Early Controversies Over Athetosis: II. Treatment

Douglas J. Lanska

1 Veterans Affairs Medical Center, 500 E. Veterans St., Tomah, Wisconsin, United States of America

Abstract

Background: Athetosis has been controversial since it was first described by William Hammond in 1871; many aspects of Hammond’s career were equally controversial.

Methods: Primary sources have been used to review treatment controversies in the 50-year period following the initial description of athetosis.

Results: The treatments used most commonly employed available pharmaceutical agents and modalities (e.g., galvanism). Initial anecdotal reports of success were seldom confirmed with subsequent experience. Several novel invasive therapies were also developed and promoted, all of which damaged or destroyed either upper or lower motor neuron pathways, and were also often associated with high mortality rates. In general, these therapies substituted paresis for abnormal spontaneous movements. These included peripheral nerve stretching, excision of a portion of the precentral gyrus, rhizotomy, nerve “transplantation” (i.e., neurotomy and nerve-to-nerve anastomoses), and “muscle group isolation” (i.e., alcohol neurolysis). There was no agreement on the appropriateness of such high-risk procedures, particularly given the intentional generation of further neurological morbidity.

Discussion: Pharmaceutical agents and modalities initially employed for athetosis had little a priori evidence-based justification and no biologically plausible theoretical framework to guide empiric treatment selection. Subsequently, all the invasive procedures employed were directed at lessening or removing the manifestations, rather than the underlying cause, of the abnormal central nervous system “irritation,” usually by imposing paresis or paralysis. Factors contributing to the disparity in outcomes between favorable initial reports and the often-disappointing results of later studies included reliance on anecdotal reports or small uncontrolled case series, placebo effects, biased observation, misdiagnosis, and biased reporting.

Keywords: History of neurology—19th century, history of neurology—20th century, athetosis, treatment

Introduction

Athetosis is an involuntary movement disorder characterized by slow, smooth, sinuous, writhing movements, particularly involving the hands.1–9 Since its description in 1871 by American neurologist William Alexander Hammond (1828–1900) (Figure 1), and subsequent elaboration by Hammond and his son Graeme Monroe Hammond (1858–1944),2–7,9–15 the disorder has been a source of controversy,1 as were many aspects of Hammond’s career, either as US Army Surgeon General during the Civil War or later as a civilian neurologist in New York.3,16–25

Although Hammond struggled to establish athetosis as a distinct clinicopathological entity, and indeed had successfully predicted the striatal pathology in his initial case (albeit somewhat serendipitously), athetosis was nevertheless considered by many late 19th and 20th century neurologists as a form of post-hemiplegic chorea or part of a continuum between chorea and dystonia.9,26–29 European neurologists, and the French in particular, initially ignored or discounted the concept.1 Additional controversies arose over whether the movements persisted during sleep, whether it was, or could be, associated with imbecility or insanity, and how it should be treated.1

The purpose of the present article is to review some of the controversies concerning treatment of athetosis in the 50-year period following its initial description. There was no agreement over how athetosis should be treated, with many anecdotal reports of benefit, which were not confirmed by subsequent experience. In particular, there was no agreement over whether heroic treatments warranted...
either the risk or the frequently associated additional morbidity. Other controversies concerning athetosis were considered in a previous paper.1

**Methods**

Reports of athetosis in the 50-year period after its description in 1871 were identified using IndexCat (the National Library of Medicine’s online version of the 61-volume Index-Catalogue of the Library of the Surgeon General’s Office, U.S. Army, Series 1–5, spanning 1880–1961), and searching other electronic databases and search engines (Google, Google Scholar, Google Books, Internet Archive, HighWire, and PubMed), and serial review of reference lists in articles/monographs. Images were identified from primary source documents on athetosis and through a search of various archival image sources (U.S. National Library of Medicine Images from the History of Medicine, U.S. National Archives Archival Research Catalog, the Library of Congress Prints and Photographs Online Catalog, Google Image, and Wikimedia Commons).

