Ken - please check the references. Best regards from Harald Fodstad

Acta Neurochir Suppl (2007) 97(1): 11–19

Printed in Austria

Electricity in the treatment of nervous system disease

H. Fodstad[1] and **M. Hariz**[2]

[1] Veterans Affairs Medical Center, New York, USA
[2] Institute of Neurology, London, UK

Summary

Electricity has been used in medicine for almost two millenniums beginning with electrical chocks from the torpedo fish and ending with the implantation of neuromodulators and neuroprostheses. These implantable stimulators aim to improve functional independence and quality of life in various groups of disabled people. New indications for neuromodulation are still evolving and the field is rapidly advancing. Thanks to modern science and computer technology, electrotherapy has reached a degree of sophistication where it can be applied relatively safely and effectively in a variety of nervous system diseases, including pain, movement disorders, epilepsy, Tourette syndrome, psychiatric disease, addiction, coma, urinary incontinence, impotence, infertility, respiratory paralysis, tinnitus and blindness.

Keywords: Deep brain stimulation; electricity; electrotherapy; nervous system; neuromodulation; neuropacemaker; neuroprosthesis; neurostimulation; stereotaxy.

"Is it a fact – or have I dreamt it – that by means of electricity, the world of matter has become a great nerve, vibrating thousands of miles in a breathless point of time? Rather, the round globe is a vast head, a brain, instinct with intelligence; or shall we say it is itself a thought, nothing but thought, and no longer the substance which we dreamed it."

Nathaniel Hawthorne (1804–1864)

Historical background

By definition, electricity is a fundamental entity of nature consisting of negative and positive charges, observable in the attractions and repulsions of bodies electrified by friction and natural phenomena, and usually utilized in the form of electric currents.

The first known use of electricity in medicine was in AD 46 when Scribonius Largus, a pharmacist from Neron and physician to the Roman Emperor Claudius applied electrical currents from the torpedo fish to treat headaches and painful gout [61, 94]:

"A chronic and intolerable headache which insistently manifests itself can be eliminated at once if treated by applying a live torpedo fish, black in color, to the site of the pain and leaving it there until the pain stops and the part is swollen."

The real breakthrough for electrotherapy came with the scientific progress of the 18th century, especially after the discovery of the Leyden jar in 1746 [11]. In 1777, Cavallo published *"A complete treatise on electricity, in theory and practice, with original experiments."* He reported cures of epilepsy, paralysis, chorea, deafness, blindness, rheumatism and glandular enlargement. He was also the first to recommend electricity as means of artificial respiration [11]. As early as 1774, Benjamin Franklin noted muscle contractions on exposure to static electricity [43]. After Franklin's invention of lightning rods in 1775, there were three important milestones in the history of electrotherapy: The discovery of animal electricity by Luigi Galvani in 1787, the discovery of bimetallic electricity by Alessandro Volta in 1794 and the discovery of inductive electricity by Michael Faraday in 1831 [34, 81] (Table 1). Volta also invented the first electric battery in 1800. In 1804 Aldini, a nephew of Galvani, recommended galvanism for deafness, insanity, amaurosis, and to produce artificial respiration [11].

Andrew Ure in 1818 used the body of a hanged criminal immediately after execution to stimulate the phrenic nerves in the chest with galvanic electricity, thereby producing contractions of the diaphragm [106]. He thought

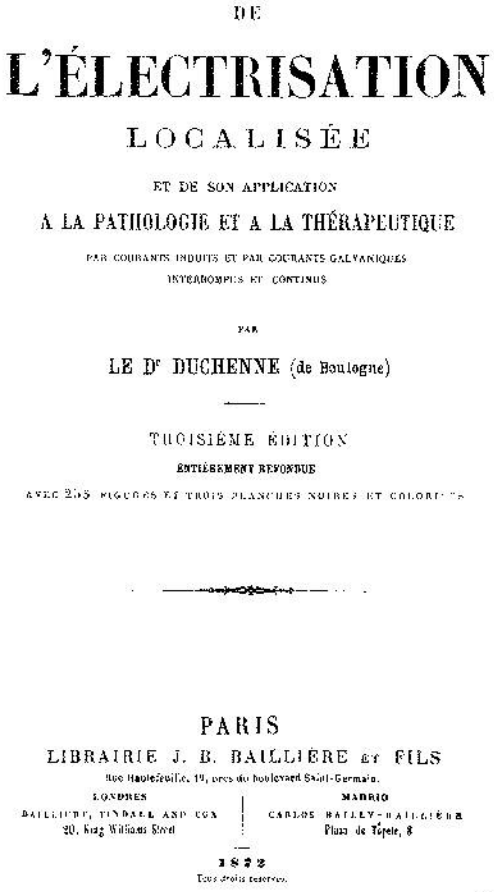
Table 1. *The evolution of electrotherapy*

Torpedo-Fish	
Scribonius Largus AD 46	
Magnetism and Static Electricity	
Gilbert	1600
– Leyden Jar	1746
– Wesley	1759
– Franklin	1775
– Cavallo	1777
Bimetallic Electricity	
– Volta	1794
Galvanization	
Galvani	1787
– Aldini	1804
– Remak	1855
Faradization	
– Faraday	1831
– Duchenne	1855
Electropuncture	
– Salandiere	1825
– D'Etiolles	1840

the method might be used to resuscitate humans with intact vital organs. Ure vividly described the events to the Glasgow Literary Society:

"The left phrenic nerve was now laid bare at the outer edge of the sterno-thyreoideus muscle, from three to four inches above the clavicle; the cutaneous incision having been made by the side of the sterno-cleido-mastoideus. Since this nerve is distributed to the diaphragm, and since it communicates with the heart through the eight pair, it was expected, by transmitting the galvanic power along it, that the respiratory process would be renewed.

