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A few thoughts on the history of epilepsy

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Abstract **The history of epilepsy is a saga of the struggle by which scientific understanding of an unusual disease was gained by a long and circuitous route. In the beginning this affliction was attributed to demon possession and defied understanding for centuries when it was still regarded as a sacred disease and surrounded by superstition and mysticism; therapy of necessity had to follow similar lines of reasoning. The gradual realisation that cerebral dysfunction was the cause of this disease was highly significant although still followed by misunderstanding and misinterpretation — those two essential steps to progress.**

Clear, inspired reasoning and lucid clinical descriptions of epilepsy by John Hughlings Jackson and William Gowers set the scene for what was to follow. Experimental neurophysiology, cortical simulation, cortical localisation, new technologies of electro-encephalography, modes of visualisation of structures histologically and radiologically led to our present-day concepts of this complex disorder. We have been brought to new thresholds of understanding through the co-operative exertions of many workers from all parts of the world and this saga tells of some of the highest scientific accomplishments in medicine.

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Prehistoric man must certainly have suffered from epilepsy and although we have no record of this, he must have experienced the amazement and awe with which this disease has been described by intelligent laymen and medical practitioners since the earliest Greek writings. The names used for it over many centuries and in many cultures reflect the perplexity with which our ancestors viewed and tried to interpret this complex disorder, which, even today, still perplexes medical and lay minds.

How far back does our knowledge about this disease extend? It is stated in the Code of Hammurabi that if a slave developed the disease *'bennu'* within a month of being bought, he could be returned to his previous owner. From the work of Karl Sudhoff it would seem that *bennu* was a spastic disease, probably epilepsy.[1]

The Greeks called it the sacred disease on the assumption that the cause of the 'seizure' was supernatural. Hippocrates was the first to use the word 'epilepsy', derived from the Greek word meaning 'to take hold of or to seize'; this also indicates clearly that the name 'sacred disease' was based on the belief of possession by a god. In his *Aphorisms*, epilepsy is frequently mentioned, e.g. 'Epilepsy which occurs before puberty may be removed but occurring after the age of 25, it continues through life'.[2] Indeed, there is an extensive ancient Greek literature on epilepsy.[3]

After Hippocrates, it was recognised that convulsions arose in the brain.

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The tendency to fall during a seizure was the basis for the Roman name, *morbus caducus*, but it was more commonly referred to as *morbus comitialis*, a term still used by Anthony Guainerius in 1488.[4] Commitia were annual assemblies of the Roman populace for the purpose of electing magistrates. If any member of the assembly suffered a seizure, the meeting was adjourned until another day.

In English the earlier designation, 'falling evil', was replaced by 'falling sickness' when the word 'sickness' came to be a general term for 'disease'.[5] The term 'commitial disease' still occurred occasionally in English in the 16th and 17th centuries.

Epilepsy in the New Testament

The gospels of Matthew, Mark and Luke contain a story of a father who brings his possessed son to Christ for healing. As each author highlights different features of the child's affliction, a very clear description of generalised seizures is obtained: 'Lord, have mercy on my son: for he is lunatic, and sore vexed; for oft times he falleth into fire and oft, into water' (Matthew 17:15, Authorised Version). The word 'lunatic' used here means afflicted by the moon, which is also the Greek term for the boy's affliction in the New Testament: moon illness.

In Mark 9: 17 - 27 of the *New English Bible* the meaning of the passage is clearer still: 'Master, I brought my son to you. He is possessed by a spirit which makes him speechless. Whenever it attacks him, it dashes him to the ground and he foams at the mouth, grinds his teeth and goes rigid. So they brought the boy to Him and as soon as the spirit saw Him, it threw the boy into convulsions and he fell on the ground and rolled about, foaming at the mouth. Jesus asked his father "How long has it been like this?" "From childhood," he replied. Jesus rebuked the unclean spirit, ". . . I command you, to come out of him and never go back." After crying aloud and racking him fiercely, it came out and the boy looked like a corpse; in fact many said, "He is dead". But Jesus took his hand and raised him to his feet, and he stood up.' Luke 9: 39 - 42 tells the same story, but adds that a sudden scream preceded the last convulsion.

The clinical descriptions are excellent and the theoretical background, i.e. possession by a spirit, was for its time perfectly acceptable. Whether Christ casts out an evil spirit or eliminates an epileptic tendency — a miracle is a miracle.

