

Learning about the brain from medical history

Phineas Gage

Phineas Gage (1823–1860) was the victim of a terrible accident in 1848

His injuries helped scientists understand more about the brain and human behaviour. Holly Story gets to grips with the grisly tale and its place in the history of neuroscience.

Phineas Gage, whose story is also known as the ‘American Crowbar Case’, was an unwitting and involuntary contributor to the history of neuroscience. In 1848, when he was just 25 years old, Gage sustained a terrible injury to his brain. His miraculous survival, and the effects of the injury upon his character, made Gage a curiosity to the public and an important case study for scientists hoping to understand more about the brain.

In 1848 Gage was working as a foreman on the construction of the Rutland and Burlington Railroad in Vermont, USA. Workers often used dynamite to blast away rock and clear a path for the railway. On 13 September, Gage was using a tamping iron (a long hollow cylinder of iron weighing more than 6 kilos) to compact explosive powder into the rock ready for a blast. The iron rod hit the rock, creating a spark that ignited the explosives. The rod was propelled through Gage’s skull, entering through his left cheekbone and exiting through the top of his head. It was later found some 30 yards away from Gage, “smeared with blood and brain”.

Despite his horrific injury, within minutes Gage was sitting up in a cart, conscious and recounting what had happened. He was taken back to his lodgings, where he was attended by Dr John Harlow. The doctor cleaned and dressed his wound, replacing fragments of the skull around the exit wound and making sure there were no fragments lodged in the brain by feeling inside Gage’s head with his finger. Despite Harlow’s efforts, the wound became infected and Gage fell into a semi-comatose state. His family did not expect him to survive: they even prepared his coffin. But Gage revived and later that year was well enough to return to his parents’ home in New Hampshire.

In 1850 Henry J Bigelow, Professor of Surgery at Harvard University, reported Gage to be “quite recovered in faculties of body and mind”.

It seems that physically, Gage made a good recovery, but his injury may have had a permanent impact on his mental condition. Although accounts from the time are sometimes conflicting and often unreliable, numerous sources report that Gage’s character altered dramatically after his accident. In 1868 Harlow wrote a report on the ‘mental manifestations’ of Gage’s injuries. He described Gage as “fitful, irreverent, indulging at times in the grossest profanity... capricious and vacillating” and being “radically changed, so decidedly that his friends and acquaintances said he was ‘no longer Gage’.”

The damage to Gage’s frontal cortex caused by the iron rod seems to have resulted in a loss of social inhibitions. The role of the frontal cortex in social cognition and decision making is now well-recognised; in the 19th century, however, neurologists were only just beginning to realise these connections. Gage’s injuries provided some of the first evidence that the frontal cortex was involved in personality and behaviour.

One of the pioneering researchers in this field at the time was David Ferrier, a Scottish neurologist who performed extensive experimental research into cerebral function. In a lecture to the Royal College of Physicians in 1878, Ferrier observed that in his experiments on primates, damage to the frontal cortices seemed to have no effect on the physical abilities of the animal but brought about “a very decided alteration in the animal’s character and behavior”. He used the experience of Phineas Gage as a case study to support his claims.

The details of Gage’s life after his accident are unclear. It is known that he worked as a coach driver for several years in New Hampshire and then in Chile and that in 1859 his health deteriorated and he returned to the USA. He died in San Francisco in 1860 after suffering seizures that resulted from his injury. His brain was not examined after his death, but in 1867 his body was exhumed and his skull was sent to Dr Harlow to be studied. It now resides, along with the tamping iron, at Warren Anatomical Museum at the Harvard University School of Medicine.

Since then, scientists have made various attempts to use the skull to reconstruct Gage's injury and establish which areas of his brain were damaged. A team led by Jack Van Horn of UCLA's Laboratory of Neuroimaging (part of the Human Connectome Project) created a new digital model of the rod's path. It suggested that the damage to Gage's brain was more extensive and severe than had previously been estimated: up to 4 per cent of the cerebral cortex and about 11 per cent of the total white matter in the frontal lobe were destroyed.

The model also indicates that the accident damaged the connections between the frontal cortex to the limbic system, which are involved in the regulation of emotions. This would seem to support some of the contemporary reports of Gage's behaviour.

In the 19th century, Gage's survival seemed miraculous. Fascination with his plight encouraged scientific research into the brain, and the continuing research into Gage's condition is proof that this same curiosity is still alive today.