The success was truly wonderful. Full, nay, laborious breathing instantly commenced. The chest heaved and fell; the belly was protruded, and again collapsed, with the relaxing and retiring diaphragm. This process was continued, without interruption, as long as I continued the electric discharges. Extraordinary grimaces were exhibited every time electric discharges were made on the


DE

L'ÉLECTRISATION

LOCALISÉE

ET DE SON APPLICATION

A LA PATHOLOGIE ET A LA THÉRAPEUTIQUE

PAR COURANTS INDUITS ET PAR COURANTS GALVANIQUES
INTERROMPUS ET CONTINUS

PAR

LE Dr DUCHENNE (de Boulogne)

TROISIÈME ÉDITION
ENTIÈREMENT REFONDUE
AVEC 253 FIGURES ET TROIS PLANCHES NOIRES ET COLORIÉES

PARIS
LIBRAIRIE J. B. BAILLIÈRE ET FILS
rue Hautefeuille, 19, près du boulevard Saint-Germain.

LONDRES
BAILLIÈRE, TINDALL AND COX
20, King William Street

MADRID
CARLOS BAILLY-BAILLIÈRE
Plaza de Topete, 8

1872
Tous droits réservés.

a

b

Fig. 1. (a) Title page of Duchenne de Boulogne's monography 3rd edn 1872. (b) Duchenne stimulating the facial muscles in a patient

supraorbital nerve. His countenance was simultaneously thrown into fearful action; rage, horror, despair, anguish, and ghastly smiles, united their hideous expression in the murderer's face, surpassing far the wildest representations of a Fuseli or a Kean. At this period several of the spectators were forced to leave the apartment from terror or sickness, and one gentleman fainted."

In 1824, Flourens in Paris reported on faradic stimulation and ablation of the cortex in experimental animals [72]. The following year Salandiere proposed the use of acupuncture needles in galvanization, so that the current could be applied directly on the desired nerve or organ. The method was called electropuncture and was used for resuscitation by Leroy-D'Etiolles in 1840 [64].

In 1855, the French physician Guillaume Duchenne de Boulogne published his pioneering monography: *"De l'electrisation localisee et de son application a la physiologie, a la pathologie et a la therapeutique"* [31] (Fig. 1a and b). Duchenne was the first to successfully use transcutaneous faradic stimulation of the phrenic nerves for artificial respiration. He was followed by Hugo von Ziemssen, who applied a DuBois-Reymond faradic stimulator (shocking coil) to the phrenic nerve to resuscitate a gas-poisoned patient [34]. At the same time Remak founded a German school of electrotherapy using galvanic current [11]. Interestingly, Duchenne was unwilling to admit the reality of the discoveries of Remak, and Remak rejected the conclusions of Duchenne. A comprehensive overview of contemporary electrotherapie was published by Erdmann in 1858 [32].

Evolution of neurostimulation and lesioning

In 1870, Fritsch and Hitzig [41] observed limb movement when stimulating the motor cortex of the dog, and in 1873 Dittmar used guided electrodes experimentally for the study of the vasomotor center in the medulla oblongata [29]. The first documented account of applying electrical stimulation to the living human brain was in 1874 by Roberts Bartholow in Cincinnati [10]. The patient was a 30 year old woman with an "epithelioma" (meningioma) and an open ulcer in the posterior portion of the skull. Bartholow was able to stimulate the parietal cortex with a "Galvano-Faradic Company double cell battery" and insulated needles. He noted muscle contractions on electrical stimulation which also triggered a grand mal seizure. In 1884, Victor Horsley applied electrical stimulation of occipital tissue in a patient with an encephalocele [109]. The conjugate eye movements he observed led him to identify the stimulated tissue as lamina quadrigemina. Ewald's investigations in Germany in 1896 may have been the first where the brains of fully awake, unrestrained animals were stimulated over a long period of time [107]. Talbert described the technique and his own extension of Ewald's work in 1900 [100].

In 1908, Victor Horsley and Robert Henry Clarke applied their stereotactic instrument and electricity to study cerebellar structures and functions in monkeys [57]. They described in detail the use of direct current (versus radiofrequency) to make lesions, a technique later adopted in animal experiments worldwide [38, 78, 84]. In 1912, Clarke wrote about his instrument [38]:

"This invention relates to what may be termed stereotaxic surgical apparatus for use in performing operations within the cranium of living human beings."

Clarke's prophecy became reality 35 years later when Spiegel and Wycis performed the first stereotactic operation in man [96, 97]. In subsequent years, electrical stimulation and recordings from selected subcortical regions through stereotactically implanted probes were performed in patients with parkinsonism, epilepsy and psychiatric disease by Magnus Petersen [107], Robert Heath [53–55], Carl Wilhelm Sem-Jacobsen [88–91], Orlando Andy [5], N P Bechtereva [12] and Jose Delgado [27]. Alberts and coworkers documented the improvement of dystonia with intracerebral stimulation in awake patients [2, 3].

Sem-Jacobsen was a controversial Norwegian psychiatrist and neurophysiologist. In 1963, he published an article about depth-electrographic observations in psychotic patients [88]. He stated that *"electrical stimulation in some regions in the ventro-medial part of the frontal lobe resulted in a temporary improvement to complete freedom from symptoms"*