In the *New English Bible*, the term 'lunatic' used in the Authorised Version of Matthew's gospel is translated as 'epileptic': 'Have pity, sir, on my son; he is an epileptic and has bad fits. . . .' This sounds more familiar to us but may be an anachronism in that the word 'epilepsy' was probably not known to those around Christ despite the Hellenic influence in the Eastern Mediterranean at the time. Could the father of the afflicted boy have been an educated Greek?

Epilepsy in the Middle Ages

During the Middle Ages there was total ignorance with regard to epilepsy, and speculation and superstition held sway. There were, however, some voices of reason.

John of Gaddesden (1280 - 1361) wrote in his *Rosa Medicinae:* 'As such, epilepsy is a complete and general spasm, from an injury in the anterior ventricle of the brain; and it is a short spasm, from an injury in the anterior ventricle of the brain; and it is a short spasm, proper to the brain itself.[6] He thus follows Hippocrates in regarding the brain as the site of origin of epilepsy but as to the cause of the disease he follows Galen in blaming it on inappropriate interaction between the four humours. In prognostication, however, he follows Hippocrates. 'If epilepsy befalls a pregnant woman, she is freed from it when her child is born. If the paroxysm is lengthy and severe and the patient does not remember it and is not ashamed of it, it is a sign that a cure is difficult or well nigh impossible. But if the paroxysm be short and easy and afterwards the patient remembers it, it is a sign that he can be cured, yet all epilepsy is cured only with difficulty. If the attacks of epilepsy come frequently, especially in old age, there is a danger of death.'

The multitude of 'cures' — including the inhalation of the gall of a wolf from pledgets of moss placed in the nostrils and the taking of boiled weasel's brain or gall — attest to the despair of those who had to manage a mysterious disease which bore the stamp of the supernatural.

Bernard of Gordon (who taught at Montpellier from 1285 to 1307) described the cause of the disease as a humour or 'coarse windiness occluding the non-principal ventricles of the brain, impeding the passage of breath to the members and therefore (the patient) is driven to fall suddenly to the ground. He feels absolutely nothing, nor can he in any way stand erect, but necessarily falls unless the epilepsy should be very mild, as will be seen. The movement of the feet and hands is agitated, disordered and so is the breathing.'

This humour, which blocks the passages of the brain and interferes with the supply of air to the limbs, was thought by medieval writers to cause the nerves to exert a mechanical pull on muscles.[7] Three centuries later, Ambroise Paré compared this process to violin strings which shrink and exert traction in dry weather, thereby highlighting the evil effect of a 'dry humour'.

The frothing at the mouth and drooling were seen by others to indicate an abundance of moisture which, in the brain, could cause occlusion of the ventricles. If there was an abundance of mucus or phlegm, other evidence of a phlegmatic individual had to be looked for as this, in turn, dictated what should be done to control the epileptic tendency by dietary means.

Bernard provides us with what is probably the first description of a seizure that is not of the grand mal type when he annotates a brief attack in a patient who simply leans against a wall and rubs his face — apparently experiencing a kind of 'absence'. He states quite clearly that he never cured chronic epilepsy — a remarkable confession in the Middle Ages!

One of the 'cures' he describes has an interesting biblical origin. During a paroxysm a person should place his mouth over the patient's ear and repeat the following verse three times: 'Gaspar bears the myrrh, Melchior the frankincense, Balthasar the gold. Whoso bears with him the names of these three kings is delivered from epilepsy by the holiness of Christ.' These words were considered equally effective if written and worn about the patient's neck.[7]

Why the three wise men? In Matthew 2:11, the Magi 'saw the young child with Mary his mother and *fell down* and worshipped him.' In medieval thought their falling down before Jesus and the fact that they were wise men, credited them with special insight and knowledge of epilepsy.[3]

Bernard's 'cures' also include powder of dessicated cuckoo! Mistletoe is good because it clings to the oak and does not fall and will therefore help prevent the falling sickness!

Epilepsy in the 17th - 19th centuries

Thomas Willis (1621 - 1675)[8] stated in his lectures: 'Epilepsy is caused by contractions of the membranes around the brain, compressing and constricting its substance and preventing the proper and equable expansion of the spirits; squeezing the pores and spaces of the brain together, one upon another; pressing out the spirits into the origins of the nerves and in the medulla oblongata so that they are forced more copiously into one or the other nerve causing a spasm in various parts of the body.' He stated even more explicitly 'to wit, that the spirits inhabiting it (the brain) being disposed to explosions, and there being exploded, bring on or cause every Falling Evil.'[9]

During the 18th century, there was little progress in the study of epilepsy, but the 19th century brought the first scientific attempts at understanding it by means of the clinical analysis of seizures and laboratory investigation by neurophysiologists.[10]

The statement by John Hughlings Jackson in 1876 that 'an epilepsy is a sudden excessive, rapid and local discharge of some part of the cerebral hemisphere'[11] summarises the scientific view held in Britain in the late 19th century. In his analysis of the loss of consciousness and other clinical features of epilepsy, Jackson based his clinical understanding of epilepsy on an understanding of the relevant anatomy, physiology and pathology. We still adhere to these premises today but with more technical sophistication.