Patient HM

Patient HM was an important case study for neurological research in the 20th century. Holly Story discovers how his life and his unique condition helped scientists to understand the brain

Henry Gustav Molaison, known to the world as 'Patient HM', has been called the most important patient in the history of brain science. He was studied by a team of neuroscientists for more than 50 years – from the age of 27 to his death aged 82 – yet he could not remember their names or their experiments. Henry Molaison suffered from profound amnesia, and his unique condition helped neuroscientists to understand more about how our memory functions.

As a child, Henry suffered from epilepsy, which may have been caused by a head injury he sustained when he was seven years old. At first his seizures were minor, but from the age of 16 they became increasingly severe. By the time Henry was 27, he was unable to work.

Undergoing surgery

In 1953 Henry was referred to neurosurgeon Dr William Beecher Scoville at Hartford Hospital, Connecticut, USA. Scoville suggested surgery to remove the part of Henry's brain that was causing his seizures. This was major and experimental surgery, but Henry was so incapacitated by his epilepsy that he agreed to undergo the procedure.

Dr Scoville performed something called a bilateral medial temporal lobe resection. This involved removing a portion of Henry's temporal lobe, including parts of the hippocampus and amygdala, from both sides of the brain. Resection is still used today to treat severe epilepsy. It is a highly precise surgical procedure, informed by advanced brain imaging and a detailed knowledge of the brain. Scoville had none of these tools at his disposal and he could not foresee the effects of his surgery.

When Patient HM woke from his surgery, he was suffering from severe amnesia. Henry could remember much of his childhood: he knew his name and family history and could remember the stock market crash of 1929. However, he struggled to remember events from the few years leading up to the surgery and could not remember some things that had happened up to 11 years before.

Henry also had severe anterograde amnesia. This means that he had lost the ability to form new memories. Later, he would describe his condition as being "like waking from a dream... every day is alone in itself".

Scoville contacted researchers at McGill University in Montreal, who had reported on two similar cases of amnesia in patients who had undergone temporal lobe surgery. Dr Brenda Milner, a psychologist from McGill, travelled to Hartford to visit Molaison and began her research into his amnesia, his remaining memory and his brain.

As Scoville never repeated the operation, Henry's case was unique. It was also well-suited to research: his amnesia was unusually severe, his condition was stable, he was a willing subject, and researchers had some knowledge of the anatomical basis for his condition.

In 1957 Dr Milner published the first results of her formal testing. She used the pseudonym 'Patient HM' to protect Henry's anonymity. This paper became one of the most cited papers in neuroscience.

Making memories

At the time of Henry's operation, it was thought that memory functions were spread throughout the brain. The fact that Henry suffered one kind of amnesia so acutely as a result of damage to one part of his brain, and yet retained his intellectual abilities, prompted researchers to reassess this assumption. It was clear that the temporal lobe must be vital for memory function.

At that stage, the scientists could not identify which structure within the lobe was specifically responsible, as several different structures – including the hippocampi, amygdalae and entorhinal cortices – had been affected by the operation. It would take years of study using animal models and great advancements in technology before the medial lobe memory system was fully understood, but Patient HM helped to lay the foundations of this vital research.

In 1962 Milner published the results of a series of trials that she had conducted with Henry, which revealed one of her most notable discoveries. In the trials she had asked Patient HM to draw a line between two outlines of a five-pointed star while watching his hand and the page in a mirror. Milner asked Henry to repeat this task several times on several different occasions. Each time Henry did not remember having completed the task before, yet his performance improved. This demonstrated that, although he was not conscious of it, Henry was able to learn new motor skills by repeated practice.

From these trials Milner was able to conclude that this form of memory, called motor learning, must be distinct from the system of memory that records new facts, faces and experiences. Furthermore, it must be located in a different part of the brain, one unaffected by Henry's operation. Milner's discovery that we have multiple memory systems and that they are located in different parts of the brain was a huge step forward in neuroscience.

Henry's legacy

Henry was always supportive of the research that he enabled and said he was glad that he could be of help to others. In 1992 he gave his consent for his brain to be used in further research after his death, and this led to the establishment of Project HM.

When Henry died in 2008, his brain was removed and scanned repeatedly using MRI. It was then sent to the Brain Observatory at the University of California. In 2009 scientists sliced the brain into 2,401 pieces, each just 70 micrometres (millionths of a metre) thick. Their aim was to create stained histological slides that would enable researchers to map the brain in new ways and connect individual anatomical structures with specific functions.

The dissection took 53 hours to complete and five blades were used in the process. Each slice was photographed and the images were posted online, and the whole procedure was streamed live on the internet.

Henry and his doctors could not have imagined the technology that would eventually be used to preserve his brain, nor could they have predicted the advances in neuroscience that would result from his operation, his condition and his generosity.

QUESTIONS FOR DISCUSSION

- Would you donate your brain to science? Why?