Henry Molaison's operation for epilepsy: a case study in medical ethics

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Abstract
Dr William Beecher Scoville, an eminent American neurosurgeon of the 1940s, offered to treat Mr Molaison for his intractable epilepsy. During the operation, he removed large portions of both of Mr. Molaison's temporal lobes. Such an operation had never been performed earlier as the function of these parts of the brain was not clearly understood and neurosurgeons such as Dr. Wilder Penfield of Canada feared they could cause grave damage to the patient.

Mr. Molaison developed severe loss of memory to the extent that a few minutes after meeting someone, he had no recollection of the meeting and he could not find his way to his own home.

Mr Dittrich, grandson of Dr. Scoville, has analysed the operation on Mr. Molaison's brain against the background of neurosurgery in the 1940s. This essay discusses the ethical aspects of Dr. Scoville's operation in the light of current understanding and practice.

Introduction
Mr Luke Dittrich, grandson of Dr Scoville, an eminent American neurosurgeon, has written a comprehensive book on the life of Mr Henry Molaison (1), Dr Scoville's most renowned patient. This account also portrays Dr Scoville, warts and all. Dittrich also tells us about Mrs Scoville's illness and her treatment by Dr Scoville.

Important lessons in the practice of medical ethics can be drawn from the interactions between the doctor, his two patients and events following Mr Molaison’s death.

Except where indicated by reference numbers, all the following quotations are from Dittrich's book.

Henry Molaison
He was born in Manchester, Connecticut on February 26, 1926. As a child, Henry Molaison wanted to be a neurosurgeon. Instead, he suffered a major, life-long handicap at the hands of a neurosurgeon, which at once rendered him incapable of looking after himself and made him an object of innumerable medical research studies.

Blond, blue-eyed Henry, aged around eight years, was returning home along the backstreets. As he heard no vehicles, he stepped off the side-walk on to the road to cross it. A bicyclist coasting down a sloping road rounded a curve and unaware of Henry, crashed into him. Henry landed on the road, hurting the left side of his head, the scalp just above his eyebrow tearing on impact. As his head rebounded off the road three times, his brain was injured. He awakened five minutes or so after the fall. The wound was stitched and he carried a bandage above his left eyes for a few days. Seizures followed, mild to start with and more intense with the passage of time. By the age of 15 years, he was suffering generalised fits attended by loss of consciousness.

To supplement the meagre income of his father, who worked as an electrician, Henry took on part-time jobs – usher at a movie theatre, helping out with the stocks at a shoe-store and in a junkyard. He attempted apprenticeship as a motor-winder. Gradually, despite drugs to control fits, he found himself greatly handicapped by the severity and frequency of his epileptic attacks.

Dr Harvey Goddard, his physician, decided to consult neurosurgeon Dr William Beecher Scoville. Dr Scoville confirmed that drugs to control epilepsy failed even when a combination of four such drugs was given 2–5 times a day. Henry, aged 27, was confined to his home for fear of injury during fits which now came on several times each day. His future was dark. Dr Scoville talked to him and his parents about operations on the temporal lobes that had helped some similar patients.

Henry's operation was carried out on August 25, 1953. Dr Scoville could find no abnormality in the temporal lobes. Records of the electrical activity of these lobes also showed no abnormality. Certainly, there was no localised area from which epileptic discharges could be identified. Had there been visible disease or an identifiable source of fits, this part of the brain could have been removed to render Henry fit-free.

Most neurosurgeons would have shrugged their shoulders and closed up the wound. Dittrich points out that at this stage, even a surgeon of the eminence of Dr Wilder Penfield would have conceded defeat, as there was no hint of the origin of the seizures. He quotes Penfield, "The neurosurgeon must balance the chance of freeing his patients from seizures against the risks and functional losses that may be associated with ablation." This was particularly important in those days when the functions of the temporal lobes were not as well understood as they are today.

"My grandfather was not Wilder Penfield," says Dittrich. Dr Scoville decided to remove the medial temporal lobes on both sides.

