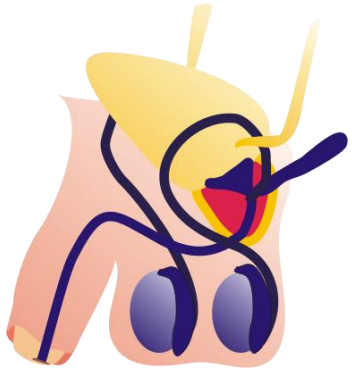
Chronic Pelvic Pain (CPP)

Daniel S. Engeler, M.D.

Department of Urology
Cantonal Hospital of St. Gallen
Switzerland

daniel.engeler@kssg.ch

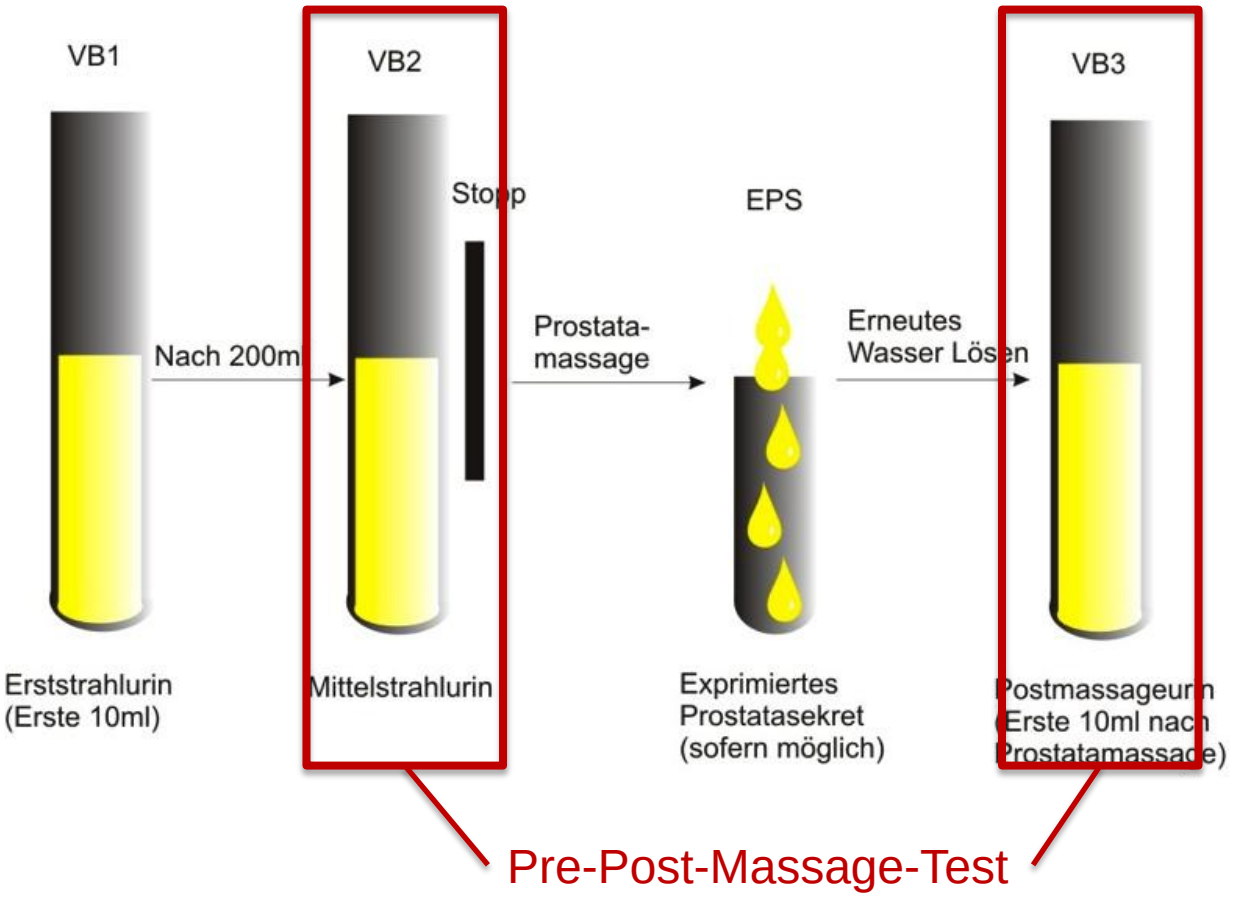
Case



History

- 38-year old male patient
- Referred for refractory pain in the region of the prostate
- **History of present illness:**
  - Started 10 months ago
  - Suggested acute prostate infection, painful micturition, frequency, urgency
  - Elevated urinary leucocytes (100/ul), but no bacteria were found
  - After short course of quinolone antibiotic therapy (ciprofloxacin), micturition symptoms (hesitancy, straining) reappeared, in addition diffuse pain in the pelvic area developped
  - Afterwards 2 to 3 antibiotic treatments were used without proven infection (including pre-/postmassage test) and without effect