**Results**

**Medications**

Hammond’s initial treatment approach in his index case utilized barium chloride, ergots, Fowler’s solution (potassium arsenite), iron, mercurials, conium maculatum (poison hemlock), and cod liver oil were applied to the treatment of athetosis, but with ultimately disappointing results, even if some initial anecdotal reports were favorable.3,4,7,27,30–47 These treatments employed non-specific drugs that were applied to the treatment of many other conditions at that time. By the 1890s, based on the pathology identified in various cases, Hammond dismissed any consideration of a pharmaceutical approach to treating athetosis: “From the nature of the lesions discovered post-mortem, it would be absurd to consider any medicinal treatment for this disease.”7

Others came to similar conclusions to those of Hammond. In 1893, Hammond’s friend and colleague, New York neurologist Landon Carter Gray (1850–1900), concluded that, “The treatment of athetosis, when it is of the organic type, is not known, for as yet no drug has been found to be of any value.”40 In 1895, Philadelphia neurologist A.O.J. Kelly similarly surmised that:

> The nature of the lesions producing the affection, so far as they are known, is such as to almost exclude the possibility of any beneficial influence being exerted by medicines. … Some cases of improvement have been reported in which galvanism, bromides, iodides, etc., were used. But unfortunately we can promise little.41

**Galvanic therapies**

Galvanic stimulation is a form of electrotherapy that involves the use of direct current applied to specific areas of the body. The “Era of Galvanization” began in 1800 with the invention of the galvanic pile (i.e., the battery) by Italian physicist Alessandro Volta (1745–1827), who was stimulated to pursue this development by his disagreements with Italian physician Luigi Galvani (1737–98) concerning “animal electricity.”42 Shortly thereafter various investigators and quacks applied galvanism indiscriminately,42,43 but as noted by American neurologists and electrotherapists George Miller Beard (1839–83) and Alphonse David Rockwell (1840–1933) in their monograph, *A Practical Treatise on the Medical and Surgical Uses of Electricity* (1871), galvanism...
failed to fulfil [sic] the extravagant expectations that had been formed of it; a reaction followed, and it fell into disrepute." Electrotherapeutics regained legitimacy in the 1850s with the work of Guillaume-Benjamin-Amand Duchenne de Boulogne in France (left) and Robert Remak in Germany (right). Thereafter, galvanic, faradic, and combined forms of electrotherapeutics enjoyed wide popularity for various conditions, and were touted in various neurology textbooks in the late 19th century, including Hammond's *A Treatise on Diseases of the Nervous System* (1871). Examples of the wide range of electrotherapeutic apparatus were also illustrated in textbooks and monographs (Figure 3).

In his index case, Hammond applied “the primary galvanic current to [the patient’s] brain, spinal cord, and affected muscles” and noted that, in combination with the internal use of barium chloride, the patient “is certainly improving, but I have little hope of any permanent result being obtained.” As it turned out, his prognostic skepticism proved well founded.

In 1876, British neurologist Sir William Gowers (1845–1915) (Figure 4) reported anecdotal improvement in the arm (but not the leg) of a post-hemiplegic case after applying a 2-month-long course of galvanic current treatments, with the positive pole applied to the nape of the neck, and the negative pole rubbed over the overacting muscles. The continuous galvanic current was applied daily, the positive pole being placed on the neck, and the negative pole on the overacting muscles and on the hand and foot. After each application he thought that his hand was steadier, and in a month the spontaneous spasm was considerably less. He could keep his hand flexed or extended, and could manage, although with difficulty, to pick up even a very small object. His great toe was less extended, and his was less halting. The applications of electricity were continued during the next two months, and the spontaneous movements became slighter and slighter, and finally

---

**Figure 2. Pioneers in Electrotherapeutics.** Electrotherapeutics regained legitimacy in the 1850s with the work of Guillaume-Benjamin-Amand Duchenne de Boulogne in France (left) and Robert Remak in Germany (right). Engravings courtesy of the U.S. National Library of Medicine.

**Figure 3. Galvanic Apparatus.** From left to right: Emil Stöhrer’s zinc–carbon (or zinc–platinum) battery, universal electrode handle with ivory interrupter, metallic electrodes of various sizes, and sponge electrode with long handle. Stöhrer (1813–1890) was a noted scientific instrument maker, who established a shop in Dresden specifically for electrotherapeutic equipment. Figure source: Beard & Rockwell, 1871.
ceased altogether. A little stiffness in the movements of the fingers was all that remained. In his leg the improvement was slighter. The foot remained inverted and the toes extended, but the pain in the ankle was considerably relieved with bromide of potassium with Indian hemp [marijuana].

Hammond and many others applied galvanic therapy for athetosis, but not often with the zeal of Gowers. Despite anecdotal reports of benefit, the positive outcomes were not reproducible and no sustained benefit was documented. As American neurologist and psychiatrist George W. Jacoby (1842–1940) concluded in 1892, “thus far the various remedies have proved of little avail. Electricity, the hope of many, is of no value.”

