Pelvic Neuromodulation

Daniel Rapoport
Urology Grand Rounds
March 14, 2007

D.O. Circa 1982,
Sherwood Park AB

“ability to void or inhibit voiding…sets humans apart from all other mammals”

Lapides
Pelvic Neuromodulation

• Definition
• Neurophysiology
• Mechanism
• Clinical aspects

Definition

• Not in stedman’s

“Fantabulous”

“Strategery”
Definition

• “therapeutic alteration of activity in the central, peripheral or autonomic nervous systems, electrically or pharmacologically, by means of implanted devices”
  North American Neuromodulation Society

• “stimulating nerves to improve bodily functions and patient symptoms”
  Resnick. Urol Clinic NA 2005

Spectrum

• Nerve stimulation
  – Cerebral
  – Spinal cord
  – Peripheral
  – Percutaneous
  – Endoscopic

• Drug Delivery
  – Intrathecal
  – Peripheral (botox)
Applications

- **CNS**
  - Pain syndromes
  - Spasticity
  - Epilepsy
  - Movement disorders

- **ENT**
  - Cochlear implants

- **Cardiac**
  - Pacemaker
  - ICD

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**Treatment of chronic ventilatory failure using a diaphragmatic pacemaker**

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Neuromodulation in Urology

• Nerve stimulation at various targets of neuraxis
  – Transurethral Bladder Stimulation
  – Direct Detrusor Stimulation
  – Spinal Cord Stimulation
  – Sacral Root Stimulation
  – Peripheral/cutaneous Nerve Stimulation
  – Pharmaconeuromodulation
Organizations

• Societies
  – International Neuromodulation Society
  – North American Neuromodulation Society

• SUFU
  – International Society of Pelvic Neuromodulation

• Fellowships
  – Several FPMRS programs include neuromodulation training
Pelvic Neuromodulation

- Definition
- Clinical aspects
- Neurophysiology
- Mechanism

The Niche

- Target Population?
  - Idiopathic voiding dysfunction
  - Chronic pelvic pain
  - Off label: DES, SUI, ED, NGB (SCI/MS)
- What does it offer?
  - Option for those failing conservative mgmt
  - Avoid irreversible surgical mgmt
Neuromodulation Indications

• FDA approved:
  – Storage disorders (urge incontinence, OAB)
  – Voiding disorders (non-obstructive retention)

• Expanding uses:
  – Chronic Pelvic Pain syndromes
  – Neurogenic bladder dysfunction
  – Stress urinary incontinence
  – Pediatric voiding dysfunction
  – Erectile dysfunction
  – Fecal incontinence/Constipation

Clinical Evaluation of Voiding Dysfunction

• History
  – Detail LUTS
  – Triggering events: diet, surgery, trauma, radiation
  – Detailed list of conservative therapies

• Questionnaires + Voiding diary
  – Objectify symptoms
  – ICIQ, OAB-q

Campbell’s 9th ed.
Siegel. Urol Clin NA; 32(1) 2005
Clinical Evaluation of Voiding Dysfunction

• Physical Examination
  – “Hurts to sit”, pelvic floor spasm
  – SUI, hypermobility, prolapse
  – Neurologic exam
  – Pelvic floor examination

• Urinalysis
  – Cytology in selected cases

• Urodynamics
  – CMG, EMG, PFS
  – Indications: previous surgery, mixed LUTS, suspect NGB, failed medical mgmt

• Cystoscopy

• Imaging
  – Ultrasound
  – MRI spine in selected cases

Camppell’s 9th ed.
Siegel. Urol Clin NA; 32(1) 2005
Defining the Disorder: OAB

• Terminology
  – Symptoms of frequency and urgency +/- incontinence, in absence of pathology

• Clinical Definition (varies)
  – 4 episodes of urgency in previous 4 wk
  – > 8 voids/day

• Epidemiology
  – 17% (9% wet) of women; 16% (2.5% wet) of men

• Natural History
  – Lack of long-term follow up data


Defining the Disorder: Idiopathic Retention

• A.K.A. Fowler Syndrome
  – Female < 30 yrs
  – Unable to void > 24 hrs
  – No urge + PVR > 1 litre
  – NO neurologic findings, MRI (-), cysto (-)
  – UDS
    • Acontractile detrusor
    • Inappropriate EUS contraction
    • Inability to relax EUS

