



Sanse-motoriske implikationer af muskelsmeketale smerter: Fokus på kroniske viscerale smerter!

Når
bevægelse
gør ondt

Stop op!
Forstå!
Gør noget!

**GLOBALT SMERTE-ÅR MED FOKUS
PÅ SMERTER I MUSKLER OG LED**

OKTOBER 2009 – OKTOBER 2010

INTERNATIONAL ASSOCIATION FOR THE STUDY OF PAIN®

Lars Arendt-Nielsen
Aalborg University
Aalborg, Denmark
LAN@HST.AAU.DK



Visceral pain conditions

Inflammatory related conditions

Pancreatitis
Cholecystitis
Diverticulitis
Appendicitis
Peritonitis
Crohn's disease
Gastroesophageal reflux disease (GERD)

Functional visceral pain disorders

IBS
Non-ulcer dyspepsia
Non-Cardiac Chest Pain

Ileus

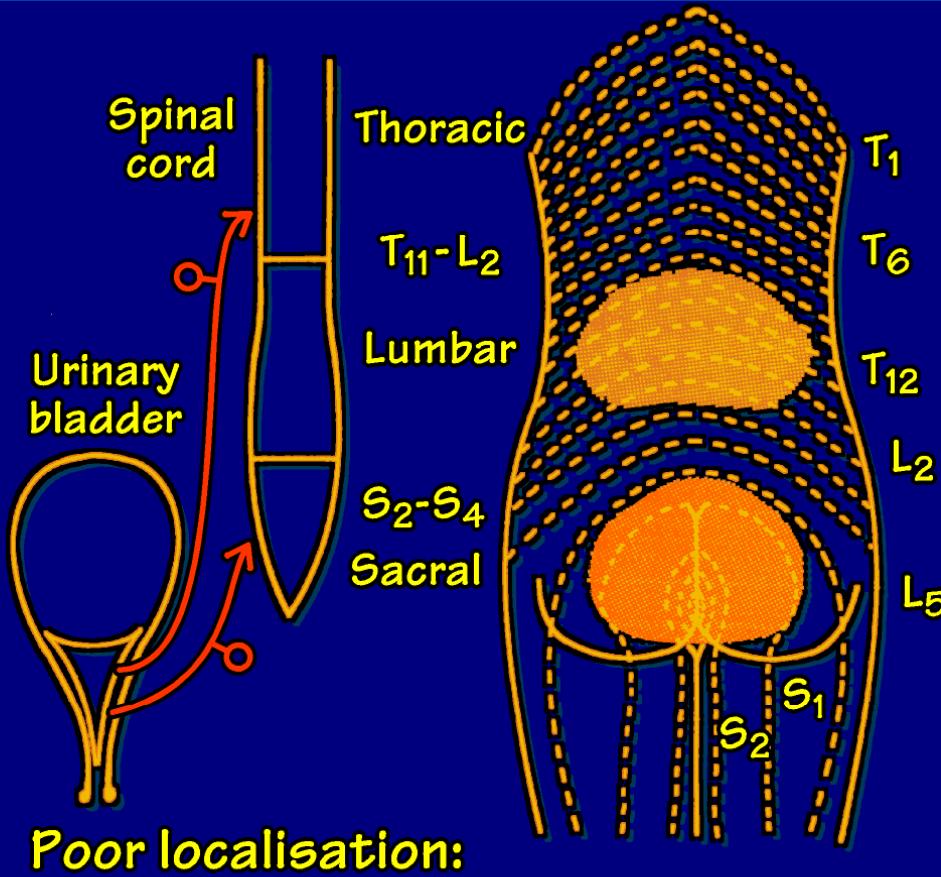
Gynaecological pain
Endometriosis
Dysmenorrhoea
Interstitial cystitis (pelvic pain syndrome)

Urological pain
Renal/urethral calculosis
~~Neuropathic visceral pain~~
Surgery/trauma/birth
Post operative pain
Major surgery
Hypoperfusion/ischemia
Visceral cancer pain

*No pain from liver, lungs, kidneys



Referred Visceral Pain



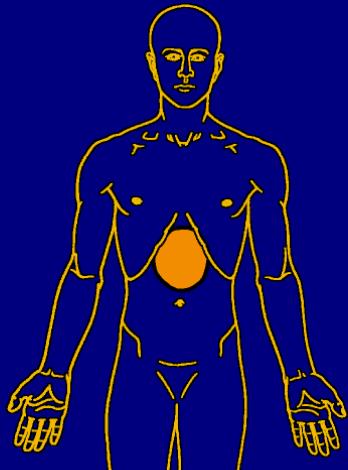
Poor localisation:

1. Projection to multiple segments
2. Low innervation density
3. Scattered spinal ramification

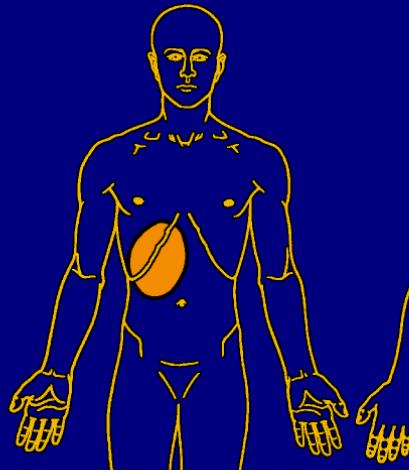


Visceral Pain

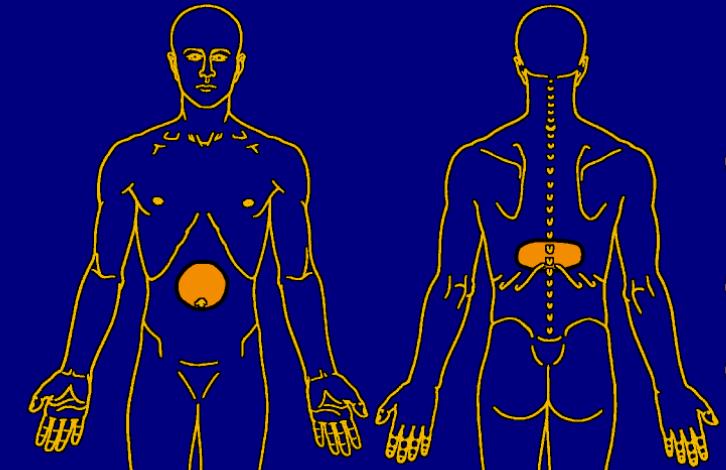
Gastric ulcer



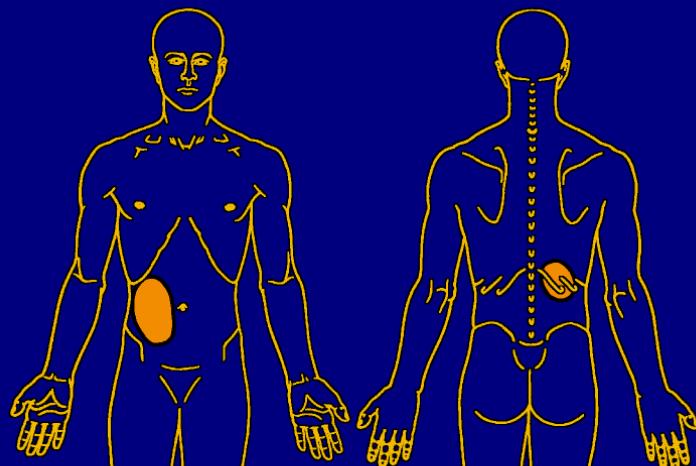
Biliary pain



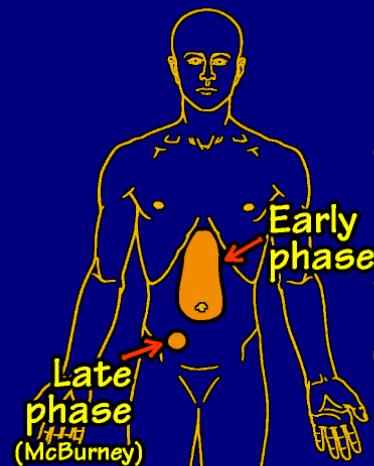
Pancreatic pain



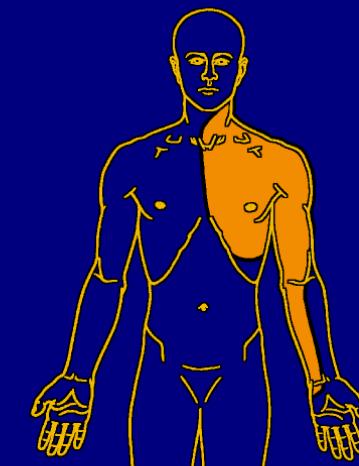
Ureter stone



Appendicitis



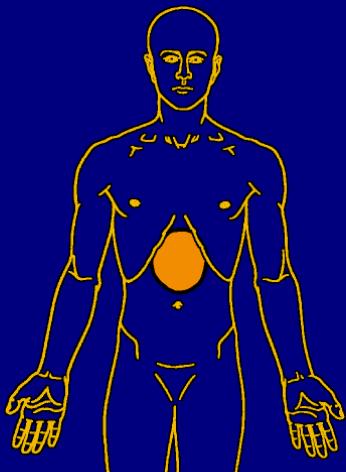
Angina pain



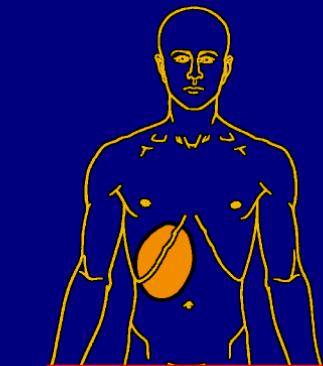


Visceral Pain

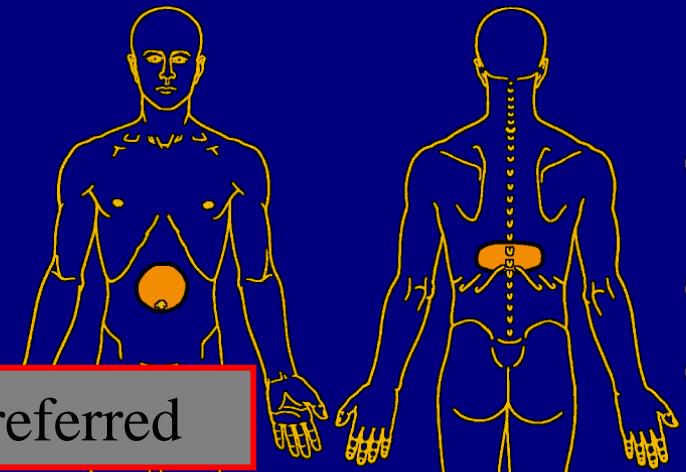
Gastric ulcer



Biliary pain

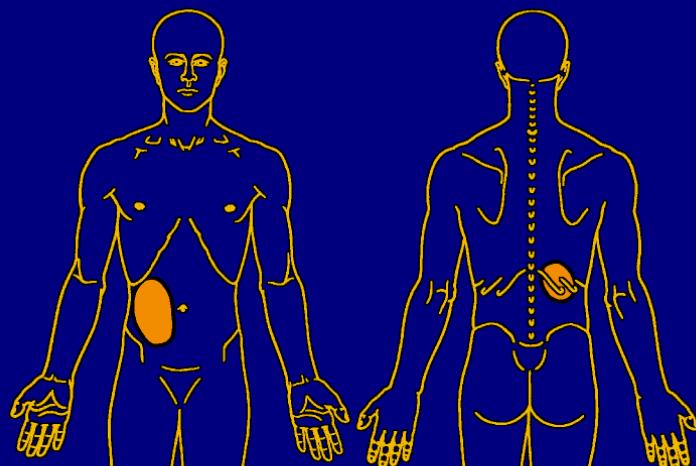


Pancreatic pain

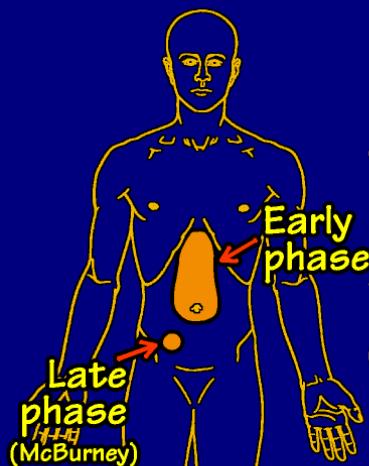


Visceral pain is diffuse and referred

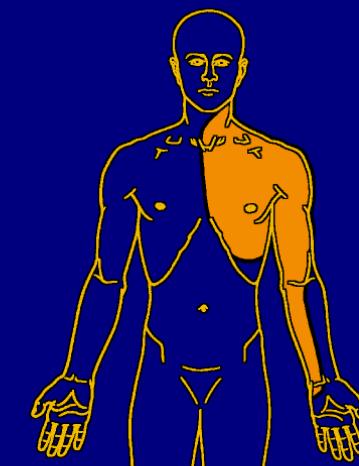
Ureter stone



Appendicitis



Angina pain

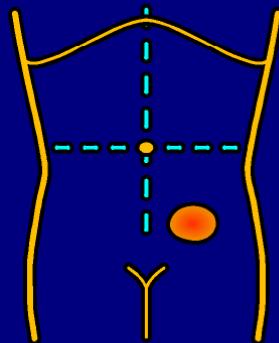




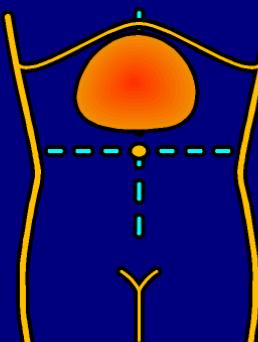
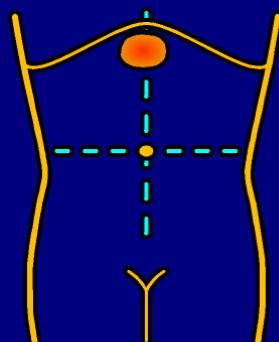
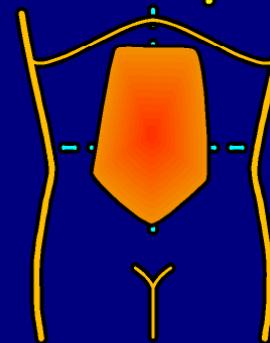
Visceral Pain

Expansion of referred pain areas

Acute pain



Chronic pain



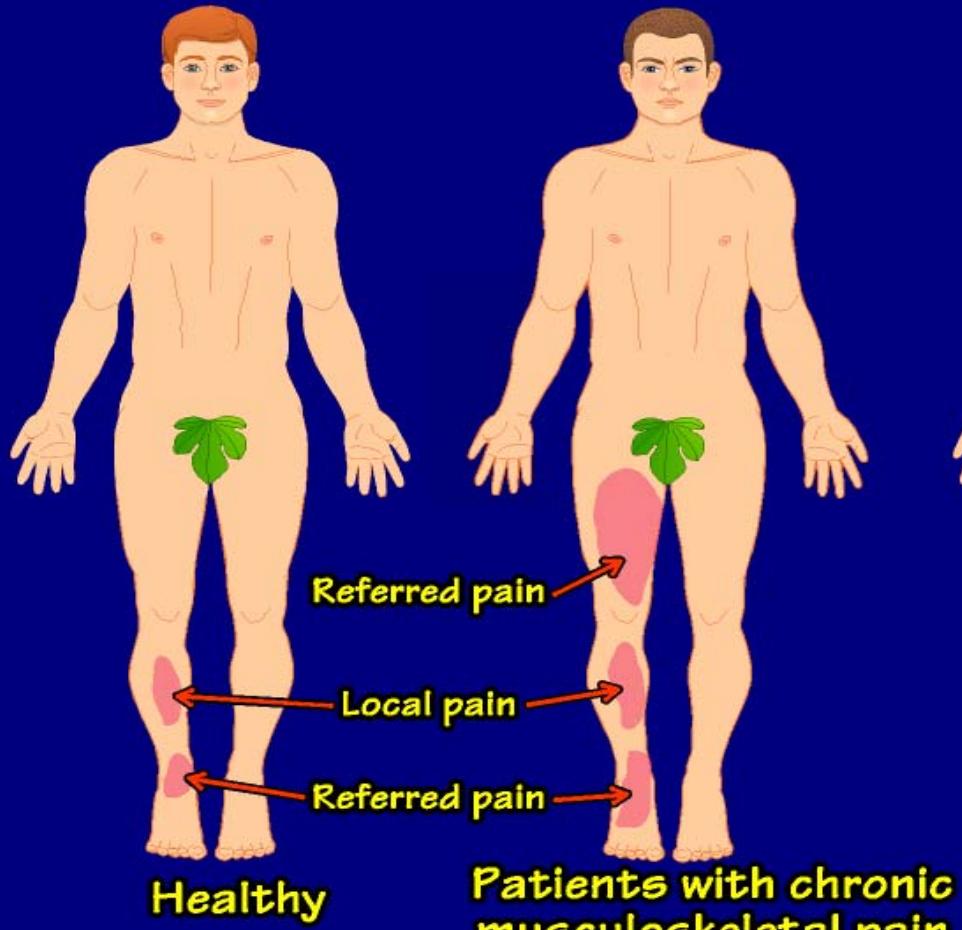
Intermittent symptoms
related to physiological events

Constant symptoms

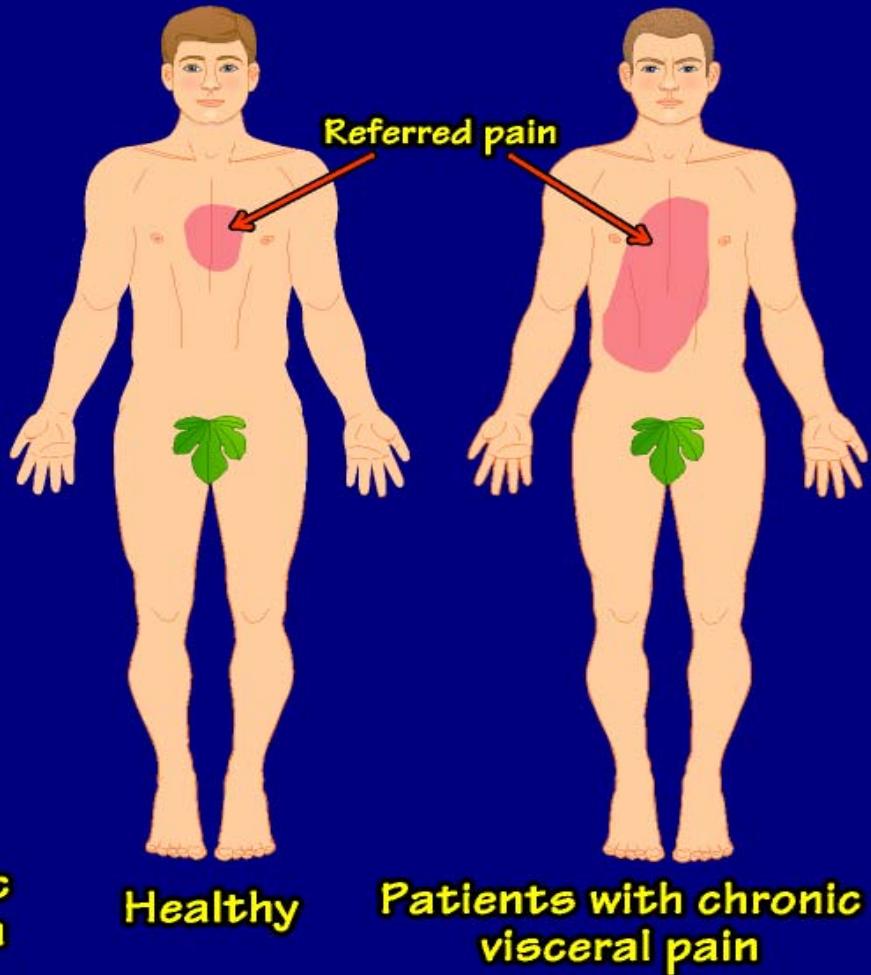


Enlarged Referred Pain Areas

Muscle stimulation



Esophageal stimulation





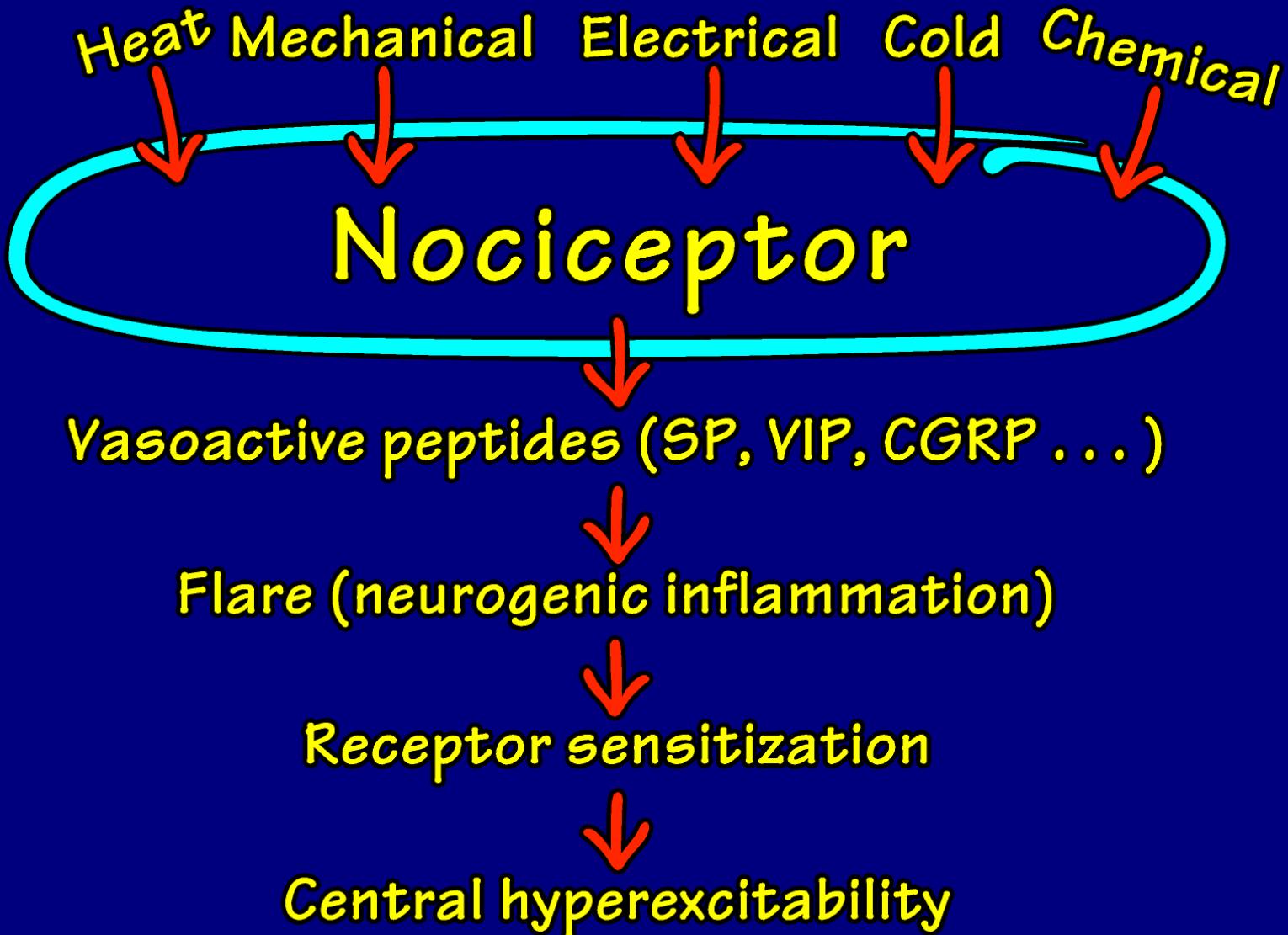
Manifestations of visceral hyperalgesia

- Visceral hyperalgesia
- Viscero-visceral convergence
 - Referred visceral hyperalgesia/allodynia
- Viscero-somatic convergence
 - Referred cutaneous hyperalgesia/allodynia
 - Referred muscle hyperalgesia/allodynia
- Somatic-somatic convergence