**Nerve stretching**

In 1872, Prussian-born Austrian surgeon Christian Albert Theodor Billroth (1829–94) (Figure 5A) operated on a patient with sciatica, but found no compression of the nerve; when the patient nevertheless reported post-surgical relief, Billroth attributed the clinical improvement to an effect of surgical manipulation of the nerve. Subsequently, based on Billroth’s report, German surgeon Johann Nepomuk von Nussbaum (1829–90) (Figure 5B) intentionally stretched the brachial plexus as a therapeutic procedure with reportedly symptomatic improvement. This positive result generated international interest in the procedure, which rapidly became a popular treatment for a wide range of disorders. In general, a short segment of

![Figure 4. British Neurologist Sir William Gowers. Gowers performed a protracted series of galvanic treatments for athetosis. Courtesy of the U.S. National Library of Medicine.](image)

![Figure 5. Pioneers of Therapeutic Nerve Stretching. Therapeutic nerve stretching originated with the work of Prussian-born Austrian surgeon Theodor Billroth (left) and German surgeon Johann Nepomuk von Nussbaum (right). In 1872 Billroth had argued that surgical manipulation of a nerve was responsible for the relief of sciatica when no compressive lesion was identified at surgery. Subsequently, Nussbaum intentionally stretched the brachial plexus as a therapeutic procedure with reportedly symptomatic improvement. Courtesy of the U.S. National Library of Medicine.](image)
a target nerve was exposed surgically, and then, using one to three fingers, the surgeon applied steady traction to the nerve in each direction.\textsuperscript{57} Pain relief was the usual therapeutic goal, but as Graeme Hammond noted in 1882 the procedure was used rather indiscriminately:\textsuperscript{10} “For the last 10 years nerve-stretching has been resorted to with more or less success in almost all spinal and cerebral cases in which there was the slightest possibility of a cure.”\textsuperscript{10} By the early 1880s, more than 250 cases of various neurological disorders (affecting either the central or peripheral nervous systems) had been reported in which nerve stretching had been applied;\textsuperscript{56} although initial experience was deemed favorable,\textsuperscript{58} many of the early results could not be reproduced, relapses in successful cases were common, and complications – including deaths – were increasingly reported.\textsuperscript{57}

At the request of British anatomist and surgeon John Marshall (1818–91), then President of the Royal College of Surgeons of England, British neurosurgeon Victor Horsley (1857–1916) (Figure 6) obtained specimens of an unstretched and a stretched peripheral nerve (Figure 7).\textsuperscript{56,59}

In the sheath or epineurium, which covers the nerve, you will find, in the unstretched specimen [Figure 7A], that the fibres are beautifully wavy, like the ordinary fibres of fibrous tissue. You find also that the tubules are, more or less, loose in their sheath, and that even the perineurium, the fine membrane lying between the epineurium and the tubules, also presents this kind of wavy contour in the unstretched state. Blood-vessels are seen at intervals lying in this position.\textsuperscript{56}

Contrasted with this specimen is one from the same median nerve stretched by a weight of twenty-eight pounds, far within its breaking strain, which would be above sixty pounds [Figure 7B]. Here you find that the epineural fibres, instead of being wavy, are in perfectly straight lines, stretched out as tight as they can be; that the perineurium is perfectly straight, and that the tubules are somewhat narrowed, and also stretched to an extraordinary degree. In a transverse section of the unstretched nerve, we see the spaces in which the fasciculi of the nerve-fibres lie, the smaller bundles being represented as combining into a larger one, the individual tubules of the nerves being represented in the centre, constituting each fasciculus. In this condition the perineurium is loose, the channels or tubes in which the nerve-fasciculi lie are more or less open, and there is a space between the fasciculus and the perineurium... The vessels [have undergone] a complete alteration. You find the epineurium or sheath again tightened in its tissue, and marked with straight rigid lines, as if the whole texture was pulled out tight, and cut in a sort of hard, solid block. You find the fasciculi compressed, and the lymphatic [sic] space

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{figure6.png}
\caption{British Neurosurgeon Sir Victor Horsley. Horsley performed histological studies of nerve stretching and also of neocortical resection of the precentral gyrus for athetosis.\textsuperscript{56,68,71} In patients with athetosis, both procedures substituted paresis for the abnormal movements. Courtesy of the U.S. National Library of Medicine.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{figure7.png}
\caption{Histology of Nerve Stretching. Longitudinal and cross-sectional drawings of an unstretched nerve (A) and a stretched nerve (B) as drawn from specimens obtained by British neurosurgeon Victor Horsley. Figure source: Marshall, 1883.\textsuperscript{56}}
\end{figure}
Obliterated, indicating, as it would appear, the compression of the bundles. ... The medullary [myelin] sheath lies in irregular masses, whilst most observers agree that the tubular part of the nerve is not broken, or that it is very rarely broken, and that the axis-cylinder [axon] is still more rarely torn across.\textsuperscript{56}

