Neuromodulation and the role of electrodiagnostic techniques

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Abstract Electrodiagnostic techniques have been utilized in surgery since the early 1960s. These techniques have been primarily used in neurosurgery; however, with the introduction of neuromodulation for voiding dysfunction, these techniques have now found their way into the field of female pelvic medicine. This article will review techniques applicable to evaluate pelvic floor function as it relates to neuromodulation. It will also review the literature describing how these techniques are used to help determine appropriate candidates as well as improve surgical outcomes. A PubMed search was conducted using the terms neuromodulation, Interstim, electrodiagnosis, electrodiagnostic techniques, electromyography with limits to the pelvic floor, and voiding dysfunction. Eight articles and three abstracts were found that directly related to the use of electrodiagnostic techniques as they apply to neuromodulation. Electrodiagnostic techniques may play a role in helping predict appropriate candidates for neuromodulation as well as improve surgical outcomes.

Keywords Electrodiagnosis · Neuromodulation · Electromyography · Sacral nerve stimulation

Introduction

Intraoperative electrodiagnostic techniques have been used since the early 1960s when Larsen et al. introduced the use of somatosensory evoked potentials (SSEPs) for monitoring responses during neurosurgical procedures [1]. These techniques were soon adopted by spine surgeons as a supplement to provide warning of compromised spinal cord function [2]. In addition to SSEPs, numerous neurophysiological monitoring methods exist, including continuous free-running electromyography (EMG), evoked EMG, compound muscle action potentials, rectal and urethral EMG, motor-evoked potential and most recently, spinal cord mapping.

In performing neuromodulation for pelvic floor dysfunction, electrodiagnostic techniques may also play a role during both the lead wire implant phase and in reprogramming the implantable pulse generator (IPG) in patients with suboptimal response [3, 4]. This provides more sensitive objective monitoring that can supplement the gross motor response. It may also be a more reliable method of determining lead wire placement when placing at alternate sites such as the pudendal nerve [5]. Electrodiagnostic techniques may also play a role in evaluating appropriate candidates for implant.

Definitions

Evoked potentials

Evoked potentials are electrical potentials recorded from the nervous system following a delivered stimulus.

Somatosensory-evoked potentials

Somatosensory-evoked potentials are elicited by tactile or electrical stimulation of a sensory or mixed nerve in the periphery (most commonly the median and posterior tibial nerves) with a resultant waveform that is picked up in several areas along the spine and scalp. The waveforms are described in terms of morphology, latency, and dispersion.

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They are used primarily to reveal or localize a lesion involving the somatosensory pathways.

Motor-evoked potentials

Motor-evoked potentials are recorded from muscles following direct stimulation of exposed motor cortex or transcranial stimulation of the motor cortex. Used widely in brain tumor resection and aneurysm surgery.

Compound muscle action potentials

A compound muscle action potential is a summation of nearly synchronous muscle fiber action potentials recorded from a muscle produced by direct or indirect stimulation of the nerve supplying that muscle. The amplitude, duration and latency are recorded. An increased latency is reflective of a neuropraxic (demyelination) injury while a decrease in amplitude indicates axonal dropout.

Electromyography

Electromyography is the recording of electrical potentials generated by the depolarization of muscle fibers. Electromyography is typically distinguished as surface or needle EMG.

Surface EMG

Surface EMG is a kinesiologic study that provides qualitative and quantitative descriptions of a muscle's activity over a period of time and thus describes more patterns of behavior. Surface EMG reflects the total muscle activity and as such gives information of total functioning mass. Examples of commonly used studies that employ surface EMG include anal manometry and urodynamics.

