Neuromodulation for pelvic floor dysfunctions: exploring tibial, sacral and pudendal nerve stimulation.

W3, 29 August 2011 09:00 - 12:00

Start	End	Topic	Speakers
09:00	09:10	Introduction	• Stefan De Wachter
09:10	09:40	Tibial, pudendal and sacral nerve stimulation: does the mechanism of action differ?	• Warren Grill
09:40	10:05	Tibial, pudendal or sacral nerve stimulation: Is there one optimal stimulation method?	• Kenneth Peters
10:05	10:30	Tibial, pudendal or sacral nerve stimulation: How to choose the suitable method for a specific patient?	• Carolynne Vaizey
10:30	11:00	Break	None
11:00	11:25	Discussion: Tibial, pudendal or sacral nerve stimulation: Is bladder and bowel management different?	All
11:25	11:50	Discussion: Tibial, pudendal or sacral nerve stimulation: sequental or parallel treatments?	All
11:50	12:00	Closing remarks - Proposal treatment algorithm	• Stefan De Wachter

Aims of course/workshop

Sacral nerve stimulation is a well accepted minimal invasive treatment for certain bladder and bowel dysfunctions, but tibial and pudendal nerve stimulation are currently emerging as alternatives.
The aim of the workshop is to guide decision making in patients in which neuromodulation therapy is considered, and to bridge the gap between bladder and bowel management.
The similarities and differences between the different forms of neuromodulation will be discussed focusing on mechanism of action, clinical efficacy, patient selection criteria and adverse events.
At the end of the workshop, the audience should have a clear overview of the different modalities and a possible algorithm to choose the optimal method for the individual patient.

Educational Objectives

Sacral nerve stimulation is a well-accepted treatment for a defined group of patients with bladder (overactive bladder dry/wet; urinary retention) and/or bowel dysfunction (faecal incontinence; constipation). However based on the results of the test stimulation and the long term efficacy results, about 50 percent of the patients involved are left insufficiently treated. Pudendal nerve and tibial nerve stimulation are less known alternatives, but they may be of benefit for some of these patients.
The aim of the workshop is to present and describe the different neuromodulatory modalities available today. The content will cover the basics on the presumed mechanism of action which will guide patient selection. The literature data will be presented by speakers from different fields (engineering - urology - colorectal surgery), which will lead to an interesting discussion between similarities and differences of the different treatments, and bridge the gap between urological and colorectal management. The final purpose is tho give the audience an algorithm how to choose the optimal treatment for the individual patient.

Electrical Stimulation for Control of Bladder Function

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The principal functions of the lower urinary tract are to store urine (continence) and expel urine (micturition). Electrical stimulation can generate either inhibition or activation of the bladder and holds promise as an approach to restore of continence and micturition.

Electrical stimulation of the sacral nerve roots is an established treatment for the symptoms of refractory non-neurogenic overactive bladder (OAB). Further, the results of clinical feasibility trials also show that stimulation of the compound pudendal nerve (PN) and stimulation of the dorsal genital nerve (DGN) can treat the symptoms of OAB. The relative efficacy of these three potential stimulation locations is unclear, and the effects of stimulation parameter variations on the efficacy of continence control is not known. We quantified the effects of acute electrical stimulation of the dorsal nerve of the penis (DNP), the PN, and the S1 sacral nerve on reflex bladder contractions and maximum cystometric capacity in adult male cats anesthetized with α-chloralose. The degree of inhibition of isovolumetric bladder contractions was significantly dependent upon stimulation location, frequency, amplitude, and the interactions between any two of these parameters. Stimulating the PN or S1 at frequencies of 7.5 Hz or 10 Hz at an amplitude of 2x the threshold to evoke a reflex EMG response in the EAS, or the DNP at frequencies of 5 Hz, 7.5 Hz or 10 Hz at 0.8x, 1x or 2x threshold generated maximal bladder contraction inhibition. Stimulation of all three locations, at frequencies and amplitudes demonstrated to inhibit isovolumetric contractions (10 Hz, 1x - 2x threshold), increased cystometric capacities as compared to control (119.1% of control ± 7.5%, mean ± s.e.m). However, maximum cystometric capacities were not significantly different from each other across the three stimulation locations. The outcome of these experiments is a quantitative comparison of the relative efficacy of three potential stimulation locations and identification of the optimal stimulation parameters at each location. This understanding could influence the selection of anatomical targets for clinical neuromodulation as well as how neuromodulation devices are programmed.

