Hugh J. McMillan
Peter B. Kang
Editors

Pediatric Electromyography

Concepts and Clinical Applications

Springer

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To my family, for their unwavering patience, tolerance, and flexibility.

—Hugh J. McMillan

To my wife Christina and our children Marian, Audrey, Louisa, and Marcus, who were very patient for many evenings as I disappeared into our home office to work on this book, and to my parents, Kwang Soo Kang and Moon Kil Kang, whose wise and enduring guidance set me on the path that eventually led me to this project.

—Peter B. Kang

Foreword

The late H. Royden Jones, Jr. (1936–2013) was a giant in the field of pediatric electromyography. A highly skilled and caring physician, he trained countless pediatric and adult neurologists and neurophysiologists throughout his long career at the Lahey Clinic and Boston Children's Hospital. His former residents and fellows now work across North America and around the world. He and two coauthors wrote what is generally recognized to be the first comprehensive textbook of pediatric electromyography which was published in 1996. We both had the privilege of training with Royden and benefited enormously from his mentorship as well as his boundless energy, kindness, and knowledge.

Hugh McMillan thanks Pierre Jacob, M.D., for introducing him to the world of neurophysiology and to Daniel Keene, M.D., for his mentorship. He is grateful to the outstanding teachers and mentors during his fellowship training: Basil T. Darras, M.D.; H. Royden Jones, Jr., M.D.; Peter B. Kang, M.D.; James A. Russell, D.O.; and Jayashri Srinivasan, M.B.B.S.

Peter Kang had the great fortune to be trained and inspired by many talented neuromuscular neurologists over the years. These include John T. Sladky, M.D., his first child neurology mentor in medical school; Mark J. Brown, M.D., and Shawn J. Bird, M.D., who taught him the basics of electromyography during residency; Gihan Tennekoon, M.D., and Richard S. Finkel, M.D., who taught him much about neuromuscular disease in childhood during residency; and Seward B. Rutkove, M.D., Elizabeth Raynor, M.D., H. Royden Jones, Jr., M.D., and Basil T. Darras, M.D., who trained him during his fellowship in clinical neurophysiology and electromyography. Basil Darras also served as a wonderful mentor during his junior faculty years at Boston Children's Hospital and Harvard Medical School. He benefited greatly from sage advice imparted over the years by Arthur K. Asbury, M.D., Robert C. Griggs, M.D., and Edward M. Kaye, M.D.; and the support of his faculty department chairs Joseph J. Volpe, M.D., Scott L. Pomeroy, M.D., Ph.D., and Scott A. Rivkees, M.D. He owes these mentors a great debt for all of their encouragement and support for many years.

We are very grateful to the talented colleagues who contributed valuable chapters to this book, many of whom we met at the biennial Paediatric EMG Congress organized for two decades by Matthew Pitt and Royden Jones.

We both thank the talented staff at Springer for this wonderful opportunity to share the very special skills of performing electromyography on the youngest and most vulnerable of our patients, especially Joanna Bolesworth, who first approached us about this project, Rajesh Sekar for supervising production of the book, and André Tournois, who provided valuable support throughout the project.

The goal of pediatric electromyography is to perform a valuable diagnostic study in as gentle a manner as possible when prompt diagnosis is crucial. We hope that this book will help encourage the lifelong acquisition of the skills needed to perform these studies properly and facilitate timely neuromuscular diagnoses for many years to come.