Various mechanisms have been suggested to explain the anecdotal reports of improvement by nerve stretching, including “breaking up of adhesions, etc., pressing injuriously upon the nerve,”\textsuperscript{63} or “trophic changes, probably induced by the disturbance of vasomotor actions.”\textsuperscript{56} None provided a particularly satisfying explanation, however, and Scottish anatomist Johnson Symmington (1851–1924) concluded that, “The manner in which a beneficial effect is produced by the operation of nerve-stretching is very obscure.”\textsuperscript{68}

In 1882, William J. Morton (1846–1920), in the department for nervous diseases at the Metropolitan Throat Hospital in New York, and shortly thereafter Graeme Hammond in the same department, independently reported anecdotal benefits of nerve stretching in patients with athetosis, at the time that this was a popular therapeutic fad.\textsuperscript{10–12,61} Morton had stretched the ulnar and median nerves with “resulting abolition of the continuous compound movements, but some numbness of the hand and an occasional twitch of the thumb persisted.”\textsuperscript{61} What Morton failed to report, though, was that he had used “such force as to render the limb permanently paralyzed.”\textsuperscript{57} Only 4 years later Graeme Hammond acknowledged that nerve stretching had initially been viewed as a panacea, and had since fallen out of favor, but he still supported its use for athetosis.\textsuperscript{13}

In nerve-stretching, which at one time cured almost every disease known to neurologists, but which at the present time has rather fallen into disrepute, we have the means of completely arresting athetosis by producing permanent paralysis of the extremity ... or we can produce temporary cessation of the movements, unaccompanied by paralysis, by employing a lesser degree of force.\textsuperscript{13}

The senior Hammond commented in 1881, in regard to the treatment of tabes dorsalis by nerve stretching, that, because the benefits were unclear and the risks were significant, the procedure should be used selectively and with only a modest stretch, an admonition that was made even more forcefully by others within only a few years.\textsuperscript{62}

Up to the present time ... seven cases of nerve-stretching for the cure of locomotor ataxia have been performed. Of these, two ... died from the effects of the operation, and one ... from the narcosis of the chloroform administered. In one ... there was no improvement. In all the others there was more or less amelioration, even in those in which death occurred. [Hammond then related his experience with 2 personal cases]. Relative to the ultimately good effects of the operation, I am by no means so confident as some European neurologists. At the same time, it appears to me that there is ground for hope that it may prove successful in some cases. I am convinced that in those instances in which gangrene, thrombosis, etc., have occurred, the nerve has been stretched too much. A very moderate extension is, I think, sufficient.\textsuperscript{62}

Gowers (Figure 4) was even more pessimistic in 1888 in regard to nerve stretching for the treatment of pain in tabes dorsalis, and noted that the procedure was gradually being abandoned.\textsuperscript{65}

In many cases the procedure has had no influence on the symptoms. If ever justified it is only as a last resort ... but it is not justifiable in any case to hold out an expectation of more than possible, and perhaps transitory relief to the one symptom. It must be remembered, moreover, that the operation is not devoid of danger of evil results; there is the risk incidental to the necessary anaesthetic [and, indeed, in the initial case treated by Lagenbuch using chloroform anesthesia, the patient died as a result of the anesthetic], and the operation has also caused death through the agencies of erysipelas and spinal haemorrhage. Its modus operandi is not easy to explain, and the theories that have been advanced to account for its influence are so inadequate as to be scarcely worth reproduction. Its common inutility is more easily intelligible. It would seem now to be passing into merited disuse.\textsuperscript{63}

Nevertheless, even after the procedure was being abandoned for other conditions, the senior Hammond continued to advocate the procedure for athetosis. Hammond noted in 1891 (and 1893) that he had several times stretched the median nerve in his original case of athetosis with beneficial but temporary results (although it was not entirely clear if the procedure was done by the senior Hammond or his son). After every operation “the spasms ceased entirely in both arm and leg, and the pain, which was severe, disappeared.”\textsuperscript{57} Relief was obtained for periods of 4–18 months, during which time the patient “could use his hand for writing, dressing himself, eating, and in fact for almost any purpose.”\textsuperscript{57} Hammond added in conclusion that, “It seems to me that nerve-stretching holds out the only hope of relief.”\textsuperscript{57}