Electrical stimulation of pudendal afferents can also generate bladder contractions [Bpggs et al. 2008a, Peng et al. 2008a, Yoo et al. 2008] and may be an effective treatment for urinary retention [Peng et al. 2008b]or bladder paralysis [Boggs et al. 2006b]. However, the mechanisms of bladder contraction evoked by pudendal afferent stimulation are unknown. We determined the contributions of sympathetic and parasympathetic mechanisms to bladder contractions evoked by stimulation of the dorsal nerve of the penis (DNP) in α-chloralose anesthetized adult male cats [Woock et al. 2011]. Bladder contractions were evoked by DNP stimulation only above a bladder volume threshold equal to 73±12% of the distension-evoked reflex contraction volume threshold. Bilateral

hypogastric nerve transection (to eliminate sympathetic innervation of the bladder) or administration of propranolol (β-adrenergic antagonist) decreased the stimulation-evoked and distension evoked volume thresholds by 25 - 39%. Neither hypogastric nerve transection nor propranolol affected contraction magnitude, and robust bladder contractions were still evoked by stimulation at volume thresholds below the distension-evoked volume threshold. As well, inhibition of distention-evoked reflex bladder contractions by 10 Hz stimulation of the DNP was preserved following bilateral hypogastric nerve transection. Administration of phentolamine (an α-adrenergic receptor antagonist) increased stimulation-evoked and distension-evoked volume thresholds by 18%, but again, robust contractions were still evoked by stimulation at volumes below the distension-evoked threshold. These results indicate that sympathetic mechanisms contribute to establishing the volume dependence of reflex contractions but are not critical to the excitatory pudendal to bladder reflex. A strong correlation between the magnitude of stimulation-evoked bladder contractions and bladder volume supports that convergence of pelvic afferents and pudendal afferents is responsible for bladder excitation evoked by pudendal afferents. Further, abolition of stimulation evoked bladder contractions following administration of hexamethonium bromide confirmed that contractions were generated by pelvic efferent activation via the pelvic ganglion. These findings indicate that pudendal afferent stimulation evokes bladder contractions through convergence with pelvic afferents to increase pelvic efferent activity.

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Sacral, Pudendal and Tibial Neuromodulation

ICS 2011-Glasgow, Scotland

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Introduction

Bladder dysfunction in the form of urinary urge, urinary frequency, and urinary urge incontinence are commonly described as overactive bladder (OAB). The International Continence Society defines OAB as a symptomatic syndrome suggestive of lower urinary tract dysfunction. It is estimated that 33.3 million adults suffer from OAB in the United States and as the population of aging adults continues to grow this number is likely to increase. Neuromodulation represents an important and ever expanding treatment option for patients suffering from OAB.

Neuromodulation is the electrical or chemical modulation of a nerve to influence the physiologic behavior of an organ. Tanagho et al. in 1989 pioneered the initial investigations into electrical stimulation for neuromodulation. Since this early work neuromodulation has become an important tool in the treatment of bladder dysfunction. Neuromodulation offers a minimally invasive, non-ablative and reversible means to treat voiding dysfunction.

Sacral Neuromodulation

Sacral neuromodulation has been FDA approved for over 10 years to treat urinary urgency, frequency, urge incontinence and non-obstructive urinary retention. The success of neuromodulation in treating voiding symptoms can be assessed by either a peripheral nerve

evaluation (PNE) or staged InterStim. The long-term success of SNM has been well-established in the literature.

Pudendal Neuromodulation

The pudendal nerve is a peripheral nerve that is mainly composed of afferent sensory fibers from sacral nerve roots S1, S2 and S3. The bulk of afferent sensory fibers are contributed by S2 (60.5%) and S3 (35.5%) according to afferent activity mapping procedures. Consequently the pudendal nerve is a major contributor to bladder afferent regulation and bladder function. Pudendal nerve entrapment often leads to significant voiding dysfunction including urinary incontinence and OAB. Because the pudendal nerve carries such a large percentage of afferent fibers this makes neuromodulation of the pudendal nerve an attractive option for refractory OAB. One study compared pudendal nerve stimulation with standard sacral nerve stimulation in a prospective, single blinded, randomized trial. Patients had both sacral and pudendal quadripolar tined leads placed in the first stage of their operation. Patients were then blinded to whether they were receiving pudendal or sacral stimulation and asked to rate their symptoms and chose a preferred site for stimulation. When patients received pudendal stimulation they had a 63% improvement in symptoms verses a 46% improvement in symptoms with conventional sacral neuromodulation. When patients were asked which lead they would prefer to receive stimulation from 79.2% of patients chose the pudendal lead and 20% chose the sacral lead. Spinelli et al also evaluated 15 treatment refractory patients with neurogenic bladder after CPNS with a tined lead placed under neurophysiologic guidance. Statistically significant reductions in incontinent episodes ($p<0.02$) and improvements in maximium cystometric capacity and pressure on urodynamics studies were seen. Constipation and fecal incontinence also improved. Currently at

our institution the most common indication for pudendal neuromodulation is for patients that have had failure of sacral neuromodulation. A recent review of our data found 41 of 44 (93.2%) who had previously failed sacral neuromodulation had a positive response to pudendal stimulation and had a permanent implant placed.

The placement of the lead is done via a posterior approach and does require electrophysiologic monitoring of the pudendal nerve action potentials intraoperatively to confirm pudendal stimulation.

Neuromodulation of the Posterior Tibial Nerve

The posterior tibial nerve is a peripheral mixed sensory-motor nerve that originates from spinal roots L4 through S3, which also contribute directly to sensory and motor control of the urinary bladder and pelvic floor. Multiple studies have demonstrated that posterior tibial nerve stimulation (PTNS) shows some efficacy in treating symptoms of OAB and altering urodynamic findings in patients with OAB. Stimulation of the nerve inhibits bladder activity by depolarizing somatic sacral and lumbar afferent fibers. Afferent stimulation provides central inhibition of the preganglionic bladder motor neurons through a direct route in the sacral cord.