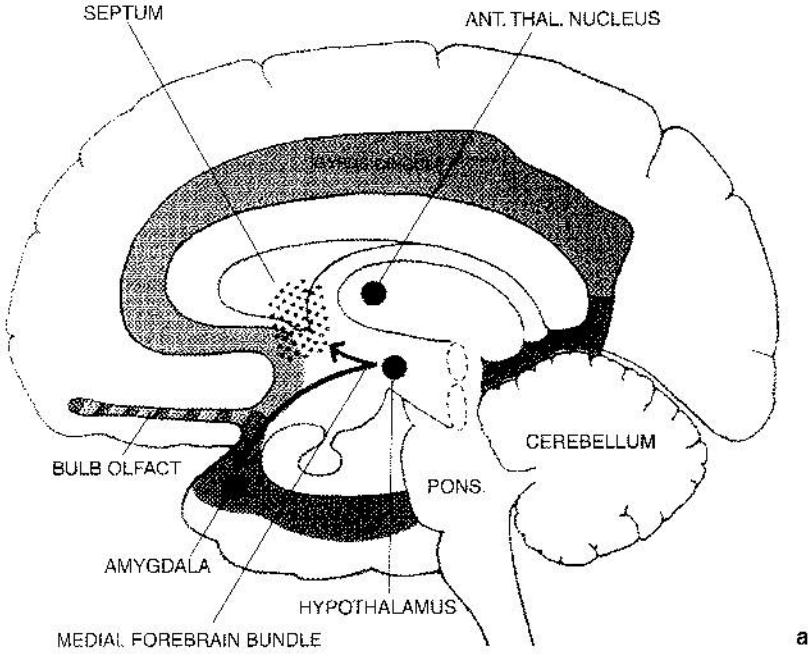
Sem-Jacobsen was accused by Norwegian colleagues of receiving grants from the CIA to perform experiments on mentally ill patients. His name was cleared by a government appointed review commission in December 2003, twelve years after his death.

Jose Delgado used remote radio stimulation of bulls' brains to abruptly stop their aggressive behavior in the arena [107]. In 1965 he summarized [26]:

"Autonomic and somatic functions, individual and social behavior, emotional and mental reactions may be evoked, maintained, modified, or inhibited, both in animals and man, by electrical stimulation of specific

cerebral structures. Physical control of many brain functions is a demonstrated fact, but the possibilities and limits of this control are still little known".

In the nineteen twenties, Walter Rudolph Hess in Switzerland and Stephen Ranson in USA used electrostimulation to explore the different regions of the hypothalamus and related neural structures in animals [56, 83]. Their experiments provided support for the speculative theory proposed in 1937 by James Papez that the limbic system (cingulate-hippocampus-fornix mamillary bodies-anterior thalamus) in conjunction with the hypothalamus may constitute the anatomical circuit which regulates emotions [79] (Fig. 2a and b). In 1948, Hess postulated that the hypothalamus consists of an anterior *trophotropic zone,* which dominates during resting and restorative activities, and a middle-posterior *ergotropic zone,* which regulates physiological reactions accompanying high arousal levels [56]. Hess received the Nobel



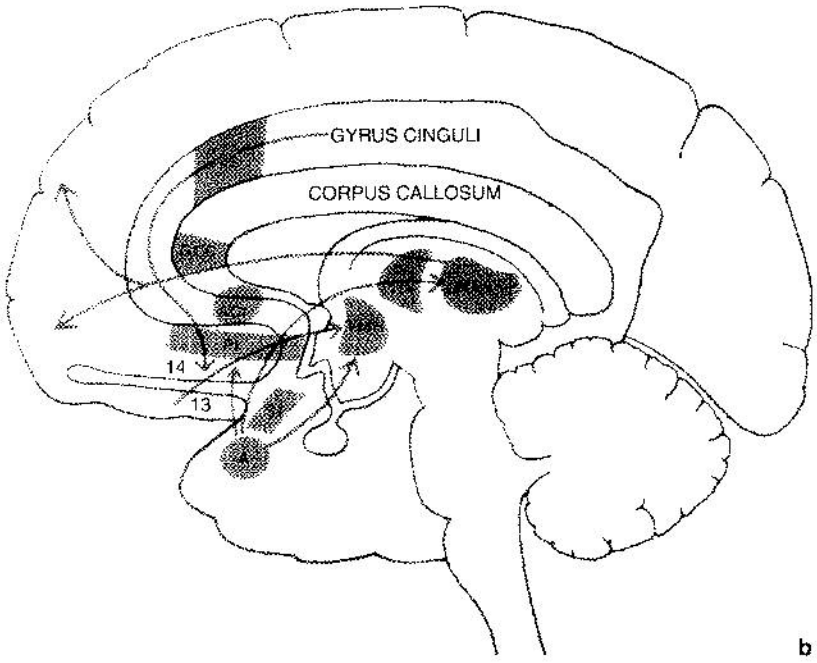


Fig. 2(a). The limbic circuit. (b) Subcortical targets in psychosurgery

Prize in Physiology and Medicine 1949 for discovering the role played by certain parts of the brain in determining and coordinating the function of internal organs. He shared the prize with the Portuguese neurologist and politician, Antonio Egas Moniz, who introduced prefrontal lobotomy for psychiatric disease [33]. This highly controversial procedure was soon to be replaced by less destructive psychosurgeries using the stereotactic technique [33, 36, 63, 75]. Concurrently, electroshock therapy for psychiatric disease and depression was introduced by Ugo Cerletti [20]. Based upon Hess' studies Sano in 1970 described the effect of electrical stimulation of the posterior hypothalamus in man [87]. Stereotactic thermolesions in the *ergotropic triangle* in 51 patients with pathologically aggressive behavior produced marked calming effect in 95% of the cases. The procedure, which was called "sedative therapy" encouraged a German group to perform stereotactic hypothalamotomies in 20 cases of pedophilia, hypersexuality and exhibitionism *"with complete harmonization of sexual and social behaviour"* [73]. A few years later, Nadvornik and his group in Bratislava published a paper on thermolesions in the anterior hypothalamus for "hedonia," which they defined as *"not only excessive smoking, tobaccoism, but also excessive inclinations to good eating and drinking, lucullianism and bacchism"* [74].

In 1974 Quaade, Vaernet and Larsson performed stereotactic stimulation and electrocoagulation of the lateral hypothalamus in obese humans [82]. Three patients with gross obesity subjected to lesions in the lateral hypothalamus showed *"a statistically significant, but transient decrease from preoperative to postoperative spontaneous calorie intake."*

Despite the reported effectiveness of hypothalamotomy as a method to control behavioral disturbances, serious moral, ethical and legal objections to these procedures have been raised [33, 65, 107].