Campbell's 9th Ed
Defining the Disorder: Idiopathic Retention

• In Males with idiopathic retention… consider:
  – Bladder neck dysfunction
    • Diagnosis by VUDS
    • Treated with A-blockers or “channel TURP”
  – Bashful Bladder
    • Low-pressure/low-flow voiding
    • Difficult to demonstrate objectively
    • Difficult to treat

Patient Selection

• Indications
  – OAB (wet or dry)
  – Idiopathic retention
• Failed conservative management
  – Behavioral; Dietary; Pelvic Floor exercises; Biofeedback; Pharmacotherapy
  – Peripheral nerve stimulation
  – Botox

Siegel. Urol Clin NA; 32(1) 2005
Predictors of Success

• Good response on trial phase is only predictor

• No clinical factors predict success of neuromodulation

Contraindications

• Absolute
  – Anatomic abnormality of sacrum or sacral nerves
  – Mental incapacity
  – Failed trial stimulation

• Relative
  – Neurologic lesion (unstable)
  – MRI studies
  – Other stimulation devices

Campbell’s 9th ed.
Siegel. Urol Clin NA; 32(1) 2005
How It’s Done

• 2 step process
  – Testing (stage 1)
  – Implantation (stage 2)

• Both can be done under combined sedation + local anesthesia

Test Phase

• Percutaneous implantation at S3 foramina
  – Fluoroscopic guidance
  – S3 reflexes: anal wink, great toe dorsiflexion

• Tined lead
  – Prevents migration (false negative)

• 1 - 4 week trial
  – Voiding diary,
  – > 50% improvement
Implantation

- Subcutaneous pouch
- Upper buttock, lower abdomen
- One implantable pulse generator per lead
  - 2 IPGs if bilateral
Efficacy

- Only 4 RCTs
  - 3 by SNS Study Group

- Several case series

- Lack of long term data
SNS STUDY GROUP
Schmidt et al. J Urol; 162(2) 1999

- Prospective multicenter (16) RCT
- Evaluate SNS for refractory urge incontinence

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age greater than 18 years</td>
<td>Neurological conditions (multiple sclerosis, diabetes with peripheral nerve involvement, spinal cord injury, stroke)</td>
</tr>
<tr>
<td>Refractory to standard medical therapy</td>
<td>Stress urinary incontinence</td>
</tr>
<tr>
<td>100 mL. bladder capacity with normal upper urinary tract</td>
<td>Primary pelvic pain</td>
</tr>
<tr>
<td>Good surgical candidate</td>
<td></td>
</tr>
<tr>
<td>Able to complete study documentation and return for followup evaluation</td>
<td></td>
</tr>
</tbody>
</table>

**Method**

- 155 patients underwent test stimulation
- 76 patients with > 50% improvement randomized to implantation or delay

**Table 1. Demographic summary of 155 patients with urge incontinence**

<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. women</td>
<td>105</td>
</tr>
<tr>
<td>No. men</td>
<td>50</td>
</tr>
<tr>
<td>Mean age ± SD (range)</td>
<td>64.6 ± 11.0 (20.2-79.9)</td>
</tr>
<tr>
<td>Mean yrs. urinary symptoms ± SD before enrollment (range)</td>
<td>7.4 ± 5.6 (0.6-30.6)</td>
</tr>
<tr>
<td>No. previous medical treatment for urinary symptoms (range)</td>
<td>139 (98.7)</td>
</tr>
<tr>
<td>Pharmacological</td>
<td>144 (92.5)</td>
</tr>
<tr>
<td>Non-surgical</td>
<td>55 (35.3)</td>
</tr>
<tr>
<td>Surgical</td>
<td>88 (56.8)</td>
</tr>
</tbody>
</table>

* Medical treatment categories were not mutually exclusive.
Efficacy Measurement

• **Clinical (Voiding Diary)**
  – Evaluated @ 1, 3, 6 mo and then q6 mo
  – Control group allowed to crossover 6 mo
  – Deactivated stimulation after 6 mo

• **QOL**
  – SF-36 Health Survey

• **Urodynamic parameters**
  – Baseline vs 6 mo
  – Treatment vs control, treatment pre & post