Posterior tibial nerve stimulation is typically performed with patients in the sitting position with the knees abducted and the soles of the feet together. A 34 gauge needle is inserted 3 cm into the skin at a level 3 fingerbreadths cephalad to the medial malleolus. A grounding electrode is placed on the arch of the ipsilateral foot. The amplitude of the stimulation is increased until the large toe curls or the toes fan. Each session lasts for approximately 30 minutes.

The lure of the tibial nerve is that it is easily accessible without requiring an operating room or an anesthetic. As with all novel techniques, the data was initially anecdotal and is now becoming more robust. A recent trial involving 100 subjects comparing PTNS to Tolterodine-LA demonstrated equivalent objective efficacy between treatment groups. The Global Response Assessment demonstrated the PTNS subjects' assessment of OAB symptoms was statistically significant for improvement or cure in 79.5% compared to 54.8% in the tolterodine subjects ($p=0.01$). A follow-up trial demonstrated that 96% maintained a clinical response at 12 months with an average of one treatment every 21 days.

Until recently, level-one evidence comparing PTNS to a sham has been lacking. This is important due to the large placebo effect encountered with interventions for voiding dysfunction. A recent randomized blinded control study offered data validating a sham for PTNS so that future investigations into this technique might be compared to a true placebo. This validated sham was used in the Sumit Trial. In collaboration with 20 clinical centers, the first sham-controlled trial on PTNS for the treatment of OAB was completed. 220 subjects were randomized and the 13-week global response assessment (GRA) showed PTNS subjects had statistically significant improvement in overall bladder symptoms with 54.5% reporting moderately or markedly improved compared to 20.9% of sham subjects ($p <0.001$). PTNS subjects had statistically significant improvements in frequency, nighttime voids, voids with moderate to severe urgency and urinary urge incontinence episodes compared to sham.

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Sacral, Pudendal and Tibial Neuromodulation

ICS 2011-Glasgow, Scotland

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Introduction

Faecal continence depends not only on the harmonious function of the internal and external anal sphincter muscles but also on the consistency of the stools and on capacity of the colon and rectum to act as a reservoir.

The prevalence of solid or liquid faecal incontinence is about 2% and 9%, respectively. The mean age of subjects with faecal incontinence is 53 years although all ages can be affected. The prevalence in men may be greater than is usually appreciated accounting for about 45% of those affected.

Neuromodulation, introduced in the form of sacral nerve stimulation in 1995, has rapidly expanded in the last 15 years as a treatment for faecal incontinence with tibial and pudendal nerve stimulation being described more recently.

Sacral Neuromodulation

Lagging many years behind our urological colleagues sacral neuromodulation was first employed by Matzel in 3 patients with weak but intact external anal sphincter muscles in 1995. Shortly thereafter our unit undertook physiological studies and showed that there was little or no enhancement of the external anal sphincter. As a direct result of this study we proposed an expansion of the application of sacral nerve stimulation including patients with thinned or disrupted internal anal sphincter muscles and even those with external anal sphincter defects. This treatment is now applied to the majority of patients who have failed all conservative therapies and remain severely symptomatic from their incontinence.

Pudendal Neuromodulation

Again following in the footsteps of our urology colleagues, pudendal nervestimulation is a rapidly developing area for the treatment of faecal incontinence. Spinelli et al evaluated 15 refractory patients with neurogenic bladder and demonstrated improvements in constipation and faecal incontinence along side the urinary effects.

In our unit we have dispended with the somewhat laborious operative intraoperative electrophysiologic monitoring of the pudendal nerve action potentials for the posterior approach relying rather on a visible contraction of the external anal sphincter muscle. We have trialled patients with complete cauda equine, both with predominant incontinence and with predominant constipation. We have also performed this type of stimulation on patients who have failed sacral nerve stimulation. At 12 months, all five of the incontinence patients were successful, as were 5 of

8 of the cauda equine patients with constipation. Of the 7 failed SNS patients 4 worked initially but one lost efficacy at 3 months.

Tibial Nerve Neuromodulation

As with many unlikely colorectal therapies tibial nerve stimulation for faecal incontinence was first described by Shafik in 2003. Using a percutaneous technique he achieved an improvement in FI in 78.2% of patients. Using transcutaneous stimulation, Queralto achieved a 60% success rate some 3 years later.

In our unit we have completed a randomized, blinded, controlled trial comparing percutaneous and transcutaneous techniques and employing a sham transcutaneous arm to avoid any acupuncture-type effects relating to a needle. Of 30 patients treated, 9 / 11 percutaneous, 5 / 11 transcutaneous and one of 8 in patients in the sham transcutaneous arm were subjectively improved corresponding to the objective feedback measures.

Conclusion

The exact mechanism of action of these treatments is still poorly understood despite extensive testing. Comparative trials in faecal incontinence are planned.

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