Needle EMG

Needle EMG is the recording and study of individual motor units (motor unit action potentials) via the insertion of a needle directly into the muscle being evaluated. A motor unit is defined as an anterior horn cell, its axon and branches, and the muscle fibers it innervates. The number of muscle fibers innervated is known as the innervations ratio. Motor unit action potentials are the summation of the potentials recorded from all muscle fibers in the motor unit within the recording range of the electrode. The advantages of needle EMG are that it is more precise and sensitive, provides information concerning denervation, re-innervation, upper and lower motor neuron function, activity and time course of the neurologic process, as well as aiding in prognosis.

Neuromodulation and electrodiagnosis

Sacral neuromodulation (SNM) was approved for the treatment of urge incontinence in 1997 and gained two further indications for the treatment of urgency/frequency and non-obstructive urinary retention in 1999. Ideal placement of the lead wire is guided by the objective motor response (bellows and/or great toe flexion) and the subjective sensory report from the patient (typically a tapping or vibration sensation in the vagina, rectum, and/or scrotum). The ideal parameter for lead placement has not been elucidated, but a report by Cohen and colleagues suggested that a motor response was far superior to a sensory response [6]. In this study, 95% of those that had a positive intraoperative motor response went on to have a successful trial and were implanted vs. 5% that elicited a sensory response only. This study emphasizes the importance of achieving an intraoperative motor response. When evaluating for a motor response, the surgeon relies on gross motor movements to determine the correct lead placement; however, this response is often elicited at much higher stimulation amplitudes than would be clinically used and may be uncomfortable for the patient. Additionally, the human eye cannot detect subtle changes in the amplitude of response. In a small series by Benson [3], electrodiagnostic techniques were utilized at the time of implant to fine tune lead wire placement. Compound muscle action potentials (cMAPs) in the levator ani muscles and urethra were recorded using a sponge