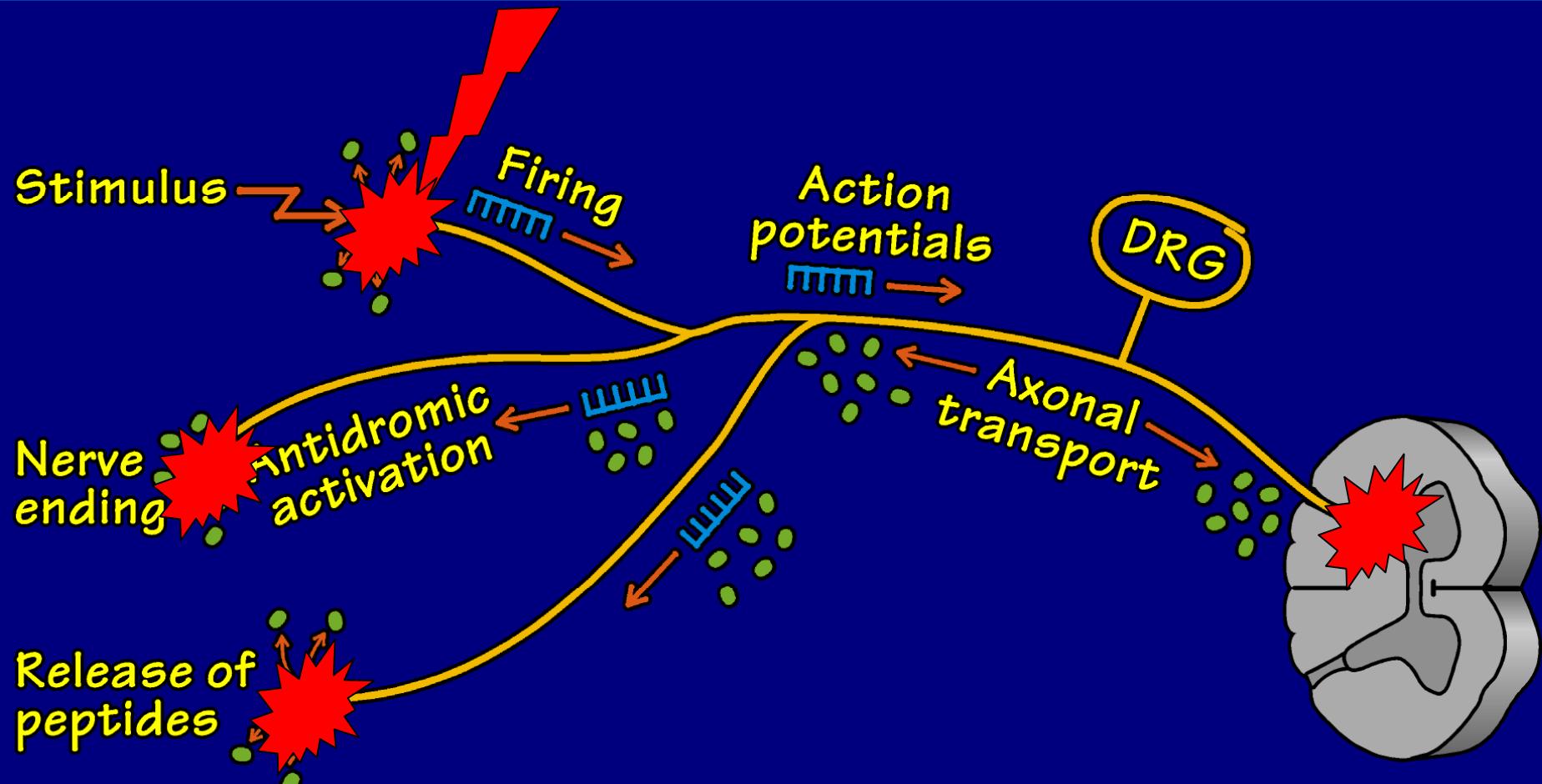
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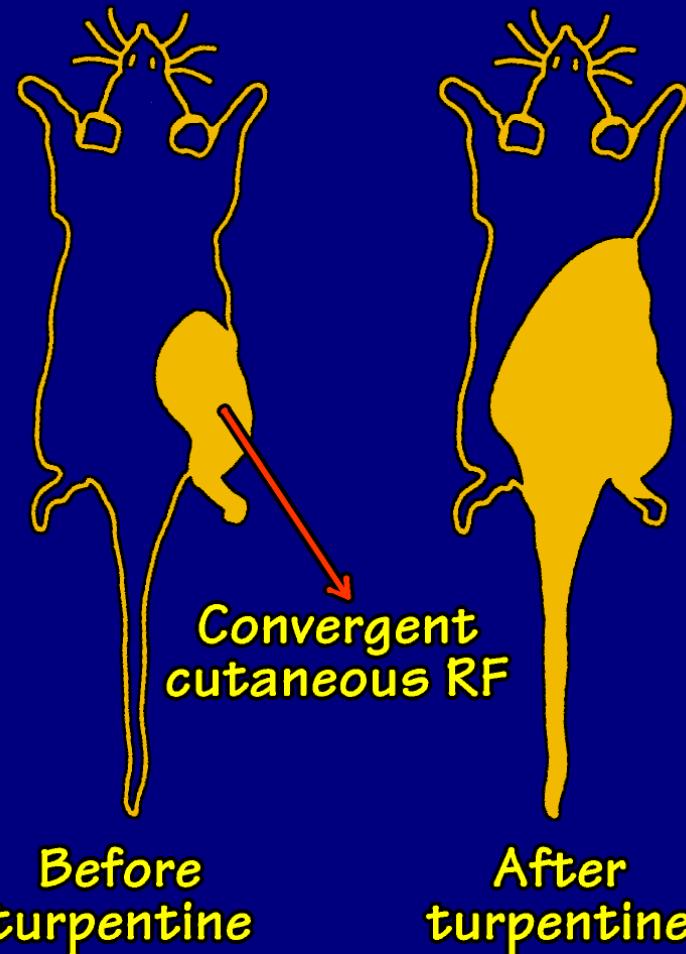
Neurogenic Inflammation



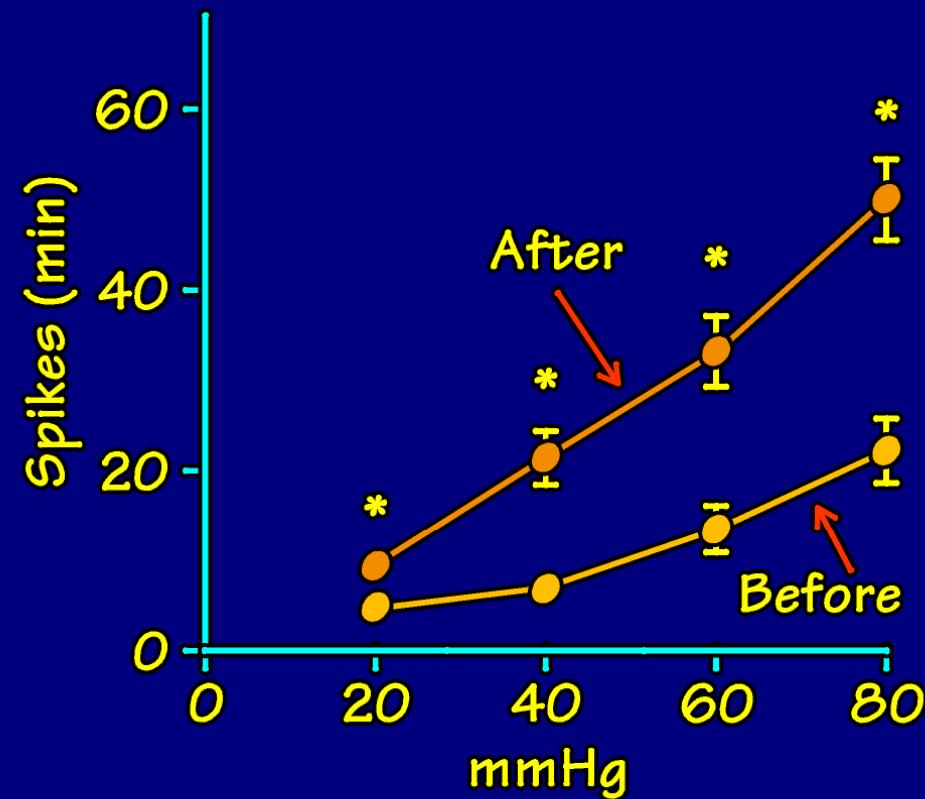


Visceral Hyperalgesia

Colorectal distension



After intracolonic mustard oil

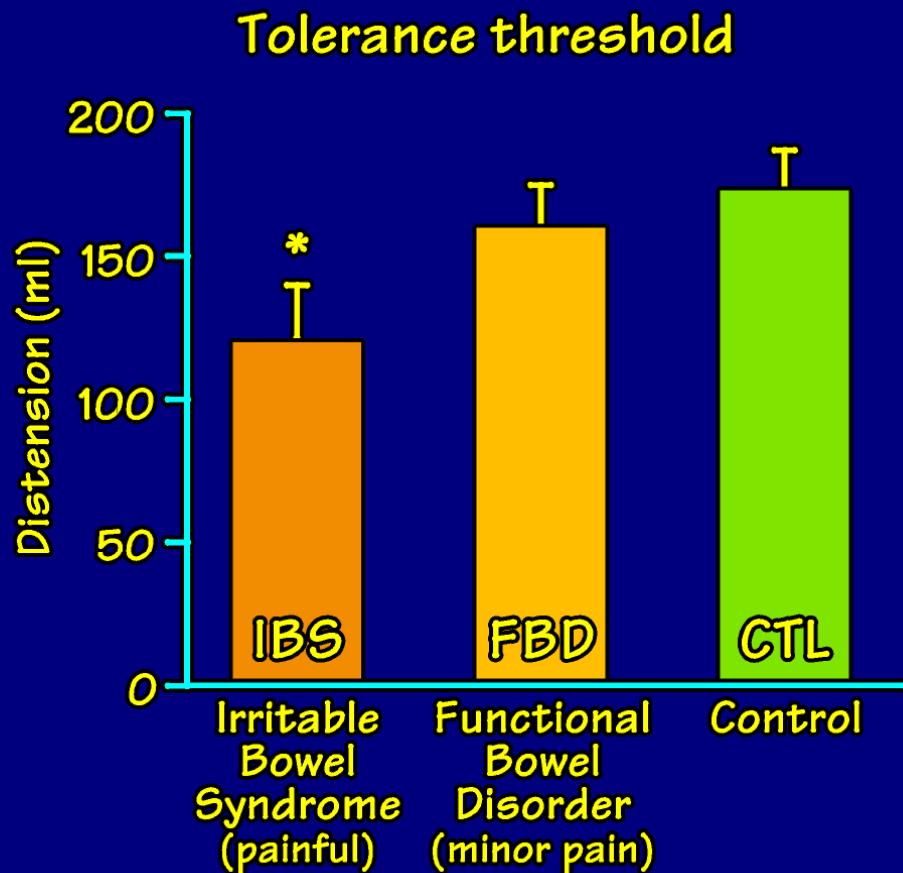


Al-Chaer et al, 1997

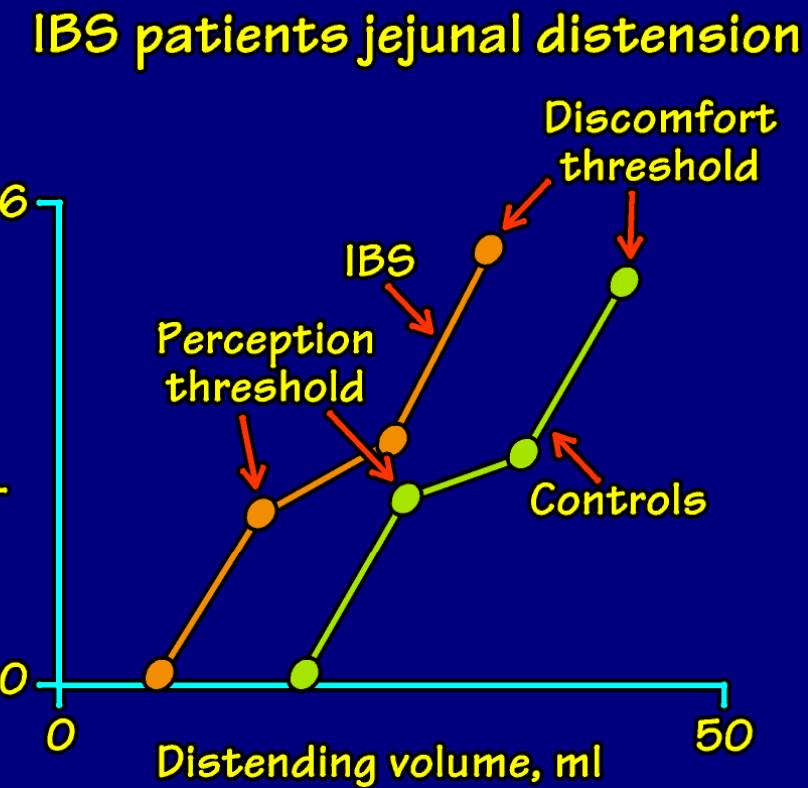


Visceral Hyperalgesia

Distension of the rectosigmoid



Whitehead et al., 1990



Accarino et al., 1995



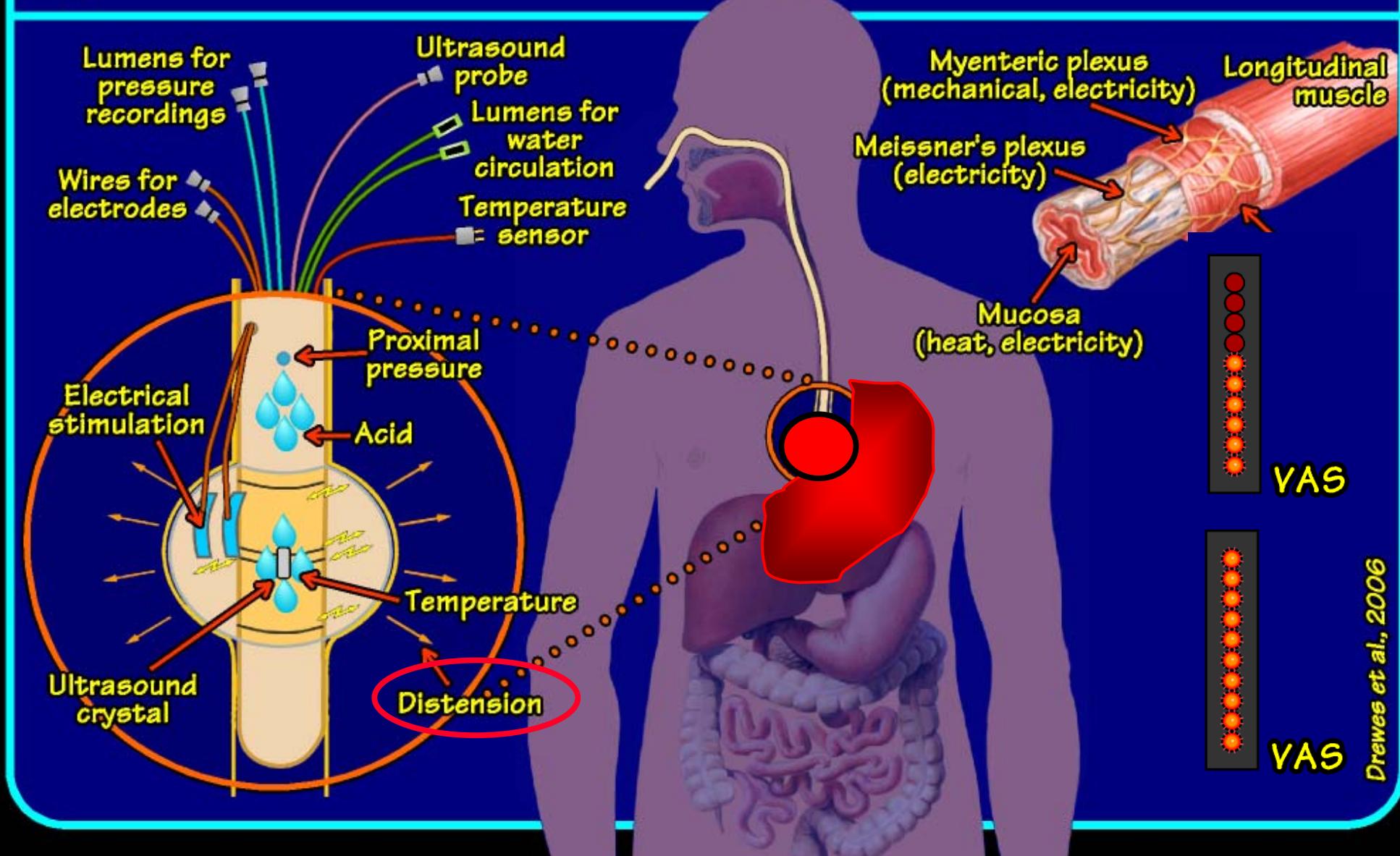
Expansion of Receptive Field

Changes in the size of a convergent, cutaneous receptive field (spinal neurons studied in dorsal horn lamina I)



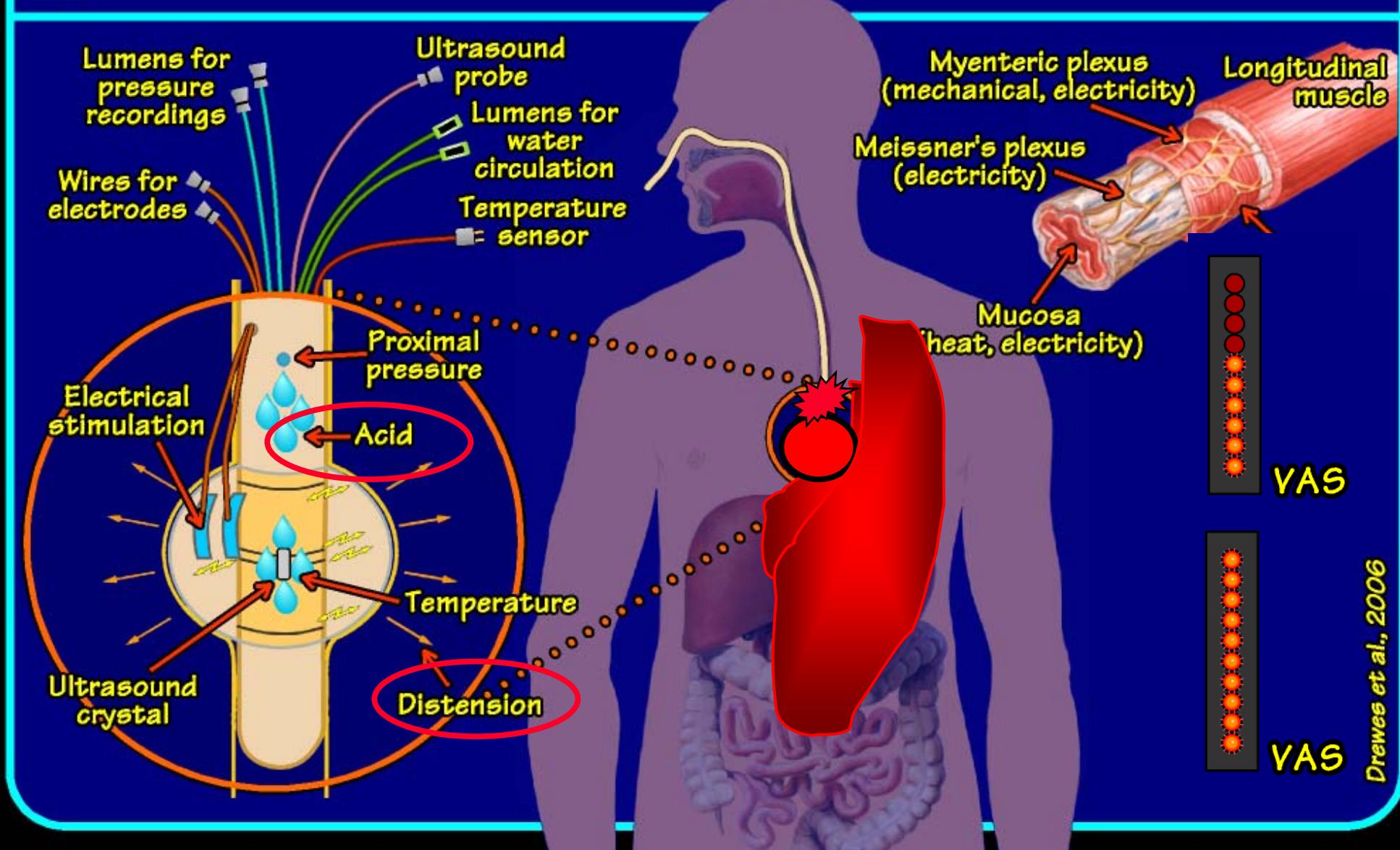


Multimodal Visceral Stimulation





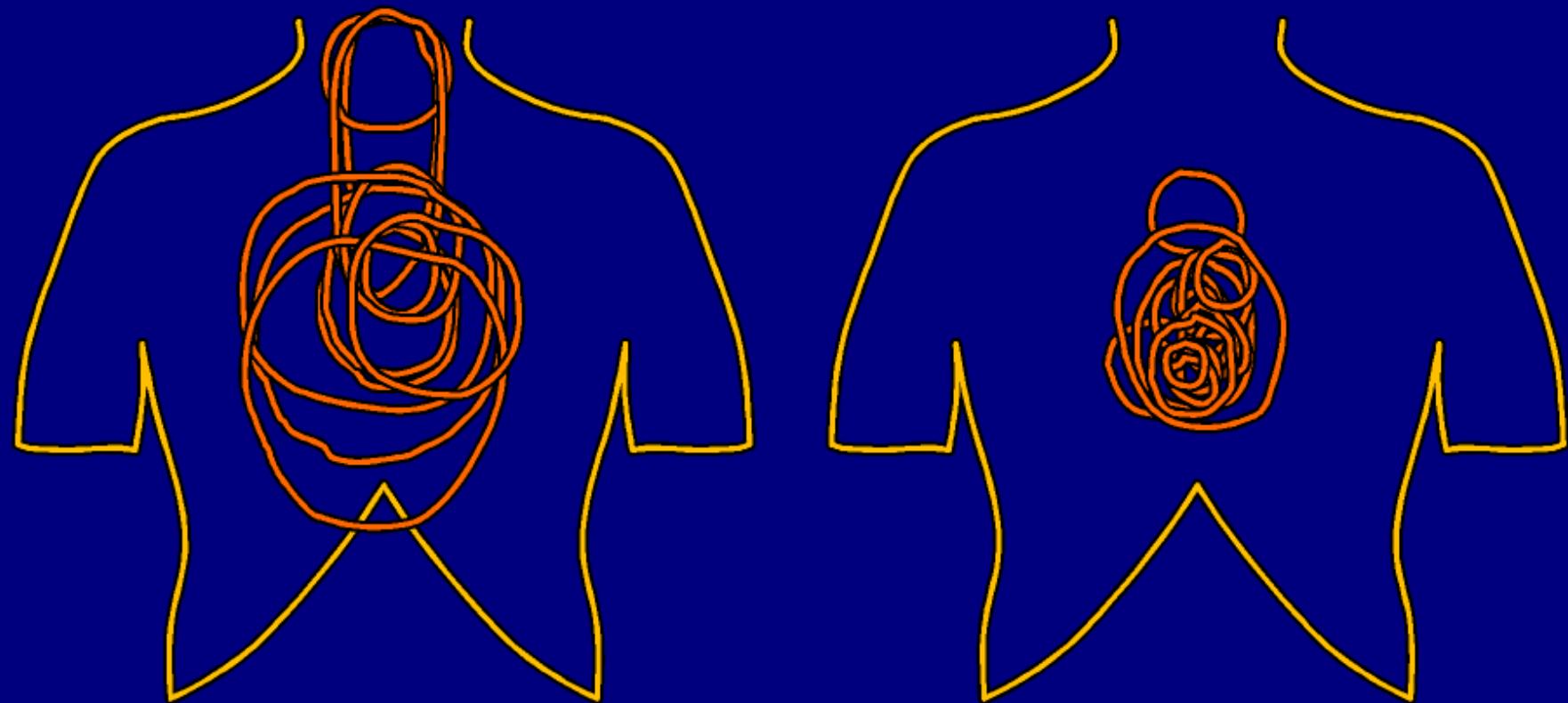
Multimodal Visceral Stimulation





Visceral Sensitisation

Distension of the esophagus (VAS = 7)



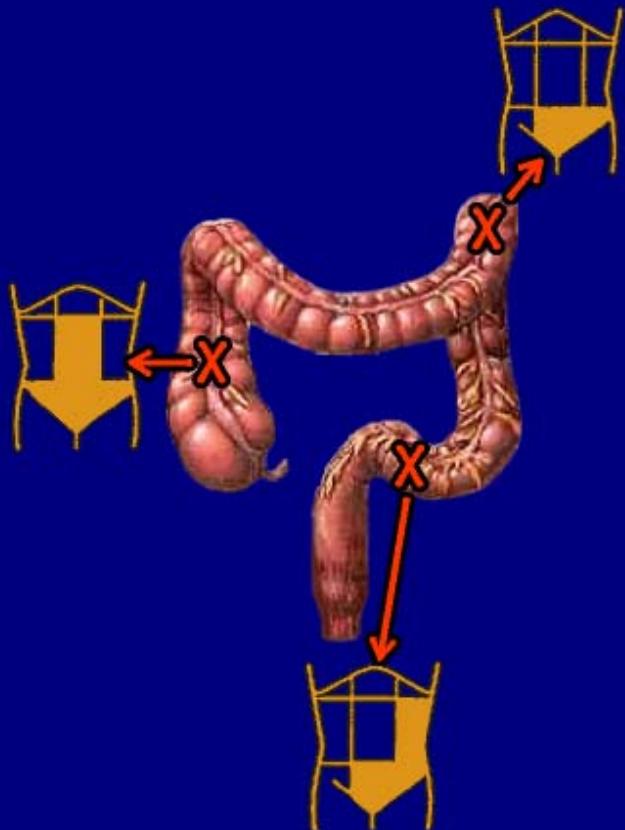
Esophagitis patients
Mean area = 49.3 cm²