In 1881 William Gowers, who had been a student of Jackson, clinically defined epilepsy as follows: 'The characteristic of the malady is the recurrence of sudden brief disturbance of some functions of the brain, varying in degree, extent and character, but generally attended with an arrest of consciousness sufficient at least to interrupt control of the muscles necessary to the maintenance of correct posture.'[5]

Given these clinical definitions of epilepsy as well as the attempts by clinicians to localise the epileptogenic focus, experimental physiologists and experimental surgeons directed their attention to cortical localisation. As a result, the history of our understanding of epilepsy is inextricably linked to the history of cerebral localisation.

The saga of cerebral localisation starts with a publication by Theodor Fritsch (1838 - 1927) in 1870. He had, in collaboration with Eduard Hitzig (1838 - 1907), explored the convexity of the dog's hemisphere (and much later would examine that of the monkey). By using platinum electrodes and weak currents they were able to elicit discreet muscle movements.

David Ferrier (1843 - 1928), with the aid of very weak currents and small electrodes less than a millimetre apart, stimulated the cortex in an attempt to elicit discreet movements rather than convulsive activity. His detailed studies of many different species, including monkeys, allowed him later to correlate his experimental work with observations in man. Ferrier, the experimental neurologist, became the link between the pure clinicians like Jackson and Gowers and pure physiologists like Charles Sherrington.

The first major scientific meeting devoted to epilepsy was the 1881 International Medical Congress in London where Friederich Goltz (1834 - 1902) of Strassburg, Ferrier of London and other researchers could discuss their contributions before a wide audience. The arguments between the localisationists (Ferrier) and the anti-localisationists (Goltz) came strongly to the fore. Their

different findings were probably the result of their using different species of experimental animals and the differing stimulating currents and electrodes utilised. Goltz used dogs while Ferrier used monkeys and it is not possible to extrapolate from one to the other.

Victor Horsley (1857 - 1916), the father of British neurosurgery, was certainly also the first experimental neurosurgeon. He performed localisation studies on the cortices of the orang-utan and man with low current electrical stimulation. He may have been a greater experimental than practical day-to-day surgeon and his experimental work greatly increased our understanding of the brain as a surgical target. Among other things he was the first to provide surface markings for structures in the underlying cortex.

Charles Scott Sherrington's (1856 - 1952) contributions to neurophysiology overshadowed those of his predecessors and determined the direction neurophysiological research would take early in the 20th century. His work on cortical localisation included not only stimulation studies, but also ablation of discreet cortical areas. He found, for instance, that fine digital movements were more widely represented than coarse proximal joint movements. His work in collaboration with Greenbaum laid the foundation for the discovery of the now universally accepted Rolandic motor and post-Rolandic sensory areas in anthropoids.

Along with clinical and experimental attempts at cortical localisation, research directed at identification of neural structures and determination of the cyto-architecture of the cerebral cortex gained momentum. Some of the greatest names in neuro-physiology were involved in this activity and from this work grew that of K. Brodmann (1868 - 1918) who, early in this century, produced cortical maps that indicated 52 different regions with evidence of histological differentiation in at least 11 major regions. The first map obtained by stimulation of the human cortex was that of Charles Frazier (1870 - 1936), a neurosurgeon, in collaboration with C. K. Mills (1845 - 1931), a neurologist. Some of this work was repeated by Harvey Cushing (1869 - 1939) in 1908. Fedor Krause (1856 - 1937) also repeated this in great detail in Germany using faradic stimulation and his observations on cortical stimulation in epileptic patients convinced him that this was an essential procedure for obtaining information about the site of the prefrontal convolution.