4-Glass Test – Pre-Post-Massage-Test



Engeler DS et al. Swiss Medical Forum 2007; 7:55-62

Case

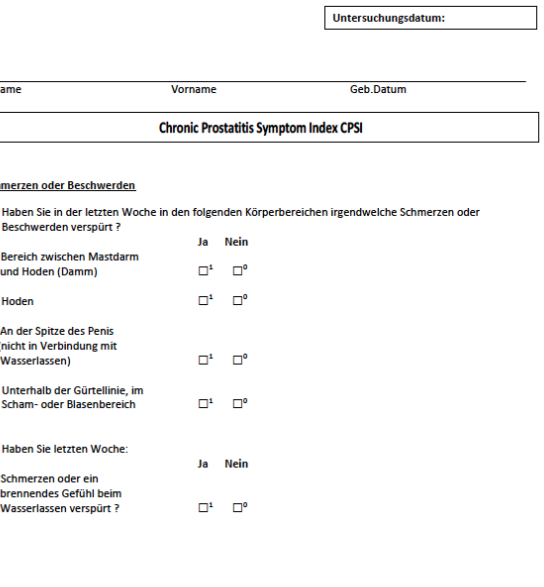
History

- **Localisation:** Pain actually perceived in the suprapubic area, left scrotum, penile tip, perineum and rectum
- **Triggers:** Long periods of walking could alleviate the pain, while longer time sitting (especially on motorbike) worsened the pain
- **Urological:** Hesitancy, straining, intermittency
- **Psychological:** Patient thinking of his pain all day long, major impact on his daily activities
- **Sexual:** Negative influence on relationship to his wife
  - Painful ejaculation -> reducing sexual activity
- **Gastrointestinal:** Passing hard stools aggravated the pain
- **Scores:** NIH-CPSI score 31 (out of 43), mean VAS for pain 7/10

Questionnaire (NIH-CPSI)

- 3 Domains
  - pain
  - symptoms
  - Auswirkung auf Lebensqualität

➢ Recommended for initial assessment and follow-up



Untersuchungsdatum:

Name Vorname Geb.Datum

Chronic Prostatitis Symptom Index CPSI

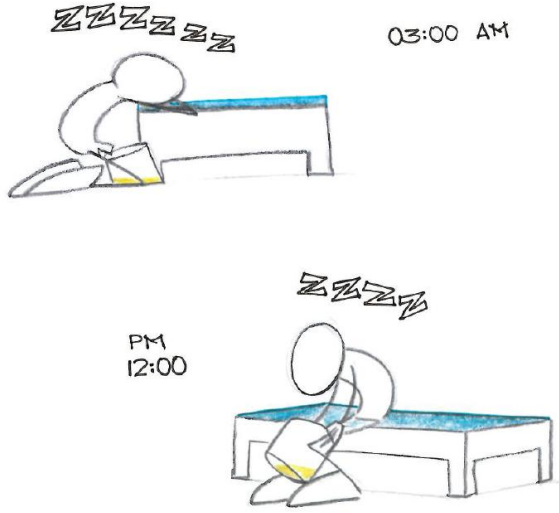
Schmerzen oder Beschwerden

1. Haben Sie in den letzten Woche in den folgenden Körperbereichen irgendwelche Schmerzen oder Beschwerden verspürt ?

	Ja	Nein
a. Bereich zwischen Mastdarm und Hoden (Damm)	□¹	□⁰
b. Hoden	□¹	□⁰
c. An der Spitze des Penis (nicht in Verbindung mit Wasserlassen)	□¹	□⁰
d. Unterhalb der Gürtellinie, im Scham- oder Blasenbereich	□¹	□⁰

2. Haben Sie letzten Woche:

	Ja	Nein
a. Schmerzen oder ein brennendes Gefühl beim Wasserlassen verspürt ?	□¹	□⁰

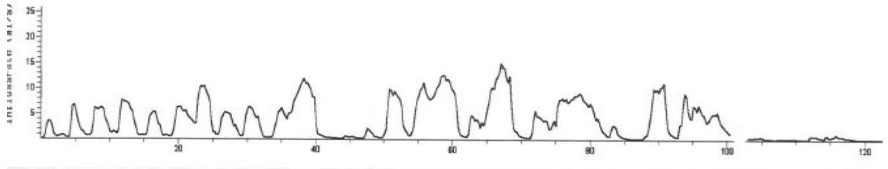


Case

Physical examination

- Pain on palpation of left epididymis
- **Rectal exam:**
  - non-relaxing pelvic floor
  - painful palpation soft prostate
  - Trigger point in the puborectalis muscle
- **Neurology:** No sensory or motor deficits in neurological examination