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Part I
Basic Concepts

Chapter 1
Historical Perspective of Electrodiagnosis

John T. Sladky

In constructing a historical context in which to view the discipline of electrodiagnostic medicine, it is difficult to determine a logical starting point. It is an elementary argument to assert that the biological underpinnings of the discipline date easily back to Galvani and Volta in the eighteenth century. Although these scientific pioneers played seminal roles in characterizing the role of electricity in the function of muscle and nervous tissue, some would credit even earlier observers with reporting the phenomenology that Galvani characterized as "the energy of life". Ultimately, it is the translational process of applying fundamental biological principles to the investigation of human disease, which has permitted the evolution of our discipline. Admitting a large measure of arbitrariness reinforced by a limited historical perspective of the scientific zeitgeist of successive eras of neurobiologists, I have cobbled together a decidedly imperfect, but well intentioned, snapshot of the conceptual ontogeny of electrodiagnostic medicine and its adaptation to pediatrics. I should apologize to bioengineers who will note that I have given short shrift to the technical aspects of the development of clinical electrophysiology. The evolution of our discipline has not been predominantly hypothesis driven but rather has been a captive of technology and has grown at a logarithmic pace as new methodologies have been adapted to investigate human neuromuscular physiology. Let me add one further disclaimer; I have not attempted to acknowledge the role of individual contributions to the body of knowledge but rather the evolution of our ongoing integration of basic scientific information into the understanding of the biological substrate of neuromuscular disease.

Notions regarding the role of what came to be understood as electrical properties in the animation and maintenance of vitality among humans and surrounding fauna date back at least to the Greeks and Romans. Practitioners at the time utilized electrical stimulation for the treatment of a range of perceived ailments. The logistics of

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this procedure required the application of torpedo fish to a patient's skin. The torpedo fish is an electric ray with electroplax organs located on each side of the head. These electric generators accorded the animal an efficient means to ward off predators and to subdue prey. The patient was persuaded to step on the animal as might occur while wading in the ocean. It was assumed that the resultant painful electrical shock experienced by the patient would imbue vigor to the recipient or provide salutary effects for a variety of common afflictions. These practices likely provided a historical context that underpinned widely held notions that conceived of electricity as the "animus" or "life force" that initiated and maintained muscle activity.

By the beginning of the eighteenth century, three well-established schools of thought dominated the hypothetical discussion of what provided the mechanistic nexus between intent and the execution of motor action. The traditionalist position, advocated by Descartes, averred that an "ephemeral force" traveled along the peripheral nerve and animated the muscle. The more pragmatic Thomas Willis felt that a vital fluid passed through hollow tubes represented by the peripheral nerves and the fluid activated the contractile mechanism in the muscle. A somewhat less tenable position was championed by Isaac Newton who conceived of a vibratory signal transmitted along the nerve which was informed by the frequency and amplitude of the oscillatory activity. Within this theoretical/philosophical milieu resided the advocates of electricity as a more plausible mechanism of signal transduction in nerve and muscle.

The ability to generate, store and direct static electricity using electrostatic generators and the Leyden jar, a technology developed by the mid-eighteenth century, instigated a wave of experimentation and perhaps an even larger swell of therapists providing treatments with tactile and visually impressive effects for common and uncommon ailments, unfortunately with little or no tangible benefit, at least for the patient. Dr. Aloisio Luigi Galvani was one of those scientists working in the final quarter of the eighteenth century drawn to the new field of inquiry based on electrical stimulation. I have read multiple iterations of the anecdotal description of the seminal experiment, none quite alike. The essential element seems to be that while Galvani and an assistant were dissecting a nerve/muscle preparation in a frog, an errant spark from a nearby electrostatic generator reached the operator resulting in an electrical spark transduced via forceps to the exposed tissue within the operating field resulting in a muscular contraction in the frog's distal leg. Despite the scintillating visual and auditory overlay that the discharge of static electricity brought to the laboratory, Galvani needed a more controlled stimulus for his experimental models. He devised an alternative method using linked pairs of dissimilar metallic electrodes to produce a direct current source for stimulation of nerves and muscles in a more regulated fashion. Galvani worked in relative silence for over a decade before finally publishing his work in 1791 [1]. In this treatise, he asserted his conclusions that electrical energy or "animal electric fluid" was demonstrably the signal transduction medium in neuromuscular transmission and muscle activity.