Healthy controls
Mean area = 23.9 cm²

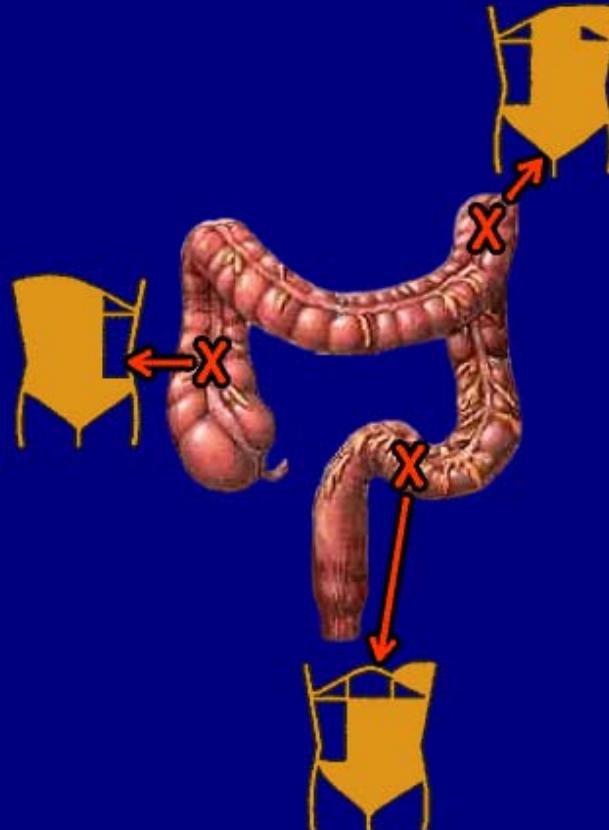


Visceral Hyperalgesia

Referred pain areas



Normal

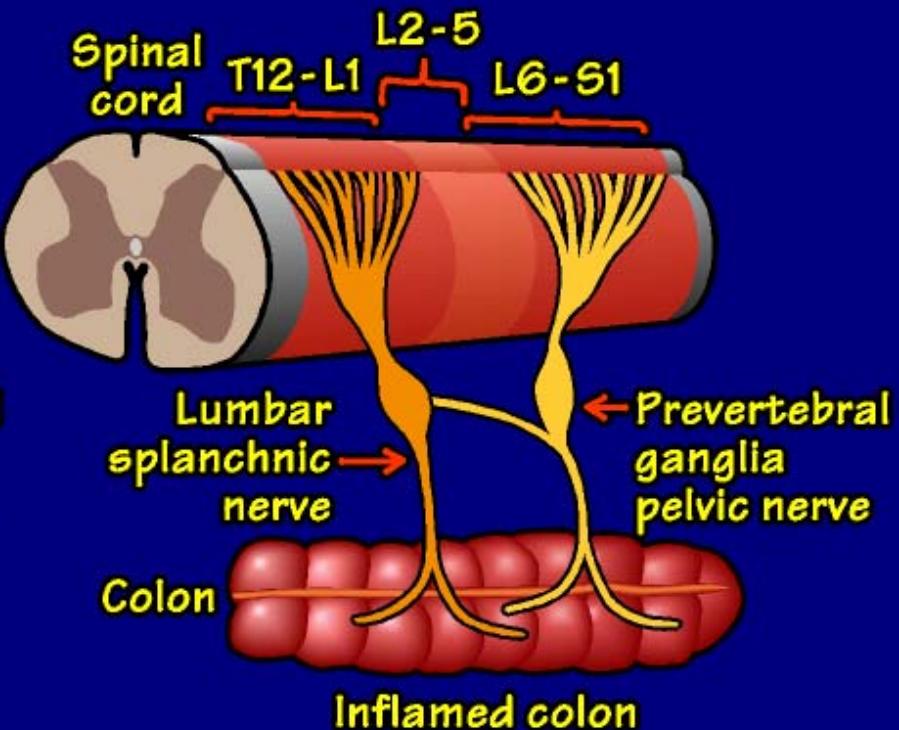
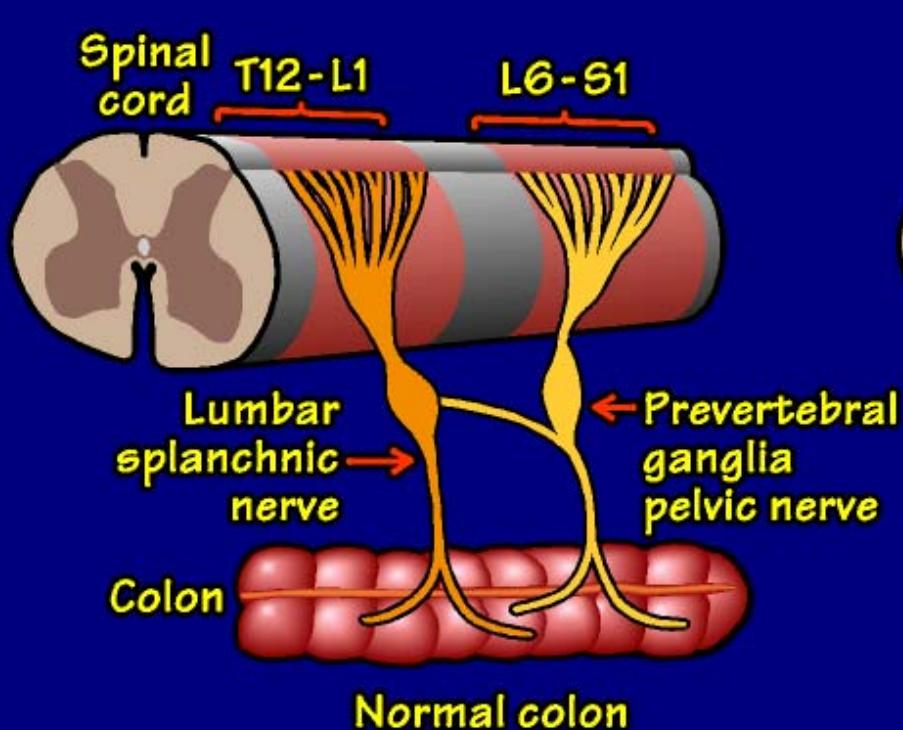


IBS patient



Expansion of Receptive Field

Increased segmental spread after colon inflammation



Visceral inflammation induced by intracolonic instillation of zymosan (3 hours) Honoré et al., 2002
Serosal, muscular and mucosal receptors in rat colon are sensitized differently Gebhart, 2004



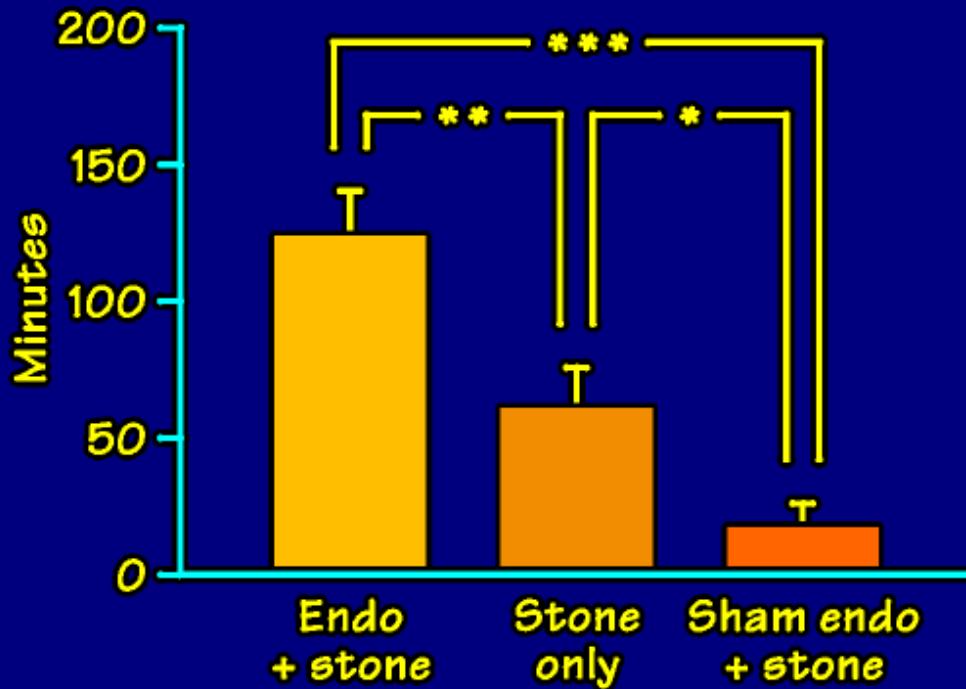
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Visceral Hyperalgesia

Duration of spontaneous “pain” behaviour responses
after 1 or 2 visceral pain conditions

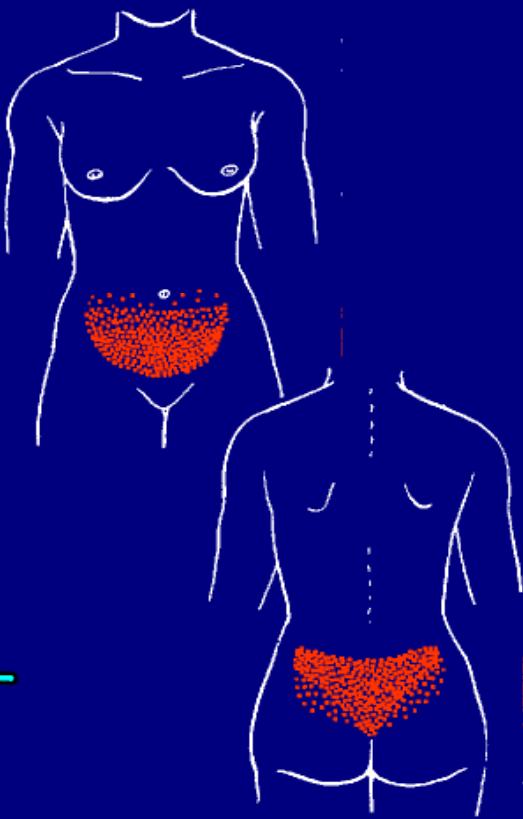
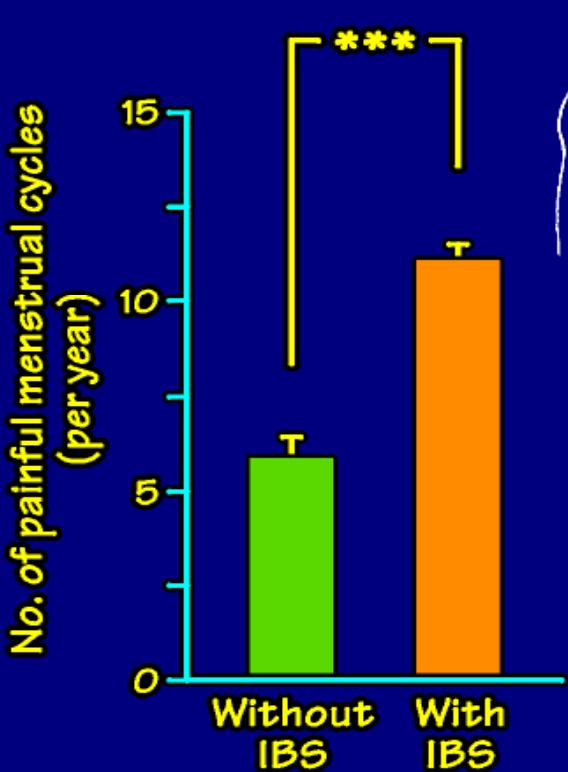


Rats with experimental endometriosis (autotransplantation of small pieces of uterus on ovary and abdominal wall) and/or experimental urinary calculosis (artificial stone in one ureter)

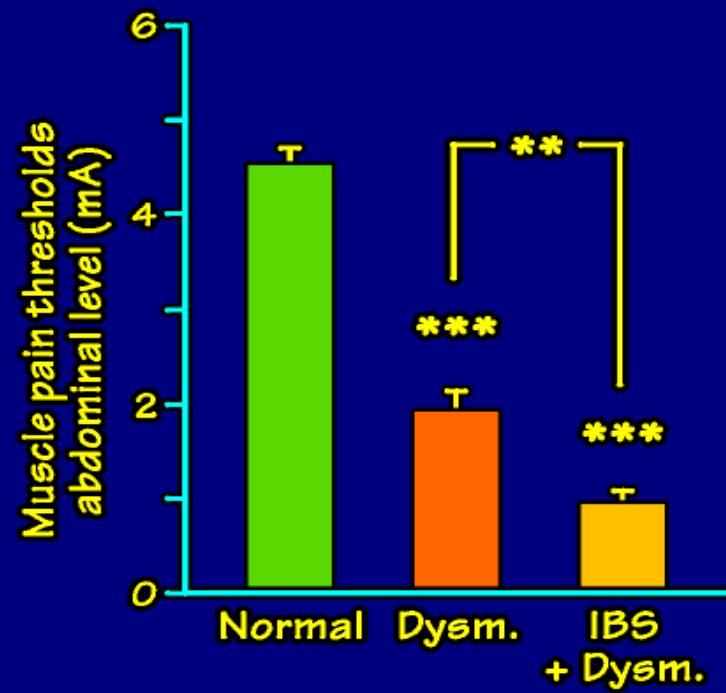


IBS + Dysmenorrhea

Spontaneous pain
from dysmenorrhea



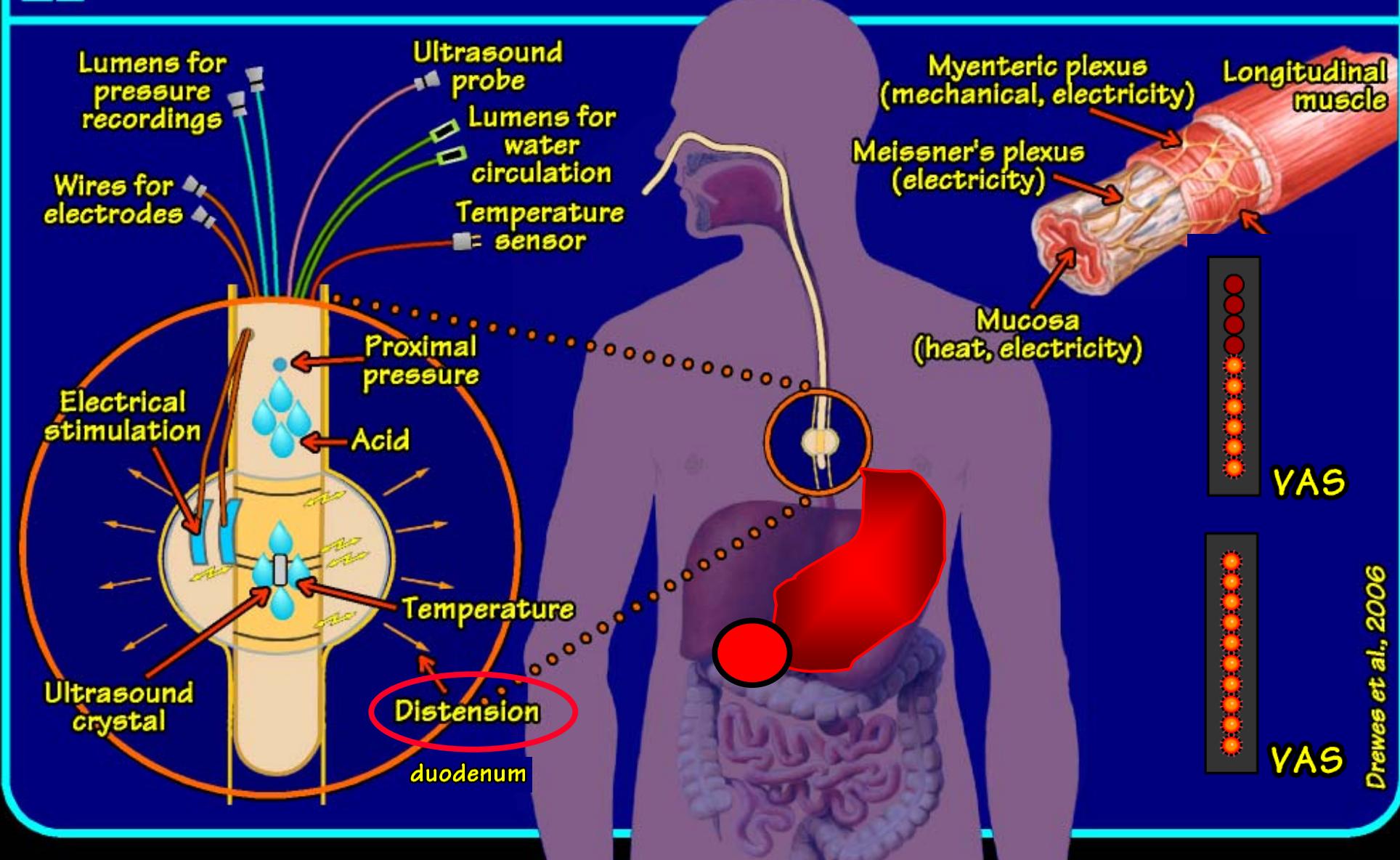
Referred hyperalgesia
from dysmenorrhea



Giamberardino et al, 2006 - unpublished data

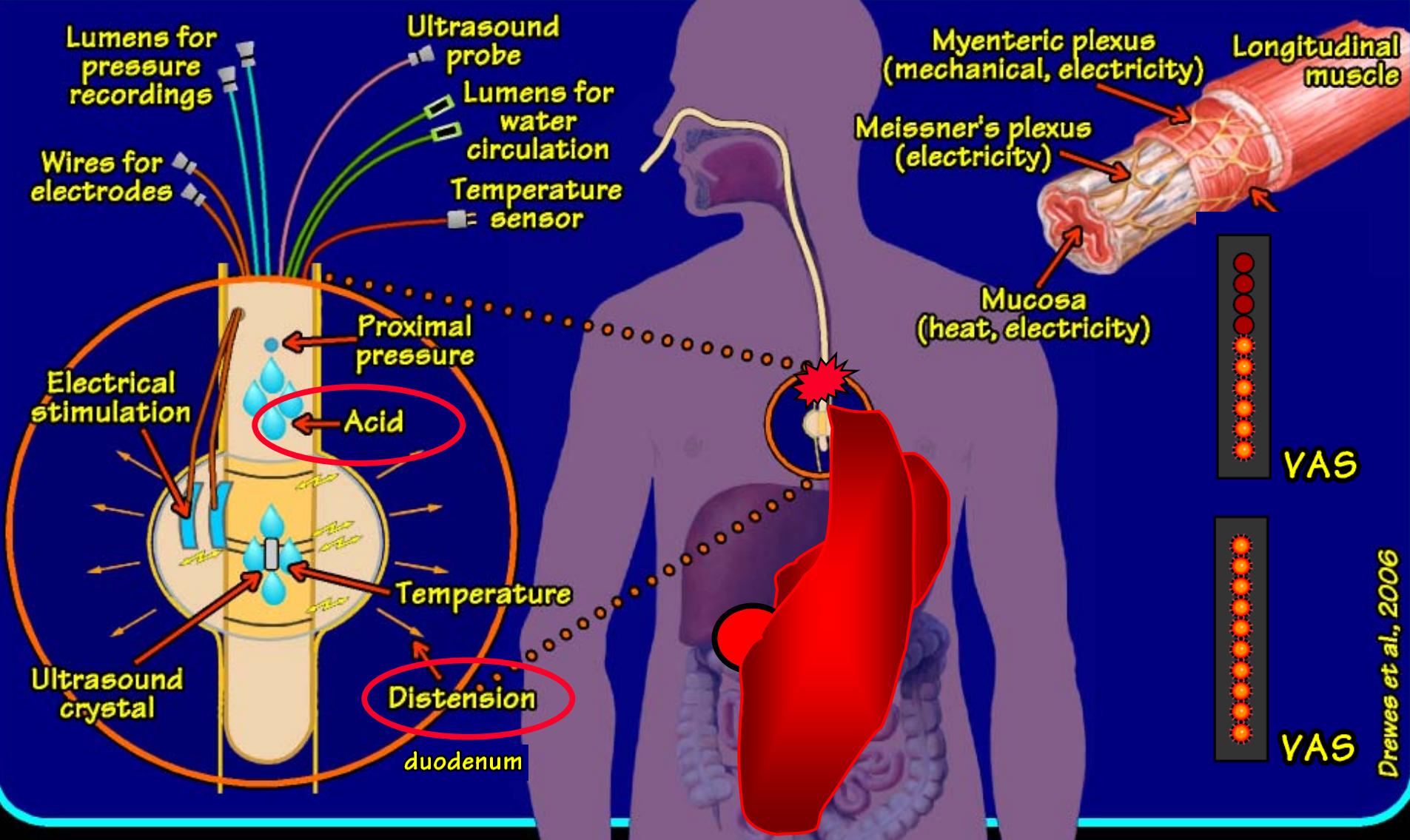


Multimodal Visceral Stimulation



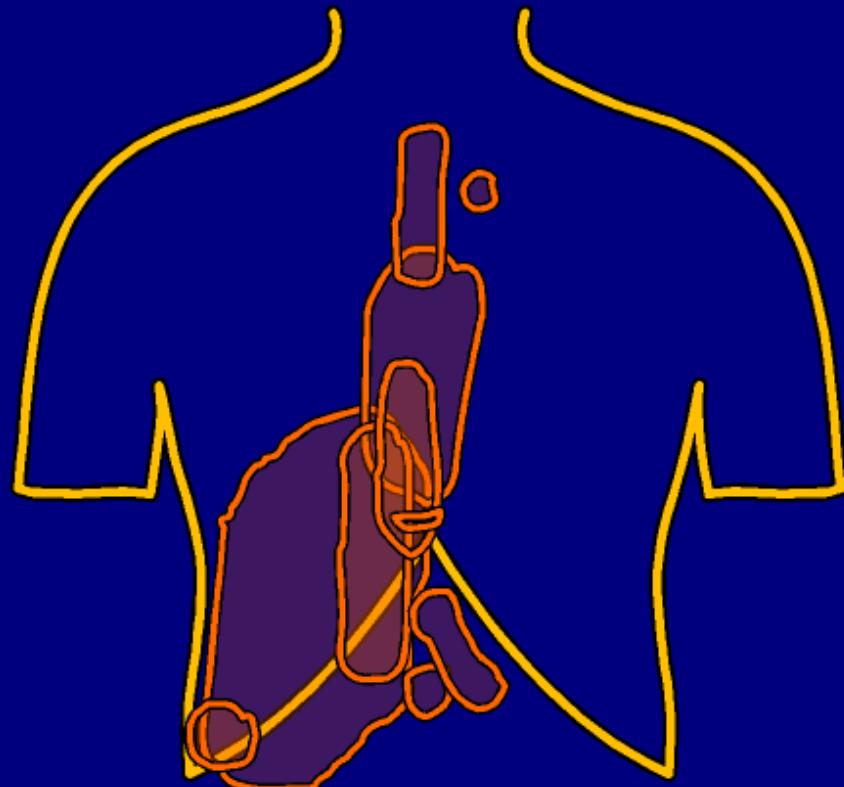


Multimodal Visceral Stimulation



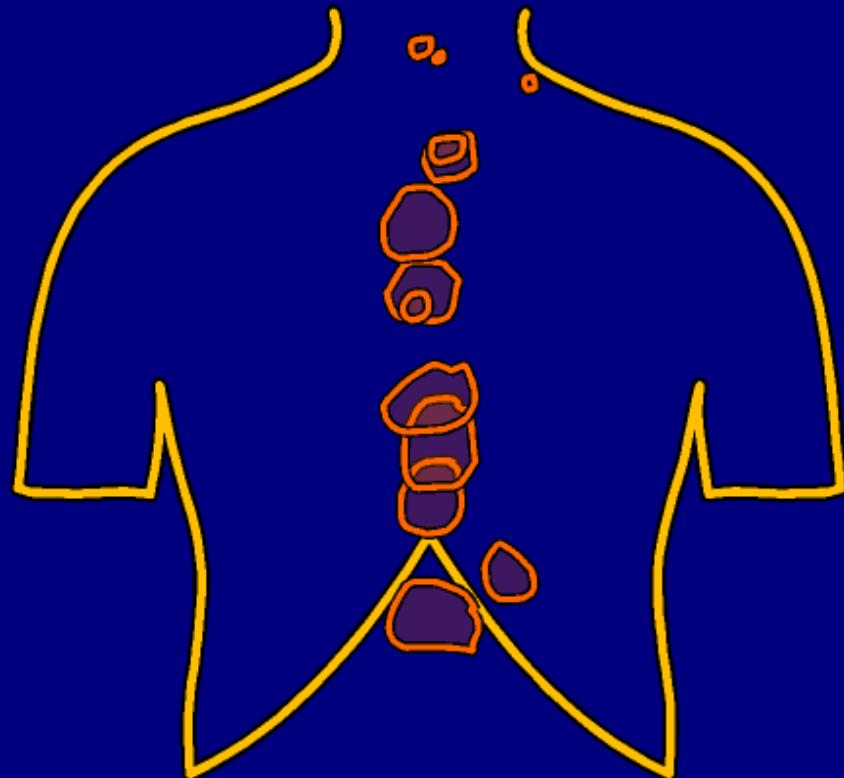


Electrical Esophageal Stimulation



Chronic pancreatitis patients
Mean area = 30.2 cm^2*

VAS=7



Healthy controls
Mean area = 6.6 cm^2



Phenomenon of symptom enhancement between different viscera which share part of their sensory innervation