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Six weeks later, Dr Scoville sent his paper on temporal lobe surgery to the Journal of Neurosurgery for publication. In the paper he reiterated what he had stated at his earlier presentation to the Harvey Cushing Society and noted that surgery on the medical temporal lobes “resulted in no marked physiologic or behavioral changes, with the one exception of a very grave, recent memory loss, so severe as to prevent the patient from remembering the locations of the rooms in which he lives, the names of his close associates or even the way to the toilet or urinal” (italics by Dr Scoville).

As Dittrich pithily puts it, in this statement Dr Scoville announced the birth of patient HM and wrote the obituary of Henry Molaison.

In a later publication (2), Scoville and Milner provided greater details on Molaison’s handicap.

After operation this young man could no longer recognize the hospital staff nor find his way to the bathroom, and he seemed to recall nothing of the day-to-day events of his hospital life. There was also a partial retrograde amnesia, inasmuch as he did not remember the death of a favourite uncle three years previously, nor anything of the period in hospital, yet could recall some trivial events that had occurred just before his admission to the hospital. His early memories were apparently vivid and intact.

This patient’s memory defect has persisted without improvement to the present time, and numerous illustrations of its severity could be given. Ten months ago the family moved from their old house to a new one a few blocks away on the same street; he still has not learned the new address, though remembering the old one perfectly, nor can he be trusted to find his way home alone. Moreover, he does not know where objects in continual use are kept; for example, his mother still has to tell him where to find the lawn mower, even though he may have been using it only the day before. She also states that he will do the same jigsaw puzzles day after day without showing any practice effect and that he will read the same magazines over and over again without finding their contents familiar.

This patient has even eaten luncheon in front of one of us (B.M.) without being able to name, a mere half-hour later, a single item of food he had eaten; in fact, he could not remember having eaten luncheon at all. Yet to a casual observer this man seems like a relatively normal individual, since his understanding and reasoning are undiminished.\(^{(2)}\)

Molaison’s extraordinary state, caused by removal of the medial parts of both temporal lobes, led to numerous research studies by those attempting to understand the functions of the temporal lobes. As these studies were carried out and reported in medical journals, Molaison’s privacy was respected by never using his full name but labelling him just as “H.M.” The full name was used again only after his death.

Access to him was restricted to those with academic credentials. One of the first to gain access was Dr Brenda Milner. She was deputed by Dr Wilder Penfield to study the consequences of this unprecedented operation. Later Dr Suzanne Corkin, a student of Dr Brenda Milner, took over the studies on Henry Molaison’s brain functions and determined who could be allowed to see him. She was to continue to study him till he died and was then able to obtain Molaison’s brain for study. Dittrich was never allowed to meet Molaison during his lifetime despite several pleas and attempts to do so.

In the 1940s, it was felt that memory was distributed across the entire cerebrum. It was not associated with any particular lobe of the brain. Ten years later, when Dr Milner studied two of Dr Penfield’s patients whose left temporal lobes were removed as they contained epileptic foci, she noted that they suffered profound loss of memory. Many other patients, whose left temporal lobes had been removed, showed no such deficit.

Drs Penfield and Milner postulated that some unidentified disease in these two patients must have damaged the medial temporal lobes on both sides. Lacking the sophisticated tests available to us today, such as computerised tomography, magnetic resonance scanning and functional magnetic resonance imaging, this remained a hypothesis.

Were Penfield willing to test the theory by actually removing both hippocampi of a patient and seeing what happened, he and Milner might have been able to obtain what they needed.

They would then have identified the seat of memory in the human brain.

But Penfield would never do that. He was too wary of causing unnecessary harm. Despite having revolutionized the field of epilepsy surgery, he was fundamentally a conservative, cautious doctor. He viewed all novelty with skepticism.

**Questionable ethics**

Dittrich commented on his grandfather’s decision to destroy the medial temporal lobes in Molaison:

This decision was the riskiest possible one for Henry. Whatever the functions of the medical temporal lobe structures were – and again, nobody at the time had any idea what they did – my grandfather would be eliminating them. The risks to Henry were as inarguable as they were unimaginable.

