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Beyond the Cuckoo's Nest : The Quest for Why Shock Therapy Can Work

R. Douglas Fields

13-17 minutes

While examining brain tissue through a microscope of hospital patients in the 1930's, Hungarian neuropathologist Ladislaus Meduna made an intriguing observation: [Brain cells, called glia](#), increased greatly in tissue taken from people with epilepsy. But samples from patients with schizophrenia and depression had far fewer glia in the cerebral cortex than normal.

Unlike neurons, glia cannot fire electrical impulses, so they were (and still are) largely ignored by most neuroscientists. But Meduna speculated that schizophrenia and depression might result from a deficiency of glial cells, so he reasoned that by inducing a seizure, he could increase their numbers and cure his

patients. On January 23, 1934, he induced a violent seizure in a man who was hopelessly catatonic from schizophrenia by injecting a chemical, camphor, into the man's bloodstream. The injection induced an explosive seizure that wracked the man's body for a full minute. Meduna's legs gave out in shock after he saw what he had done. The scientist collapsed and two nurses had to help him back to his apartment to recover. Undeterred, Meduna four days later induced another seizure in the same man—who for four years had never spoken or moved and who had been fed continuously through a tube. By the fifth seizure he induced on February 10, 1934, the man awoke, dressed himself, requested breakfast and greeted Meduna cheerfully by name. “I hear them talking that you were going to make some crazy experiment? [Did you do it?](#)” he asked

This success inspired others: Ugo Cerletti and Lucio Bini in Italy used electricity to induce a seizure by applying electrodes they had obtained from a pig slaughterhouse to the head of one of their mental patients on April 11, 1938. Did the patient get better? In some cases, patients who underwent these primitive procedures experienced improved mental states

noticeably. But they could also induce violent, whole-body contractions that sometimes dislocated joints and broke bones.

Kinder and Gentler ECT

Today, electroconvulsive therapy (ECT), as it is referred to by physicians, is still a part of the psychiatric armamentarium. But the patients who now receive it—after having failed other treatments, whether pharmaceuticals, talk therapy or even other forms of electrical stimulation—undergo less of an ordeal than did Meduna's patient.

Wendy Marie Ingram, a psychiatric epidemiologist at Geisinger Health System in Pennsylvania, is studying ECT to determine which patients are most likely to benefit from the procedure, described the first time she witnessed a patient under go ECT. “The first person I saw was a male,” Ingram says. “The previous week he was *completely* nonresponsive [catatonic]—couldn't even respond to his name.” The anesthesiologist inserted a soft rubber guard into the man's mouth to prevent him from biting his tongue, and while he was under anesthesia, resting tranquilly under the influence of muscle relaxants, the technicians applied two

electrodes to his head and delivered pulses of high-voltage electricity into his brain. “It was amazing how calm everybody was...efficient, like watching a surgery,” she notes. “Everyone was warm and kind and spoke to the patient, even though he wasn’t particularly responsive [because of his catatonia].”

In contrast to the horrifying scenes dramatizing shock therapy in movies like *One Flew Over the Cuckoo’s Nest*, violent seizures did not wrack the patient’s body when the high-voltage switch was thrown. “You see the body tense for a period of time and then it relaxes—that’s it,” Ingram says. “It’s amazing,” she adds, “patients who are severely depressed, suicidal or catatonic are given ECT and two weeks later they are up, happy, chatting with the physicians and nurses.”

Used on over [100,000 people a year in the U.S.](#), ECT is highly effective in treating severe depression, bipolar disorder and other mental illnesses. But it does not always work—and some health providers now shy away from the procedure. “I was watching people stay sick, says [Jessica Eure](#), professional counselor at the Virginia Center for Neurofeedback, recalling her work in a mental hospital with severely psychotic, suicidal and homicidal patients. “They give them ECT and it gets

them perked up for a couple of months—but then you are back to where you were, but maybe with some memory loss. It was really upsetting to me.”