- **Ischemic Heart Disease - Gallbladder Calculosis**
[Heart - Gallbladder (T5)]
- **Irritable Bowel Syndrome - Dysmenorrhea**
[Colon -Uterus (T10-L1)]
- **Dysmenorrhea - Urinary Calculosis**
[Uterus - Urinary Tract (T10-L1)]



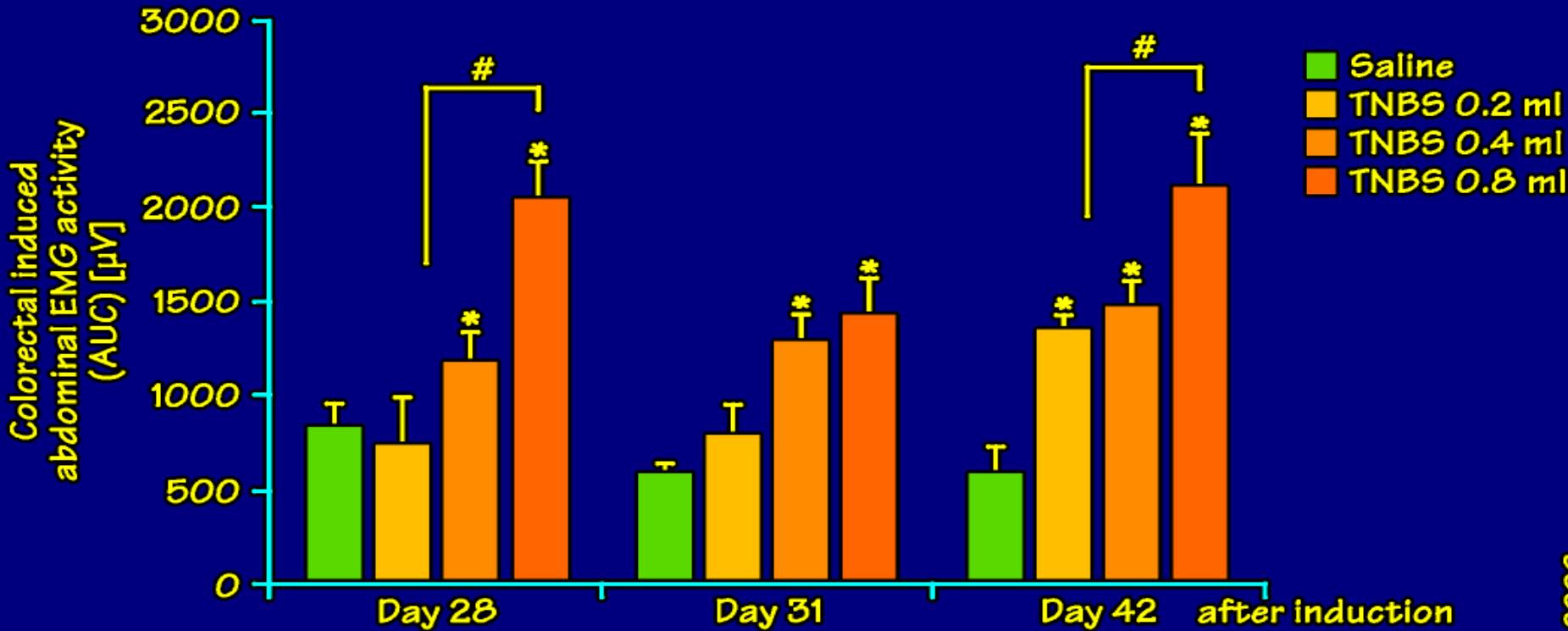
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Visceral Pain and Hyperalgesia

Transient visceral pain causes long lasting hyperalgesia

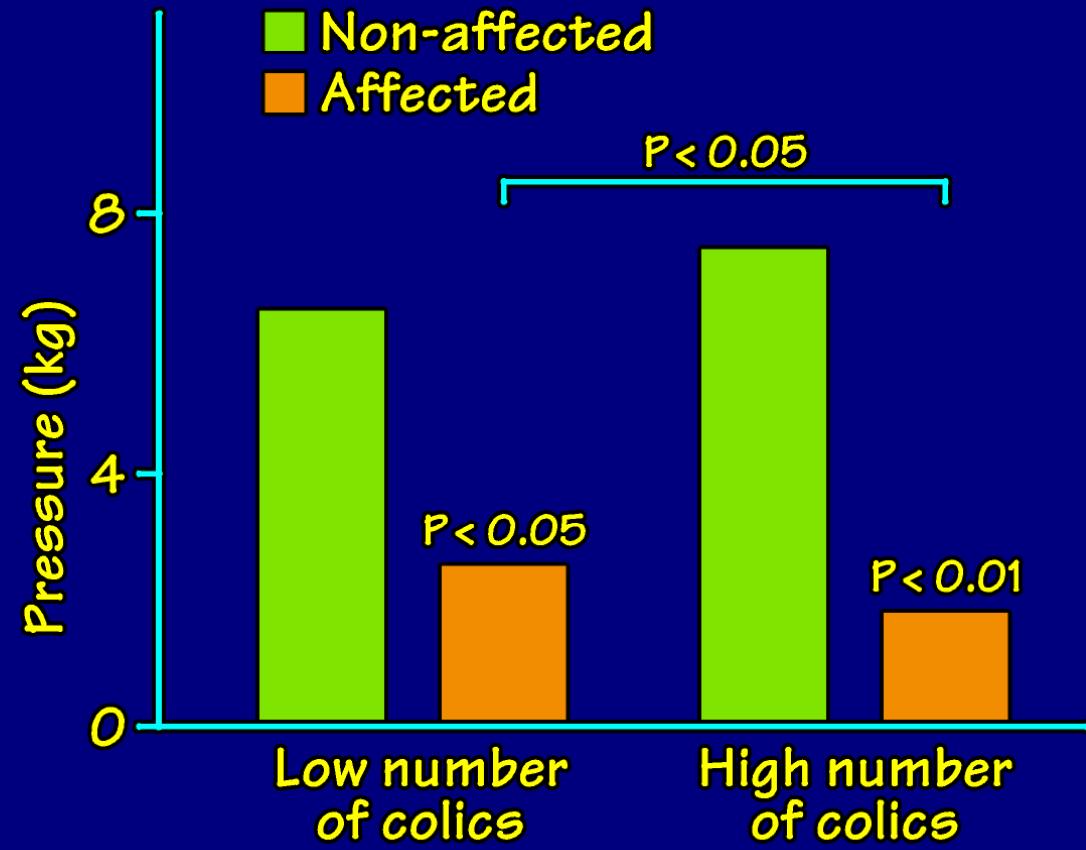
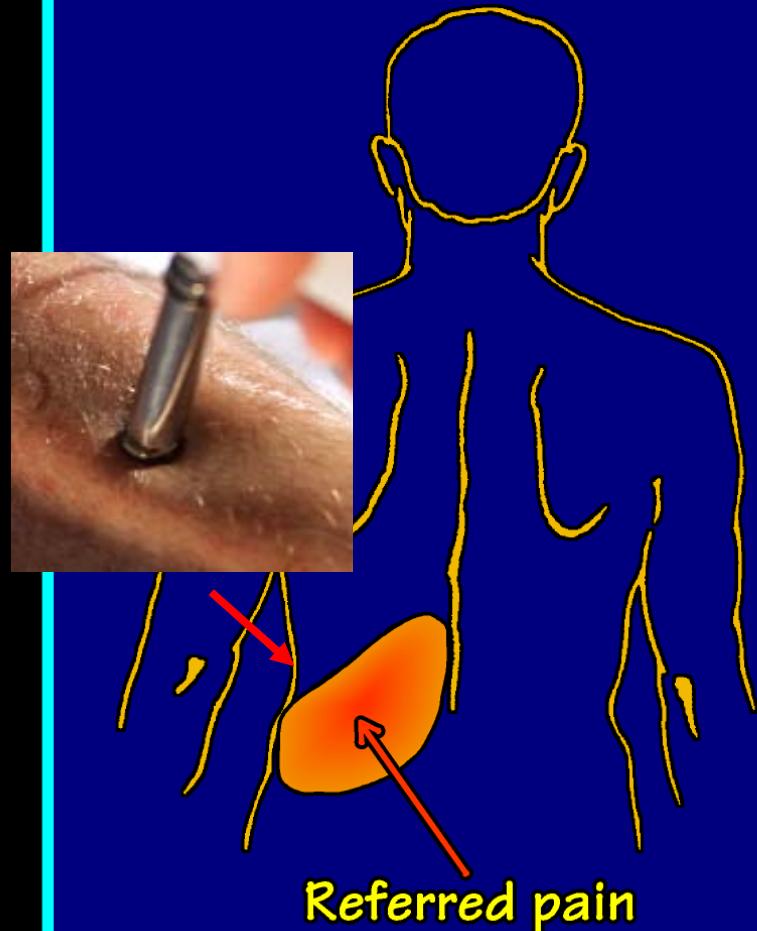


Transient colitis induced by various doses of trinitrobenzenesulfonic acid (TNBS). In patients with a long-standing remission of inflammatory bowel disease a 2- to 3-fold higher prevalence of IBS-like symptoms has been reported compared to normal population (Simren et al., 2002).



Referred Hyperalgesia from Viscera

Calculus of one upper urinary tract

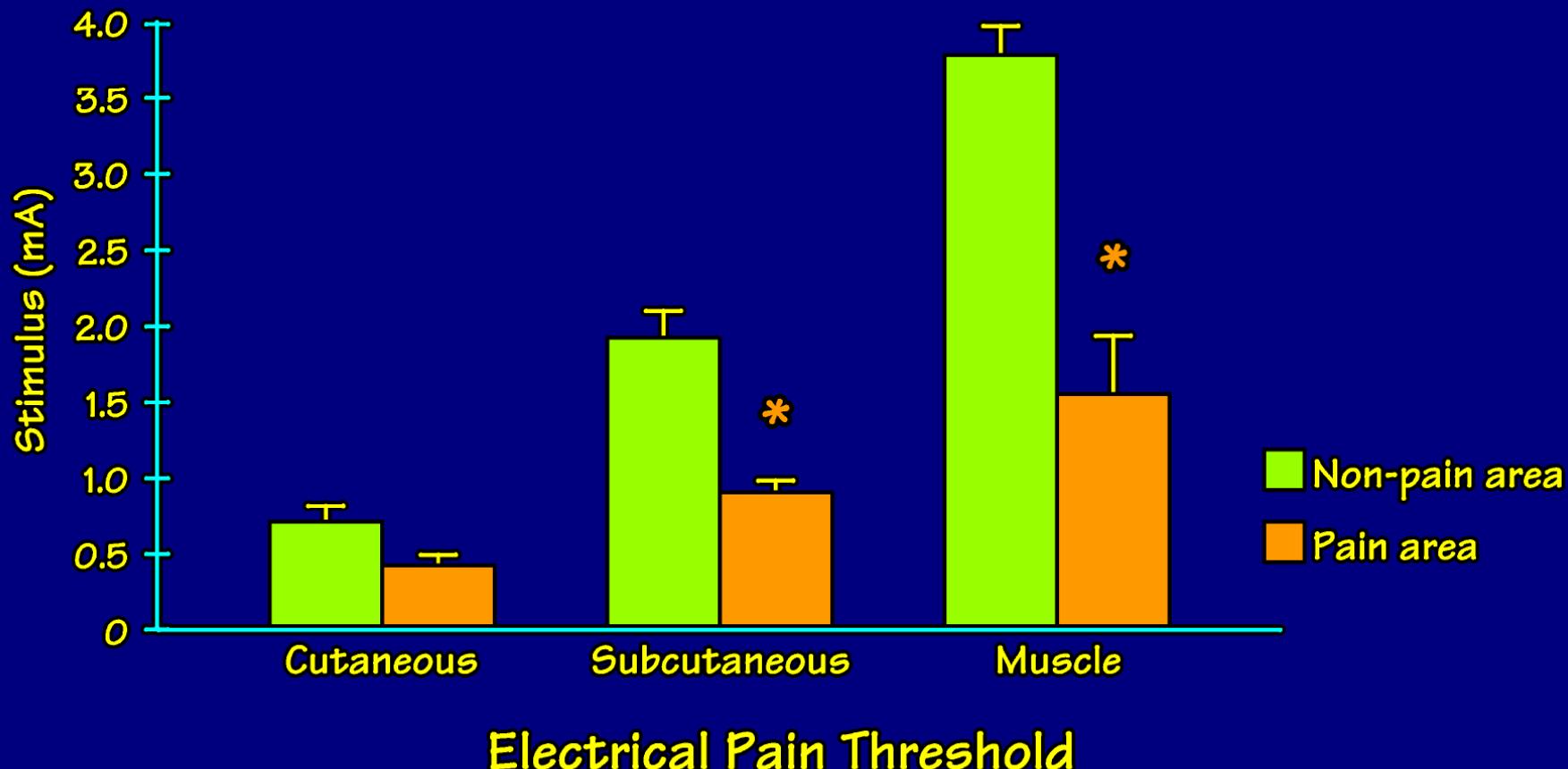


Giamberardino et al., 1993



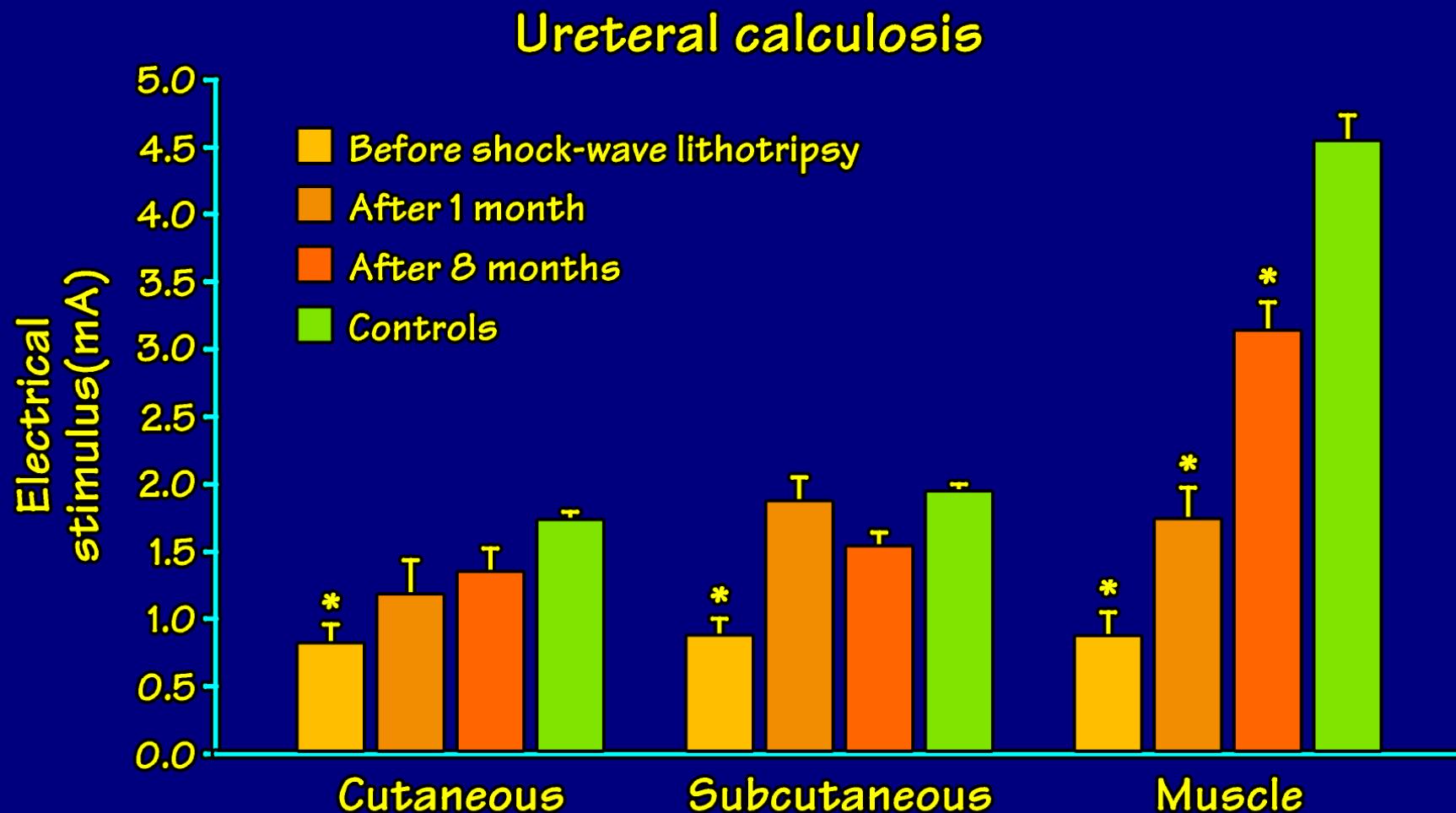
Visceral Pain and Referred Hyperalgesia

Renal/ureteral Calculosis





Referred Hyperalgesia



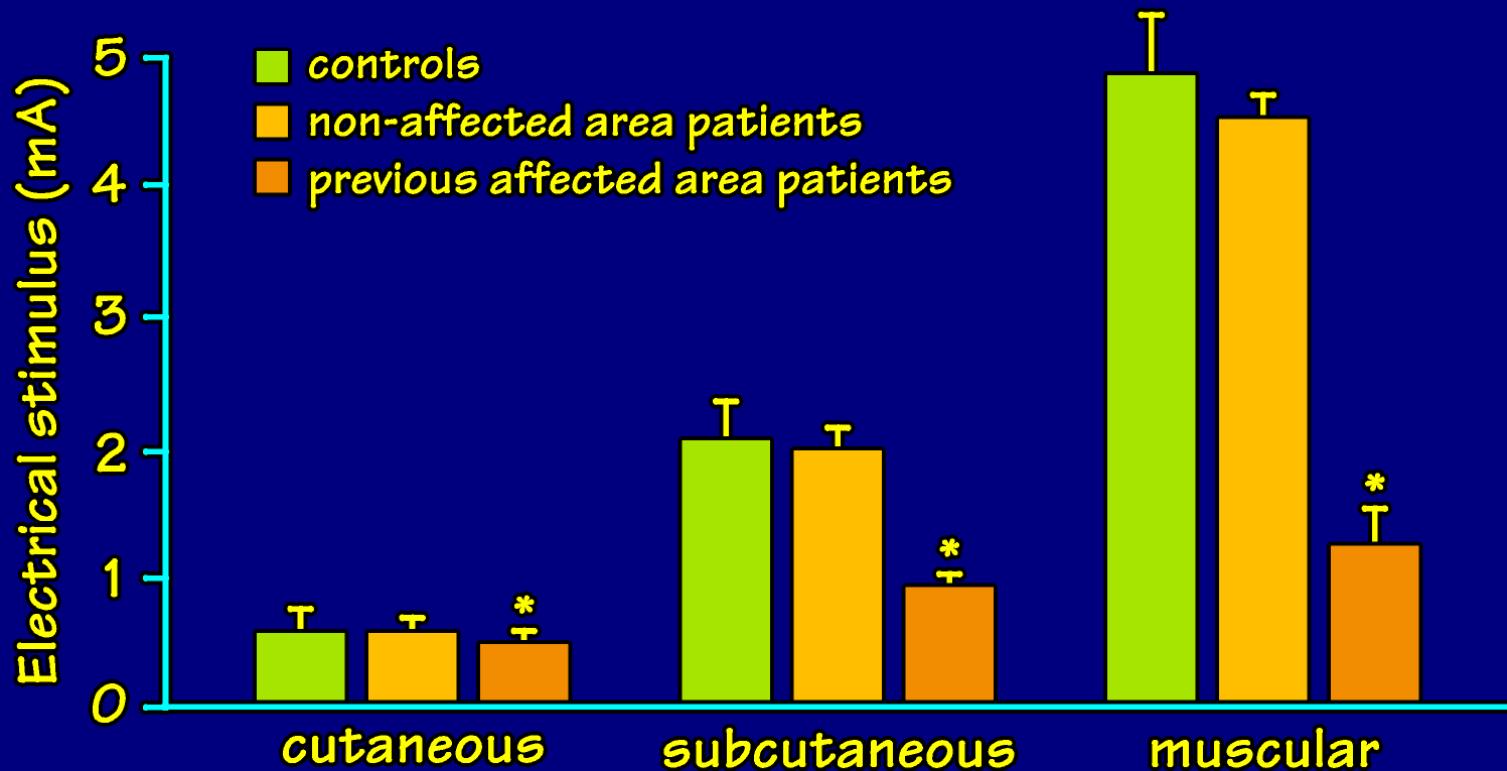
* = different from controls

Giamberardino et al., 1994



Referred Hyperalgesia from Viscera

3-10 years after renal/ureteral colics

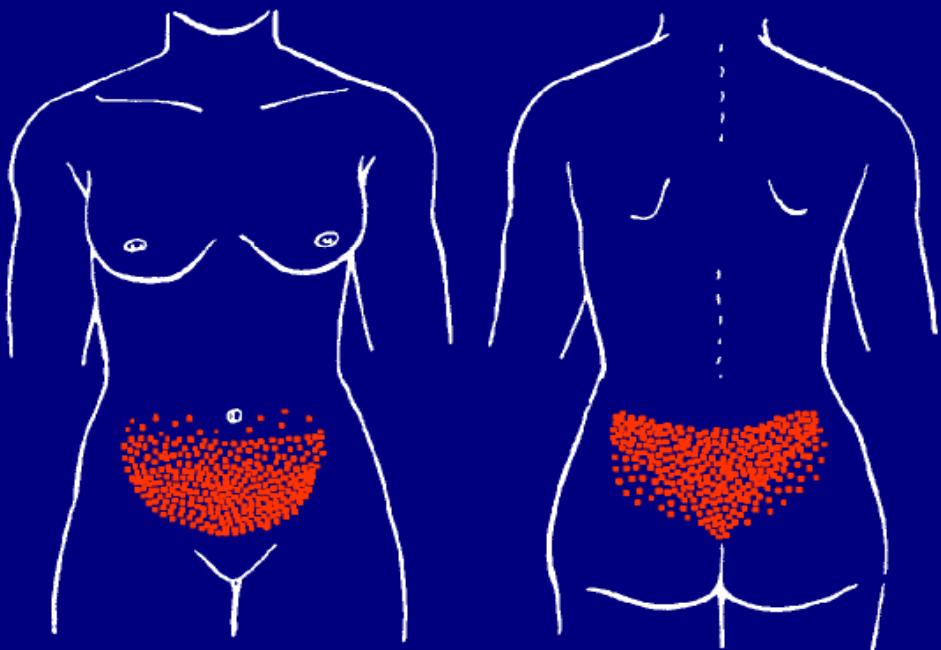
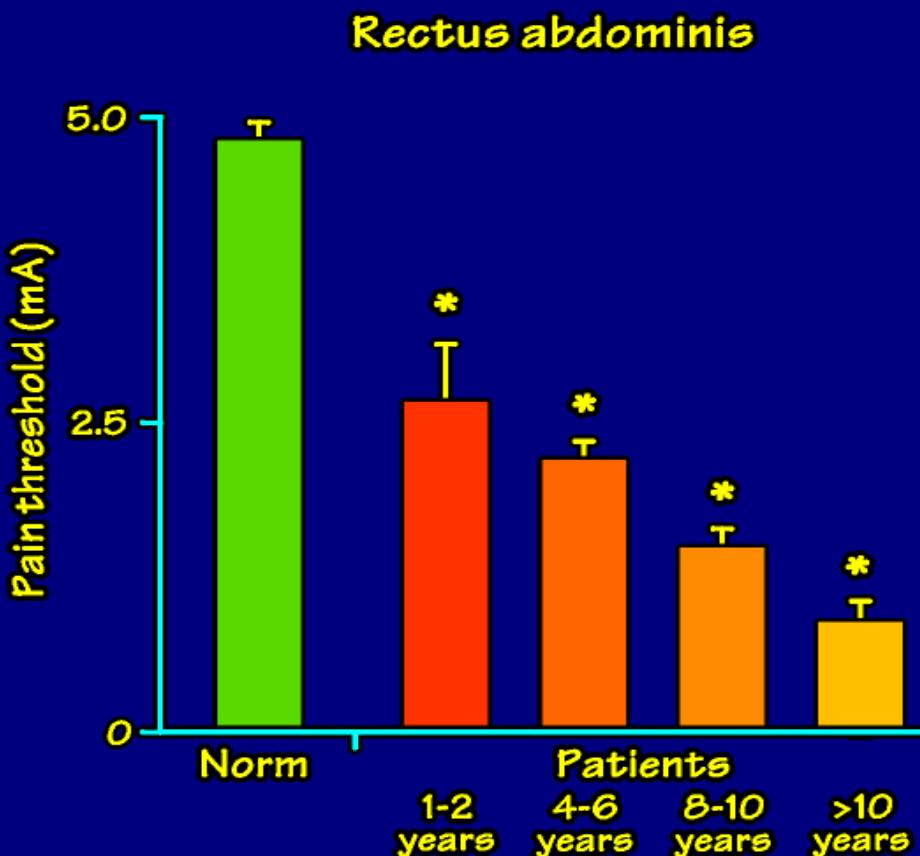