Uroflowmetry



- Intermittent stream, reduced maximal flow rate
- No resting urine

Case

Flexible cystoscopy

- Normal except for painful passage of hyperactive external urinary sphincter

MRI

- Previous MRI of pelvis normal

Case 3

Diagnosis

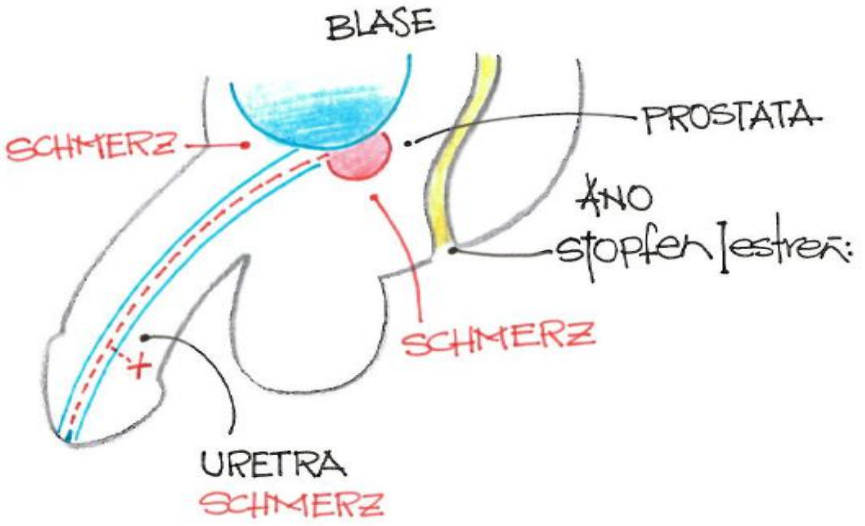
- **Prostate pain syndrome (PPS)**

Prostate pain syndrome (PPS)

- Aim of diagnostic procedures:
  - Exclusion of chronic prostate pain associated with specific disease
    - (e.g. infection, carcinoma, stricture, neurogenic disease)
  - After exclusion of specific disease associated pain one should diagnose the patient with prostate pain syndrome (PPS)
  - Phenotyping (e.g. predominantly micturition symptoms)

Definition of PPS according to IASP/EAU 2012

Prostate pain syndrome	PPS is the occurrence of persistent or recurrent episodic pain (which is convincingly reproduced by prostate palpation). There is no proven infection or other obvious local pathology. PPS is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction.



Case 3

Therapy

- **Patient information/education:**
  - Nature of pain syndrome was explained to the patient and his wife
  - Including lack of evidence for cancer
  - Expectation: realistic aims!
- **Behaviour:**
  - Advice given regarding avoidance of pain promoting factors such as sitting on cold and hard surfaces
  - Motivation for physical activity
- **Physiotherapy:** Local warming pad on a regular base, pelvic floor muscle exercises, biofeedback and electrostimulation
- **Oral medical therapy:** α-blockers for urinary symptoms and diclofenac to treat periods of worsening pain