Discouraged by ECT, Eure now uses neurofeedback that monitors a patient’s brain waves to treat people with a range of mental illnesses.

The efficacy of any medical treatment depends on scientific understanding of the disorder, and how the treatment is applied. But that insight is largely lacking with ECT—and there is no consistent method of administering the technique throughout the U.S. A survey of legislation across the nation, just published online in advance of print in the [*The Journal of ECT*](#), finds laws regulating ECT vary widely from state to state. Six states have no regulation at all on ECT, limiting who can administer or receive the treatment, who can provide consent, how it is practiced or administrative requirements on reporting. Other states are so restrictive, a court order is required in some cases.

The methods of administration also differ. “The power, the frequency, the electrode placement...the number of treatments and the duration of the treatments are also variable,” Ingram says. “The piece that is really missing

is, what *is* a therapeutic seizure?” According to Ingram, extremely long seizures are associated with worse adverse events such as memory loss. But weaker ones, like those induced by stimulating only the right side of the head instead of both sides, produces less memory loss, but also has less therapeutic benefit. Why one procedure might be better than the other is unclear. “The neuroscience is completely unknown. It’s baffling to me,” Ingram says. It is not even clear the seizure itself is the most important factor. The amount of suppression of brain activity that is often, but not always, seen immediately following the seizure, called postictal suppression, may be a better indicator of therapeutic benefit.

A better understanding of how the procedure works is needed to allay concern for undesirable side effects and fear of potential abuse fuel negative stereotypes about ECT. “The procedure has been so horrifically portrayed in media...showing it being used in mental facilities as punishment, not for its tremendous therapeutic effects,” Ingram says. [Nazi doctors even perverted shock therapy](#) to systematically euthanize thousands of mental patients in the abhorrent “racial hygiene” program, beginning in 1944

Frustrations of Medical Records

To gain a better grasp of ECT, Ingram and her colleagues Sharon Larson, Stanley Poler and Fatin Nahi sifted through electronic medical records of 127 patients in [Geisinger Health System](#). In total, the patients had undergone a total of 2,023 individual ECT treatments between 2013 and 2017. Their goal: to find clues to how ECT works, why it sometimes fails, why some people experience significant side effects and to identify the best procedures to maximize the benefit of the procedure and reduce its risks.



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One key question they decided to explore is whether anesthesia—used to prevent convulsions—undercut the effectiveness of the procedure. Ingram presented preliminary data on her group's findings at the 2017 Society for Neuroscience meeting in Washington, D.C., in November. The data showed the type of anesthesia did have a significant effect on the duration of the seizure. The anesthesia propofol, the study found, reduced seizure duration significantly more than the

anesthetic methohexital. Neither drug affected the postictal suppression. With this finding, the researchers set about trying to determine whether it was the seizure duration or the postictal suppression that produced the best outcome by assessing whether patients who had received either anesthetic showed the greatest reduction in depression following ECT. Depression is measured quantitatively by the Beck Depression Inventory, a series of questions psychiatrists use to score the severity of a patient's depression.

Inspecting the medical records more closely revealed to what degree ECT has become a medical backwater. The electronic medical records showed that only 21 patients had been given the diagnostic test after the treatment, making any correlations researchers might find too weak to achieve statistical significance.

Contrast this with almost any other medical treatment. Would any doctor fail to record changes in their patient's blood pressure after prescribing a drug treatment? Ingram then attempted to compare the number of patients who had been readmitted to the hospital after the treatment with the anesthesia they had received, but only 18 patients relapsed within 30 days of receiving ECT. This provides a clue to the

efficacy of the treatment, although it leaves researchers with too little data to answer the critical scientific questions necessary to make ECT as safe and effective as possible.