Acknowledging the above, it seems reasonable to assert that the modern era of clinical electrophysiology began in mid-nineteenth century Paris with Dr. Guillaume-Benjamin-Armand Duchenne du Boulogne (1806–1875). By the

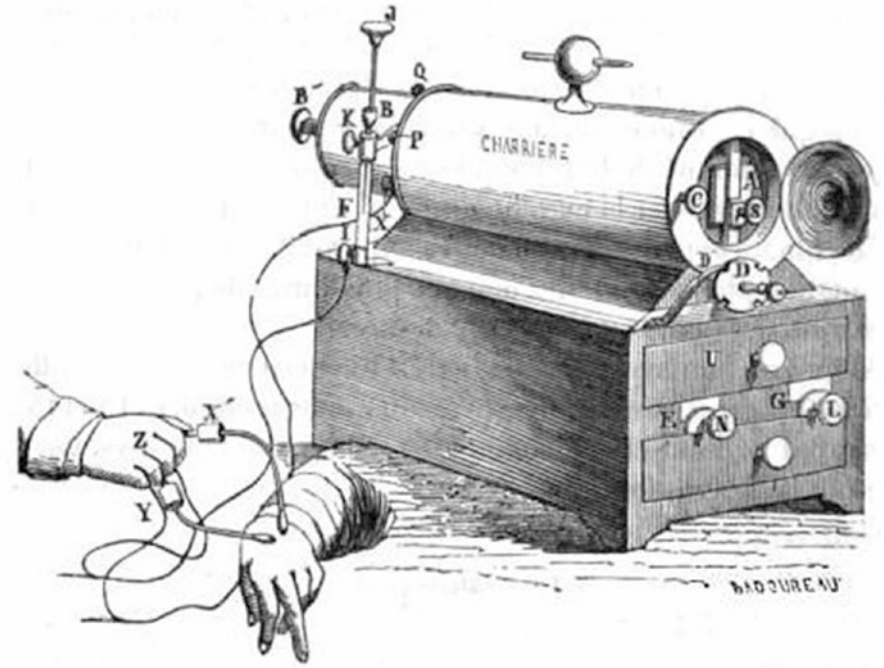

Fig. 1.1 Duchenne's handmade direct current electrostimulation device. Non-invasive surface electrodes could be placed for precise stimulation of small muscles of the hand and face

turn of the nineteenth century, many practitioners in Europe and North America endorsed electrotherapy for a host of neuropsychiatric and other conditions. Duchenne conceived of using electrical stimulation of muscle and nerve for diagnostic purposes [2]. He devised a portable direct current source along with a series of specialized surface electrodes, which permitted non-invasive stimulation of nerve and muscle and obviated the complication of wound infection that frequently ensued after placement of subcutaneous electrodes, which was the custom at that time (Fig. 1.1). He understood that stimulation of the nerve triggered contraction of a constellation of functionally related muscles and developed electrodes for the isolation and stimulation of individual muscles to investigate their specific role in volitional movements. Early in his career he became interested in the muscles of facial animation and in utilizing "localized faradization" (focused electrostimulation of individual muscles or muscle groups) to distinguish upper from lower motor neuron facial paralysis (Fig. 1.2). Duchenne designed and built his stimulating device to permit individual or trains of repetitive electrical stimuli to be selectively delivered to individual or constellations of muscles. His aim at the bedside was to be able to elicit a convincing supramaximal stimulus and to grade the resultant contractile response using visual and tactile measures, which could be incorporated into serial testing protocols. He applied lessons gleaned from these studies to the evaluation of appendicular muscles affected by nerve or spinal cord injury.