Otfrid Foerster (1873 - 1941), a great admirer of Jackson and Sherrington, was the father of functional neurosurgery. He was really an experimental neurophysiologist who utilised every opportunity to observe the function of the brain by direct cortical stimulation as well as other experiments. He was not only an outstanding neurologist but, out of necessity, also became a very ingenious functional neurosurgeon; posterior root section for pain, anterolateral cordotomy and cortical localisation are but a few of the procedures that he pioneered. Foerster performed a large number of cortical stimulation experiments on the simian cortex and he can be seen as one of the originators of systematic, scientific cortical localisation.[12] After World War I, he dealt with many patients with post-traumatic epilepsy caused by cerebral scars that had resulted from war wounds. He tried to control these attacks by excision of the scar which he thought to be the stimulus for the seizure.[13]

Despite Caton's detection of weak electrical currents from the brains of rabbits and monkeys in 1875, it was Hans Berger (1873 - 1941) who, with scalp electrodes, first recorded electrical activity from the human brain in 1929.[14] Electro-encephalography (EEG), as it was called, had far-reaching effects on the study, diagnosis and management of epilepsy, both clinically and surgically.

John Fulton (1899 - 1960), the American neurophysiologist who was a student of Foerster, had a great influence on a generation of neurosurgeons who became interested in the surgery of epilepsy. His work focused on localisation of function in the primate motor cortex and cerebellum and was the basis for the first frontal leucotomies, performed by Egaz Moniz (1874 - 1955) and Pedro Almeida Lima in 1935. His student, J. G. Dusser De Barenne of Utrecht, introduced physiological neuronography, i.e. electrocorticography and depth recording utilising topical cortical stimulation with strychnine. This fostered a new understanding of the cerebral cortex based not only on the basic structure but also on cortico-cortical and extrinsic connections of individual areas.

Foerster's student who made the greatest contribution to cortical localisation and the surgery of epilepsy was Wilder Penfield (1891 - 1976). He had also been a student of Sherrington and is the man with whom surgical treatment of epilepsy in the 20th century is associated. The Montreal Neurological Institute at McGill University was established by him in 1934 and on the basis of its research, the concept of cortical excision as a treatment for certain types of epilepsy became established neurosurgical practice. Meticulous observations on the surgically exposed brain by him and his co-workers, Jasper, Rasmussen and others, gave us much of the clinical certainty we have today.

It is impossible to name all the neuroscientists who played a part in unravelling the brain's localisation of function, particularly with regard to epilepsy. The structure and functional characteristics of the epileptic neuron have been established by the activities of research workers in many parts of the world. Their work laid the foundations of what is taken for granted today and determined the quality and scope of neurological/neurosurgical practice which has, in turn, provided an abiding stimulus for this work to continue.

Surgery for epilepsy

The first venture into surgery for epilepsy involved scar excision for focal epilepsy after cortical injury, but with functional localisation the outstanding contribution was surgery for temporal lobe seizures. That behavioural disturbances may be associated with temporal lobe lesions was substantiated by the work of Kiüver and Bucy in monkeys in 1939; the temporal lobe as the site of origin of psychomotor seizures was established by the work of Jasper and Kershmann in 1941. E. L. Gibbs and F. A. Gibbs in 1947 showed that focal spike discharges on EEG recording from the anterior temporal lobe occurred in the majority of these patients and could best be detected during drowsiness and sleep. Percival Bailey of Chicago was the first to do temporal lobectomies for psychomotor seizures at the insistence of the neurologists, Gibbs and Gibbs, and was also the first to use electro-corticography for intra-operative localisation.

What was previously known as psychomotor, temporal lobe, or limbic epilepsy and is now called partial complex epilepsy, has since then been treated very successfully by anterior temporal lobectomy in selected cases. This is a direct development of localisation which made it possible to separate the limbic system or 'visceral brain' from the neo-cortex, which is mostly concerned with higher intellectual function.[10]

One must not forget that an original and remarkable contribution was made to the surgery of epilepsy by the first South African neurosurgeon, Roland Krynauw (1907 - 1990). Hemispherectomy is to this day one of the most well-directed surgical attacks on epilepsy and

probably one of the most successful when done for the correct indications.

In our attempts at surgical localisation, we are still dependent mainly on a good clinical history and examination as well as observation of the seizures, both visually and electrically. These endeavours have greatly benefited from advances in technology (EEG, video tape recordings, etc.). Computed tomography and magnetic resonance scanning have made a big difference since the days when we had to rely on air encephalography and arteriography as our only means of visualising the brain in attempts at anatomical localisation.

We have come a long way and we have a long way to go. Perhaps methods of investigation will shift towards those which show actual function of the brain, such as positron emission tomography scanning, so that therapeutic intervention will be at a functional level, probably more pharmacological than surgical. The clinical methods of analysing and understanding seizures, aided by the advances in appropriate technology, is continuing.

Sir Gordon Holmes's warning to clinicians should, however, not be forgotten. He quoted Oliver Wendell Holmes as follows: 'If I wished to show a student the difficulties of getting at the truth from clinical experience, I would give him the history of epilepsy to read.'[15]

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