Case 3

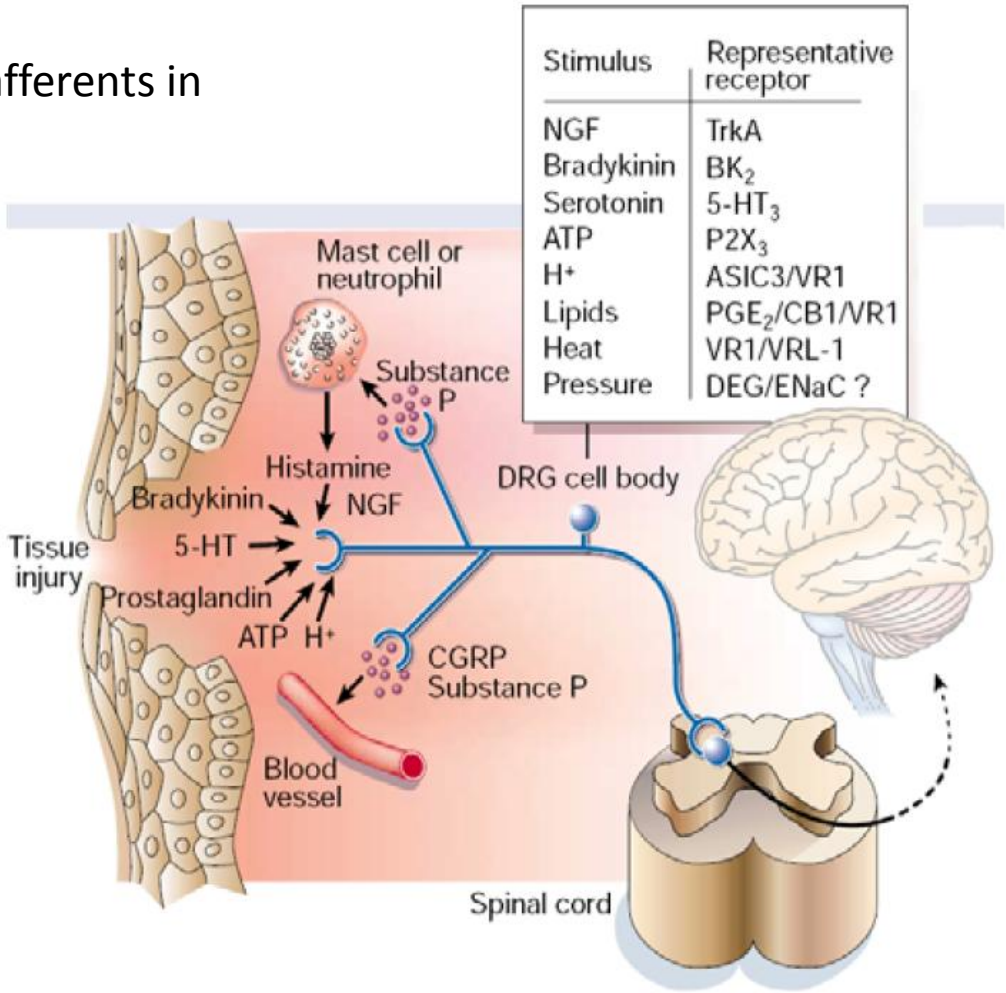
Outcome

- After 5 months, fluctuating improvement of the pain to a mean VAS of 2-3/10
- Lower urinary tract symptoms slightly improved
- Could overall live with the pain and accept his situation much better than before

Peripheral Sensitisation

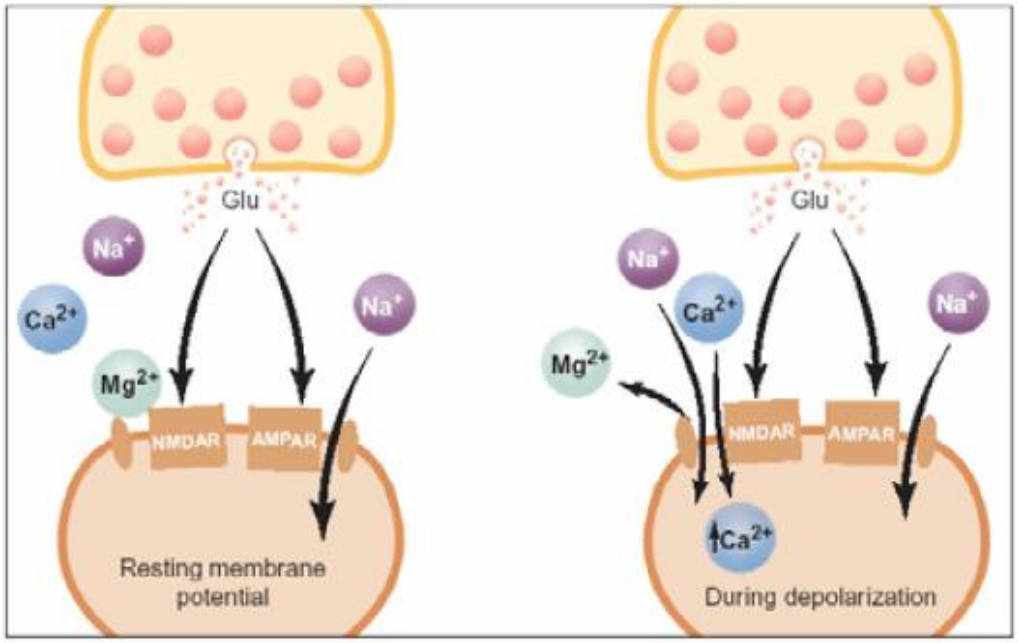
Peripheral sensitisation
of nociceptive primary afferents in
inflammatory „soup“

- Inflammation of tissue releases mediators sensitizing receptors
- threshold↓, response on nociceptive trigger↑



Central Sensitisation

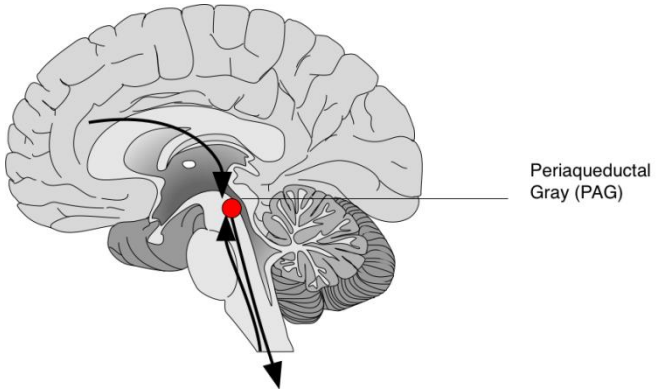
- Multiple mechanisms
  - Example: NMDA Receptor (spinal)

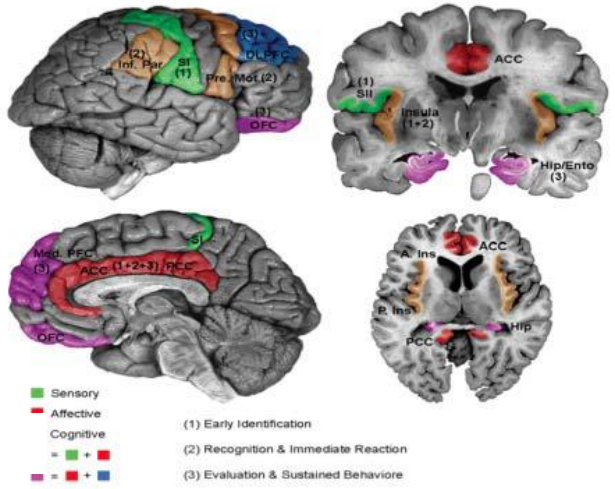


Elevated concentration of glutamate leads to reduced blockage from Mg2+ of NMDA -> Intracellular calcium-concentration rises with the concequence of a reduced activation threshold of the secondary neuron