Stimulation: lumbar (L1) area

Vecchiet et al., 1992



Referred Hyperalgesia in Dysmenorrhea

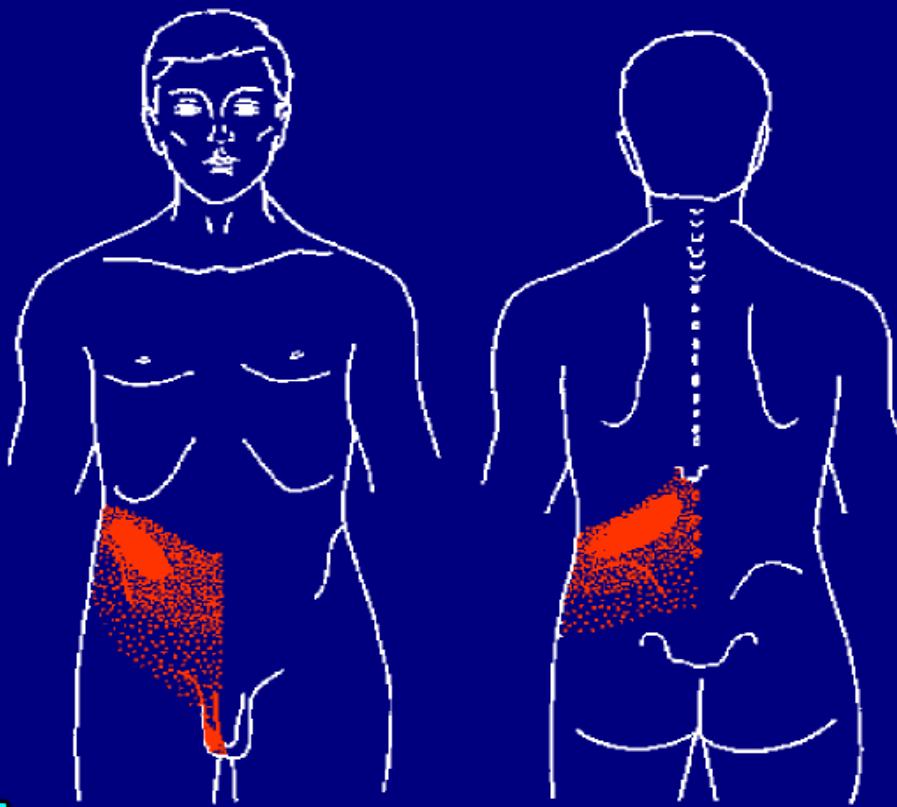
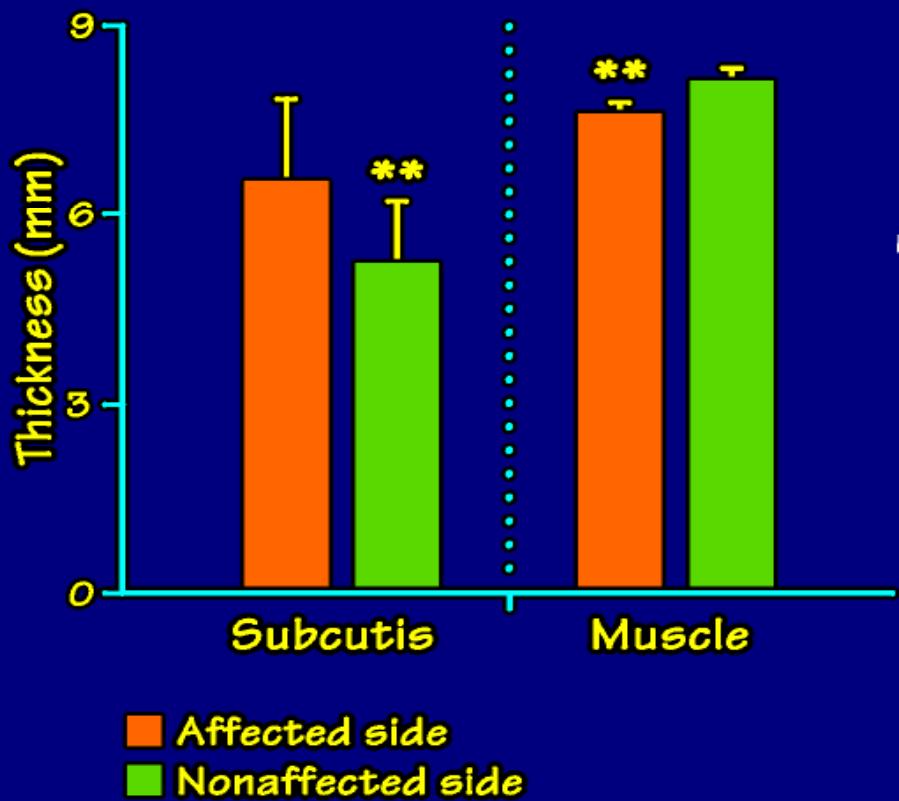


Giamberardino et al., 1997, 2006



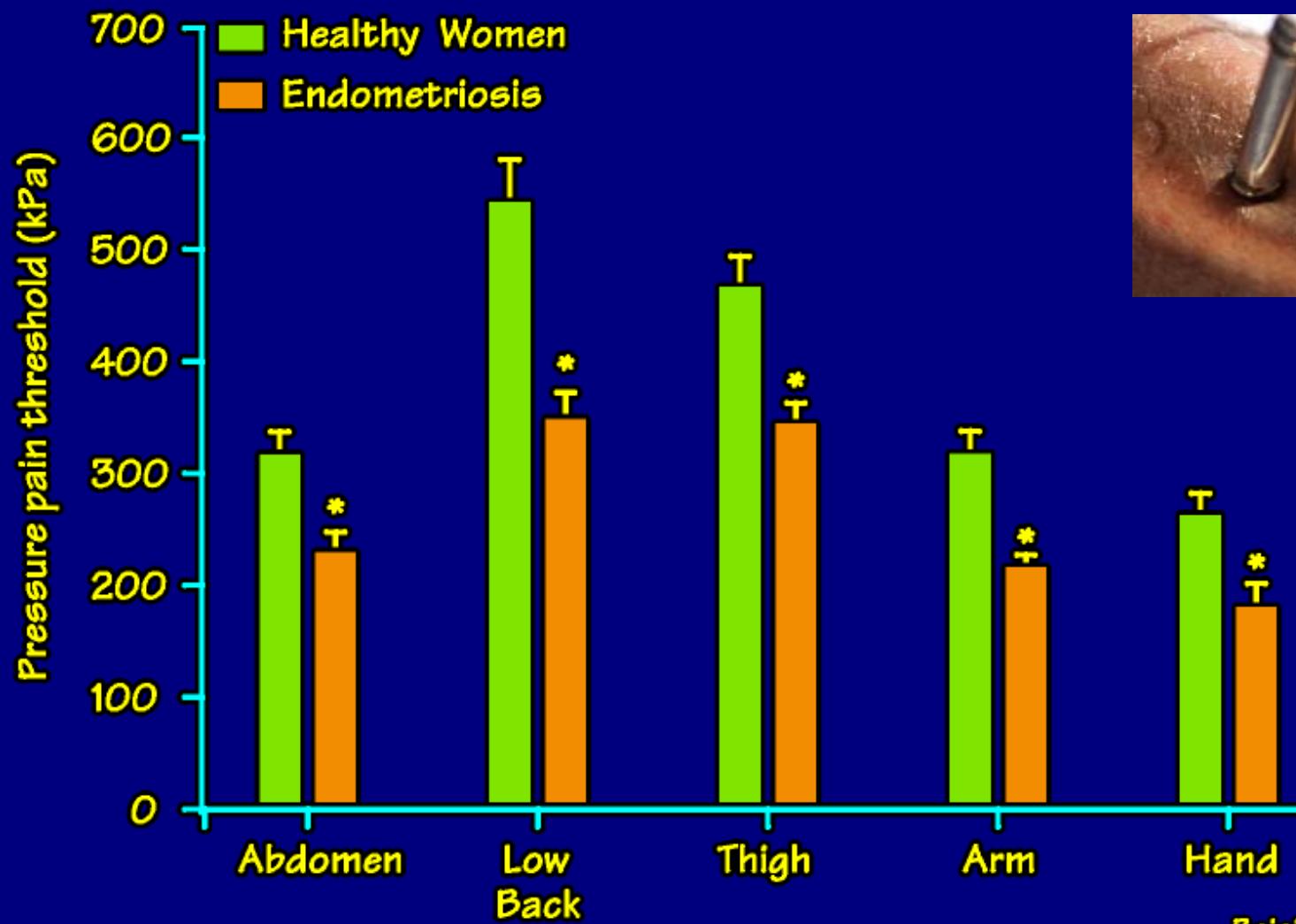
Referred Trophic Changes In Urinary Colics

Symptomatic urinary calculosis
subcutis and muscle thickness
ultrasound evaluation





Sensitisation in Endometriosis

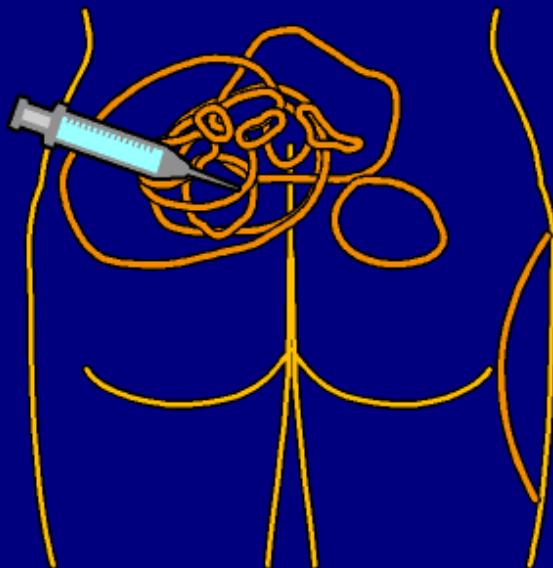


Bajaj et al., 2002



Visceral Pain and Sensitisation

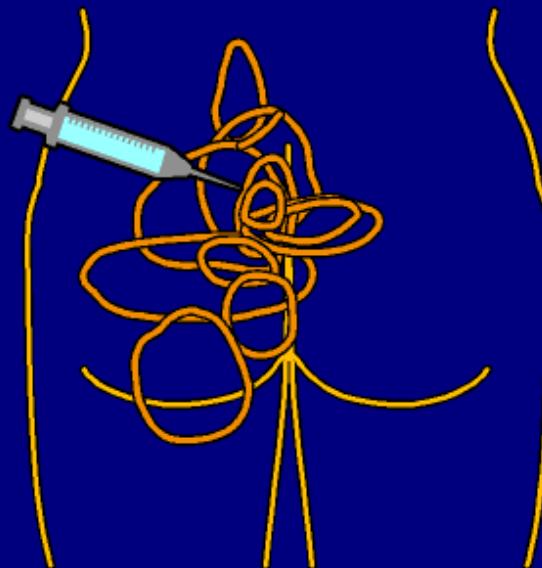
Healthy controls (N=10)



Area = $3.1+/-1.0$ AU

VAS = $2.0+/-0.3$

Endometriosis (N=10)



Area = $4.1+/-1.8$ AU*

VAS = $2.7+/-0.5$ *

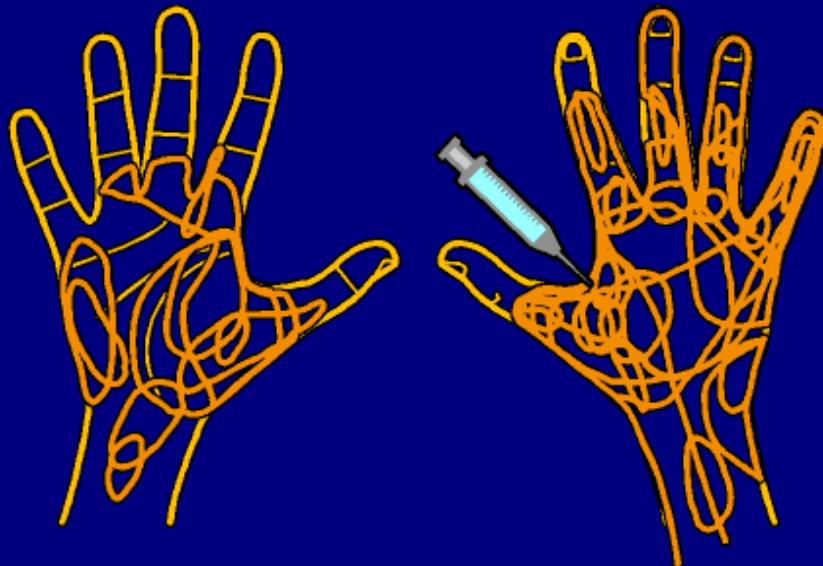
Hypertonic saline (0.5 ml, 6%) in multifidus muscle (menstrual pain referral)

* P<0.06 (NS)



Visceral Pain and Sensitisation

Healthy controls (N=10)



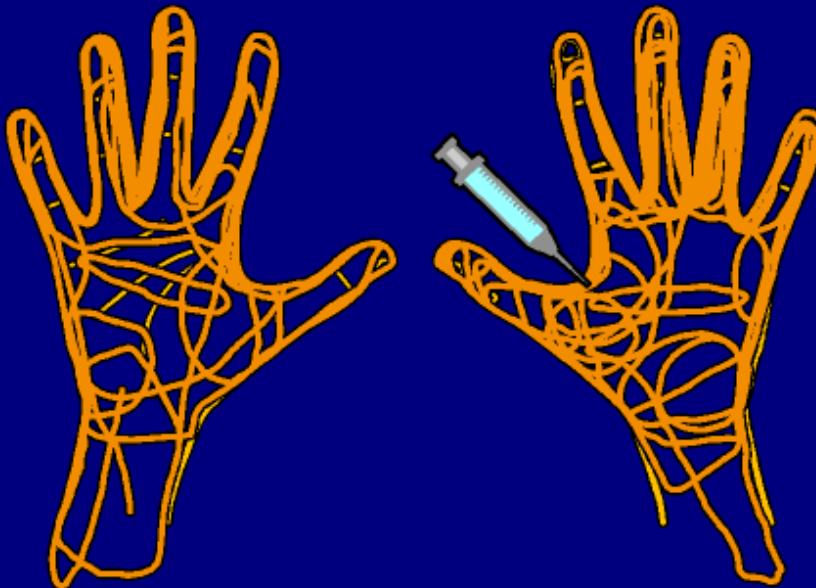
Plantar

Dorsum

Total area = 24+/-3 AU

VAS = 4.6+/-0.5

Endometriosis (N=10)



Plantar

Dorsum

Total area = 56+/-7 AU*

VAS = 6.3+/-0.3*

Hypertonic saline (0.5 ml, 6%) in first dorsal interosseous muscle
(non pain site, central sensitisation)