As stereotactic neurosurgery progressed, stimulation became routine for localization of targets in the brain. Hassler, a former graduate researcher with Rudolph Hess, recognized that thalamic stimulation caused cessation of tremor and might mimic the same effect as a lesion [51, 52]. Similar observations of the stimulation of various subcortical targets were made by Spiegel and colleagues [43, 98] and Ronald Tasker and his group [101].

Melzack and Wall's "gate control theory of pain" published in 1965 [69] laid the foundation for the start of pain management by neuromodulation, including transcutaneous electrical stimulation (TENS) [62], peripheral nerve stimulation [99, 111], spinal cord stimulation [76, 92], cortical stimulation [60, 105], and deep brain stimulation (DBS) [58, 70, 85]. DBS and spinal cord stimulation were also used for treatment of spasticity and dyskinesia [93, 95]. Early neurostimulators consisted of extracorporeal parts (radiotransmitter and antenna) and implanted components (receiver and electrode) [42].

Electrophrenic stimulation (diaphragm pacing) for chronic ventilatory insufficiency was developed by William Glenn in the 1960's [45, 46]. The initially enthusiastic reports on spinal cord stimulation in multiple sclerosis could not be substantiated in later trials [21, 43]. Visual cortex stimulation for blindness was first described by Brindley in 1968 [18], and the first clinical study on the use of vagal nerve stimulation for intractable epilepsy appeared in 1990 [47].

Current use of neuromodulation

Neuromodulation is defined as the use of electrical stimulation by implanted stimulators to treat various neurological conditions [1, 43]. Neurostimulation has experienced a renaissance in the past two decades with the introduction of totally implantable neuropacemakers and image guided surgical systems, and the field is rapidly advancing [66]. Neuroaugmentation to subcortical structures via implanted electrodes has largely replaced lesioning all over the world. DBS is a nonablative and reversible procedure with a low incidence of permanent complications, and it is considered safer than ablative lesions. The anatomical targets in the brain for DBS remain more or less the same as for stereotactic radiofrequency lesioning.

The current FDA (Food and Drug Administration) approved indications for DBS in the United States are unilateral or bilateral stimulation of the ventralis intermedius (Vim) nucleus of the thalamus for essential tremor and parkinsonian tremor, and unilateral or bilateral stimulation of the internal globus pallidus (GPi) and subthalamic nucleus (STN) in Parkinson's disease [13, 14, 71]. FDA approval was based on the report of 'The Deep-Brain Stimulation for Parkinson's Disease Study Group' published in 2001 [103]. However, the report has been subjected to criticism for inaccurate documentation of side effects [49]. Benabid introduced STN as the main target in Parkinson's disease, but STN stimulation is hampered by psychiatric side effects due to the nucleus' proximity to hypothalamus and the limbic circuitry [14, 80].

Some DBS surgery complications may be closely related to the experience and techniques of the neurosurgical team. Hardware complications (electrode migration, lead breakage, stimulator malfunction) and other side effects occur in a significant number of patients [16, 42, 50, 77]. The use of single-cell microelectrode recordings for alleged accurate target placement of the electrode, which has become routine in many centers, may increase the surgical complications, including hemorrhage [48]. The modern neuropacemakers require repeat programming of the electrical paradigms by a specially trained health employee to meet the changing needs of each individual patient. The implanted non-rechargeable batteries need to be changed every three to five years.

The exact mechanism of action of DBS is not yet known. Possible mechanisms include depolarization blockade, channel blocking, synaptic failure, antero- and retrograde effects, effects on non-neuronal cells, effects on the local concentrations of ions or neuroactive molecules, and neuronal energy depletion [68]. The long-term effect of chronic electrical stimulation on brain tissue and function is not well understood.

The indications for DBS in movement disorders include (but are not limited to) tremor, bradykinesia, dyskinesias, rigidity, dystonia and gait disturbance [7, 17, 24]. In addition, DBS has been reported to be successful in treating chronic deafferentation pain [58], cluster headaches [9, 39], epilepsy [15, 22, 108], obsessive-compulsive disorder [4, 6], Tourette syndrome [110], depression [59, 67], violent behavior [40] and other neuropsychiatric disorders [86]. Motor cortex stimulation has been applied for chronic pain [60, 105] and the auditory cortex has been stimulated magnetically and electrically for intractable tinnitus [25]. Transcranial non-invasive magnetic stimulation has been reported by several authors to be effective in controlling intractable epilepsy [28, 102]. Neurostimulation and neuromodulation is also used for restoration of hand function and gait [1], improvement of peripheral circulation [8, 30], bladder control [76], fertility management [1], respiratory paralysis [37, 46], chronic hiccup [35], blindness [44], cerebral palsy [23] and coma [104].

DBS is now an established method in treating movement disorders and pain. Thanks to functional imaging, new areas in the brain are shown to be involved in some pathological processes. These areas are now being subject to DBS to see if they can be electrically inhibited [9, 66]. DBS should still be regarded as experimental in psychiatric disease and embryonic in many other mentioned disorders until the reported results have been verified in controlled studies in a larger number of patients. DBS should be considered only for patients in whom other established therapeutic modalities have been carried out. Current practice and ongoing trials of DBS including brain targets are shown in Table 2a and b.

History seems to repeat itself, as electricity is currently being tried for almost any kind of nervous system disease with physicians looking for specific stimulation targets in the brain for certain symptoms and diseases. Neuronal circuits rather than specific nuclei are frequently targeted, and different targets often respond equally to electrostimulation for the same disorder. The voluminous recent literature on DBS indicates that it is in danger of becoming a new method in search for more diseases.