Fig. 1 a Ring electrode mounted on a 14-French catheter placed at the mid-urethra. b Sponge Electrode—placed transvaginally or transrectally
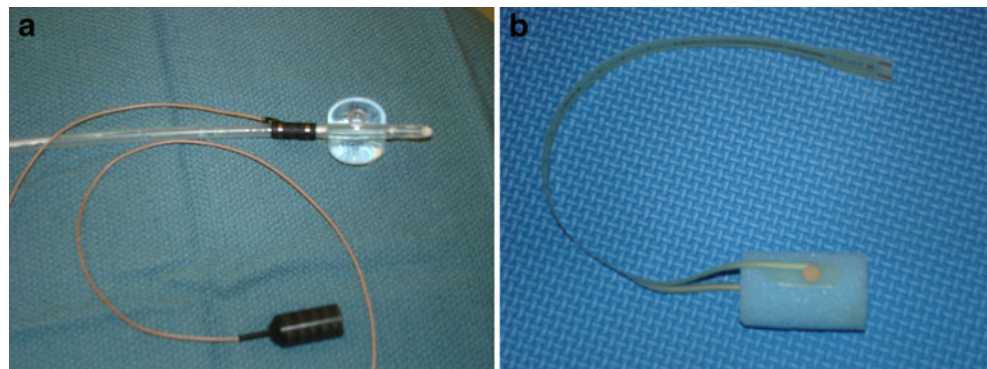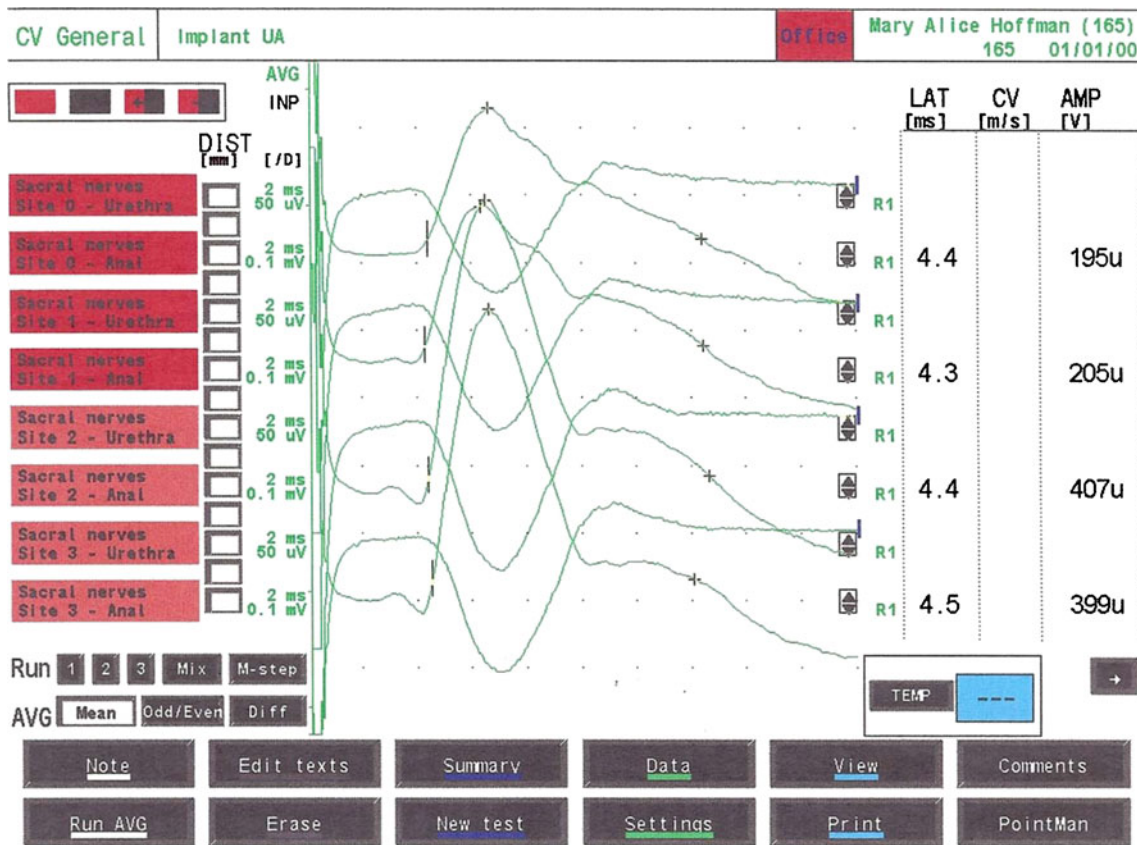
Fig. 2 Evoked potentials generated by the implantable pulse generator and recording in the urethral rhabdosphincter and external anal sphincter. The urethral leads are inverted in this particular tracing. Note the recordings are obtained from each of the four electrodes

electrode placed vaginally or rectally, and a ring electrode placed on a Foley catheter (Fig. 1a, b). The resulting wave forms were analyzed with regard to latency and amplitude (Fig. 2). The advantage of analyzing the motor response with this technique is that small decrements in response can be measured electrodiagnostically. These subtle changes in amplitude cannot be appreciated with the naked eye when looking for a motor response. Using this technique, Benson achieved an 80% implant rate, which at the time of publication, was significantly higher than the 50% response being reported. Since the introduction of the tined lead, no other study has evaluated the use of electrodiagnostic techniques on outcomes.

Benson et al. also found that utilizing electrodiagnostic techniques was a valuable tool for screening appropriate candidates for implant. Preoperatively, 46 patients underwent electrodiagnostic evaluation of the pelvic floor, including motor conduction studies of the pudendal nerve (inferior hemorrhoidal and perineal branches) as well as sacral reflex testing. The sacral reflexes included the clitoral–anal reflex (CAR), the urethral–anal reflex, and the bladder–anal reflex (BAR). Of those 46 subjects, 15 had urinary retention with the remaining categorized as urgency/frequency and/or urge incontinence. In

looking for factors predictive of "responders" vs. "non-responders," they found in the urgency/frequency group that a normal CAR latency and an elevated BAR sensory threshold were associated with improved outcomes. In both the urge incontinence and retention groups, the presence of an increased CAR sensory threshold was predictive of being a responder [7]. Unfortunately, this data was only published in abstract form and no further studies have been conducted to confirm these findings. In a related study, Mutone et al. found a direct relationship