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### Voiding Diary Effect

**Table 3. Sustained clinical benefit 18 months after implant**

<table>
<thead>
<tr>
<th></th>
<th>% 6 Mos. After Implant (38 pts.)</th>
<th>% 12 Mos. After Implant (38 pts.)</th>
<th>% 18 Mos. After Implant (31 pts.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any leaking episode:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dry</td>
<td>47</td>
<td>46</td>
<td>32</td>
</tr>
<tr>
<td>50% Reduction or greater</td>
<td>28</td>
<td>34</td>
<td>24</td>
</tr>
<tr>
<td>Total clinical success</td>
<td>75</td>
<td>79</td>
<td>78</td>
</tr>
<tr>
<td>Heavy leaking episodes:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eliminated</td>
<td>77</td>
<td>79</td>
<td>84</td>
</tr>
<tr>
<td>50% Reduction or greater</td>
<td>13</td>
<td>19</td>
<td>89</td>
</tr>
<tr>
<td>Total clinical success</td>
<td>90</td>
<td>80</td>
<td>84</td>
</tr>
<tr>
<td>Absorbent pads or diapers replaced daily:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eliminated</td>
<td>57</td>
<td>55</td>
<td>57</td>
</tr>
<tr>
<td>50% Reduction or greater</td>
<td>26</td>
<td>21</td>
<td>13</td>
</tr>
<tr>
<td>Total clinical success</td>
<td>83</td>
<td>76</td>
<td>78</td>
</tr>
</tbody>
</table>

Schmidt et al. J Urol; 162(2) 1999
Deactivation after 6 months

- N = 52
- 3-7 day deactivation

<table>
<thead>
<tr>
<th></th>
<th>SNM ON</th>
<th>SNM Off</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leaks/day</td>
<td>2.9</td>
<td>9.5</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Severity</td>
<td>.8</td>
<td>2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Pads/day</td>
<td>1.2</td>
<td>5.8</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Schmidt et al. J Urol; 162(2) 1999

QOL Effect

- Significant improvement in perceptions of physical health status
- No treatment patients got worse
Urodynamic Effect

- No significant changes
- No de novo retention
- No de novo detrusor overactivity

SNS STUDY GROUP
Urgency-Frequency

- 29 patients, 2 yr f/u
- Voiding Diary
  - 56-64% significant (>50%) improvement in
    - Voids per day
    - Voided volumes
    - Urgency score
- QOL
  - Statistically significant improvements in several domains of SF-36

Hassouna et al. J Urol; 163(6) 2000
SNS STUDY GROUP
Idiopathic Retention

• 42 patients, 2 yr f/u
  – 5.6 cath/day, 343 mL/cath

• Voiding Diary
  – 70% significant (>50%) reduction in cath volumes
  – 58% eliminated cath usage altogether

Jonas et al. J Urol; 165(1) 2001

Durability

• Prospective case series (OAB)
• 45 patients, mean f/u 47 months
• 60% significant improvement
  – 20% cured
• Reasons for failure
  – Recurrent lead migration/breakage
  – Explantation for infection
• All failures occurred w/in 18 mo

Bosch. J Urol; 163(4) 2000
**Expanding Indications: IC**

- **25 patients**
  - NIDDK criteria IC
  - Failed behavioral, drugs and hydrodistention after 6 months
- **Underwent test stimulation**
  - 7 days, Voiding diary
- **Data measured**
  - Daytime frequency, nocturia
  - Voided volume
  - IC symptom and problem index scores

Comiter. J Urol; 169(4) 2003

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**Comiter. J Urol; 169(4) 2003**

- **17 patients had > 50% improvement**
  - Implanted
- **Mean 14 mo f/u**
  - Improved freq/noct
  - Improved pain scores
  - Improved voided volumes
  - Improved ICSI/ICPI

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Post</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime Frequency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nocturia</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Graph showing improvement in frequency and nocturia.
Safety