Table 2. *(a) Routine use of dbs*

Parkinson's disease
– Nucleus ventralis intermedius (Vim), globus pallidus internus (GPi), subthalamic nucleus (STN), zona incerta
Dystonia
– Globus pallidus internus (GPi)
Tremor (essential, cerebellar and MS)
– Nucleus ventralis intermedius (Vim), zona incerta
Choreoathetosis
– Nucleus ventralis intermedius (Vim), nucleus ventro-oralis posterior (Vop), globus pallidus internus (GPi), zona incerta
Deafferentation pain
– Nucleus ventro-postero-medialis (VPM), nucleus ventro postero-lateralis (VPL), Centromedian nucleus (CM), periaqueductal gray (PAG), periventricular gray (PVG)

Table 2. *(b) Current trials of dbs*

Epilepsy
Anterior thalamus, centromedian nucleus (CM), subthalamic nucleus (STN), hippocampus
Cluster headaches
– Posteromedial hypothalamus
Obsessive compulsive disease
Anterior limb of the internal capsule, nucleus accumbens
Tourette syndrome
– Centromedian nucleus (CM), nucleus ventro-oralis internus (Voi), globus pallidus internus (GPi), periventricular gray (PVG)
Depression
– Anterior limb of the internal capsule, nucleus accumbens, anterior cingulum
Drug addiction
– Nucleus accumbens
Violent behavior
– Posteromedial hypothalamus
Obesity
Anterior hypothalamus

The only commercially available deep brain stimulator (Medtronic Inc) is unreasonably expensive, and aggressive marketing and sponsoring by the sole supplier raises concerns about conflicts of interest.

Thanks to past trials and errors together with scientific progress and technological advancements, we have reached a point where electricity can be applied relatively safely and effectively in the management of a great variety of nervous system diseases. However, improvements in screening and standardization of techniques will be needed in the future. There remains no consensus on best DBS practices, and the refinement of transplantation procedures and controllable genetically engineered stem cells may render these systems irrelevant and obsolete in the future. In the world of contemporary neuroaugmentative procedures, one must always keep in mind the cautionary words of Malcolm Carpenter, renowned neuroanatomist [19]:

"Personally, I feel that stereotaxic surgery has much to offer, if properly controlled and used judiciously. Some of the wild things that are done without a scientific rational jeopardize the entire effort."

References

1. Al Moutaery K, Ansari S (2001) Neurostimulation & neuromodulation. An introduction. Pan Arab J Neurosurg. MSD Printing Press, pp 1–189
2. Alberts WW, Feinstein B, Levin G, Wright EW, Darland MG, Scott EL (1965) Stereotaxic surgery for parkinsonism. Clinical results and stimulation thresholds. J Neurosurg 23: 174–183
3. Alberts WW, Feinstein B, Levin G, Wright EW (1966) Electrical stimulation of therapeutic targets in waking dyskinetic patients. Electroencephalogr Clin Neurophysiol 20: 559–566
4. Anderson D, Ahmed A (2003) Treatment of patients with intractable obsessive-compulsive disorder with anterior capsular stimulation. Case report J Neurosurg 98: 1104–1108
5. Andy OJ (1966) Neurosurgical treatment of abnormal behavior. Am J Med Sci 252: 232–238
6. Aouizerate B, Cuny E, Martin-Guehl C, Guehl D, Amieva H, Benazzouz A, Fabrigoule C, Allard M, Rougier A, Bioulac B, Tignol J, Burbaud P (2004) Deep brain stimulation of the ventral caudate nucleus in the treatment of obsessive-compulsive disorder and major depression. Case report J Neurosurg 101: 682–686
7. Ashby P, Strafella A, Dostrovsky JO, Lozano A, Lang AE (1998) Immediate motor effects of stimulation through electrodes implanted in the human globus pallidus. Stereotact Funct Neurosurg 70: 1–18
8. Augustinsson LE, Carlsson CA, Holm J, Jivegard L (1985) Epidural electrical stimulation in severe limb ischemia. Pain relief, increased blood flow, and a possible limb-saving affect. Ann Surg 202: 104–110