Higher Center Modulation of Spinal Nociceptive Pathways

- Complex system of ascending and descending neuronal pathways
- PAG plays an important role in spinal modulation
- Input from centers associated with thought and emotion
- Projections to the dorsal horn through relay centers can inhibit nociceptive messages (via opioids, 5-hydroxytryptamine, noradrenaline)





Sensitisation in CPPS

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PAIN SENSITIZATION IN MALE CHRONIC PELVIC PAIN SYNDROME: WHY ARE SYMPTOMS SO DIFFICULT TO TREAT?

CLAIRE C. YANG,* JAY C. LEE,† BRENDA G. KROMM, MARCIA A. CIOL AND RICHARD E. BERGER‡

From the Departments of Urology (CCY, JCL, BGK, REB) and Rehabilitation Medicine (MAC), University of Washington, Seattle, Washington

- Clinical study: Patients with CPPS (N=36) vs controls (N=66) reported computerized visual analog scale as a reponse to noxious stimuli at perineum an thigh

- CPPS report higher visual analogue scale scores than controls to short bursts of noxious heat stimuli to the perineum but not to the anterior thigh.

TABLE 3. *Summarized COVAS data*

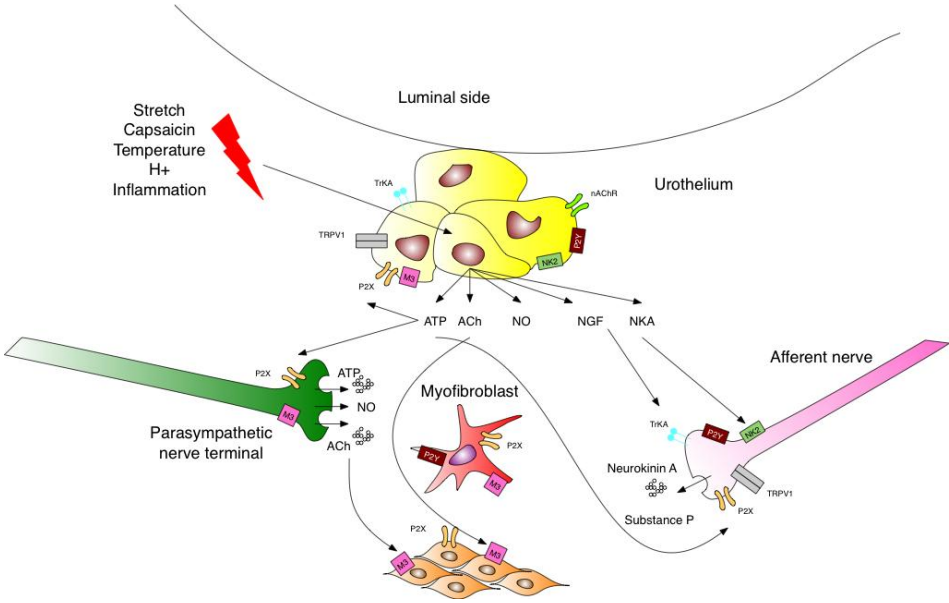
Variables (series No.)	Mean (SD)* Control	Mean (SD)* CPPS	p Value†
Perineum:			
Av peak COVAS (1)	29.5 (17.8)	37.4 (18.4)	0.041
Av peak COVAS (2)	29.7 (21.6)	38.8 (19.4)	0.037
Av time to peak COVAS (1)	2.6 (0.7)	2.9 (0.5)	0.017
Av time to peak COVAS (2)	2.5 (0.6)	2.8 (0.5)	0.003
Thigh:			
Av peak COVAS (1)	30.4 (20.0)	35.7 (21.0)	0.230
Av peak COVAS (2)	28.5 (21.7)	30.5 (18.0)	0.620
Av time to peak COVAS (1)	2.9 (0.5)	3.2 (0.8)	0.032
Av time to peak COVAS (2)	2.7 (0.6)	3.1 (0.7)	0.023

Pain scale 0 to 100 (0, no heat sensation to 100, most intense heat sensation imaginable). Time measured in seconds.

➢ This implies <u>altered sensation in the perineum</u> compared with healthy controls similar to other chronic pain syndromes.