* P<0.01



Peripheral and central sensitisation





Central sensitisation



Pin Prick Hyperalgesia

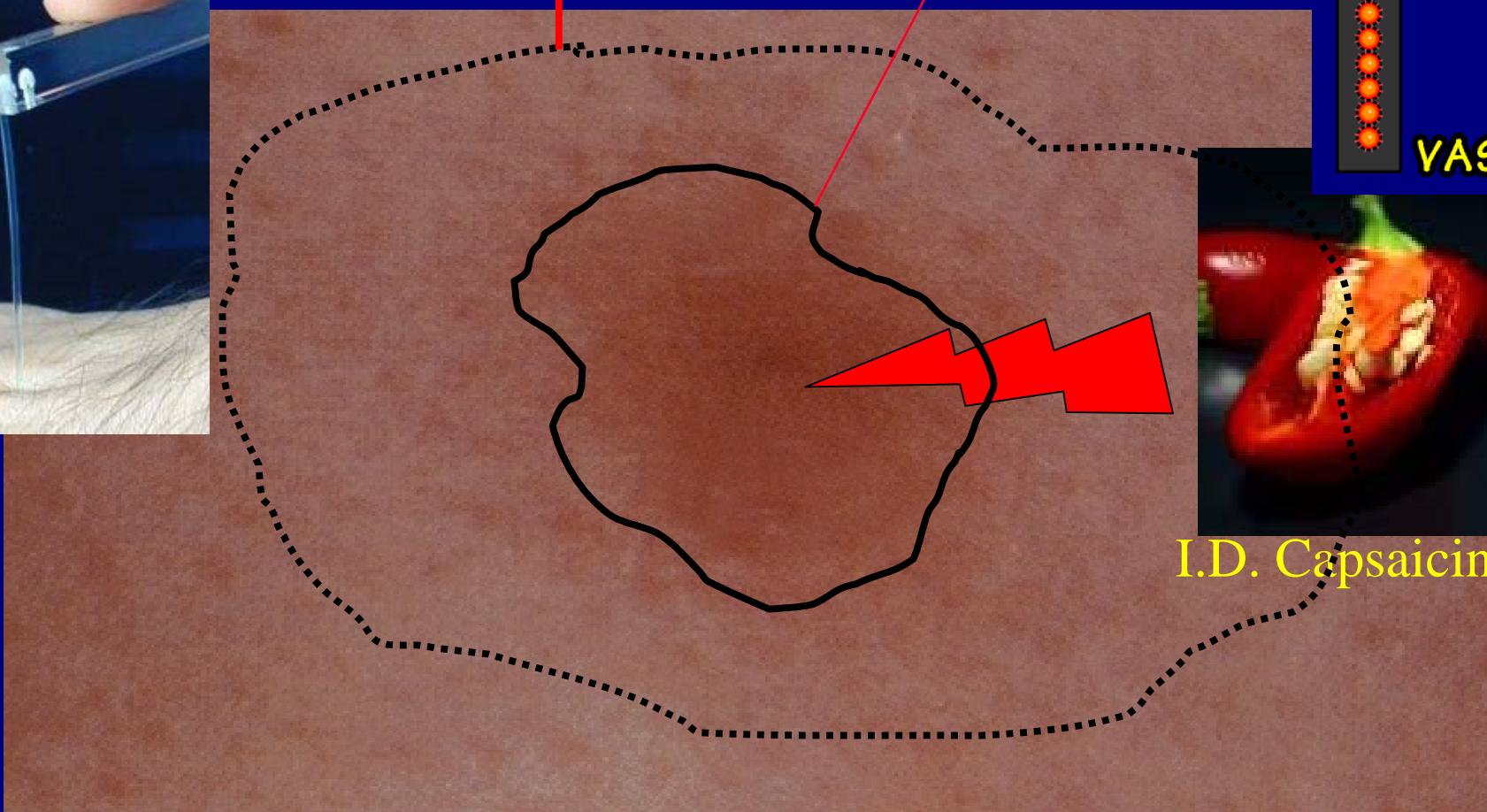
Flare



VAS



I.D. Capsaicin



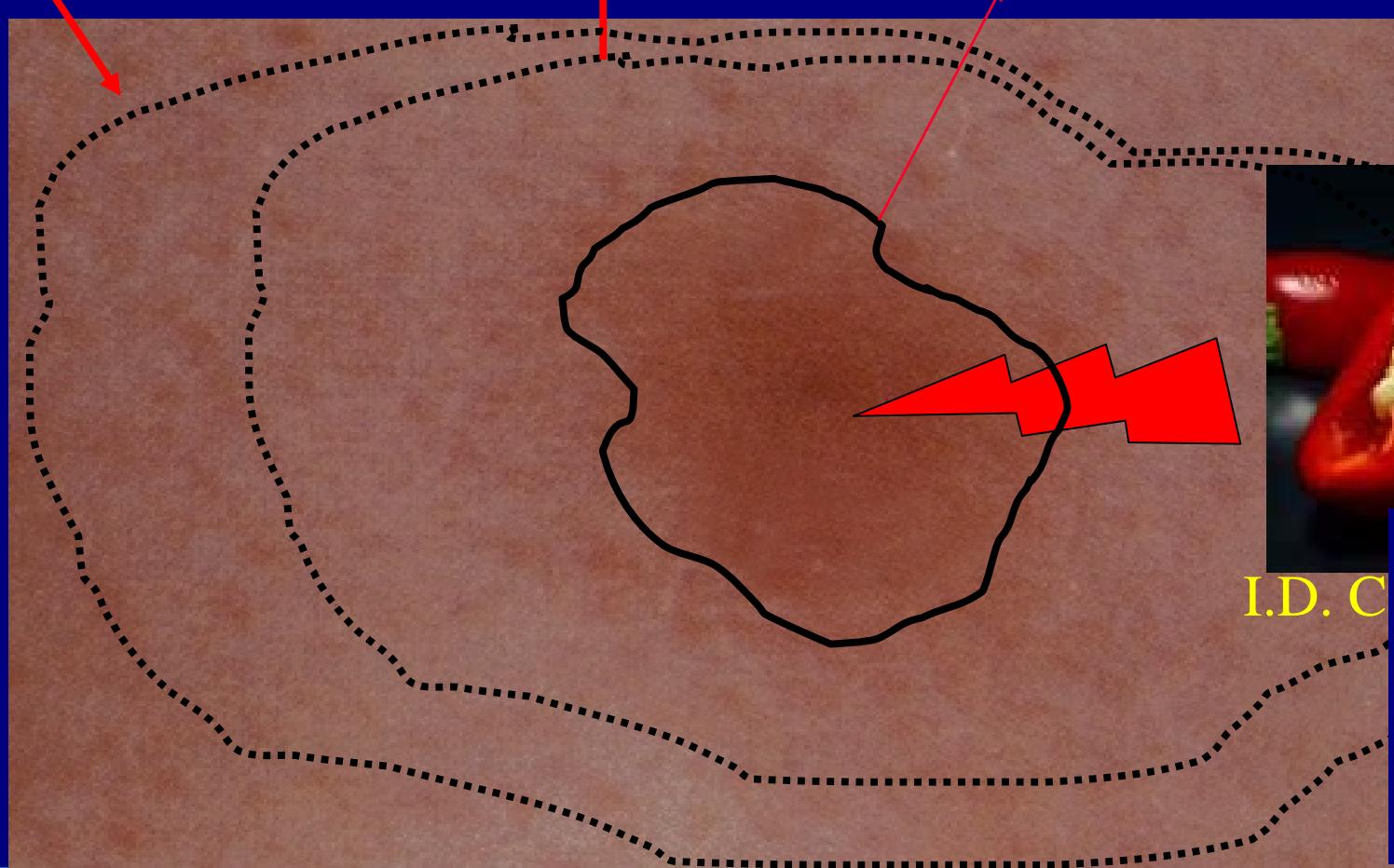


Central sensitisation

Vulvodynia

Pin Prick Hyperalgesia

Flare



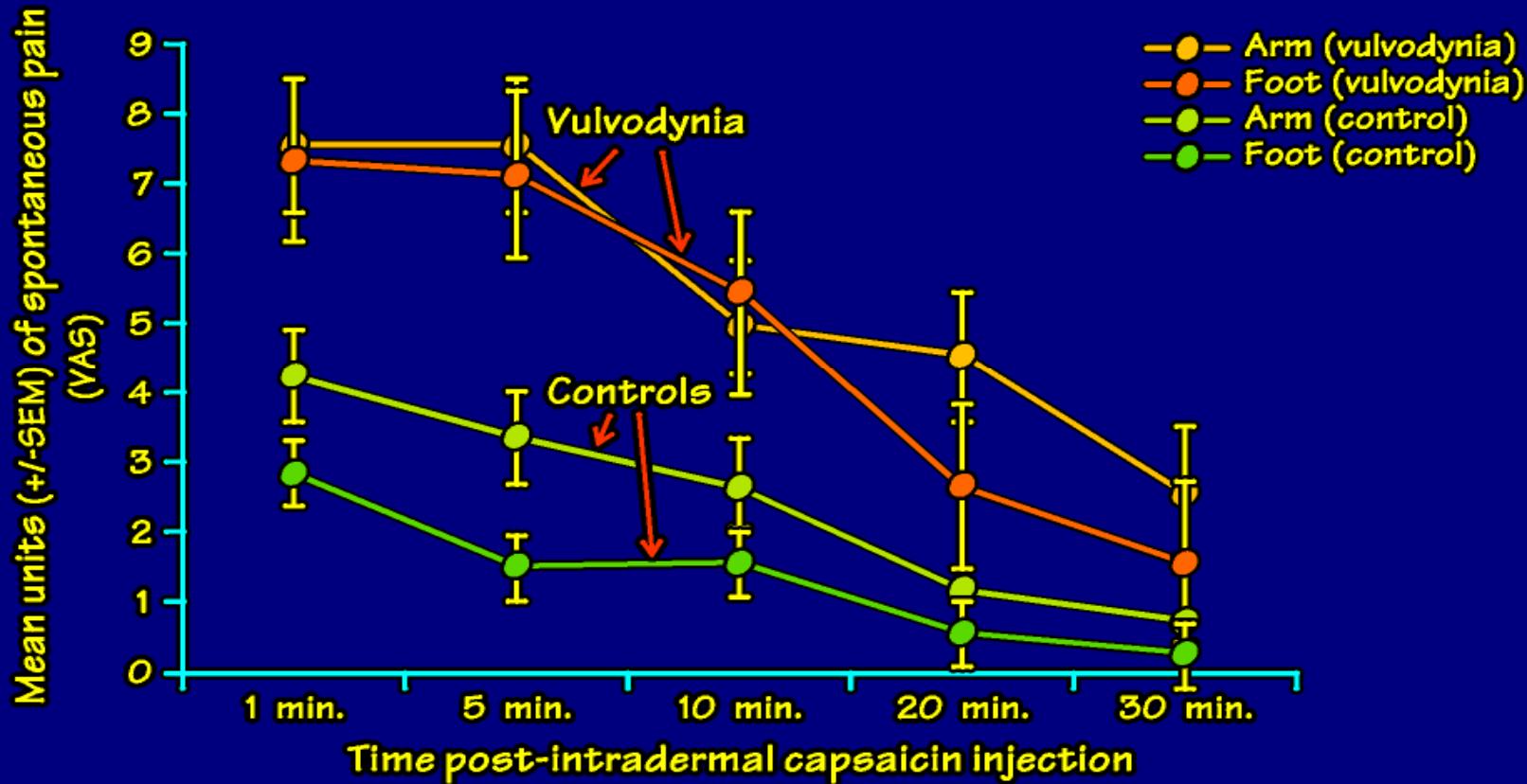
VAS

I.D. C

VAS



Central Sensitisation in Vulvodynia

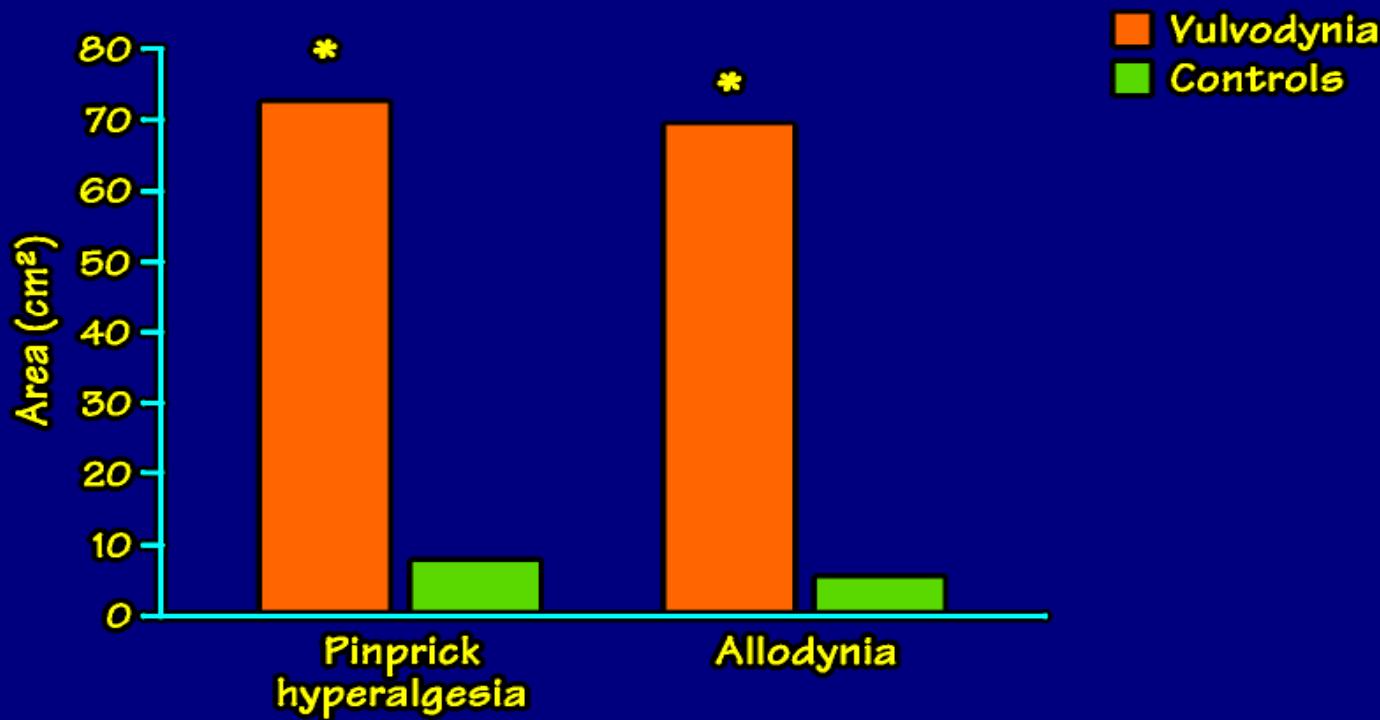


10mg 0.1% intradermal capsaicin

Foster et al., 2005



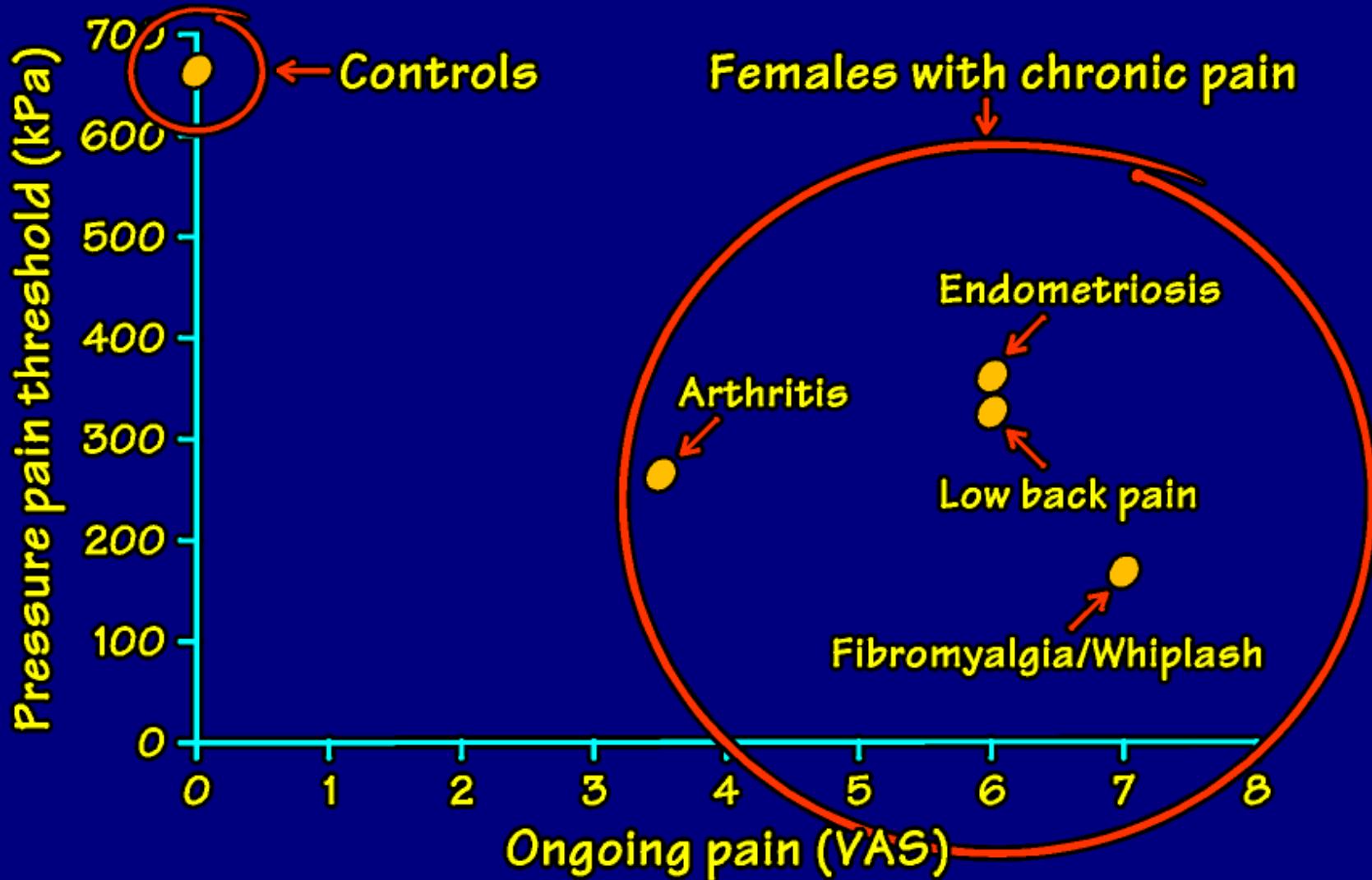
Central Sensitisation in Vulvodynia



10mg 0.1% intradermal capsaicin



Muscle Hypersensitivity

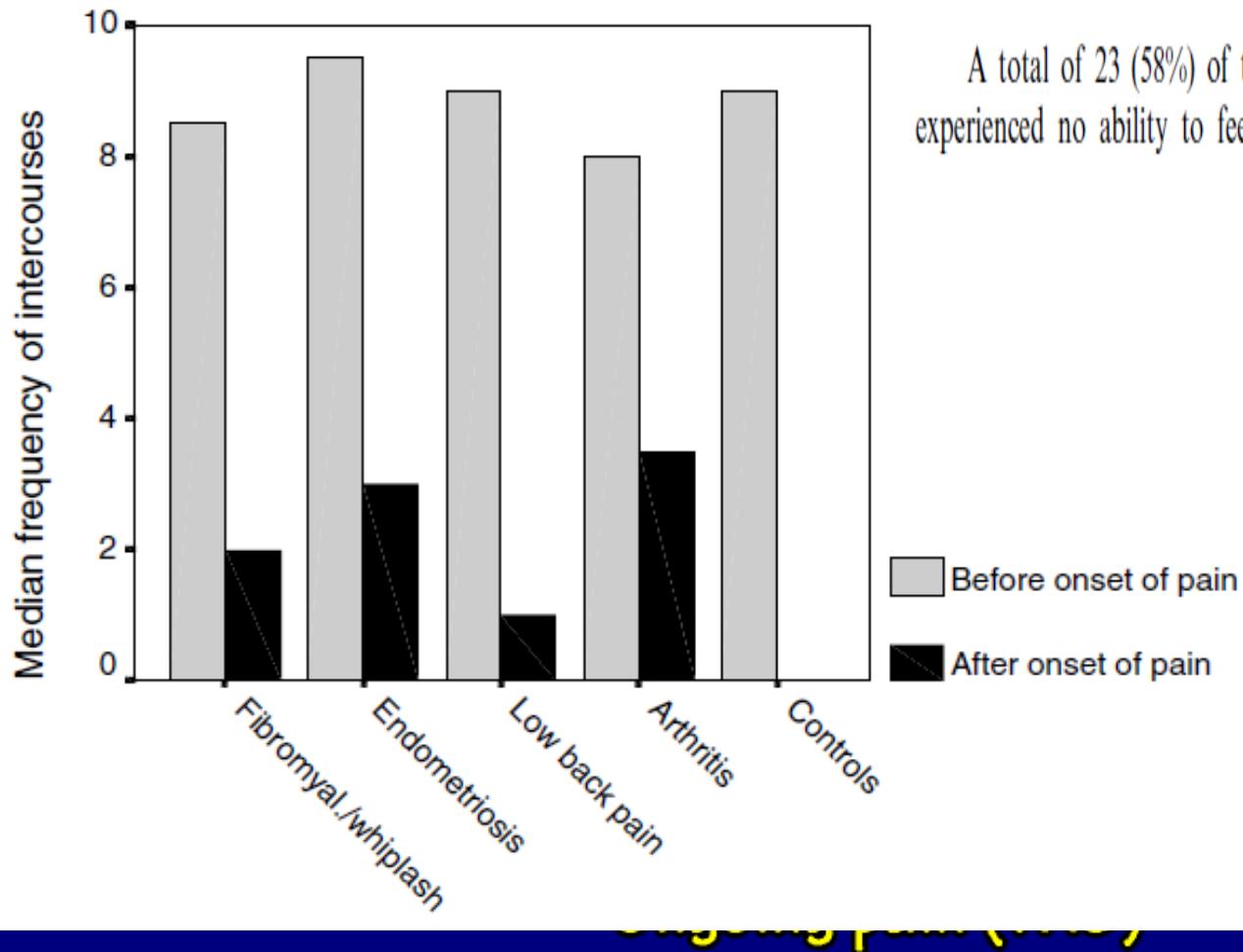


Laursen et al., 2003

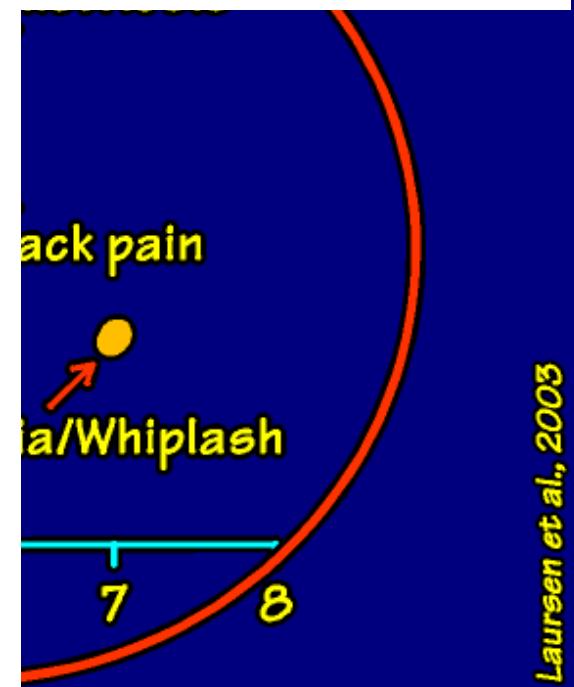


Muscle Hypersensitivity

Frequency/month of sexual intercourses



A total of 23 (58%) of the females with chronic non-malignant pain experienced no ability to feel sexual desire at all,



Laursen et al., 2003



Sensitisation

Primary
dysmenorrhea

Restless legs

Post traumatic
stress disorder

Whiplash

FMS

OA

Neuropathic
pain

CLPB

Pelvic pain/
interstitial
cystitis

Vulvodynia

IBS

Migraine

TTH/CTTH

TMD

Myofascial
pain syndrome



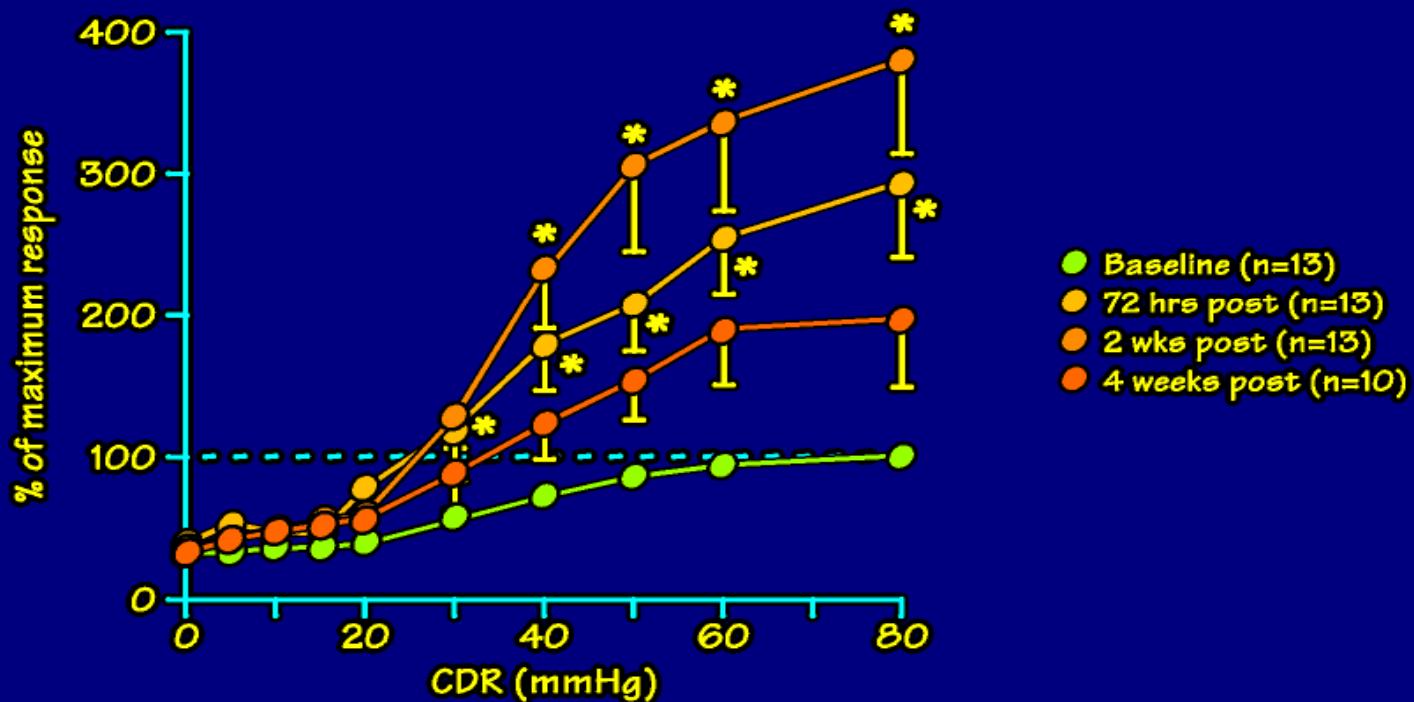


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Somatic-Visceral Interaction



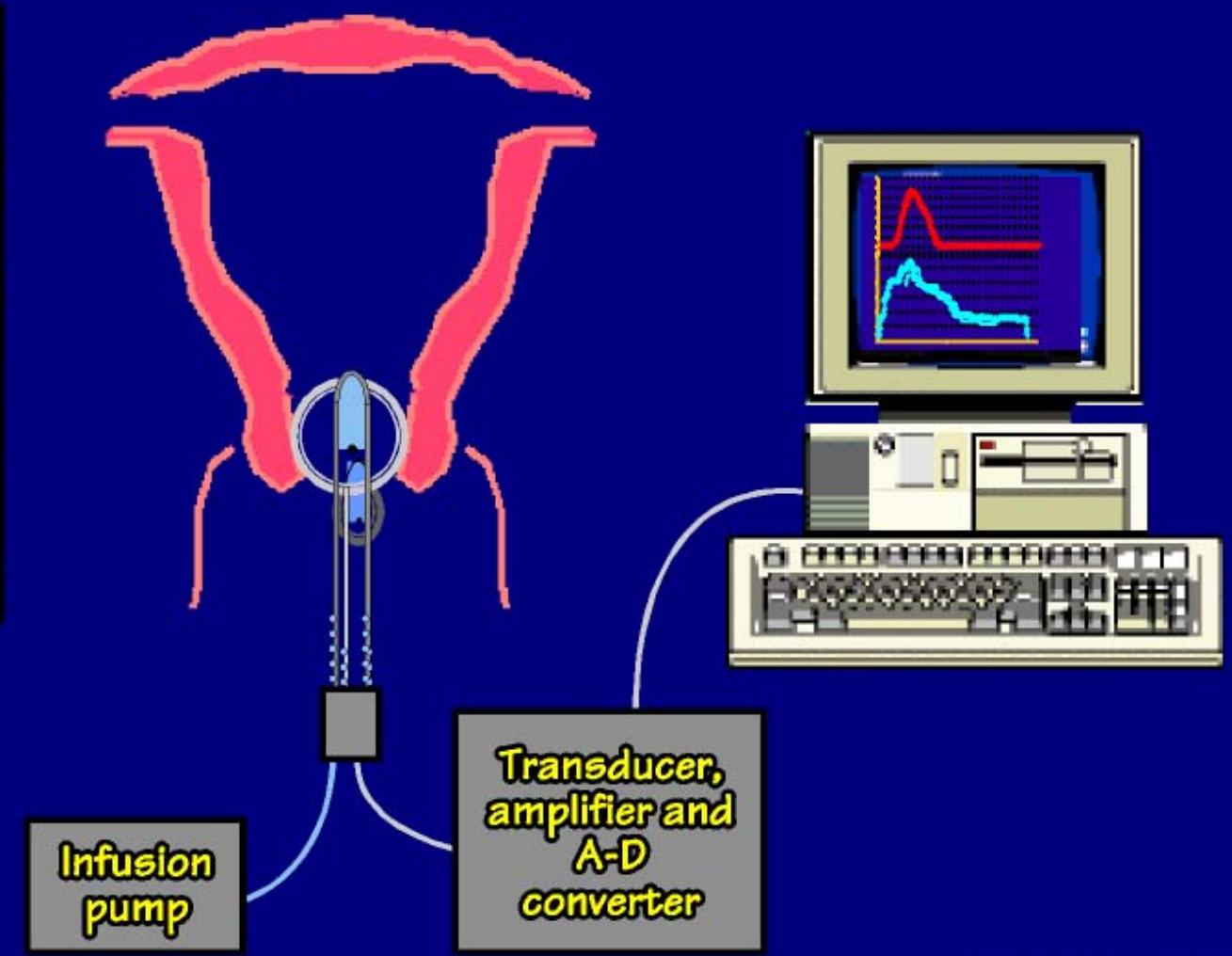
Colo-rectal distension (CRD) before and after intramuscular inflammation (low pH=4) in gastrocnemius muscle in rats