**Surgical therapies**

In the 50-year period after the description of athetosis, a variety of invasive and risky surgical procedures were also developed, generally with little justification and no experimental support, and typically with serious expected (and realized) secondary morbidity. The range of heroic surgical therapies included trephining,\textsuperscript{72} excision of the precentral gyrus, posterior (and sometimes concomitant anterior) rhizotomy, peripheral nerve “transplantation” (i.e., neurotomy and nerve-to-nervan anastomosis), alcohol neurolysis of peripheral nerves, and even amputation of the most affected limb.\textsuperscript{64–67}

**Excision of the precentral gyrus**

In 1890, Victor Horsley (Figure 6) reported neocortical excision of a portion of the precentral gyrus in a patient with athetosis, but despite Horsley’s unshakeable belief that the operation would be
successful if a large enough excision had been done, the patient in fact sustained no benefit. Horsley’s justification for the procedure was quite limited: “The pathology of athetosis is as yet obscure. I have, however, always regarded it as a form of cortical discharge.” English neurologist and anatomist Charles Edward Beevor (1854–1908) had asked Horsley to operate on the patient, who was considered a “hopeless case, and one in which [Beevor], having detected a successive invasion of segments by the movement commencing in the thumb [akin to Jacksonian epilepsy], was led to conclude that the affection was one of cortical origin.” Horsley therefore removed the neocortical “focus for the representation of the movements of the thumb,” and for about 2 weeks the movements were arrested, but the movements soon returned “as the cortex around resumed its functional activity.” Horsley did not question the utility of a failed operation, but instead concluded that he had not been aggressive enough: “it is evident therefore that the whole representation of the part must be removed, a course which the paralysed state of the limb fully warrants. This operation, in fact, offers the only means of relieving the condition of spasm.

Although Horsley’s able surgical technique was generally acknowledged, few followed his lead with extirpation of portions of the precentral gyrus, even when others had the skill to perform the procedure. Pioneering Philadelphia neurosurgeon William Williams Keen (1837–1932), whose initial professional recognition came as a neurological collaborator of Silas Weir Mitchell (1829–1914) during the US Civil War, was one who questioned the appropriateness of Horsley’s procedure, and one who showed greater restraint in applying such risky procedures (Figure 8).

The advisability of operating in these cases is as yet doubtful. Mr. Horsley regards athetosis as a form of cortical discharge, and has reported one case in which he operated without benefit. ... He urges the removal of the entire area innervating the part involved if, I suppose, the disease be limited to a single extremity; he would scarcely propose to remove both an arm and leg centre, producing an entire hemiplegia [or conduct bilateral procedures]. ... In a case under my own care, in which the athetosis is limited to the left arm ... I have not thus far thought it right to operate on the brain. The patient is an adult and still finds the arm somewhat useful. I stretched the brachial plexus above the clavicle [akin to more distal peripheral nerve stretching procedures], but the operation was not followed by any improvement. When the disease arises in childhood, especially in conjunction with the cerebral palsy of children, I should certainly advise against operation, with our present knowledge. It is, however, but just to say that our experience is as yet too limited for us to be dogmatic.

Occasionally surgeons did attempt the procedure, but no clear success was reported. As subsequently reported by Philadelphia neurologist and neuropathologist William Gibson Spiller (1863–1940) and colleagues, a young man who had athetosis from around 2 years of age had undergone an unsuccessful excision of the “cortical centre for his left upper extremity” at the Philadelphia General Hospital prior to 1905. After the surgery, the man suffered “two or three convulsions, in which he lost consciousness at times for ten minutes” and it was also noted that “since the operation his left arm has been more rigid, the pain in his right arm has been more pronounced, and his condition has grown steadily worse.”