<table>
<thead>
<tr>
<th>Complication</th>
<th>Probability of occurrence (Siegel series)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain at neurostimulator site</td>
<td>15.5%</td>
</tr>
<tr>
<td>New pain</td>
<td>9.0%</td>
</tr>
<tr>
<td>Suspected lead migration</td>
<td>6.4%</td>
</tr>
<tr>
<td>Infection</td>
<td>6.1%</td>
</tr>
<tr>
<td>Transient electric shock</td>
<td>5.5%</td>
</tr>
<tr>
<td>Pain at lead site</td>
<td>5.4%</td>
</tr>
<tr>
<td>Adverse change in bowel function</td>
<td>3.0%</td>
</tr>
<tr>
<td>Technical problems</td>
<td>1.7%</td>
</tr>
<tr>
<td>Suspected device problems</td>
<td>1.6%</td>
</tr>
<tr>
<td>Change in menstrual cycle</td>
<td>1.0%</td>
</tr>
<tr>
<td>Adverse change</td>
<td>0.6%</td>
</tr>
<tr>
<td>Involuntary bladder</td>
<td></td>
</tr>
<tr>
<td>Persistent skin irritation</td>
<td>0.5%</td>
</tr>
<tr>
<td>Suspected nerve injury</td>
<td>0.5%</td>
</tr>
<tr>
<td>Device rejection</td>
<td>0.5%</td>
</tr>
<tr>
<td>Others</td>
<td>9.5%</td>
</tr>
</tbody>
</table>

Complications of SNS

- **Test Stimulation (18% complication rate)**
  - Lead migration
  - Technical problems
  - Pain
- **Post-implantation (15% complication rate)**
  - Pain at IPG site
  - Infection
- **33% re-operation rate**
  - Revision and explantation
Cleveland Clinic Case Series

• 167 patients, 2 yr follow-up
• Indications
  – OAB, IUR
  – IC
  – Neurogenic retention

Vasavada. Urol Clin NA; 32(1) 2005

CCF: Stage 1 Complications

• 72% went on to implantation
  – 2-4 wk test stimulation
  – Percutaneous tined lead
• Of the 28% test leads removed
  – 92% poor clinical response
  – 8% infection
• 12% required revision
  – Marginal response
  – Migration/lead problem
CCF: Stage 2 Complications

• 12% Explant
  – 56% infection
  – 43% to maintain response

• 20% Revisions
  – Infections, mechanical reasons

Generator Site Infection

• Best management is explantation
• Salvage often not successful
  – Ie. Relocation

• Pain at generator site, no infection
  – Generator relocation
Management of Response Decrease

• Impedance testing
  – Open circuit
    • High impedance, no current flow
  – Short circuit
    • Low impedance, high current flow (to wrong area)
    • Body fluid/tissue intrusion into wires
    • Current follows path of least resistance

Management of Response Decrease

• Response-related revision are most common case of stage 2 revisions
Future

• Special Populations
  – Pediatrics
  – Neurogenics
• Expanding Indications
  – ED
• Technical advances/improvements

• 9 women with NGB and incontinence
  – 2 MS, 2 myelitis, 5 SCI
  – All had neurogenic DO
  – refractory to antichol.
  – 5 with DESD
• 40 mo f/u
  – Improved urodynamic and clinical parameters in most
  – Increased DO in 1 patient
• 23 children age 6-15
• Severe DES
  – Negative work-up (US, VCU, UDS, MRI)
  – Failed 6 mo conservative/medical mgmt
  – “highly motivated’ families
• 21/23 responded to test stimulation

Preliminary Results of Sacral Neuromodulation in 23 Children
Mitchell R. Humphreys, David R. Vandersteen, Jeffery M. Slezak, Pam Hollatz, Craig A. Smith, Janet E. Smith and Yuri E. Reimberg
• Definition
• Clinical aspects
• **Neurophysiology**
• Mechanism
Overview

• Neuroanatomy
  – Peripheral
  – Central
• Neurophysiology
  – reflexes

Peripheral Efferent Pathways

1. Sacral parasympathetics
   – excite bladder, inhibit outlet

2. Thoracolumbar sympathetics
   – inhibit bladder, excite outlet

3. Pudendal nerves
   – excite external sphincter
### Peripheral Efferent Pathways

<table>
<thead>
<tr>
<th>Parasympathetic</th>
<th>Structures</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S 2,3,4</td>
<td>Voiding</td>
</tr>
<tr>
<td></td>
<td>Ganglia in detrusor wall</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pelvic plexus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Perirectal)</td>
<td></td>
</tr>
<tr>
<td>Sympathetic</td>
<td>T 10 – L2</td>
<td>Storage</td>
</tr>
<tr>
<td></td>
<td>Sympathetic chain ganglia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inferior mesenteric ganglia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypogastric nerves</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pelvic Plexus</td>
<td></td>
</tr>
<tr>
<td>Somatic</td>
<td>S 2,3,4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Onuf’s nucleus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pudendal nerve</td>
<td></td>
</tr>
</tbody>
</table>