Peripheral Sensitisation in Bladder Pain Syndrome

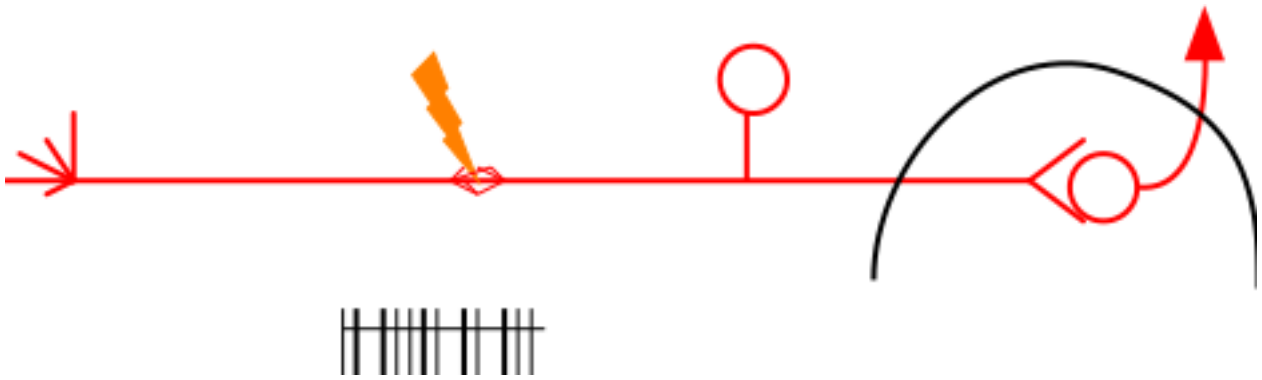
- Changes in chemical communication between urothelium and capsaicin sensitive C-fibre afferents may be responsible for afferent sensitization
  - ATP release from urothelium excites sensory nerves via $P2X_{2/3}$ receptors
  - Upregulation of different urothelial receptors
  - Prostaglandins from urothelium trigger hyperalgesia through changes in voltage gated channels on afferent nerves
- Experimental models
  - NGF expression is enhanced in rats with experimental cystitis
  - Low-threshold A-type K+ current controlling excitability in afferent neurons is reduced in experimental cystitis in rats or feline interstitial cystitis
- Enhanced signalling my trigger painful sensations



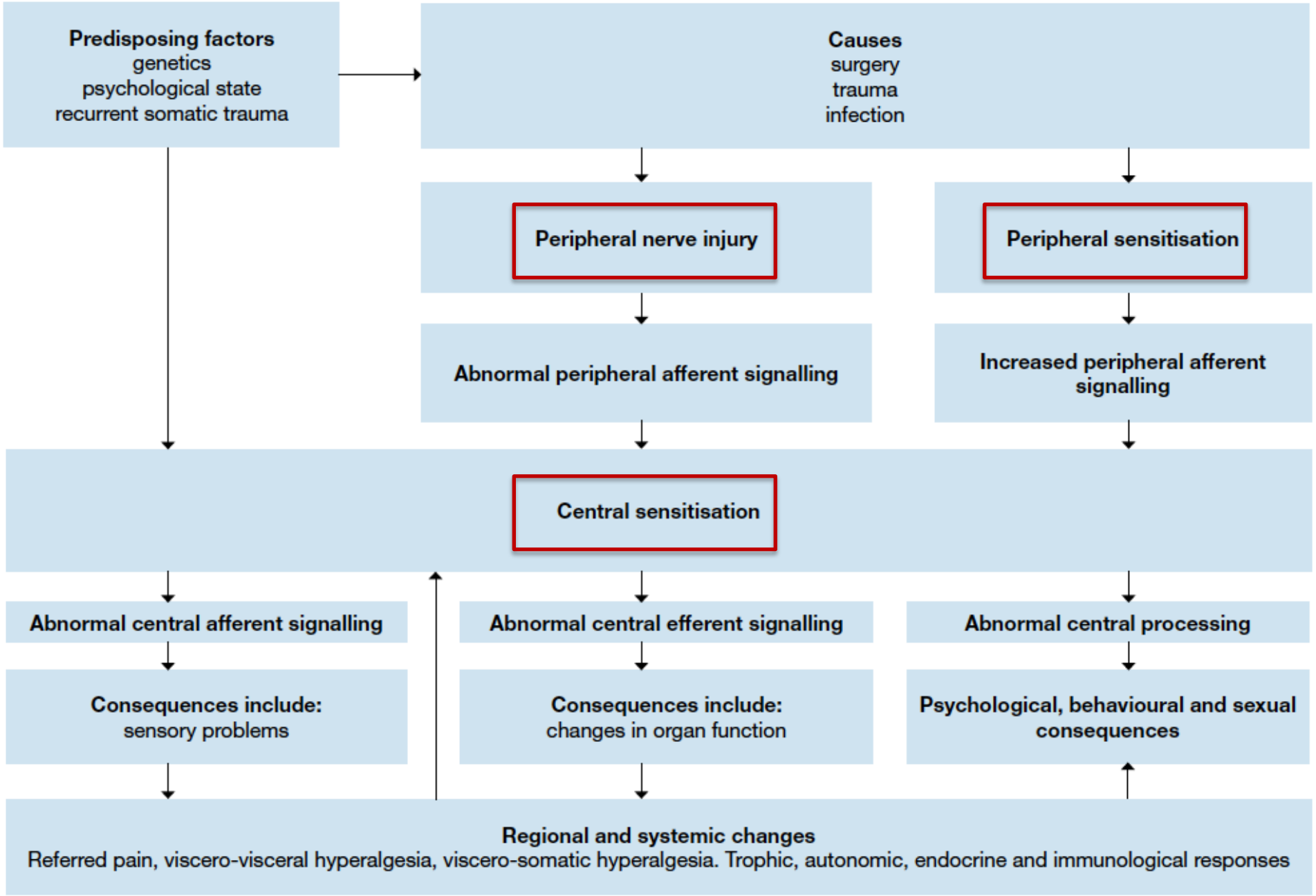
Sun Y, et al. J Urol 2001;166:1951–1956
Sculptoreanu A, et al. J Pharmacol Exper Therap 2004;310:159–168