Dr Scoville did this operation despite the experimental findings by Heinrich Klüver (1897–1979) and Paul Bucy (1904–1992) in 1939 (3, 4). Klüver and Bucy had built upon the description by Hughlings Jackson (1835–1911) of uncinate fits with the causal foci in the temporal lobes. They carried out experiments in Rhesus monkeys to study the effects of removal of the medial temporal lobes. They showed, especially in the aggressive female monkey named Aurora, that removal of both temporal lobes reduced previously aggressive animals into docile, “psychically blind” individuals. The term “psychically blind” was used to describe the inability of these monkeys to recognize objects by sight even when their vision was unimpaired. They concluded that damage to both temporal lobes “disrupted
the processes by which the meaning of a sensory precept is appreciated. Their ability to understand what they perceived was abolished.

The unprecedented surgery on Molaison’s brain, without any scientific backing for the infliction of such damage, left him amnesic. As he expressed it so well, “Every day is alone in itself. Whatever enjoyment I’ve had and whatever sorrow I’ve had.” The next day, his slate had been wiped clean with no trace of bygone events.

As noted above, a more prudent surgeon such as Dr Wilder Penfield would have stopped once no abnormality was detected on inspection, and on a study of cortical electrical recordings. Not so Dr Scoville who proceeded with the destruction of the mechanisms for memory in Henry Molaison.

Were such an operation to be performed under modern circumstances, the neurosurgeon would find himself in deep trouble. At the least, Dr Scoville would have been accused of medical adventurism, acting outside accepted medical practice.

The permanent handicaps that Henry Molaison suffered would result in heavy damages imposed by a court of law.

**Mrs Scoville**

In the mid-1940s, Dr Scoville’s wife displayed evidence of mental illness. After hospitalisation, she was subjected to hypothermia, fever therapy (her body temperature being elevated to 105–106 degrees Fahrenheit), electroconvulsive therapy and insulin shock therapy. The description of Mrs Scoville’s descent into madness is wrenching, especially since before her illness she had been assessed as being markedly above the average in intelligence and a true lover of music.

Dr Scoville wrote to his parents, “I have been so happily married and am utterly heartbroken.”

Her own assessment of the marriage was different, being influenced by Dr Scoville’s infidelity and promiscuity. Dittrich describes a Thanksgiving dinner, “my grandfather holding court at the head of the table, his second wife to one side, my grandmother sitting mostly silent a few seats away.” He had, by then, performed bilateral frontal lobotomies on her.

Dittrich, very fond of his grandmother, wrote:

> Whatever they did to my grandmother at the asylums, however bad it got, whatever they took, whatever he took… What remained was strong… In 1957… my grandmother took a trip to Reno, Nevada. She walked into one of the local shops that specialized in quick no-contest divorces. She filled out each of the form they gave her… She left my grandfather, moved to New York City on her own… She started over…

**Questionable ethics**

Given his infidelity and promiscuousness, Dr Scoville's destructive surgery on both her frontal lobes raises major ethical questions. He knew that such surgery would render an agitated person docile.

Decision on her treatment should have been made by an objective third party. Knowledge of the permanent consequences of the destructive operation would have hindered most surgeons, especially since prior to her illness she had been described as being markedly above the average in intelligence and a true lover of music.

Her behaviour almost two decades after the operation, her devotion in the late 1950s to the blind and her affection for her grandchildren show that the damage inflicted by Dr Scoville had not quelled her indomitable spirit.

**Henry Molaison’s brain**

Towards the end of his life, Molaison was besieged with other illnesses – a recurrence of fits requiring large doses of anticonvulsants, a need for antidepressants and anxiolytics, brittle bones, fractures, and a stroke.

Dr Corkin brought in neuroanatomist Dr Jacopo Annese to see Molaison. The purpose was to ensure that a proper study of Molaison’s brain would follow his death. Molaison never consented to an autopsy. He was deemed to suffer from dementia and consent was therefore given by a third cousin, Tom Mooney, who claimed he had looked after Molaison during his last days. The first cousins of Henry Molaison were not informed of the research being carried out on him or his death. Their consent was not sought.