**Function Structures**

- S: genitalia, pelvic viscera
- M: EUS contraction
Peripheral Afferent Pathways

1. Somatic: pudendal nerves
   - sensory info from genitals, pelvic viscera

2. Autonomic: pelvic and hypogastric nerves
   - A-delta fibres:
     • Located in smooth muscle
     • Sense bladder fullness
   - C-fibres:
     • Located in mucosa and smooth muscle
     • Sense noxious stimuli

De Groat. Urol Clin NA; 23(2), 1996
Leng. Urol Clin NA; 32(1) 2005

C-Fibres

• Most are silent
• Recruitment with inflammation/pathology
• Become mechanosensitive, low threshold
• Implicated in detrusor overactivity
• Therapeutic target
  – Capcaisin
  – RTX
  – Neuromodulation

Leng. Urol Clin NA; 32(1) 2005
Central Pathways

<table>
<thead>
<tr>
<th>Structures</th>
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<tbody>
<tr>
<td>Cortex</td>
<td>Frontal</td>
</tr>
<tr>
<td></td>
<td>ACG</td>
</tr>
<tr>
<td></td>
<td>Sensation, social context Control</td>
</tr>
<tr>
<td></td>
<td>“on-off” spinal reflexes</td>
</tr>
<tr>
<td></td>
<td>external sphincter</td>
</tr>
<tr>
<td>Brainstem</td>
<td>PMC</td>
</tr>
<tr>
<td></td>
<td>Coordinates bladder and sphincter</td>
</tr>
<tr>
<td></td>
<td>Reflex and voluntary</td>
</tr>
<tr>
<td>Spinal Cord</td>
<td>Afferent pathways</td>
</tr>
<tr>
<td></td>
<td>- dorsal</td>
</tr>
<tr>
<td></td>
<td>Efferent Pathways</td>
</tr>
<tr>
<td></td>
<td>- ventral</td>
</tr>
<tr>
<td></td>
<td>Interneurons</td>
</tr>
<tr>
<td></td>
<td>Interface between brain and periphery</td>
</tr>
<tr>
<td></td>
<td>Interface b/w peripheral afferents &amp; efferents</td>
</tr>
</tbody>
</table>

Efferents to LUT activated by

- Signal from peripheral afferents
  - Eg. Reflex voiding in infants
- Signal from brain
  - Eg. Volitional voiding
- Unique organ:
  “Visceral organ under mostly voluntary control”
Overview

• Neuroanatomy
  – Peripheral
  – Central

• Neurophysiology
  – reflexes
Storage Reflex

• Passive ("default mode")
• Reflex arc contained within spinal cord
• Low bladder wall tension → low-intensity afferent signal results in:
  – Sympathetic outflow to bladder & outlet
  – Somatic outflow to external sphincter
  – Inhibition of parasympathetic outflow

De Groat. Urol Clin NA; 23(2), 1996

Storage Reflex

• External sphincter contraction (somatic)
• Internal sphincter contraction (sympathetic)
• Detrusor inhibition (sympathetic)
• Parasympathetic inhibition (sympathetic)

De Groat. Urol Clin NA; 23(2), 1996
Emptying Reflex

• Voluntary or reflex initiation
• Mediated by PMC (Spino-bulbar-Spinal)
• High bladder wall tension $\rightarrow$ high-intensity afferent signal results in:
  – Parasympathetic outflow to bladder & outlet
  – Somatic outflow to sphincter
  – Inhibition of sympathetic outflow

De Groat. Urol Clin NA; 23(2), 1996

Emptying Reflex

• Inhibit external sphincter (somatic)
• Inhibit internal sphincter (parasymp.)
• Detrusor contraction (parasymp.)
• Inhibit sympathetic outflow (parasymp.)