Table 1 Relative contribution of the sacral nerve roots to the urethra, levator, anal sphincter, and great toe (abductor hallicus)

	Primary root (mean % amplitude)	Secondary root (mean % amplitude)	Tertiary root (mean % amplitude)
Urethra	S3 (61%)	S2 (24%)	S4 (15%)
Levator	S3 (75%)	S4 (19%)	S2 (6%)
Anal sphincter	S2 (45%)	S3 (44%)	S4 (11%)
Abductor hallicus	S2 (90%)	S3 (8%)	S4 (2%)
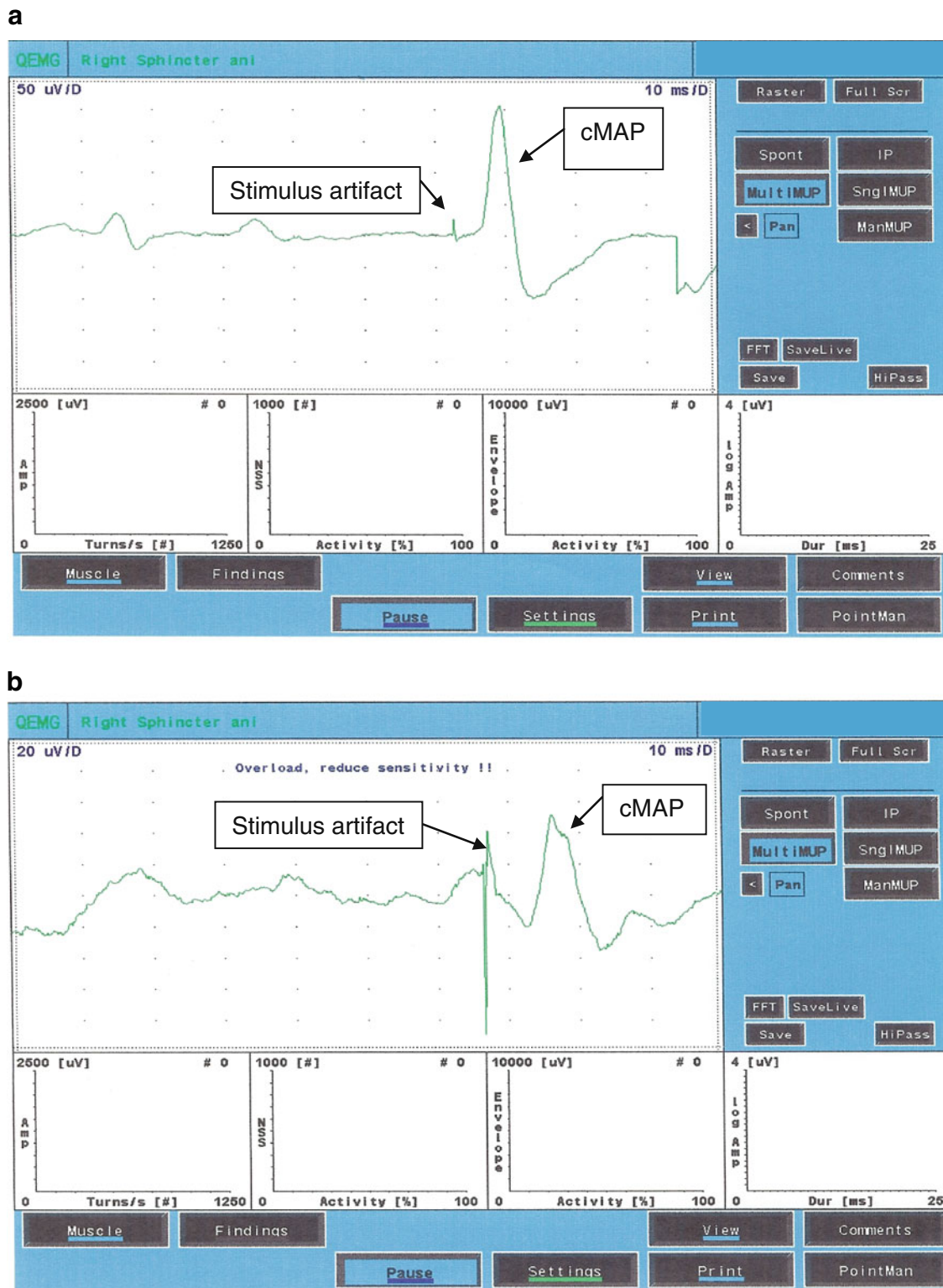
Fig. 3 Recorded cMAP from the levator ani muscle in patients with an implanted InterStim system. The first figure demonstrates a very small stimulus artifact indicating that only a small amount of energy is required to obtain a motor response. In the second example, the stimulus artifact is larger indicating a greater amount of energy is required to get the motor response