Molaison died in 2008. Dr Corkin ensured that the body was kept refrigerated. Magnetic resonance scans of the dead brain were carried out at the Massachusetts General Hospital before the brain was removed for preservation and study. As Dr Corkin accompanied the brain to the airport for the flight to San Diego, the *New York Times* revealed HM’s full name for the first time, describing him as “the most important patient in the history of brain science” (5). Dr Annese was at the airport to take charge of the precious organ. He took it with him to the Brain Observatory at the Institute for Brain and Society, which he had founded in San Diego.

Dr Annese studied the brain in detail and released a digitised 3-dimensional model of it that can be accessed by anyone. A disagreement between Dr Corkin and Dr Annese led to an ugly dispute over the custody of the brain and its slices. In April 2010, Dr Corkin asked Dr Annese to send her everything related to Henry Molaison’s brain. By then Dr Annese had spent thousands of hours working on the brain and spent $750,000 in grant money over the studies. Bickering and meetings followed. Lawyers were brought in. Dr Corkin’s stated reason for insisting on retaining the brain and its slices was that these precious resources should be in good custody so that future researchers could benefit from them.

Dittrich’s descriptions of his meetings with Dr Corkin do no credit to her. When asked for her notes of fifty years of interviews with Molaison, she blandly told Dittrich that they had been destroyed (6). How then was Molaison’s legacy in the form of data to be made permanently accessible by future researchers?
Controlled human infection models for vaccine development: Zika virus debate

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Abstract
An ethics panel, convened by the National Institute of Health and other research bodies in the USA, disallowed researchers from the Johns Hopkins University and University of Vermont from performing controlled human infection of healthy volunteers to develop a vaccine against Zika virus infection. The members published their ethical analysis and recommendations in February 2017. They have elaborated on the risks posed by human challenge with Zika virus to the volunteers and other uninvolved third parties and have systematically analysed the social value of such a human challenge experiment. They have also posited some mandatory ethical requirements which should be met before allowing the infection of healthy volunteers with the Zika virus. This commentary elaborates on the debate on the ethics of the human challenge model for the development of a Zika virus vaccine and the role of systematic ethical analysis in protecting the interests of research participants. It further analyses the importance of this debate to the development of a Zika vaccine in India.

Introduction
In December 2016, an ethics panel convened by the US National Institutes of Health (NIH), the National Institute of Allergy and Infectious Diseases (NIAID) and the Department of Defense Walter Reed Army Institute of Research (WRAIR) reviewed a proposal by researchers from the Johns Hopkins University and the University of Vermont College of Medicine in the USA to conduct controlled infection of healthy human volunteers with the Zika virus (ZIKV) to develop a vaccine against the virus. The panel published its recommendations in February 2017, halting the progress of any such experiments, as it deemed such research unethical in the current context of research on and development and understanding of the ZIKV (1). This evoked mixed opinions and led to vociferous debates between the proponents of the controlled human infection models (CHIM) for ZIKV vaccine development and the bioethicists, who view the risks to the participants and other uninvolved third parties as too high to allow the experiments (2,3).

ZIKV is a mosquito-borne flavivirus, causing a febrile exanthematous (fever with rash) illness in humans. Though it was isolated and identified in 1947, the first major human outbreak was only in 2007 in the Island of Yap, in the Pacific (4). In July 2015, Brazil reported an association between ZIKV and Guillain-Barre syndrome (GBS – a severe form of nervous disorder due to immunological problems caused by the ZIKV); and in October of the same year, an association between ZIKV infection of pregnant women and microcephaly (small head) of new-borns with severe neurological damage (4). Most illness caused by ZIKV infection is mild and not apparent. However, its association with GBS and congenital Zika syndrome (CZS) are the major causes for concern. The virus is transmitted by the bite of the Aedes mosquito, as well as by sexual transmission and vertical transmission from the mother to the foetus (5). The virus rapidly spread to Mexico, Central America, the Caribbean, and all over South America. Given these concerns and the possibility of the spread of the virus to other tropical and subtropical areas, the World Health Organisation declared the disease a Public Health Emergency of International Concern in January 2016 (4). Since then, the ZIKV has been a dreaded emerging infectious disease, and laboratory research and animal experiments have been conducted to understand