A new model for gynaecological pain



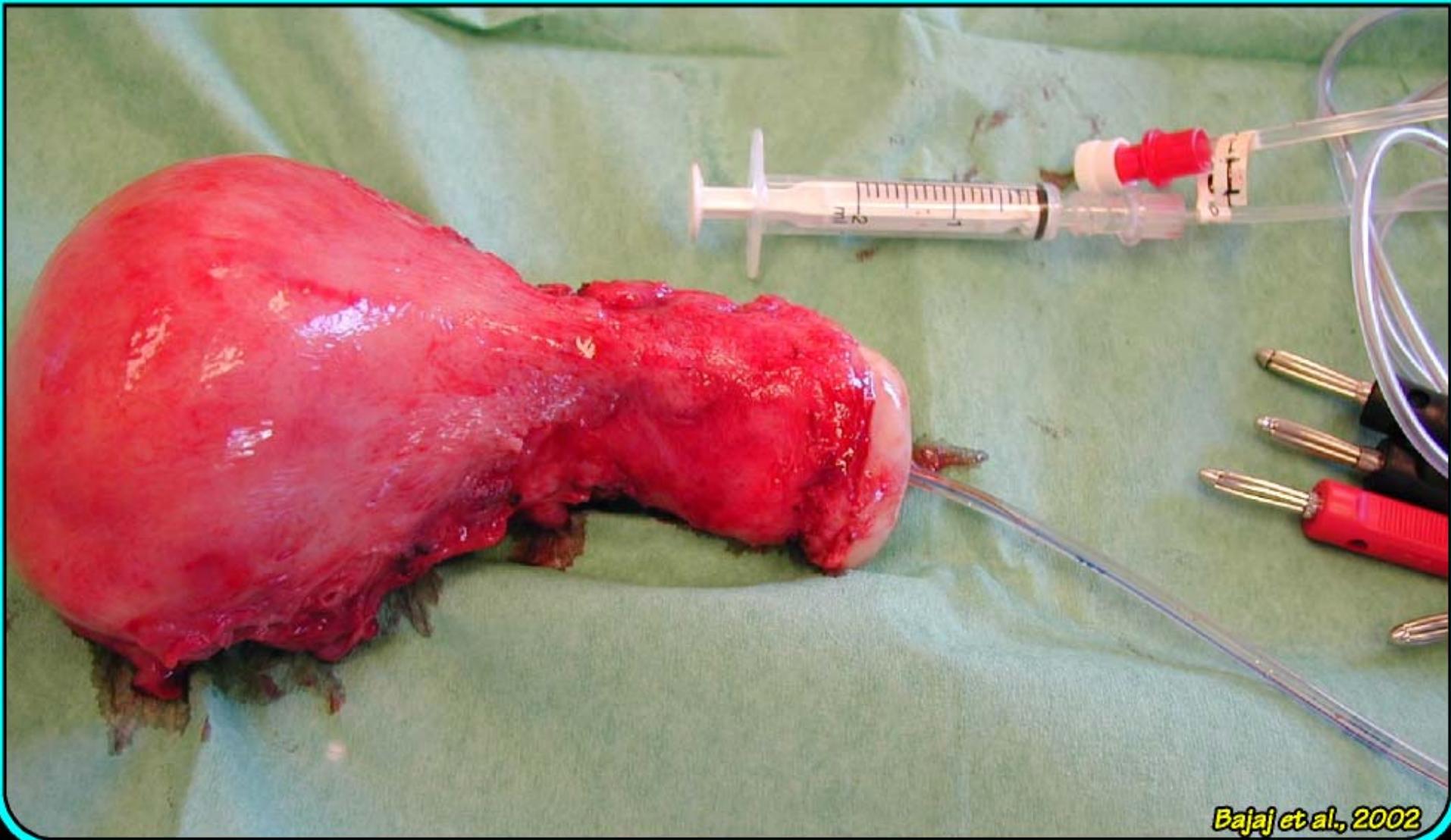
Cervix Dilatation



Bajaj et al., 2002



Cervix Dilatation



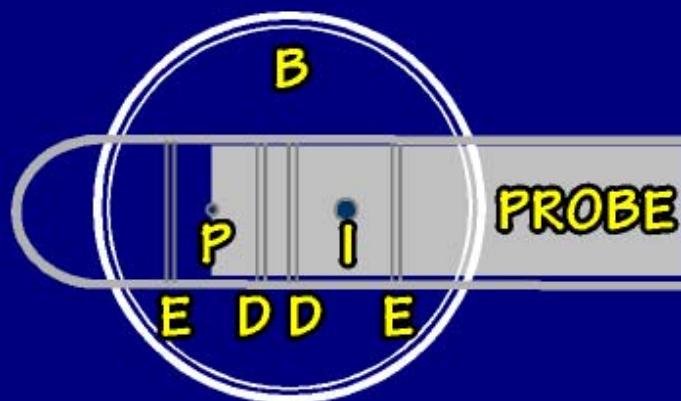
Bajaj et al., 2002



Cervix Dilatation



probe assembly with undistended balloon



probe design

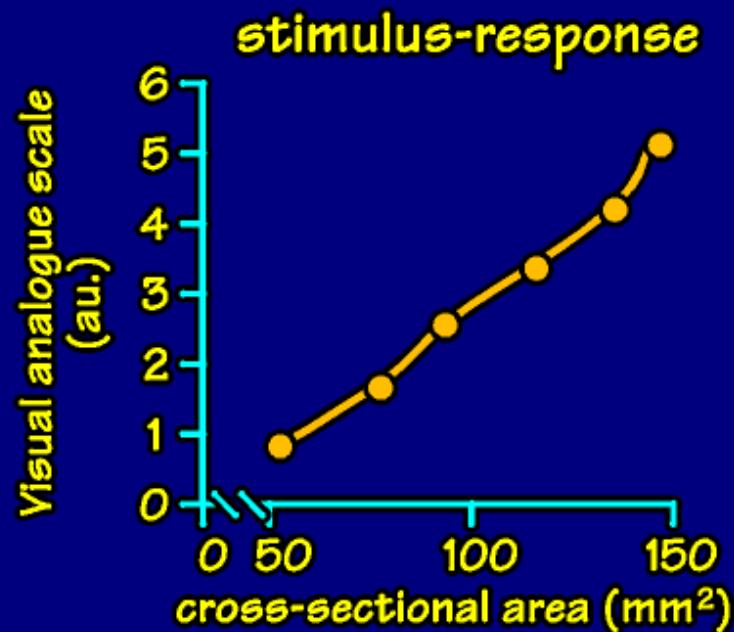
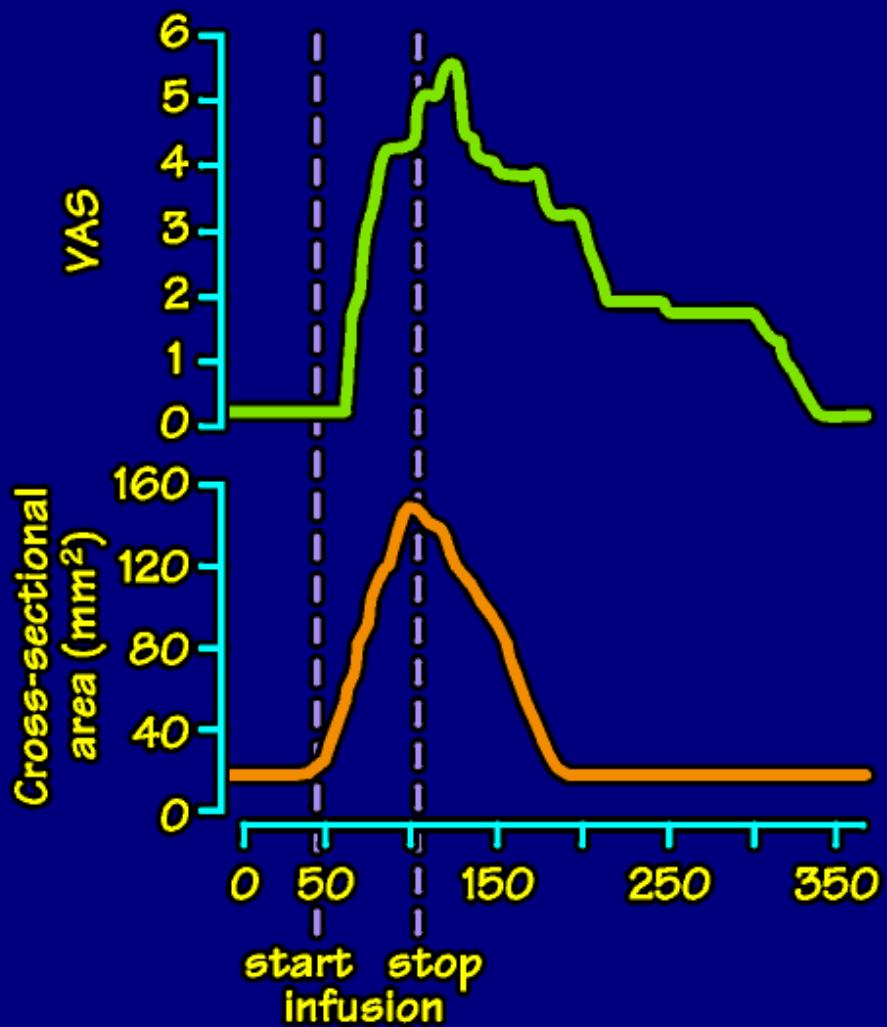
B = balloon; P = pressure channel;
I = infusion channel; E = excitation
electrode; D = detection electrode



*distended
balloon*



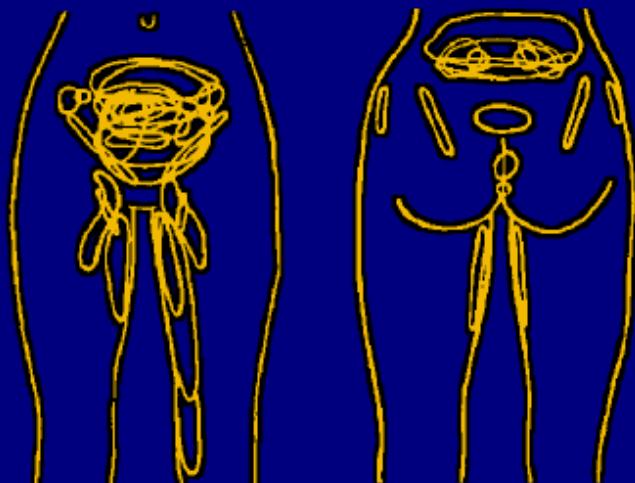
Cervix Dilatation





Mapping of Cervical Pain

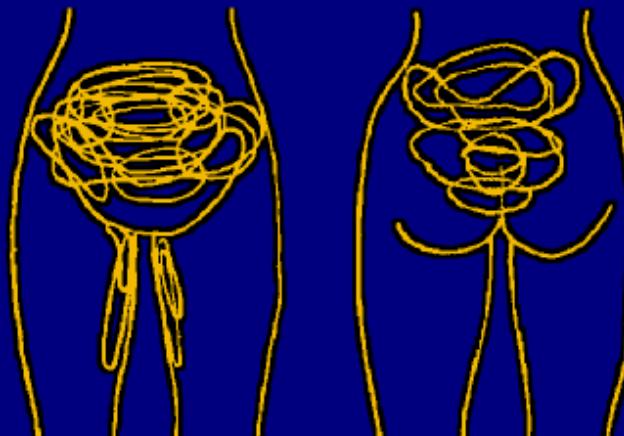
Experimental cervical dilatation



Anterior

Posterior

Menstrual pain

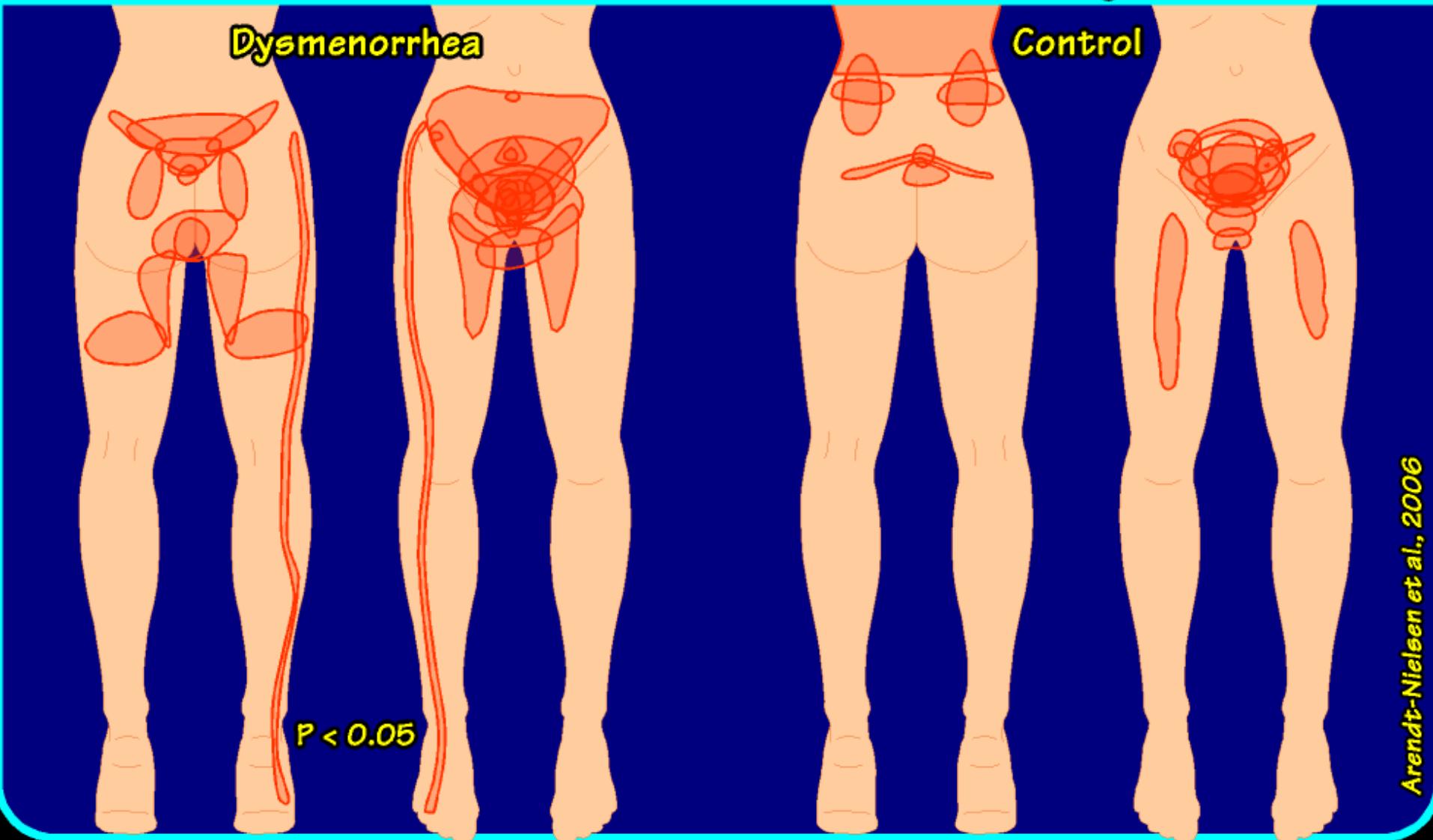


Early labor pain
Bonica (1980)



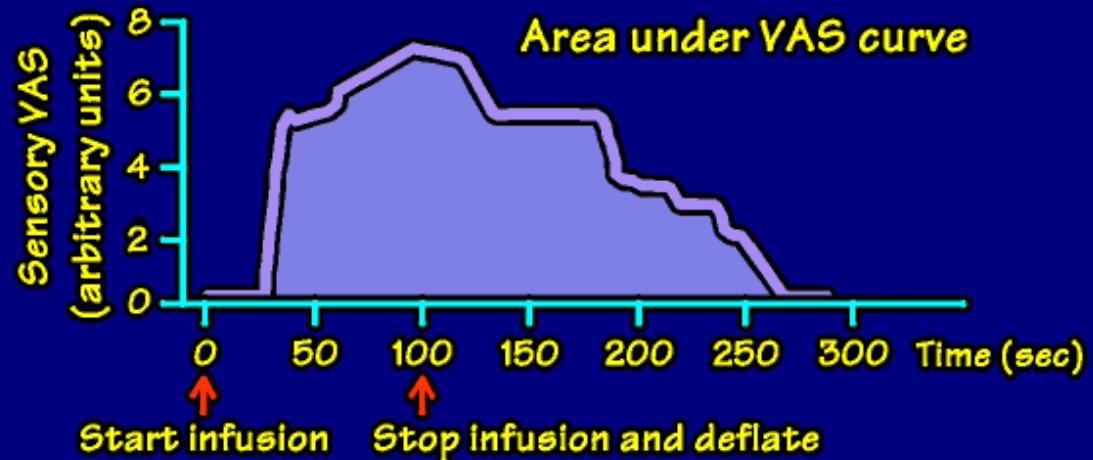
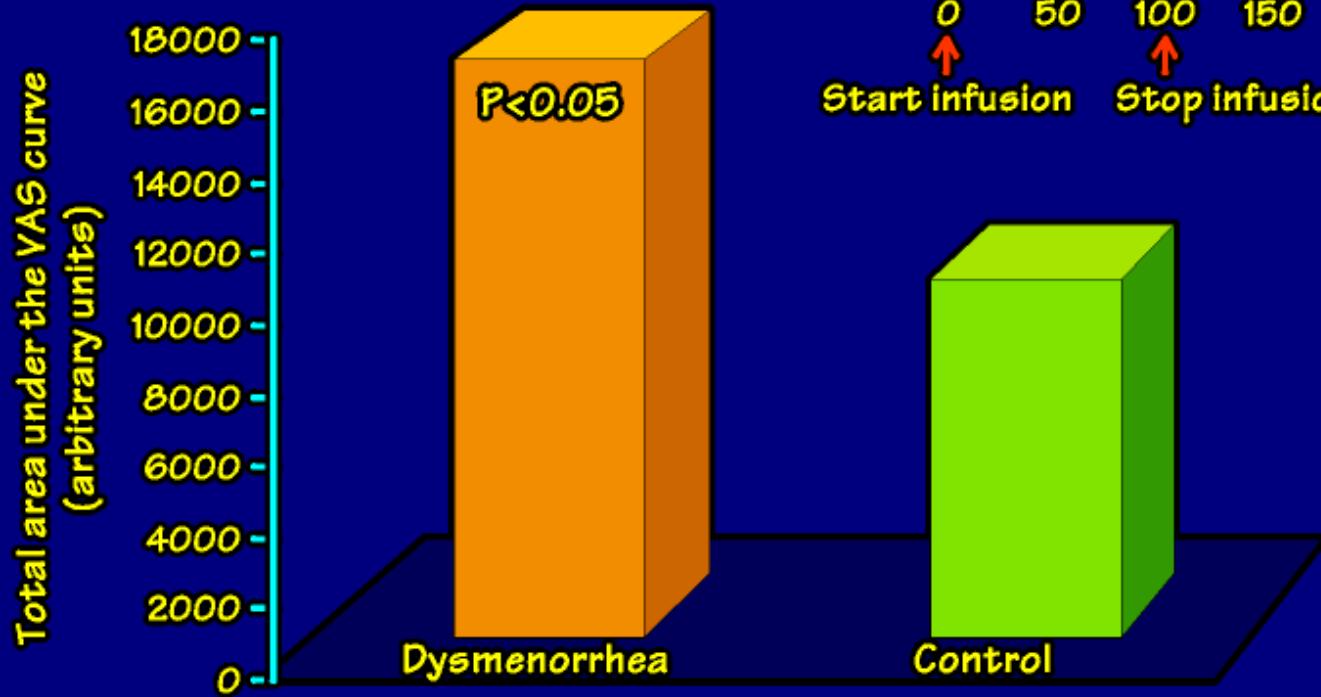
Referred Pain to Cervix Dilatation

Pain threshold stimulation intensity





Cervix Dilatation in Dysmenorrhea





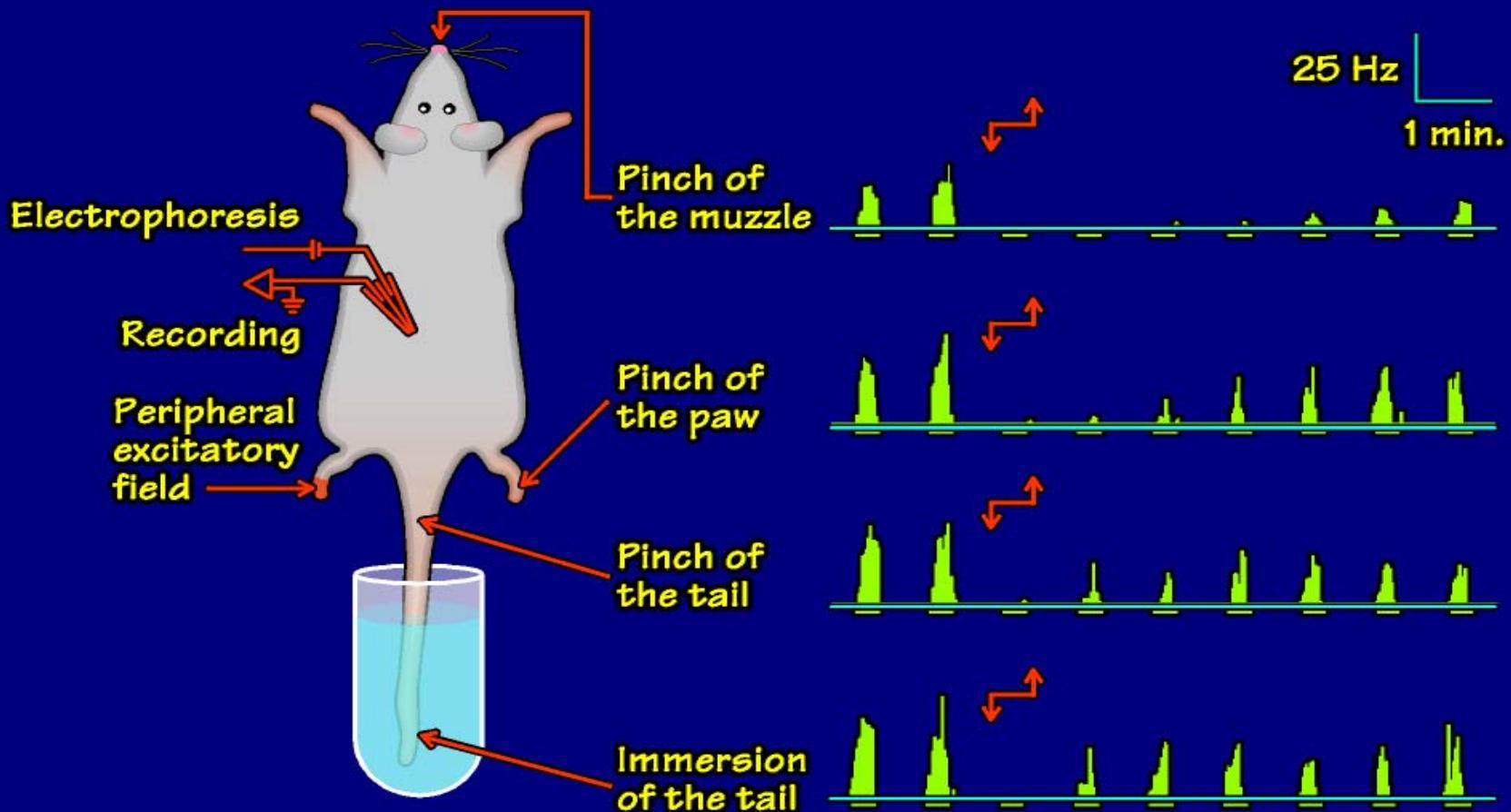
Neurophysiologic parameters translating into patients with visceral pain



- Impaired descending control
- Central spreading of sensitisation
- Central integration