De Groat. Urol Clin NA; 23(2) 1996
Interneurons

- Interneurons in spinal cord allow for communication between sympathetic, parasympathetic and somatic pathways

  - GABA, glycine, enkephalin mediated

Reflexes and Neuromodulation

- Reciprocal autonomic reflex arcs
  - Sympathetic (storage) vs Parasympathetic (emptying)
  - “off balance”
    - Afferent over/underactivity
    - Efferent over/underactivity
    - Central signalling dysfunction
- Autonomic, Somatic & Central pathways converge in spinal cord
  - Activation of one effects the other
  - Gate-control theory
• Definition
• Clinical aspects
• Neurophysiology
• Mechanism

Neuromodulation Mechanism
Neuromodulation Mechanism: What is “known”

• Efferent outflow to the LUT is activated by
  – Periphery: autonomic afferents (reflex) or
  – Central: supraspinal efferents

• Somatic spinal afferents (pudendal nerves) can modulate voiding function
  • Eg. Vincent’s Curtsy, Kegel’s

De Groat. Urol Clin NA; 23(2), 1996

Neuromodulation Mechanism: What is “Known”

• Primary action: triggers somatic afferents
  – Stimulus under threshold for autonomies/motor
  – Common pathway to affecting micturition and storage reflexes

Leng. Urol Clin NA; 32(1) 2005
Van der Pal. Curr Opin Urol;16(1) 2006
Neuromodulation Mechanism: What is “Known”

- Somatic afferent stimulation secondary effects:
  - Autonomic efferents
    - Directly
    - Indirectly (through afferent limb of reflex arc)
  - Autonomic afferents
    - Directly
    - Through interneurons
  - Supraspinal centres
    - Direct
    - Indirect
    - Chronic changes (neuroplasticity)

Neuromodulation Mechanism: What is “Proposed”

- Induces physiologic changes in sphincter muscle and pelvic floor
- Induces chronic changes (neuroplasticity) in higher centers
- Enhances nerve regeneration stimulation of neurotrophin secretion
Storage Disorders (OAB)

• Proposed pathophysiology:
  – Increased afferent firing and reflex voiding
    • C-fibre recruitment
    • establishment of new low threshold pathways
  – Altered CNS inhibition of reflex voiding

Storage Disorders (OAB)

• Proposed therapeutic mechanism:
  – Inhibit afferent firing
    • Inhibit parasympathetic efferent
  – Re-establish central inhibition
Storage Disorders (OAB): Peripheral Effect

- Inhibit bladder afferents **
- Inhibit parasympathetic efferents
  - Indirect reflex inhibition
  - Indirect activation sympathetic efferents
- Direct stimulation of Onuf’s nucleus (not supported)
  - No direct sphincter contraction

Van der Pal. Curr Opin Urol;16(1) 2006
Leng. Urol Clin NA; 32(1), 2005

Storage Disorders (OAB): Central Effect

- Activates central inhibitory areas
  - Functional MRI evidence
    - activation of somatosensory and somatomotor cortex

- ? Chronic brain changes (neuroplasticity)

Van der Pal. Curr Opin Urol;16(1) 2006
Leng. Urol Clin NA; 32(1) 2005
Idiopathic Retention

• Proposed pathophysiology:
  – Brain unable to turn off guarding reflex
    • Bladder-sympathetic reflex
  – Pelvic floor spasm leads to reflex inhibition of detrusor
  – Essentially DSD without SCI

Van der Pal. Curr Opin Urol;16(1) 2006
Leng. Urol Clin NA; 32(1) 2005

Idiopathic Retention

• Proposed therapeutic mechanism:
  – Inhibit afferent limb of guarding reflex
    • Indirectly inhibit sympathetic outflow to bladder/urethra
  – Stabilize pelvic floor
  – Activate PMC
Idiopathic Retention: Peripheral and Central Effect

- Inhibit afferent limb of guarding reflex**
  - Reflex inhibition of sympathetic efferents to bladder and outlet
- Elimination of pelvic floor/sphincter spasticity
- Activation of PMC
  - Conflicting data from PET studies

Van der Pal. Curr Opin Urol; 16(1) 2006
Urol Clin NA, 32(1) 2005

Chronic Pelvic Pain / IC

- Gate-control theory (Melzack and Wall, 1965)
  - Activity in low threshold afferents inhibits firing of nociceptive afferents through an inhibitory interneuron
  - Activity in pudendal afferents/A-delta afferents inhibit firing of c-fibres through interneurons in substantia gelatinosa

Alo. Neurosurgery; 50(2), 2002
Van der Pal. Curr Opin Urol; 16(1) 2006