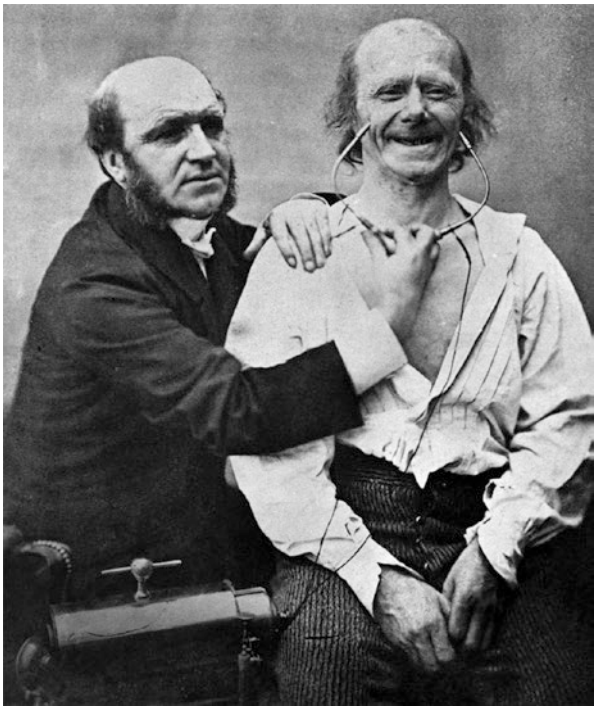

Fig. 1.2 "Faradization" of facial muscles. Duchenne used this device to distinguish upper from lower motor neuron palsies. He also used the techniques he developed to investigate the relationship between facial expression and emotion. He observed an association between involvement of the extraocular muscles along with the lower facial muscles when the smile was born out of happiness as opposed to social convenience. The term "Duchenne smile" has joined the formal lexicon of academic physiognomy to denote the sincerity of the facial expression

Poliomyelitis was endemic among the children of mid-nineteenth century Paris, especially in crowded urban environments where public hygiene was limited. Although the communicable nature of the disease was gaining recognition, a mechanistic understanding of the cause of paralysis was lacking. It was commonly held that the paralysis in this disease was "essential" in nature, an obfuscational proposition that declared that the pathogenic process existed in a realm beyond the ken of contemporary medical science and hence, was indescribable and unknowable. Duchenne, thought to be somewhat of a contrarian among his colleagues, noted homologies in his observations of electrical muscle and nerve stimulation in patients with facial palsy, poliomyelitis and spinal cord injuries. He used electrostimulation of muscles and nerves to examine patients with spinal cord diseases, including those presumed to be poliomyelitis, to characterize patterns of affected muscles as excitable or not. He demonstrated that those atrophic muscle groups, which were unresponsive to direct electrical stimulation, generally did not recover while contiguous muscles, which exhibited a tangible response to supramaximal electrical stimulation, would exhibit the capacity to regain function. He was able to discern that this testing could be performed early in the disease and might provide important prognostic insights. Given the high incidence of poliomyelitis in urban centers of the period and the fact that most of the acutely affected were children since a majority of adults were rendered immune by prior infection, children constituted a large segment of Duchenne's patients. He focused on this experience in his writings and in didactic sessions with his fellow neurologists in Paris. Imagine Duchenne

explicating the fine points of the electrodiagnostic evaluation of a child with acute paralysis before Charcot and his contemporaries at the Hôpital Universitaire Pitié-Salpêtrière during the 1860s. Duchenne correctly inferred that the site of the primary lesion in poliomyelitis must be the anterior horn cells in the spinal cord. At the time, autopsy studies in individuals with poliomyelitis had been performed on patients with longstanding paralysis who died from unrelated causes. Visual inspection of post mortem pathological specimens of the spinal cord failed to demonstrate evidence of definite abnormality. Microscopic anatomy of the spinal cord, however, had not been studied in this disease. Duchenne argued that the key to understanding the pathogenesis lay in a more scrupulous examination of the spinal cord in these patients. Over the ensuing decade, Duchenne's hypothesis was confirmed by several observers, including his younger colleague Dr. Jean-Martin Charcot in a paper published in 1870. Duchenne came to be highly regarded for his clinical and pathophysiological acumen and was referred to by Charcot as "mon maître en neurologie" or my mentor in neurology.