Horsley nevertheless persisted with the procedure and reported a second case in his Linacre Lecture at St. John’s College, Cambridge on May 6, 1909. The patient was a 14-year-old male who “at the age of 7 had gradually developed athetoid movements of the left hand, which then developed into violent convulsive movements of the whole upper limb” and had consequently been referred to Horsley by neurologist James Risien Russell (1863–1939). Horsley “advised that the arm area in this case should be delimited by excitation [i.e., mapped by electrical stimulation] and then removed.” In 1908, Horsley resected “the whole depth of the [contralateral] gyrus pre-centralis” (Figure 9) with resulting “disappearance of spasmodic movements” that persisted for at least a year after surgery, but with significant sensory loss and weakness of the arm, which gradually improved to a modest degree (Figures 10 and 11).
Rhizotomy (posterior and anterior)  

Another surgical procedure first performed for athetosis shortly after Horsley’s operation was sectioning of posterior (and sometimes concomitantly selected anterior) nerve roots. In 1888, in a letter to New York surgeon Robert Abbe (1851–1928), New York neurologist Charles Loomis Dana (1852–1935) (Figure 12) had proposed sectioning the posterior spinal roots in patients with intractable chronic pain.\(^{65}\) Abbe (Figure 13) soon adopted this posterior rhizotomy procedure and called it “Dana’s operation,” ultimately applying it to a variety of conditions.\(^{65}\) One of the cases Abbe reported in 1911 had suffered from infantile hemiplegia and “athetoid paralysis” involving, in particular, the right arm and hand and, to a lesser degree, the right foot.\(^{65}\) “Constant excessive athetoid movements” and pain led sequentially to amputation of the forearm, stretching of the brachial plexus, and then amputation at the shoulder.\(^{65}\) It was at this point in 1894 that Abbe performed a posterior rhizotomy at C5–C8, and an anterior rhizotomy at C7–C8 to help control the pain and “incessant spasms” (Figure 14).\(^{65}\) Abbe reported that the man was “discharged [a month later] with very great improvement” and, in particular, that “the constant athetoid spasms had gone.”\(^{65}\) Abbe followed him over the next 16 years until his death in 1910, and noted that although the patient “said he suffered … the old athetoid spasms did not return.”\(^{65}\) Up to the time of his death, the man “complained moderately and took his morphine.”\(^{65}\)

Philadelphia neurosurgeon Charles H. Frazier (1870–1936) (Figure 15), Professor of Clinical Surgery at the University of Pennsylvania, also used posterior rhizotomy in a case of athetosis, after the persistent urging of Spiller who was then Professor of Neuropathology and Associate Professor of Neurology at the University of Pennsylvania.\(^{71,72}\) However, although the “results seemed at first very promising …. [when] we saw him again, some three years later, athetosis in the operated limbs had almost disappeared, but contraction had become pronounced and interfered greatly with voluntary motion.”\(^{71}\) Spiller added that, “Improvement in this case … is distinct, but tenotomy may be needed on account of the shortening of the flexor muscles at the elbows.”\(^{71}\)

Spiller was aware of criticism of the procedure, but saw no insurmountable obstacles, and in fact felt the issue had been largely solved:\(^{71}\)

In regard to some of the objections made to the treatment, I acknowledge that the operation is serious …. [Nevertheless] I would say that a means has been devised full of promise for selected cases of spasticity and athetosis, and that these conditions which formerly perplexed and baffled us have in a considerable measure yielded to treatment. Undue enthusiasm is to be deprecated, as bringing the method into disrepute. Cases must be carefully selected, and only those are available in which spasticity is great and weakness is comparatively slight.\(^{71}\)

Despite Spiller’s continued advocacy of the procedure, in 1915 neurosurgeon Charles A. Elsberg (1871–1948), at the Neurological Institute of New York, argued that posterior rhizotomy “should never be attempted in other motor disturbances such as athetosis or torticollis” because “in these cases the muscular spasms are not due to an increased influx of sensory stimuli to the cord, but to an increased afflux [sic] of motor impulses from higher centers.”\(^{73}\) Similarly in 1918, New York neurologist Moses Allen Starr (1854–1932) concluded, “The operation performed by Spiller of division of the sensory nerve roots along the spine [posterior rhizotomy] does not appear to have had any permanent beneficial effect.”\(^{74}\) The procedure was never widely adopted for this condition.

Nerve “transplantation” (motor neurotomy and nerve-to-nerve anastomosis)  

Somewhat earlier, in 1905, prior to the efforts of Spiller and Frazier with posterior rhizotomy, Spiller had suggested that nerve “transplantation” might be a means of altering the balance of neural discharges to an affected limb, which might produce an increase in function.\(^{64,75}\) Spiller’s idea was to section, or partially section, motor
nerves, and then to anastomose the sectioned ends with other nerves to lessen or rebalance the motor discharges causing the abnormal movement (Figure 16). This was the same procedure Spiller had advocated in 1902 for the treatment of some cases of poliomyelitis and cerebral palsy:

There must in cases in which athetosis exists be an irritation of the motor system somewhere... We can not hope to remove the irritation in the brain. We can not hope to cut the central motor fibers. Such a procedure would be unjustifiable. Can we accomplish anything by operation upon the peripheral nerves? ... Theoretically the proper procedure might be to cut the posterior roots of the affected limbs ... but this is always a serious operation, and the results have at times been
unexpectedly grave. It is possible that if we were to divide one or more of the motor nerves of the affected limb and immediately suture the divided portions we might lessen the involuntary activity and weaken the muscles only slightly.75

It occurred to me that if we could switch off, so to speak, some of this excessive innervation of the flexors into the extensors by nerve transplantation, we might be able to establish a more nearly normal relation between certain groups of muscles and their opponents, and by division of nerves be able to lessen the athetoid movements probably permanently.64

Spiller and colleagues studied a case of athetosis treated with this nerve “transplantation” procedure.64,75,76 A 19-year-old male, who had undergone a unsuccessful craniotomy and resection of the part of the precentral gyrus, underwent three further nerve “transplantation” procedures. The first, performed by Frazier in 1905, was a lateral anastomosis of the divided left median and ulnar nerves to the radial nerve (Figure 17), and the second, performed a month later by Jean Jacques Abram Van Kaathoven (1877–1928), Assistant Instructor of Surgery, under the direction of Frazier, was done on the same arm, with the axillary and musculocutaneous nerves being divided and subsequently “an end-to-end anastomosis effected between the central end of the one and the distal end of the other, and vice versa” (Figure 18).64

Two months after the second procedure, the patient underwent “very much the same procedure in the right arm,” performed by J.J.A. Van Kaathoven.64 Nine months later Spiller reported that the man “had now little or no athetosis in the muscles operated upon, and a very considerable return of power” (Figure 19).76

Spiller further summarized the results in the patient in positive terms:

It may be said that the operation was a attempt to influence a cerebral lesion by disturbing peripheral nerves, and this, indeed, is what it was. We could not remove the source of the irritation, but, if we could remove the manifestations of this irritation, without causing the patient more discomfort, we might consider the operation a success. This is what he have accomplished. There is no doubt that this man’s condition is far better than it was before any operation was attempted, and we may hope for still greater restoration of power. He has now returned to his

Figure 12. New York Neurologist Charles Loomis Dana. Dana proposed posterior rhizotomy, later called “Dana’s operation,” in 1888.65 Courtesy of the U.S. National Library of Medicine.

Figure 13. New York Surgeon Robert Abbe. Abbe performed the posterior rhizotomy procedure (Dana’s operation) in a patient with athetosis. Photograph from Notable New Yorkers: 1896–1899 (1899) by Moses King.
occupation of selling papers, and is very happy over his improved condition.

Nevertheless, British neurologist Sir James Purves-Stewart (1869–1949) suggested snidely to Spiller, after seeing his patient, that “if in epilepsy we could cut all the motor nerves we should arrest the convulsions and produce a condition similar to that seen in our patient, so far as arrest of involuntary movements is concerned, but we should not cure the epilepsy.” Undaunted, Spiller parried, “I fully agree with him in this statement, but if we have arrested the athetoid movements, even though we have not removed the cerebral lesion, we have accomplished much.” Despite his initial advocacy, though, Spiller soon moved to advocacy of posterior rhizotomy in preference to this peripheral nerve procedure.

“Muscle group isolation” (alcohol neurolysis)

In 1909, Sidney I. Schwab (1871–1947), Professor of Nervous and Mental Diseases at St. Louis University, along with orthopedic surgeon Nathaniel Allison (1876–1932) (Figure 20) at Washington University in St. Louis, reported initial results of what became a series of papers on “muscle group isolation” for athetosis and spasticity. Using alcohol neurolysis the authors “isolated” the muscles they deemed at fault in athetosis or spasticity “by cutting off from the central nervous system the connection along which the abnormal impulses ... are transmitted.” Injection of alcohol into the nerve resulted in “an immediate paralysis of the physiologically stronger group of muscles without interfering with the free muscular use of the antagonists.” The initial case was a patient with athetosis in whom the ulnar nerve was regarded as primarily involved, but “as the case presented a median nerve complication,” the median nerve was subsequently injected. This proved to be the only case of athetosis that they treated, and according to one of their reports in 1910 after the patient’s nerves were injected with alcohol, “the athetosis completely disappeared and did not return.” In 1912, Russian-American neurologist Lewis John Pollock (1886–1966) (later a charter member of the American Board of Psychiatry and Neurology I 1934 and president of the American Neurological Association in 1942), and neurologist Earl B. Jewell at the University of Illinois in Urbana-Champaign reported a further six cases using the procedure and concluded that, “It is preferable to suffer with athetosis and possess function, than to be relieved of the athetosis and have function disappear.” Pollock and Jewell also warned “against the injection of alcohol into any nerve possessing important motor functions, as the ulnar, median, etc.”
Discussion