9. Bahra A, Matharu MS, Buchel C, Frackowiak RS, Goadsby PJ (2001) Brainstem activation specific to migraine headache. Lancet 357: 1016–1017
10. Bartholow R (1874) Experimental investigations into the functions of the human brain. Am J Med Sci 67: 305–313
11. Beard GM, Rockwell AD (1875) Practical treatise on the medical and surgical uses of electricity. 2nd edn. Lewis, London, pp 214–318
12. Bechtereva NP, Bondarchuk AN, Smirnov VM (1972) Therapeutic electrostimulations of the deep brain structures. Vopr Neirokhir 1: 7–12
13. Benabid AL, Pollak P, Loveau A, Henry S, de Rougemont J (1987) Combined (thalamotomy and stimulation) stereotactic surgery of the VIM thalamic nucleus for bilateral Parkinson disease. Appl Neurophysiol 50: 344–346
14. Benabid AL, Pollak P, Gross C, Hoffmann D, Benazzouz A, Gao DM, Laurent A, Gentil M, Perret J (1994) Acute and long-term effects of subthalamic nucleus stimulation in Parkinson's disease. Stereotact Funct Neurosurg 62: 76–84
15. Benabid AL, Minotti L, Koudsie A, de Saint Martin A, Hirsch E (2002) Antiepileptic effect of high-frequency stimulation of the subthalamic nucleus (corpus Luysi) in a case of medically intractable epilepsy caused by focal dysplasia: a 30 month follow-up: Technical case report. Neurosurgery 50: 1385–1392
16. Beric A, Kelly PJ, Rezai A, Sterio D, Mogilner A, Zonenshayn M, Kopell B (2001) Complications of deep brain stimulation surgery. Stereotact Funct Neurosurg 77: 73–78
17. Brice J, McLellan L (1980) Suppression of intention tremor by contingent deep-brain stimulation. Lancet 1: 1221–1222
18. Brindley GS, Lewin WS (1968) The sensations produced by electrical stimulation of the visual cortex. J Physiol 196: 479–493
19. Carpenter MB (1987) Personal communication (letter)
20. Cerletti U (1956) Electrochock therapy. In: Marti-Ibanez F, Sackler AM, Sackler MD, Sackler RR (eds) The great psychodynamic therapies in psychiatry. Hoeber-Harper, New York, pp 91–120
21. Cook AW (1976) Electrical stimulation in multiple sclerosis. Hosp Pract 11: 51–58
22. Cooper IS, Amin I, Riklan M, Waltz JM, Poon TP (1976) Chronic cerebellar stimulation in epilepsy. Clinical and anatomical studies. Arch Neurol 33: 559–570
23. Cooper IS, Riklan M, Amin I, Waltz JM, Cullinan T (1976) Chronic cerebellar stimulation in cerebral palsy. Neurology 26: 744–753
24. Coubes P, Cif L, El Fertit H, Hemm S, Vayssiere N, Serrat S, Picot M-C, Tuffery S, Claustres M, Echenne B, Frerebeau P (2004) Electrical stimulation of the globus pallidus internus in patients with primary generalized dystonia: long-term results. J Neurosurg 101: 189–194
25. De Ridder D, De Mulder G, Walsh V, Muggleton N, Sunaert S, Moeller Aa (2004) Magnetic and electrical stimulation of the auditory cortex for intractable tinnitus. Case report. J Neurosurg 100: 560–564
26. Delgado J (1965) Evolution of physical control of the brain. Proceed Am Mus Nat Hist New York, pp 1–54
27. Delgado J (1968) Intracerebral radio stimulation and recording in completely free patients. J Nerv Ment Dis 147: 329–340
28. Dhuna A, Gates J, Pascual-Leone A (1991) Transcranial magnetic stimulation in patients with epilepsy. Neurology 41: 1067–1071
29. Dittmar C (1873) Ueber die Lage des sogenannten Gefaesszentrums in der Medulla oblongata. Berl Saechs Ges Wiss (Leipzig) 25: 449–469
30. Dooley DM, Kasprak M (1976) Modification of blood flow to the extremities by electrical stimulation of the nervous system. South Med J 69: 1309–1311
31. Duchenne G (1872) De l'electrisation localisee et de son application a la pathologie et a la therapeutique, 3rd edn. Baillere, Paris, pp 1–914
32. Erdmann BA (1858) Anwendung der Elektricitaet in der Physiologie, Pathologie und Therapie. Verlag von Joh. Ambr. Barth, Leipzig, pp 1–266