Duchenne first illustrated the superficial phenomenology of brachial plexus palsy in 1862 in association with a photograph of a 6 year old boy exhibiting the sequellae of a brachial plexus injury sustained at birth. Even before that publication, he had recognized a stereotypical constellation of features which he termed "obstetric palsy of the brachial plexus". It required another decade to collect and publish his anatomical observations on three patients with that injury in 1872. Duchenne surmised that the injury was related to traction of the head against the after coming shoulder with concomitant injury to the plexus in the course of delivery of an infant with shoulder dystocia. It is fitting that the baton was metaphorically passed in this fashion as Dr. Wilhelm Heinrich Erb (1840–1921) published his findings on the physiological and anatomical substrates for this malady in 1874 [3]. Erb was familiar with Duchenne and his opinions regarding the disease along with his studies of anatomy and clinical electrophysiology. He freely acknowledged his colleague's precedence in describing the nature of the injury. Erb's singular contribution was the amalgamation of electrophysiology and neuroanatomy with the use of electrodiagnostic methods to localize the site of the anatomic lesion to the upper trunk of the brachial plexus. He employed a needle electrode inserted at the medial border of the supraclavicular fossa beneath the insertion of the sternocleidomastoid to stimulate the brachial plexus near the confluence of cervical nerve roots five and six at the origin of the upper trunk. Tetanic stimulation at that site in normal subjects elicited a constellation of simultaneous muscle contractions resulting in the assumption of what was described as a "fencer's posture" with abduction of the shoulder, flexion of the biceps and supination of the forearm. The agonist muscles activated by electrical stimulation of the brachial plexus near "Erb's point" predicted the pattern of weakness resulting from an injury to the upper trunk of the brachial plexus at that site. Anatomic studies confirmed Erb's notion of the localization of the injury with evidence of consequent chronic denervation in muscles downstream from the injury.

There are many interesting analogies and distinctions within the personal and professional lives of Duchenne and Erb that deserve more attention than can be provided here. Both came from working class families. Duchenne was never warmly embraced by the medical establishment in Paris. He was never inducted into the

Academy of Sciences in his native France. He was, however, internationally known and later in his career was elected to membership in prestigious academic societies in multiple countries outside of France. He also established close relationships with several of the seminal figures in clinical neurology working in Paris, probably the epicenter of clinical neuroscience at the time. Duchenne was highly regarded in that circle and was referred to by Charcot as "my mentor in neurology". Erb, by contrast, migrated from his rural beginnings in the Bavarian countryside to Heidelberg, one of the most prestigious academic institutions in Europe, for his education where he studied under Dr. Jakob Henle and Dr. Nikolaus Friedreich. He remained on the faculty at the University for the balance of his career with the exception of a 3 year hiatus when he accepted the position and served as Chair of Internal Medicine at the University of Leipzig from 1880–1883. He returned to Heidelberg to accept an appointment as Chair of Internal Medicine after Friedreich's death. Like Duchenne, Erb viewed neurology as an independent field of inquiry within the discipline of medicine and played a seminal role of establishing the field of clinical neurology as a unique academic and clinical niche in the biological sciences.

The evolution of clinical electrodiagnosis at the outset of the twentieth century would be held in abeyance while technical progress continued in research laboratories focusing on signal processing and characterization in nerve and muscle. Though the cathode ray tube, the basis for the development of the oscilloscope, was invented just before 1900, the triggered sweep oscilloscope would not become widely available for clinical applications until after the Second World War.

Like so many arenas in pediatrics new translational approaches are usually hand me downs from our adult colleagues who have developed these experimental techniques among populations competent to provide informed consent until their safety and reliability has been confirmed. Such was the case with clinical electrodiagnosis which by the mid-1950s had been embraced at multiple centers as a potential means to refine and focus the evaluation of patients with neuromuscular disease.