All of the treatments developed in the 50-year period after the description of athetosis that showed any apparent efficacy in stopping the movements did so because of, or at least concomitant with, the development of significant weakness, and often with additional sensory loss and other morbidity. All of the responsible surgeons viewed these cases as successful, because of demonstrated technical success in lessening or aborting the abnormal movements, even if only transiently, and in spite of the often serious resultant secondary morbidity. All of them accepted the concomitant morbidity as a reasonable trade-off for resolving the abnormal movements. Although these pioneering surgeons are often hailed for introducing these procedures, most of the patients who were operated upon received little overall benefit, and all of these patients were left with significant additional morbidity.

In 1886, Graeme Hammond acknowledged the overall futility of treatment, recognizing that available technologies could not begin to resolve the underlying pathology: "On the treatment of athetosis this is very little to be said. The very nature of the lesions which have been found to produce athetosis, precludes the possibility of their ever being removed by any remedial measures that we are able to resort to at the present time." In 1905 Spiller, expressing his frustration at the lack of an adequate treatment for athetosis, commented: "Athetosis is one of the most distressing forms of involuntary movement, and the failure

Figure 16. Spiller and Frazier’s Approach to Peripheral Nerve “Transplantation.” This procedure combined section of motor nerves and various modes of nerve-to-nerve anastomosis. In the diagram, A represents the “unaffected” nerve and B represents the “affected” nerve. Spiller advocated these techniques to modulate the activity of the specific motor nerves that were felt most involved in the expression of athetosis in a given patient. Figure source: From Spiller, Frazier, and Van Kaathoven, 1905.

Figure 17. Nerve-to-Nerve Anastomoses after the First Procedure. The specific nerve anastomoses performed by Charles Harrison Frazier on the patient’s left arm. Figure source: Spiller, Frazier, and Van Kaathoven, 1905.

Figure 18. Nerve-to-Nerve Anastomoses after the Second Procedure. The specific nerve anastomoses performed by Frazier on the patient’s left arm. Figure source: Spiller, Frazier, and Van Kaathoven, 1905.
to control it in any degree is a reproach to medicine." Similarly, as summarized by Starr in 1918, nearly half a century after the original description of athetosis, "There appears to be no treatment for this condition."

The initial treatment approaches used for athetosis utilized available pharmaceutical agents (e.g., bromides, arsenicals) and modalities (e.g., galvanism) that were employed in a non-specific manner to many other conditions at the time; there was little a priori evidence-based justification for the use of such treatments in this condition, and no biologically plausible theoretical framework to guide empiric treatment selection. Later, various novel invasive therapies were directed at relatively accessible portions of the central nervous system (e.g., precentral gyrus), the nerve roots, or peripheral motor nerves. With the exception of amputation and pure dorsal rhizotomy (i.e., in the absence of concomitant anterior rhizotomy), all of these invasive procedures were directed at lessening activity in either upper or lower motor neurons serving the targeted limb. All of the invasive procedures employed were directed at lessening or removing the manifestations rather than the underlying cause of the abnormal central nervous system "irritation," usually by imposing a degree of weakness, but sometimes by inducing complete paralysis or even amputation.

With the development of such novel invasive therapies, several factors likely contributed to the disparity in outcomes between the favorable initial reports and the often-disappointing results of later studies, including reliance on anecdotal reports or small uncontrolled case series, placebo effects (augmented by the novelty and apparent sophistication of the methods employed), biased observation, misdiagnosis, and biased reporting (for example, initial reports of invasive treatments that did not at least have a positive technical outcome were generally not published). The early proponents of such invasive procedures often continued to blindly support them despite increasing evidence of their futility or harm. Although later reports were not inherently better than the initial uniformly positive reports, often the later investigators were less invested in a positive outcome (i.e., a finding or demonstration of treatment "success" or effectiveness) and were able to more carefully deal with potential biases. Learning from anecdotal reports or case series is possible, but is "fraught with difficulty, uncertainty, and error." Unfortunately, while controlled trials would have minimized or eliminated these problems, few such studies were carried out in this era, particularly for invasive surgical procedures, and were in any case entirely lacking among the treatment studies for athetosis.
References