Diffuse Noxious Inhibitory Control

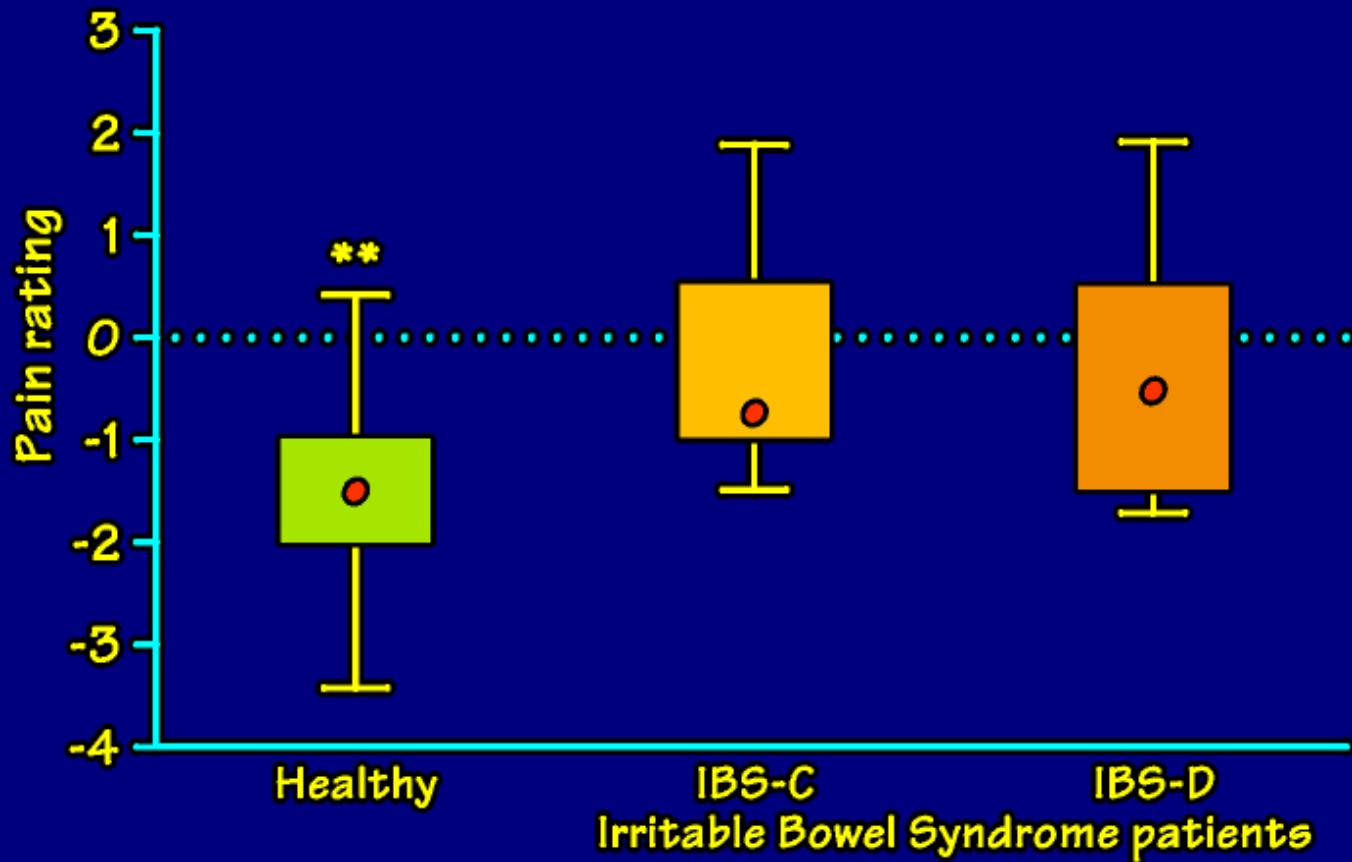


Villanueva et al., 1984



Impaired DNIC in IBS

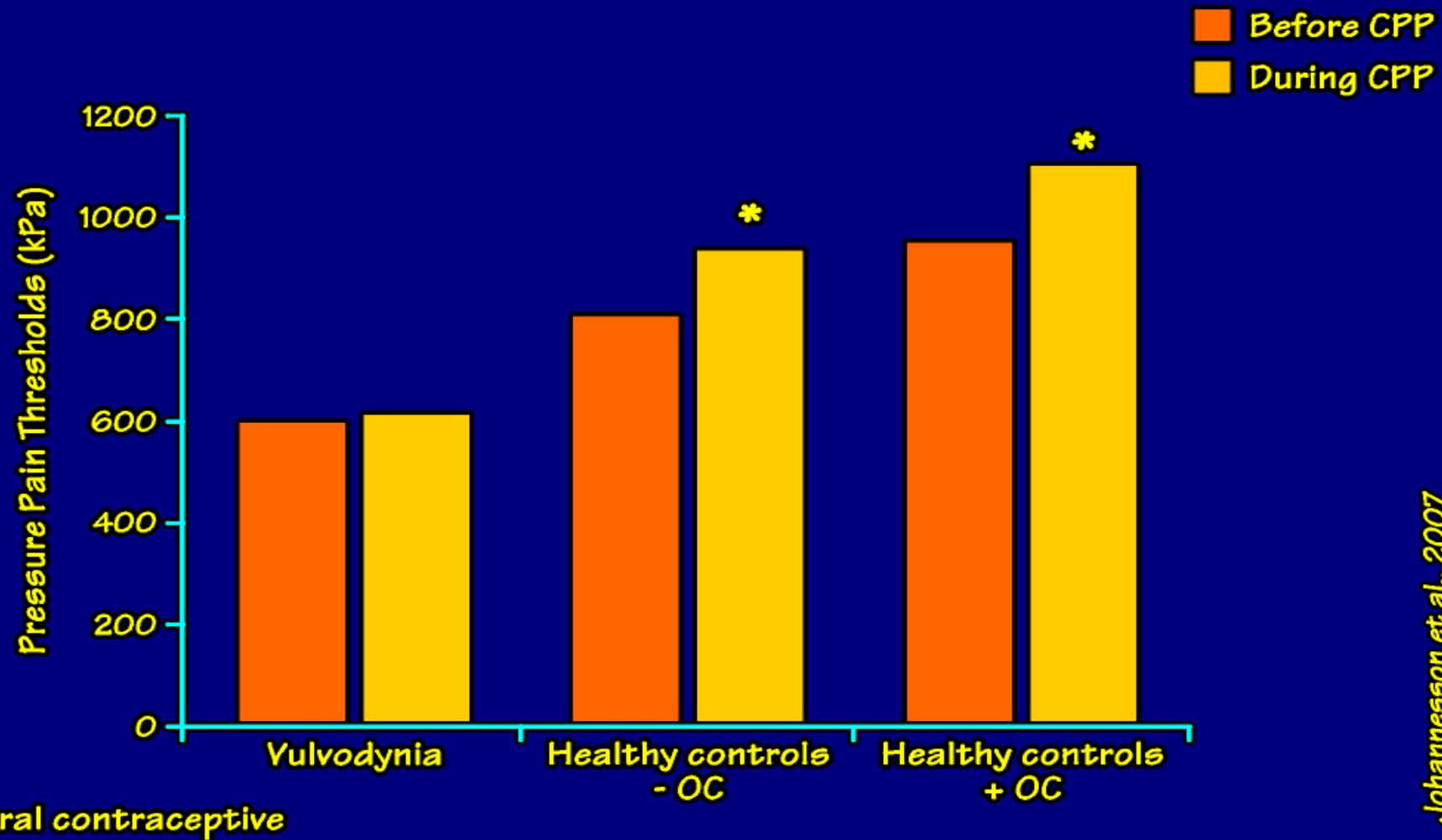
Differences in rectal distension pain ratings with and without painful ice water immersion of the foot



10 healthy subjects and five constipated (IBS-C) and five diarrhoeic (IBS-D)



Impaired Descending Inhibition in Vulvodynia



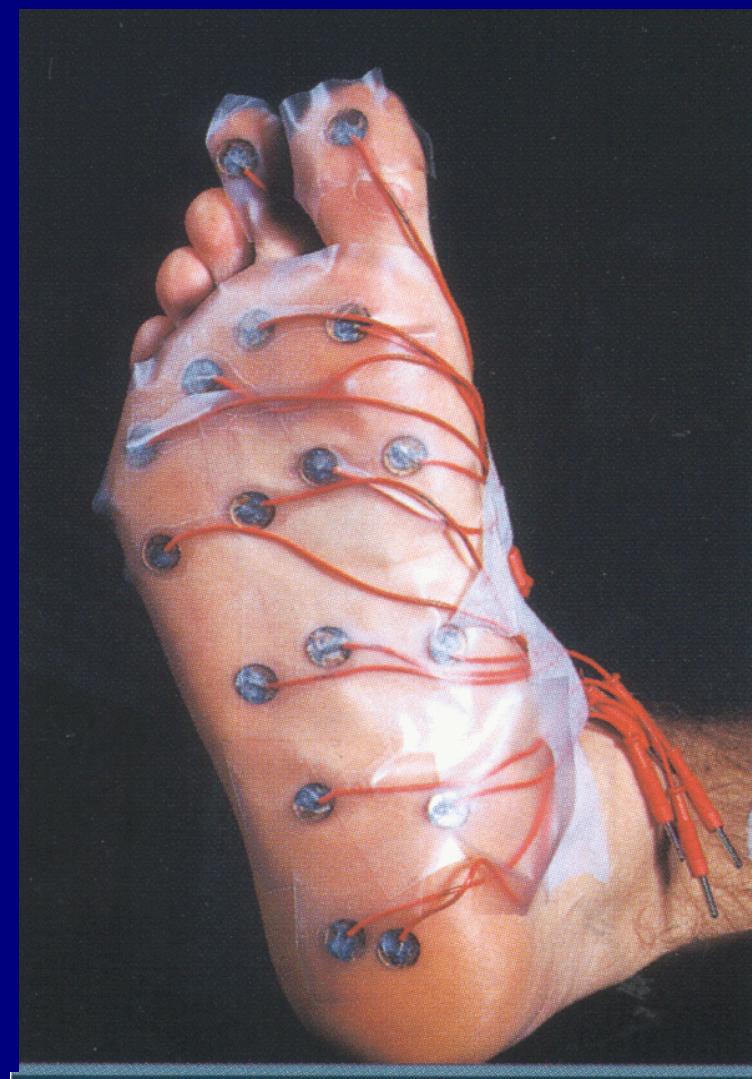
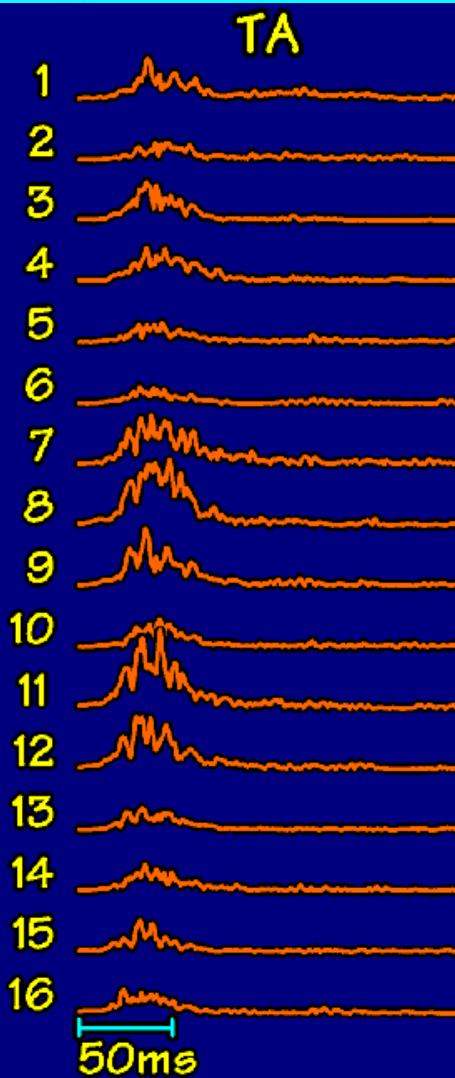
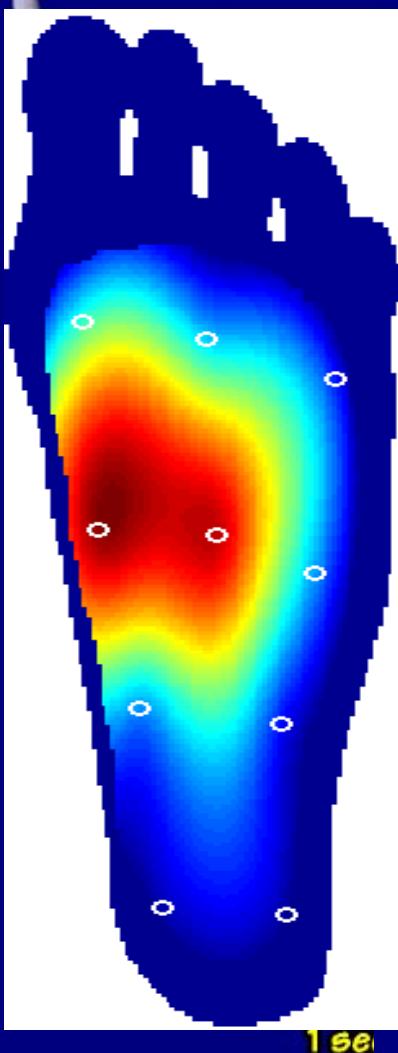
Johannesson et al, 2007



- Impaired descending control
- Central spreading of sensitisation
- Central integration



Reflex Receptive Fields



Weng and Schouenborg, 1998



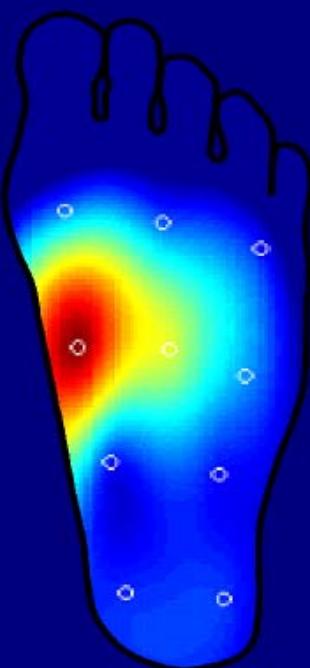
Reflex Receptive Field

Rats



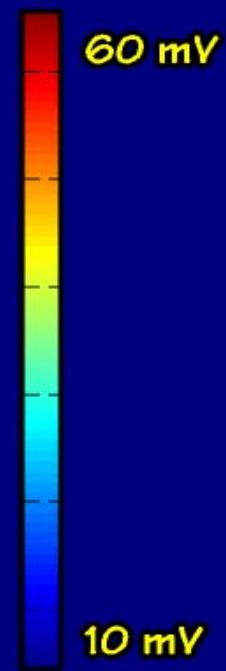
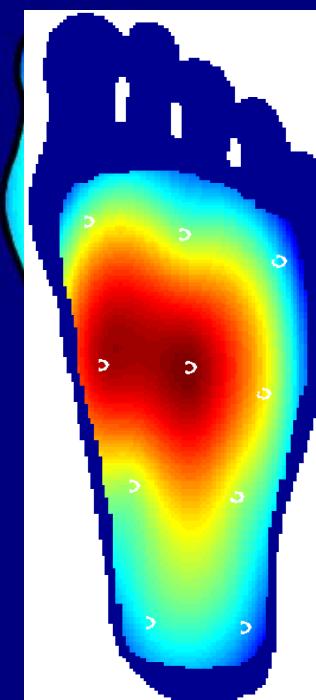
Schouenborg 2002

Healthy human



Andersen et al. 2001

Endometriosis



Reflex receptive field by stimulation of the foot sole and recording from tibialis anterior

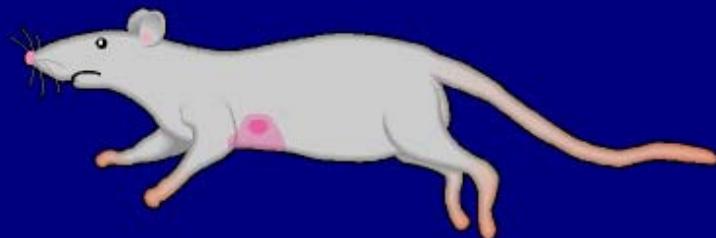


- Impaired descending control
- Central spreading of sensitisation
- Central integration

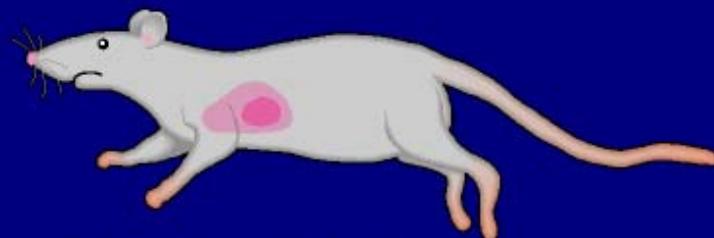
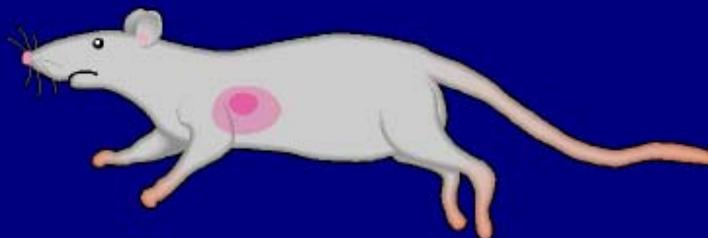


Receptive Fields and Visceral Nociception

*Changes in the size of convergent, cutaneous receptive fields
(spinal neurons studied in dorsal horn lamina I)*



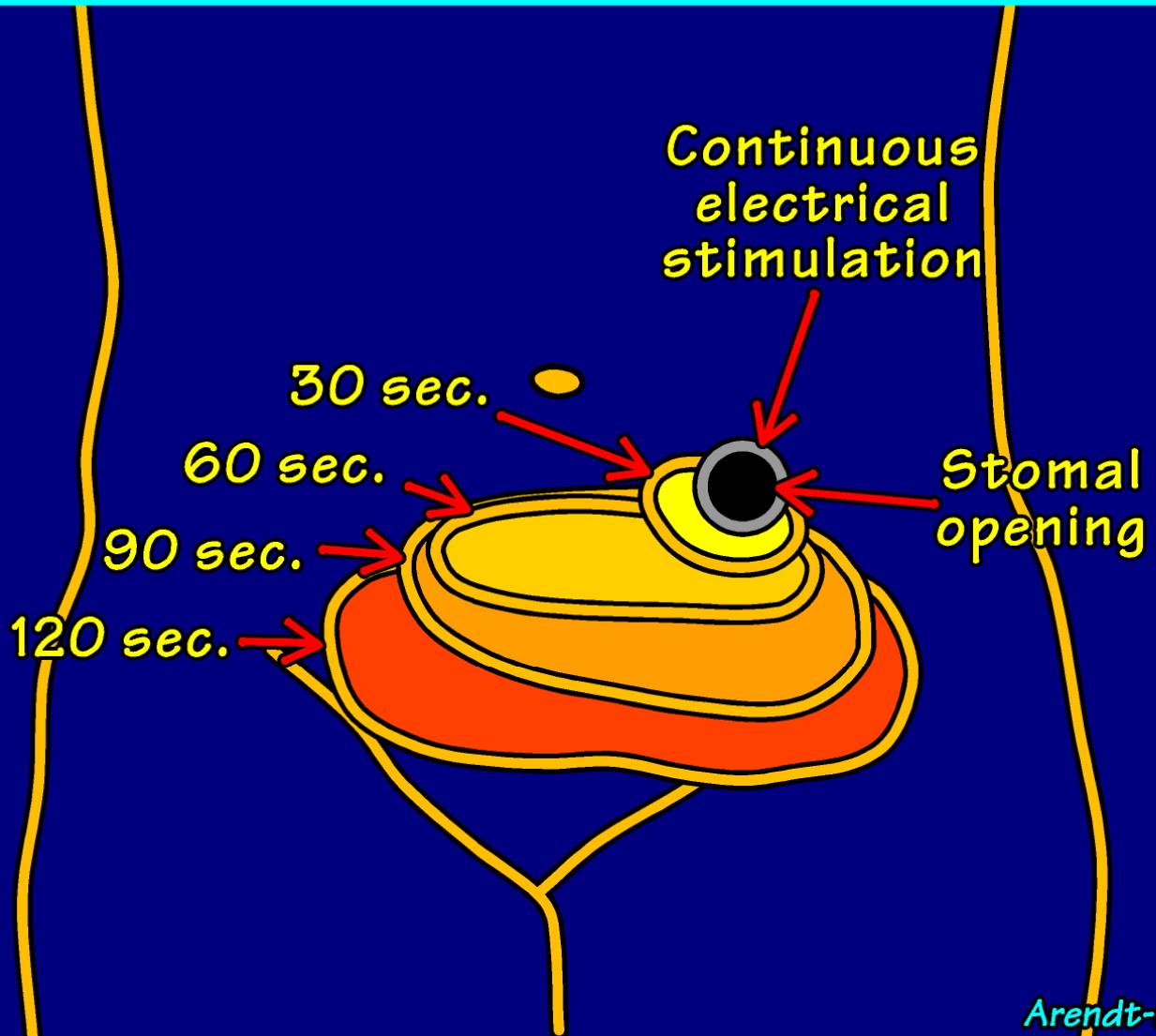
- Originally cutaneous receptive field
- Expanded cutaneous receptive field following 10 to 15 distentions given every 6 min.



Repetitive esophageal distension (1.25 mL, 30 sec)



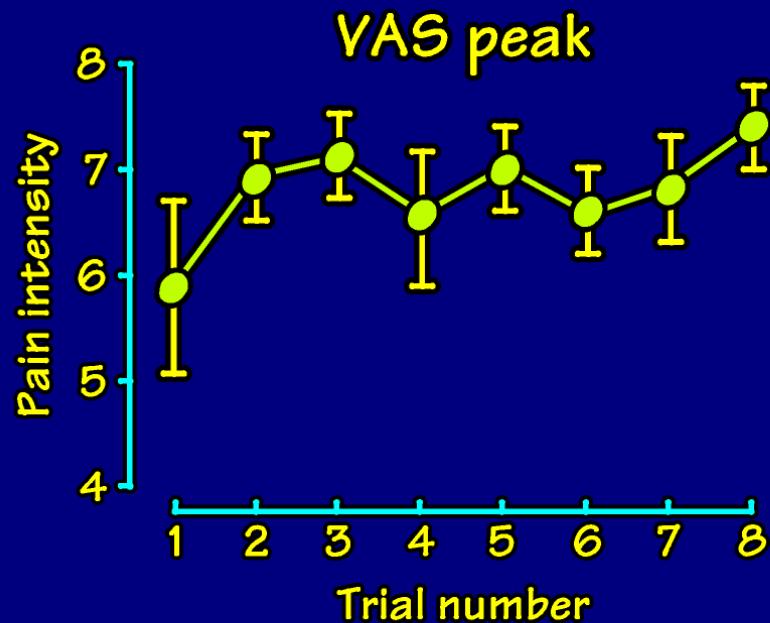
Temporal Summation of Visceral Pain





Visceral Hyperalgesia

Repeated Filling of the Urinary Bladder



Stimulation: 8 repeated fillings, 7 min apart.

VAS peak increased by 25%

Referred pain area increased by 72%



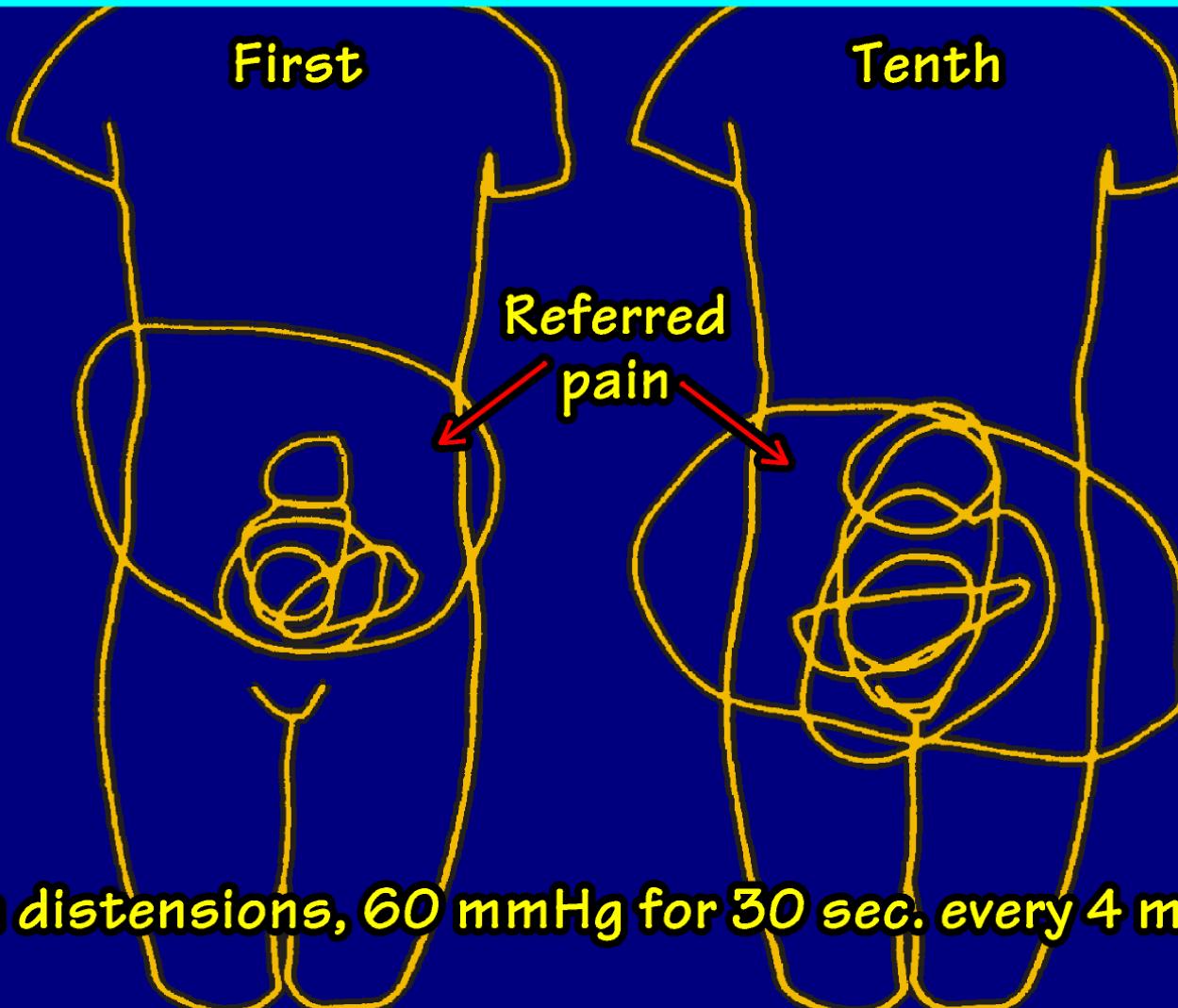
First trial



Last trial



Temporal Summation of Visceral Pain



Colon distensions, 60 mmHg for 30 sec. every 4 minutes

Nes et al., 90



Conclusion

- Neurophysiological mechanisms in animals translate into patients
- Visceral pain is referred and may amplify pain from other viscera, from muscles or from skin
- Referred visceral pain is a dynamic phenomena and is enlarged in recurrent or chronic visceral pain conditions
- Different manifestations of visceral hyperalgesia exist but little is known about the implications for treatment