33. Feldman RP, Goodrich JT (2001) Psychosurgery: a historical overview. Neurosurgery 48: 647–659
34. Fodstad H (1995) Phrenico-diaphragmatic pacing. In: Roussos C, Clenfant C (eds) The thorax. Marcel Dekker Inc, New York Basel Hong Kong, pp 2597–2617
35. Fodstad H, Nilsson S (1993) Intractable singulitus: a diagnostic and therapeutic challenge. Br J Neurosurg 7: 255–262
36. Fodstad H, Strandman E, Karlsson B, West KA (1982) Treatment of chronic obsessive compulsive states with stereotactic anterior capsulotomy or cingulotomy. Acta Neurochir (Wien) 62: 1–23
37. Fodstad H, Blom S, Linderholm H (1983) Artificial respiration by phrenic nerve stimulation (diaphragm pacing) in patients with cervical cord and brain stem lesions. Scand J Rehab Med 15: 173–181
38. Fodstad H, Hariz M, Ljunggren B (1991) History of Clarke's stereotactic instrument. Stereotact Funct Neurosurg 57: 130–140
39. Franzini A, Ferroli P, Leone M, Broggi G (2003) Stimulation of the posterior hypothalamus for treatment of chronic intractable cluster headaches. The first reported series. Neurosurgery 52: 1095–1101
40. Franzini A, Marras C, Ferroli P, Bugiani O, Broggi G (2005) Stimulation of the posterior hypothalamus for medically intractable impulsive and violent behavior. Stereotact Funct Neurosurg 83: 63–66
41. Fritsch G, Hitzig E (1870) Ueber die elektrische Erregbarkeit des Grosshirns. Arch Anat Physiol Wiss Med 37: 300–332
42. Gildenberg PL (1977) Neurosurgical statement on neuroaugmentive devices. Appl Neurophysiol 40: 69–71
43. Gildenberg PL (2005) Evolution of neuromodulation. Stereotact Funct Neurosurg 83: 71–79
44. Girvin JP, Fodstad H (1998) Visual prosthesis. In: Gildenberg PL, Tasker RR (eds) Textbook of stereotactic and functional neurosurgery. McGraw-Hill, pp 1999–2004
45. Glenn WWL (1978) Diaphragm pacing: present status. Pacing Clin Electrophysiol 1: 357–370
46. Glenn WWL, Brouillette RT, Dentz B, Fodstad H, Hunt CE, Keens TG, Marsh HM, Pande S, Piepgras DG, Vanderlinden RG (1988) Fundamental considerations in pacing of the diaphragm for chronic ventilatory insufficiency: a multi-center study. Pace 11: 2121–2127
47. Hammond EJ, Uthman BM, Reid SA, Wilder BJ, Ramsey RE (1990) Vagus nerve stimulation in humans: Neurophysiological studies and electrophysiological monitoring. Epilepsia Suppl 31: 51–59
48. Hariz MI, Fodstad H (1999) Do microelectrode techniques increase accuracy or decrease risks in pallidotomy and deep brain stimulation? A critical review of the literature. Stereotact Funct Neurosurg 72: 157–169
49. Hariz MI, Fodstad H (2002) Deep-brain stimulation in Parkinson's disease: letter to the editor. N Engl J Med 346: 452–453
50. Hariz MI, Shamsgovara P, Johansson F, Hariz G-M, Fodstad H (1999) Tolerance and tremor rebound following long term chronic thalamic stimulation for parkinsonian and essential tremor. Sterotact Funct Neurosurg 72: 208–218
51. Hassler R, Dieckmann G (1982) Stereotactic treatment of spasmodic torticollis. In: Schaltenbrand G, Walker AE (eds) Stereotaxy of the human brain. Thieme, Stuttgart, pp 522–531
52. Hassler R, Riechert T, Mundinger F, Umbach W, Ganglberger JA (1960) Physiological observations in stereotaxic operations in extrapyramidal motor disturbances. Brain 83: 337–350
53. Heath RG (1963) Electrical self-stimulation of the brain in man. Am J Psychiatry 120: 571–577
54. Heath RG (1972) Pleasure and brain activity in man. J Nerv Ment Dis 154: 3–18
55. Heath RG, Monroe RR, Mickle WA (1955) Stimulation of the amygdaloid nucleus in a schizophrenic patient. Am J Psychiatry 111: 862–863
56. Hess WR (1964) The central control of the activity of internal organs. In: Nobel Lectures, Physiology or Medicine 1942–1962. Elsevier, New York
57. Horsley VA, Clarke RH (1908) The structure and functions of the cerebellum examined by a new method. Brain 31: 45–124
58. Hosobuchi Y, Adams JE, Rutkins B (1973) Chronic thalamic stimulation for the control of facial anesthesia dolorosas. Arch Neurol 29: 158–161
59. Jimenez F, Velasco F, Salin-Pascual R, Hernandez JA, Velasco M, Criales JL, Nicolini H (2005) A patient with resistant major depression disorder treated with deep brain stimulation in the inferior thalamic peduncle. Neurosurgery 57: 585–593
60. Katayama Y, Yamamoto T, Kobayashi K, Kasai M, Oshima H, Fukaya C (2001) Motor cortex stimulation for phantom limb pain: Comprehensive therapy with spinal cord and thalamic stimulation. Stereotact Funct Neurosurg 77: 159–162
61. Kellaway P (1946) The part played by electric fish in the early history of bioelectricity and electrotherapy. The William Osler Medical Essay. Bull Hist Med 20: 112–137
62. Laitinen L (1976) Placement of electrodes in transcutaneous stimulation for chronic pain. Neurochirurgia (Stuttg) 22: 517–526
63. Laitinen L (1980) Psychosurgery. In: Kisker KP, Meyer J-E, Mueller C, Stroemgren E (eds) Psychiatrie der Gegenwart. Springer, Berlin Heidelberg New York, pp 351–378
64. Leroy-D'Etiolles M (1840) De l'asphyxie. J Soc Gen Naufragie 4: 53–76
65. Ljunggren B, Fodstad H (1991) Surgical intervention in the brain's most sacred area – the hypothalamus. Emirates Med J 9: 167–172
66. Lozano AM (2001) Deep-brain stimulation: Challenges to integrating stimulation technology with human neurobiology, neuroplasticity, and neural repair. J Rehabil Res Dev 38: 10–19
67. Mayberg HS, Lozano AM, Voon V, McNeely HE, Seminowicz D, Hamani C, Schwalb JM, Kennedy SH (2005) Deep brain stimulation for treatment-resistant depression. Neuron 45: 651–660
68. McIntyre CC, Takor NV (2002) Uncovering the mechanisms of deep brain stimulation for Parkinson's disease through functional imaging, neural recording, and neural modeling. Crit Rev Biomed Eng 30: 249–281
69. Melzack R, Wall PD (1965) Pain mechanisms: A new theory. Science 150: 971–979
70. Merienne L, Mazars G (1982) Traitement de certaines dyskinesies par stimulation thalamique intermittente. Neurochirurgie 28: 201–206
71. Mogilner AY, Rezai AR (2003) Brain stimulation: History, current clinical application, and future prospects. Acta Neurochir Suppl 87: 113–120
72. Morgan JP (1982) The first reported case of electrical stimulation of the human brain. J Hist Med Allied Sci 37: 51–64
73. Mueller D, Roeder F, Orthner H (1973) Further results of stereotaxis in the human hypothalamus in sexual deviations. First use of this operation in addiction to drugs. Neurochirurgia (Stuttgart) 16: 113–126
74. Nadvornik P, Sramka M, Patoprsta G (1977) Transventricular anterior hypothalamotomy in stereotactic treatment of hedonia. In: Sweet WH, Obrador S, Martin-Rodriguez JG (eds) Neurosurgical treatment in psychiatry, pain and epilepsy. University Park Press, Baltimore, pp 445–449
75. Narabayashi H (1973) Stereotaxic operations for behavior disorders. Progr Neurol Surg 5: 113–158
76. Nashold BSJ, Friedman H, Glenn JF, Grimes JH, Barry WF, Avery R (1972) Electromicturition in paraplegia. Implantation of a spinal neuroprosthesis. Arch Surg 104: 195–202
77. Oh MY, Abosch A, Kim SH, Lang AE, Lozano AM (2002) Long-term hardware-related complications of deep brain stimulation. Neurosurgery 50: 1268–1276

