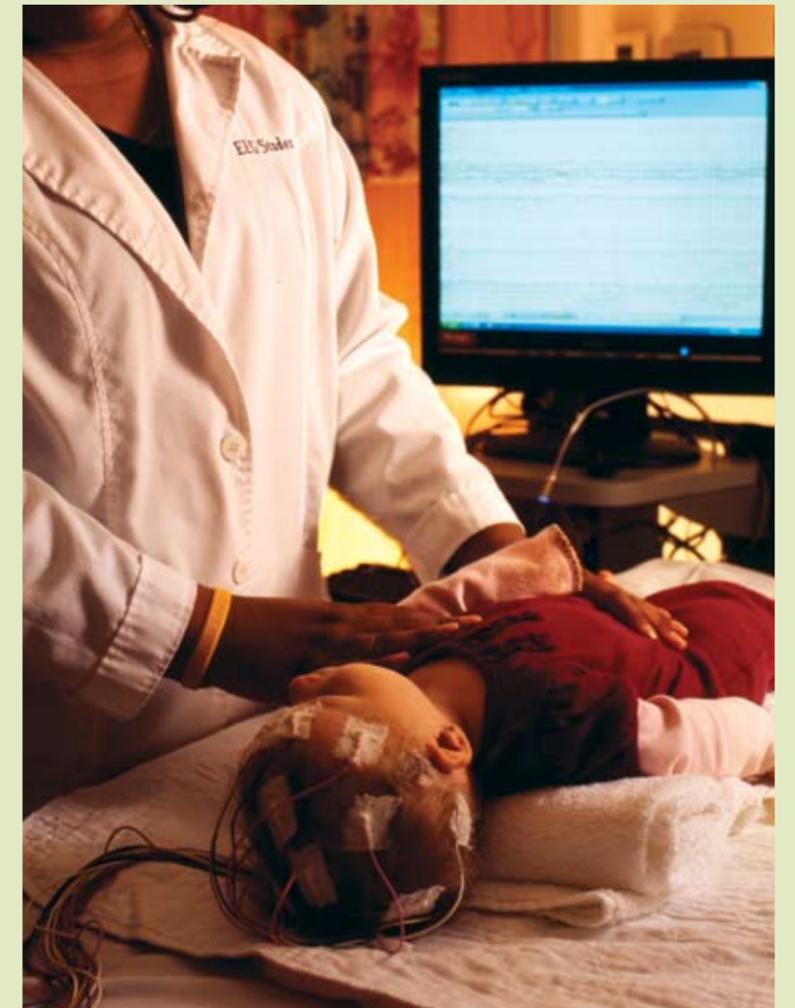
Either way, hemispherectomies do come with a price. They always leave the patient with weakened motor function on the side of the body opposite from the hemisphere that’s removed. Usually, that means limited or no mobility in that arm, some vision loss in each eye and a limp. Patients also have partial weakness in their face muscles (since the face is controlled by both sides of the brain). The trade-off, though, can be enormous. “Sometimes patients refer to this surgery as a second birth,” says Blaise Bourgeois, MD, director of Epilepsy and Clinical Neurophysiology. “A child can wake up completely free from epilepsy with a new life.”

After a night in intensive care, neurosurgeons visited Melodie to see if she could speak and asked her the standard question, ‘Do you know what day it is?’ To everyone’s shock, Melodie cheerfully replied, correctly, ‘It’s my birthday!’ The doctors didn’t know whether to be more pleased by the fact that she was fully alert or that her seizures had completely stopped. For her mother, regaining a daughter she thought she’d lost was by far the best part. “She had an immediate and complete personality change,” Learned says, and one that Melodie herself became fully aware of. Not long after the operation, she announced to her mother, “I’m not the old Melodie any more.”

The reason Melodie’s personality and cognition were freed along with her body isn’t clear. “It’s still a mystery and we have to be in awe of it,” says Madsen. Every day, Melodie is improving, working hard in speech therapy and in physical therapy to regain strength in her weakened right side. She regularly sees her Children’s epileptologists, who are weaning her off the few medications she’s still taking. Despite weakness on her right side, Melodie is walking, using a small brace, and talking up a storm. “She’s blossomed,” says Learned. “She has friends and can understand and learn. She’s genuinely happy for the first time in her life. After everything, it shows there really can be happy endings.”

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IN ORDER TO PINPOINT THE ORIGIN OF EPILEPSY, a patient receives continuous electroencephalogram monitoring, during which electrodes attached to her scalp are connected to a monitor. Doctors record her brain’s seizure activity, shown on the screen above, using sensitive equipment that picks up even the small seizures that don’t lead to physical convulsions.

Ground-breaking epilepsy research

Melanie’s brain recordings, combined with those of other epilepsy patients, are allowing Children’s researchers the rare opportunity to consider questions about the brain’s function—much of which is still very much a mystery. One such scientist is Gabriel Kreiman, PhD, whose findings shed light on how the brain stores visual memory. He’s found what’s called the “Halle Berry cell,” a single neuron that consistently reacts to a picture of a particular famous person or landmark. The Halle Berry cell fires when the patient looks at an image of the actress, whether she’s in a gown at the Oscars or in a Catwoman costume. Remarkably, the same cell fires if the patient is shown a drawing of Berry or even just the letter string “Halle Berry.”

Another researcher, Frances Jensen, MD, director of epilepsy research, studies the relationship between epilepsy and learning. She’s found that half of all epileptics have cognitive or psychiatric problems, and her research suggests that abnormal activity in the brain in between seizures could actually be what’s so disruptive to an epileptic child’s learning—not merely the seizures themselves. She’s also exploring causes of epilepsy on the cellular level and is putting together a clinical trial to test a new drug.