Neuropathic Pain

Damage to peripheral nerve may change its properties

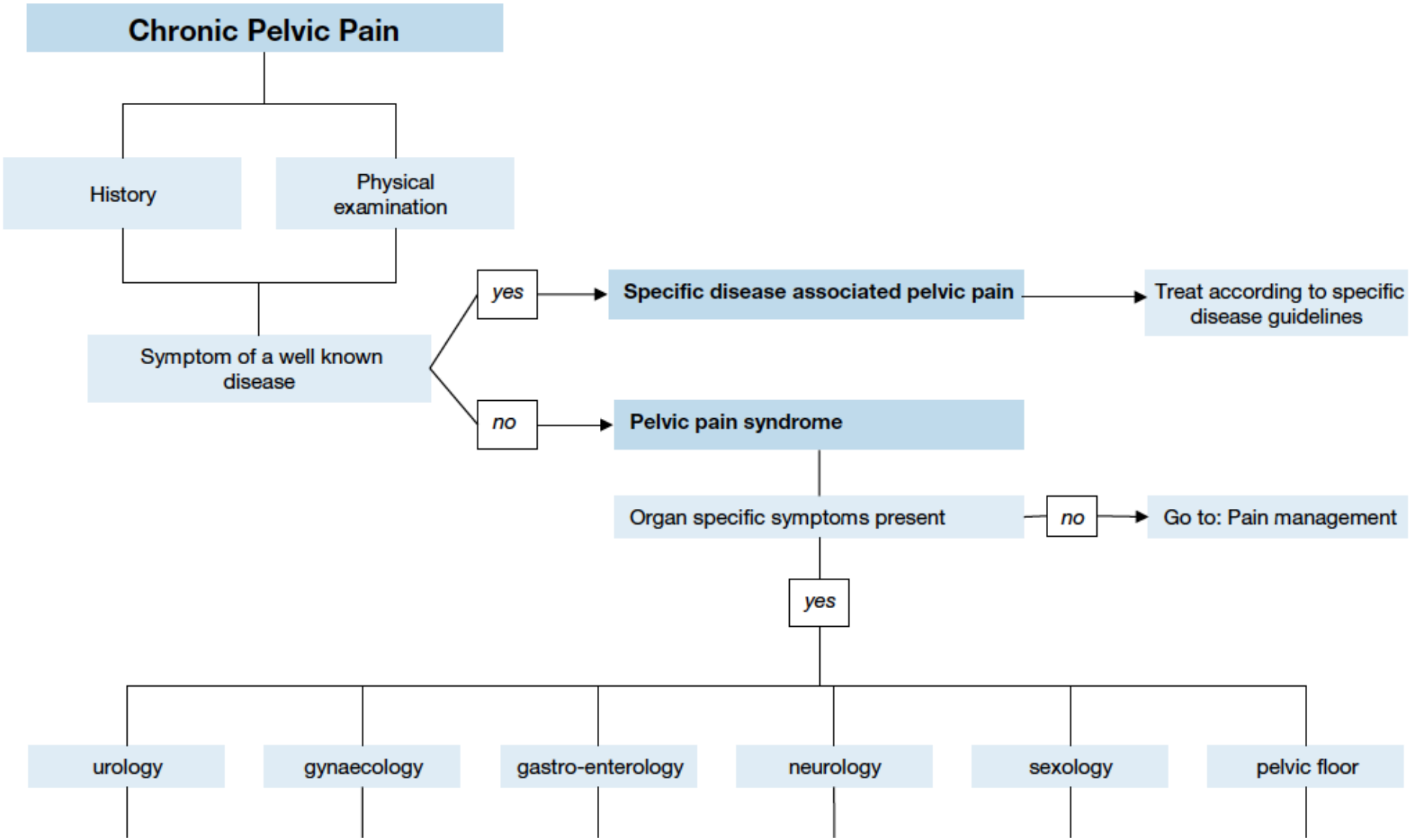


Changes in Na+ and K+ channels
➔Overexcitability and spontaneous activity
➔Hyperalgesia and continuous pain