between the relative change in amplitude in the urethral cMAP and degree of improvement in bladder function in subjects who underwent repeat testing. There was no relationship to the absolute amplitude of the urethral or levator cMAP [8].

Sacral neuromodulation generally involves placement of the lead through the S3 foramen, but is this the optimal nerve root? In a small series of three subjects undergoing sacral neuromodulation test stimulation, each of the nerve roots S2-S4 were stimulated [9]. The cMAPs were simultaneously recorded from four sites; the urethral rhabdosphincter via the ring electrode, the levator ani via the vaginal sponge electrode, the external anal sphincter via the monopolar needles, and the abductor hallicus (great toe) via the surface electrode. The results demonstrated that the innervation of the urethra and levator was predominantly S3, with only a small contribution from S4. The S2 and S3 nerve roots contributed equally to the innervation of the external anal sphincter (Table 1). These findings suggest that S3 is the most logical choice from an electrodiagnostic standpoint.

McLennan [4] reported on the use of electrodiagnostic techniques in the reprogramming of patients who had a delayed suboptimal response to sacral nerve stimulation despite having maintained a sensory response. Using surface EMG that involved placing patch electrodes on either side of the anal sphincter, she was able to record evoked potentials produced by stimulation from the implantable pulse generator (Fig. 3). She evaluated ten patients with complaints of delayed device failure. Five of the ten were able to be reprogrammed using electrodiagnostics. These five patients were noted to have a more robust cMAP at an alternate electrode and were reprogrammed to that setting and had return of efficacy. Three patients had no cMAP noted at any of the four electrodes and underwent revision of the lead wire, two of whom had return of efficacy. Two were reprogrammed to the same electrode with changes in frequency and pulse width parameters and had improved response. Overall, using these techniques, they were able to restore response in 90% of patients.

More recently, alternate sites of stimulation, namely the pudendal nerve, are being investigated. Peters et al. [5] have compared pudendal to sacral nerve stimulation with very promising results in the pudendal group. In determining proper lead placement, Peters utilized electrodiagnostic techniques to confirm its placement along the nerve. Needle electrodes were placed in the anal sphincter to measure the cMAP produced from stimulation at the pudendal nerve. The senior author feels it is imperative to utilize electrodiagnostic techniques when placing the pudendal lead to insure that it is the pudendal nerve being stimulated and not just stimulation of the pelvic floor muscles directly. Should pudendal placement prove to be more efficacious and become an approved technique, the use of electrodiagnostics may become more mainstream.