Ingram, a neuroimmunologist and biophysicist, turned to epidemiological research because she felt her laboratory study at the cellular and molecular level was not leading to the needed understanding that would result in treatments for mental illness. “You have to use clinical informatics to study *people*, especially with these *complicated*, human-specific mental illnesses, and especially affective disorders—depression, bipolar, schizophrenia, which are unique to humans,” she says, and then use those findings to inform biological experiments in animal models. What is urgently needed, she adds, is better reporting of ECT treatments in medical records from all institutions into a central database for epidemiologists to analyze. Depression, bipolar disorder and other mental illnesses affect nearly everyone directly or indirectly. Of those 18 years of age and older in the U.S., [1.1 percent of the population](#) will develop schizophrenia—and according to Ingram, the incidence is even higher for bipolar disorder (2.5 percent) and major depression (5

percent). Suicide is the second-most common cause of death in the U.S. for people in the prime of life (ages of 10 to 34), according to U.S. Center for Disease Control and Prevention statistics ([pdf](#)).

In an interview after her presentation, Ingram's passion broke through the dry clinical detachment of a scientist discussing data points. "Depression is a *life-risking* disorder," she says. Retaining her professional composure, but suddenly gripped with emotion she adds, "I lost my cousin to suicide and depression. One of the last-ditch efforts was ECT therapy and it failed, and she ended up committing suicide." Her research on depression predated this personal loss but the tragic experience infuses her scientific work. "One of the most important things that is preventing us from getting at the mechanisms of treatments and the mechanisms of the etiology of the disease is the social stigma against mental illness in general. Society needs to change its mind and acknowledge that mental illness, especially mood disorders, is not a decision of the individual, it is not a character flaw, it is a biological disease, and it has genetic and environmental and behavioral components." This stigma discourages people from seeking treatment, stifles their participation in scientific

studies and reduces research funding for mental illness, Ingram says, noting the National Institutes of Health budget for cancer research in fiscal year 2017 is [\\$5.5 billion](#) in comparison to only [\\$1.5 billion for mental health](#). “We conducted this study with only a \$2,000 internal grant.” (The White House’s proposed budget for 2018 would cut funding for both institutes to \$4.4 billion and \$1.2 billion, respectively.)

Legal and Funding Gaps

Negative stereotypes have thwarted the effort to achieve best practices and legislation for ECT treatments. [Justin Coffey](#), one of the co-authors of the study on legal regulations on ECT in the U.S. and an associate professor of psychiatry and behavioral Sciences at Baylor College of Medicine in Houston, is especially concerned about the harm caused by overregulation. “Laws that protect patients are good,” Coffey says. “In the case of ECT, however, some state laws do just the opposite—they restrict access to what is an extremely safe and often lifesaving medical treatment. Such laws are not based on medical science. “In Texas, where I practice, I see 14-year-old kids with severe depression and certain forms of

autism, conditions where ECT can be lifesaving—but the law does not allow me to provide the care they need, the care that is medically indicated.” Coffey says he is sometimes forced to direct families to seek professional help in other states where ECT is “not hindered by laws based on stigma rather than fact.

For her part, Ingram places medical knowledge about mental disorders, in general, within a larger context. “Cancer 50 years ago is where we are at right now with mental illness, back when we didn’t know anything about the causes,” she says. “When we didn’t have anything to treat it well, people hid it. They would get a lump in their body and they would hide it. It was taboo, and there was fear around it.” Along the way the attitude toward cancer changed. “People now wear proudly the ribbons of breast cancer survivor, and they have contributed to research that is associated with that disease, she says. “It is normalized; it is medicalized. The same thing needs to happen with mental illness in order for us to make the big leaps we need to.”

ABOUT THE AUTHOR(S)

R. Douglas Fields is a senior investigator at the

National Institutes of Health's Section on Nervous System Development and Plasticity. He is author of *Electric Brain: How the New Science of Brainwaves Reads Minds, Tells Us How We Learn, and Helps Us Change for the Better* (BenBella Books, 2020). Credit: Nick Higgins