78. Olds J, Milner B (1954) Positive reinforcement produced by electrical stimulation of the septal area and other regions of the rat brain. J Comp Physiol Psychol 47: 419–426
79. Papez JW (1937) A proposed mechanism of emotion. Arch Neurol Psychiat 38: 725–743
80. Piasecki SD, Jefferson JW (2004) Psychiatric complications of deep brain stimulation for Parkinson's disease. J Clin Psychiatry 65: 845–849
81. Pruel MC (1997) A history of neuroscience from Galen to Gall. In: Greenblatt SH, Dagi TF, Epstein MH (eds) A history of neurosurgery. Association of Neurological Surgeons, Park Ridge, pp 99–130
82. Quaade F, Vaernet K, Larsson S (1974) Stereotaxic stimulation and electrocoagulation of the lateral hypothalamus of obese humans. Acta Neurochir (Wien) 30: 111–117
83. Ranson SW (1937) Some functions of the hypothalamus. Harvey Lecture, Bull. N.Y. Acad Med 13: 241–271
84. Reynolds DV (1969) Surgery in the rat during electrical analgesia induced by focal brain stimulation. Science 164: 444–445
85. Richardson DE, Akil H (1977) Pain reduction by electrical brain stimulation in man. 1. Acute administration in periaqueductal and periventricular sites. J Neurosurg 47: 178–183
86. Roth RM, Flashman LA, Saykin AJ, Roberts DW (2001) Deep brain stimulation in neuropsychiatric disorders. Current Psychiatry Reports 3: 366–372
87. Sano K, Mayanagi Y, Sekino H, Ogashiwa M, Ishijima B (1970) Results of stimulation and destruction of the posterior hypothalamus in man. J Neurosurg 33: 689–707
88. Sem-Jacobsen CW (1963) Depth-electrographic observations in psychotic patients. Proc Gaustad Ment Hospital, Oslo, pp 412–416
89. Sem-Jacobsen CW (1965) Depth electrographic stimulation and treatment of patients with Parkinson's disease including neurosurgical technique. Acta Neurol Scand Suppl 13: 365–377
90. Sem-Jacobsen CW (1966) Depth-electrographic observations related to Parkinson's disease. J Neurosurg 24: 388–402
91. Sem-Jacobsen CW, Torkildsen A (1960) Depth recording and electrical stimulation in the human brain. In: Ramey ER, O'Doherty DS (eds) Electrical studies on the unanesthetized brain. Paul B Hoeber, New York, pp 275–290
92. Shealy CN, Mortimer JT, Reswick JB (1967) Electrical inhibition of pain by stimulation of the dorsal columns. Preliminary clinical report. Anesth Analg (Cleveland) 46: 489–491
93. Siegfried J (1977) Two different aspects of neurosurgical treatment of spasticity. Cerebral intervention and stimulation of the posterior spinal cord. Neurochirurgie 23: 344–347
94. Siegfried J (1978) Introduction – Historique. In: R Sedan R, Lazorthes Y (eds) La Neurostimulation Electriques Therapeutique. Neurochirurgie 24 Suppl 1: 5–10
95. Siegfried J (1986) Effect of stimulation of the sensory nucleus of the thalamus on dyskinesia and spasticity. Rev Neurol (Paris) 142: 380–383
96. Spiegel EA, Wycis HT, Marks M, Lee AJ (1947) Stereotaxic apparatus for operations on the human brain. Science 106: 349–350
97. Spiegel EA, Wycis HT, Umlauf CW (1950) Electroenecephalographic studies before and after thalamotomy. Monatsschr Psychiatr Neurol 120: 398–411
98. Spiegel EA, Wycis HT, Szekely EG, Soloff L, Adams J, Gildenberg P, Zanes C (1964) Stimulation of Forel's Field during stereotaxic operations in the human brain. Electroencephalogr Clin Neurophysiol 16: 537–548
99. Sweet W, Wepsic JG (1968) Treatment of chronic pain by stimulation of fibers of primary afferent neuron. Trans Am Neurol Assoc 93: 103–107
100. Talbert GA (1900) Ueber Rindenreizung am freilaufenden Hunde nach J. R. Ewald. Arch Anat Physiol 24: 195–208
101. Tasker RR, Organ LW, Hawrylshyn PA (1982) The thalamus and midbrain of man. A physiological atlas using electrical stimulation. Charles C Thomas, Springfield
102. Tergau F, Naumann U, Paulus W, Steinhoff BJ (1999) Low frequency repetitive transcranial magnetic stimulation improves intractable epilepsy. Lancet 353: 2209–2213
103. The deep-brain stimulation for Parkinson's disease study group (2001) Deep-brain stimulation of the subthalamic nucleus or the pars interna of the globus pallidus in Parkinson's disease. N Engl J Med 345: 956–963
104. Tsubokawa T, Yamamoto T, Katayama Y, Hirayama T, Maejima S, Moriya T (1990) Deep-brain stimulation in a persistent vegetative state: follow-up results and criteria for selection of candidates. Brain Inj 4: 315–327
105. Tsubokawa T, Katayama Y, Yamamoto T, Hirayama T, Koyama S (1991) Chronic motor cortex stimulation for the treatment of central pain. Acta Neurochir Suppl 52: 137–139
106. Ure A (1819) An account of some experiments made on the body of a criminal immediately after execution, with physiological and practical observations. J Sci Arts (London) 6: 283–294
107. Valenstein ES (1973) Brain control. A critical examination of brain stimulation and psychosurgery. John Wiley & Sons, New York, pp 13–197
108. Velasco F, Velasco M, Velasco AL, Menez D, Rocha L (2001) Electrical stimulation for epilepsy: stimulation of hippocampal foci. Stereotact Funct Neurosurg 77: 223–227
109. Vilenski JA, Gilman S (2002) Horsley was the first to use electrical stimulation of the human cerebral cortex intraoperatively. Surg Neurol 38: 425–426
110. Visser-Vandewalle V, Temel Y, Boon P, Vreeling F, Colle H, Hoogland G, Groenewegen HJ, van der Linden C (2003) Chronic bilateral thalamic stimulation, a new therapeutic approach in intractable Tourette Syndrome. Report of three cases. J Neurosurg 99: 1094–1100
111. Wall PD, Sweet WH (1967) Temporary abolition of pain in man. Science 155: 108–109

Correspondence: H. Fodstad, 130 East 18 St. Apt. 17H, New York, NY 10003, USA. e-mail: Mail4viking@gmail.com