In Rochester, Minnesota, Dr. Edward H. Lambert, a neurophysiologist, and Dr. Peter J. Dyck, who specialized in peripheral nerve histopathology, collaborated on a landmark study of individuals and kinships with dominantly inherited neuropathy conforming to a diagnosis of Charcot-Marie Tooth disease (CMT). The patients included in this study were phenotypically similar and were all members of kinships with what appeared to be dominantly inherited peripheral neuropathies. In 1957, Thomas and Gilliatt reported the observation of profound slowing of motor nerve conduction velocity in an individual with a phenotype consistent with CMT [4]. It was discovered that clinically similar patients with this disease were heterogeneous based on sensory and motor nerve conduction studies and could be segregated into two groups based on the motor conduction velocity of the ulnar and median nerves in the forearm. They divided the patients into those with conduction velocities above and below 35 m/s and correlated those groups with histopathology from sural nerve biopsies. This work codified the clinical, electrodiagnostic and histopathological characteristics of these patients and provided the biological substrate for the initial classifications of demyelinating or axonal CMT. They showed that these clinical traits bred true within the kinships and hence could infer that there were probably

independent autosomal dominant genes involved in producing the distinctive electrophysiological and histopathological phenotypes associated with the demyelinating and axonal forms of the disease. Later the nosology would evolve into hereditary motor and sensory neuropathy types I and II (HMSN I and HMSN II), though many still use the traditional terminology CMT1 and CMT2. After that came the deluge.

It was understood that CMT was dominantly inherited but the disease seemed entirely capricious in terms of its age of onset and pace of progression in affected individuals. Families wanted to know whether their toddler was affected and as much information as could be garnered regarding what the future might hold for that child. In order to begin to attempt to answer some of these questions it was necessary to understand more about the developmental biology of the peripheral nervous system in children, more specifically, the ontogeny of motor conduction velocity as a function of age. To that end, Lambert set out to characterize age specific normative values for ulnar motor nerve conduction in a cohort including 6 premature infants, 42 term newborns and 98 children less than 15 years of age [5]. He and his colleagues showed that saltatory conduction in the ulnar motor nerve changes significantly with age and that what may be normal nerve conduction velocity in a toddler would be classified as consistent with demyelinating CMT if it were documented in an adult. The fact of the evolution of nerve conduction velocity with age was not a revelation, however, without a precise understanding of the normative values for electrophysiological measurements at different ages in children, the technology held limited value in the evaluation and management of children with neuromuscular disease.

At nearly the same time, Dr. Fritz Buchtal in Copenhagen and Dr. Ingrid Gamstorp, a child neurologist in Uppsula, Sweden were grappling with similar issues in the context of newborn infants of different conceptional ages in the neonatal nursery and later in childhood. Buchtal set out to systematically study cohorts of infants born at different gestational ages to develop accurate normative data for nerve conduction measurements in infants. Not surprisingly, he was able to demonstrate that nerve conduction velocities in infants were dependent on the age since conception and could be used to quite accurately predict the conceptional age of a newborn or an older infant independent of the age of the child from birth. Gamstorp evaluated motor conduction in median, ulnar and peroneal nerves in normal individuals ranging in age from newborn to adult [6]. Nerve conduction velocities, like EEG patterns, were stereotypical in their tempo of growth toward an apogee in the mid-first decade and ultimately a regression in later adulthood.

By the 1970s clinical electrophysiology had been widely validated as a useful tool for the study of neuromuscular disease in children. While these techniques were becoming widely employed in adult populations, their application in younger individuals remained largely confined to tertiary pediatric centers. There were, perhaps, two handfuls of neurologists who were vocal advocates for the incorporation of electrodiagnostic techniques into the evaluation of pediatric neuromuscular disease. Only a few stood on the front lines and developed centers dedicated to expanding our understanding of the neurobiology of clinical electrophysiology codifying that knowledge in the medical literature and passing down lessons learned in