Others have used these techniques to investigate the mechanism of action in sacral neuromodulation in both voiding dysfunction and anal incontinence. Fowler et al. studied a series of women with urinary retention [10]. They measured the latency of anal sphincter contraction with peripheral nerve stimulation of S3. The mean latency measured was 98 ms, and she concluded the anal sphincter contraction was due to a sensory afferent-mediated pathway. Whether or not this was a spinal or supraspinal reflex could not be determined. Malaguti and colleagues [11] studied the specific action of sacral neuromodulation on the sensory cortical areas by using somatosensory-evoked potentials (SEPs) from the pudendal and posterior tibial nerves in patients who were responders and non-responders to therapy. They recorded the SEPs prior to implant (T0) and 1 month after placement of the chronic lead in S3 at 21 Hz (T1) and at 40 Hz (T2). All patients in the group of responders demonstrated a significant decrease in the pudendal SEP P40 latency between T0 and T2, and between T2 and T1 which was seen with either ipsilateral or bilateral stimulation. This was not consistently demonstrated with posterior tibial nerve stimulation, indicating the specificity of pudendal sensory-evoked potentials in measuring the effect of sacral neuromodulation on the cortical sensory area via the afferent pathway. In the group of non-responders to SNM, there was no significant difference in latencies between T0 and T2. This finding demonstrates the lack of a modulating effect in the cortical areas in these patients which correlated to a lack of clinical efficacy. In the group of responders, the difference seen between the two frequencies indicates a possible improved response to a higher frequency of stimulation. Based on these findings, the authors indicate they are preferentially programming patients to these higher rates. Their study confirmed previous observations that SNM works via the afferent pathway at the cortical level and further concluded that the effect was specific to the pudendal

Table 2 Summary of how neurodiagnostic techniques benefit neuromodulation

• Implant of the lead wire (sacral and pudendal)

• Reprogramming of the IPG

• Understanding the mechanism of action of neuromodulation in the treatment of

  ◦ Overactive bladder (urge/frequency, urge incontinence)

  ◦ Urinary retention

  ◦ Anal incontinence

SEPs. This technique may also prove to be useful in predicting those patients who will respond to therapy.

In a study of ten patients, Wyndaele et al. found that SNM in the on vs. off mode improved the sensory thresholds within the bladder but not in the urethra or peripheral skin. Although this provided further evidence that SNM works via the afferent pathways via the pelvic nerves, there was no correlation of these findings to clinical outcomes and the authors recommended further study [12].

Perhaps combining some of these modalities in patients with both successful and unsuccessful responses to SNM may provide more clinical insight as to the mechanism of action and predict who may be a good candidate for implant.

Although not currently approved in the United States for the treatment of anal incontinence, SNM is approved for this indication in Europe. Additionally, many are now looking at treating constipation disorders with SNM. Several studies have demonstrated the efficacy of this therapy in treating anal incontinence, yet few have looked at the potential mechanism of action. In a recent study by Vitton et al., using a cat model, they were able to demonstrate that SNM inhibited colonic activity as well as enhanced internal anal sphincter activity. These findings were seen with stimulation of the dorsal nerve roots, whereas stimulation of the central end of the nerve roots resulted in an increase in colonic activity [13]. Dinning et al. studied the effects of SNS on patients with proven slow-transit constipation and found that stimulation of the S3 nerve root significantly increased the pan-colonic antegrade propagating sequence. In contrast, stimulation of the S2 nerve root resulted in a significantly increased retrograde propagation sequence. These preliminary findings may have an implication in choosing the most appropriate location for stimulation based on the presenting symptom.

Conclusion

Sacral neuromodulation has gained wider acceptance and the number of implants has risen exponentially over the past few years. Despite the vast improvements in technique for lead placement, tools for predicting good candidates for therapy or optimizing the surgical outcomes have lagged behind. The use of electrodiagnostic techniques has been shown in small studies to have benefit in both these areas, as well as helping to elucidate the mechanism of action (Table 2). Additionally, these techniques may prove to be a valuable tool in reprogramming refractory patients. As we

move on to alternate sites for implant and expand our indications for neuromodulation, the use of electrodiagnostic techniques may become an essential part of the procedure.

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