Engeler D, Baranowski AP, Elneil S, Hughes J, Messelink EJ,

Algorithm



Engeler D, Baranowski AP, Elneil S, Hughes J, Messelink EJ,

„Phenotyping“ UPOINT

Phenotyping	Assessment
Urology	Urinary flow, micturition diary, cystoscopy, ultrasound, uroflowmetry
Psychology	History of negative experiences, important loss, coping mechanism, depression
Organ specific	Ask for gynaecological, gastro-intestinal, ano-rectal, sexological complaints Gynaecological examination, rectal examination
Infection	Semen culture and urine culture, vaginal swab, stool culture
Neurological	Ask for neurological complaints (sensory loss, dysaesthesia). Neurological testing during physical examination: sensory problems, sacral reflexes and muscular function
Tender muscle	Palpation of the pelvic floor muscles, the abdominal muscles and the gluteal muscles

Nickel JC, et al. J Urol. 2009; 182:155-60.

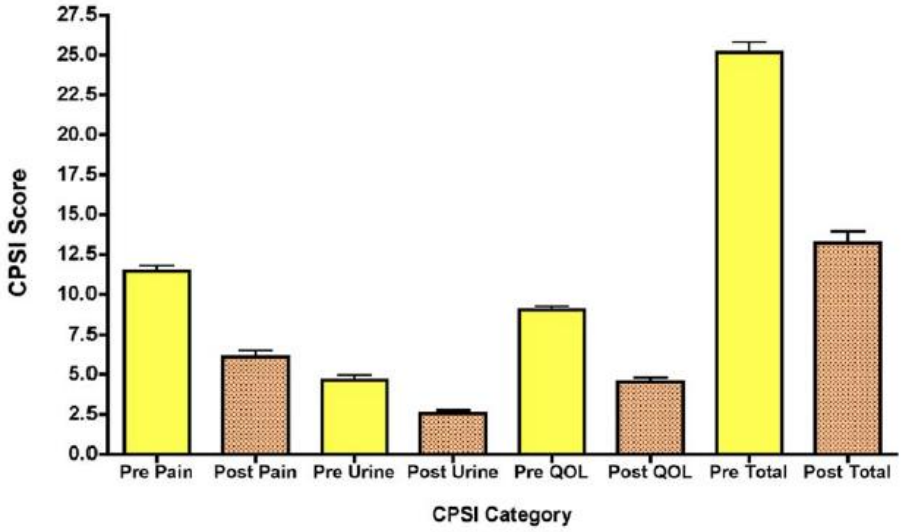
Differences in Visceral and Somatic Pain

	Visceral pain	Somatic pain
Effective painful stimuli	Stretching and distension, producing poorly localised pain.	Mechanical, thermal, chemical and electrical stimuli, producing well localised pain.
Summation	Widespread stimulation produces significantly magnified pain.	Widespread stimulation produces a modest increase in pain.
Autonomic involvement	Autonomic features (e.g., nausea and sweating) frequently present.	Autonomic features less frequent.
Referred pain	Pain perceived at a site distant to the cause of the pain is common.	Pain is relatively well localised but well recognised.
Referred hyperalgesia	Referred cutaneous and muscle hyperalgesia is common, as is involvement of other visceral organs.	Hyperalgesia tends to be localised.
Innervation	Low density, unmyelinated C fibres and thinly myelinated A∂ fibres.	Dense innervation with a wide range of nerve fibres.
Primary afferent physiology	Intensity coding. As stimulation increases afferent firing increases with an increase in sensation and ultimately pain.	Two fibre coding. Separate fibres for pain and normal sensation.
Silent afferents	50-90% of visceral afferents are silent until the time they are switched on. These fibres are very important in the central sensitisation process.	Silent afferents present, but form a lower percentage.

EAU Guidelines on Chronic Pelvic Pain 2012

Multimodal Therapy

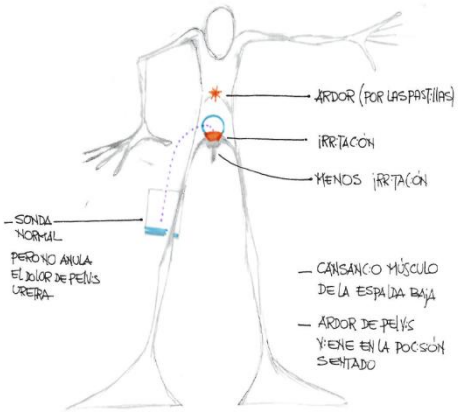
- There is no single standard therapy for most of the pelvic pain syndromes
- Multimodal phenotype directed therapy possibly more successful



For each pair, $p<0.0001$

Change in CPSI subscores and total score before and after therapy.

84% improved



Take home messages

- Mechanisms of CPPS are well defined and include aspects of neuroplasticity and neuropathic pain
- „Pain as a disease“
- Phenotyping for treatment selection
- Combined and phenotypically directed therapies for CPPS probably more successful than monotherapies


HI