



Persistent Postsurgical Pain:

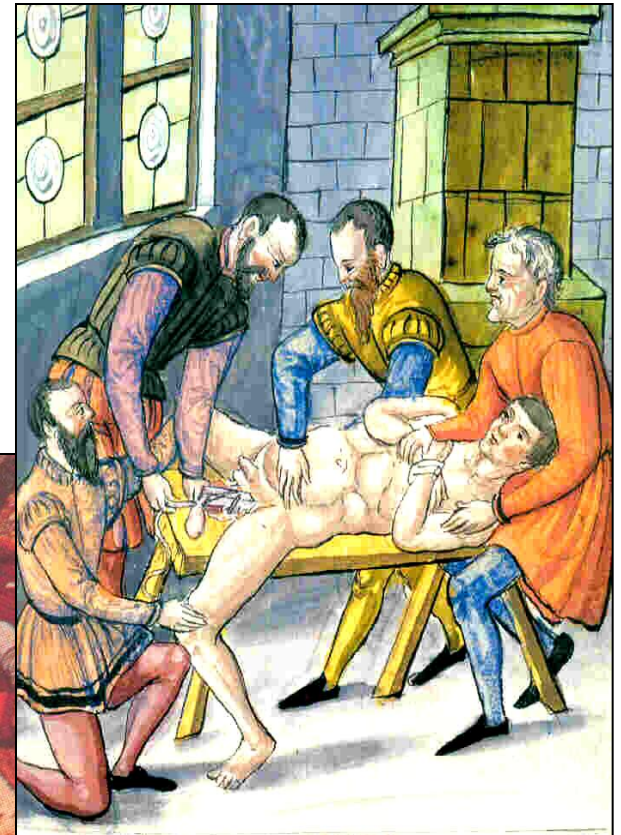
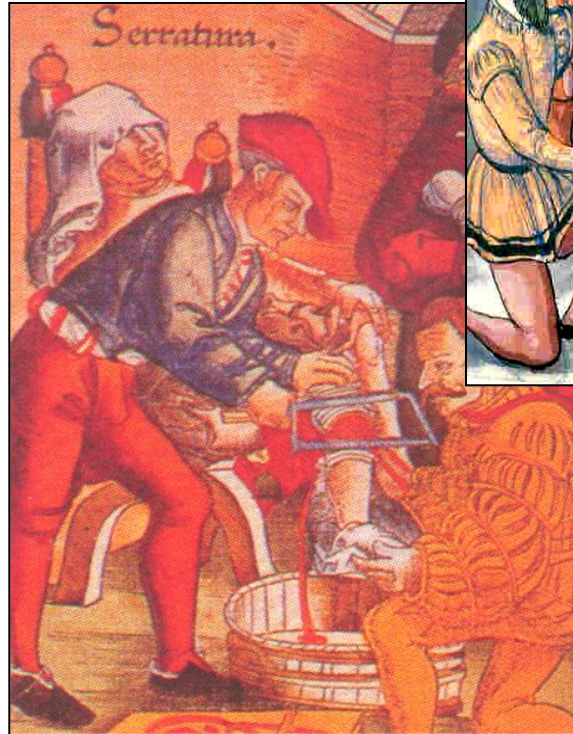
A Neuropathic pain condition

Hong Kong Pain Society April 24-25, 2010



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Aarhus University Hospital, Denmark

Surgery and pain: Acute but what about Chronic ?



Chronic Postoperative Pain

- Postoperative pain
- Neuropathic pain
- Mechanisms
- Types of operations
 - Mastectomy
 - Herniotomy
 - Hip arthroplastic
 - Hysterectomy
 - Limb amputation
- Conclusions



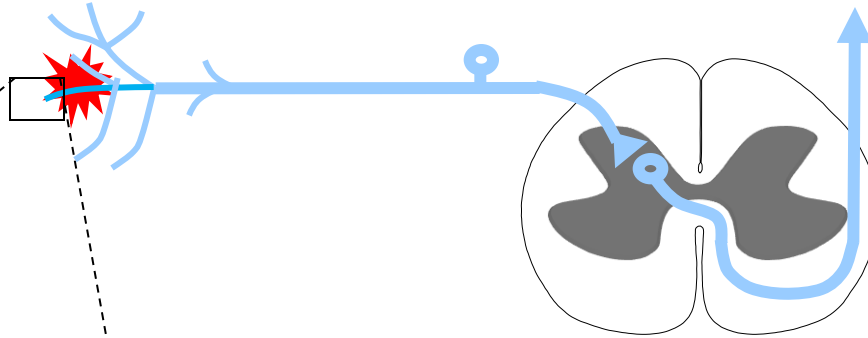
Epidemiology of chronic Postoperative pain

Surgical procedure	Incidence of Pain	Severe pain
Limb amputation	30-50%	5-10%
Breast surgery (mastectomy)	30-40%	5-10%
Inguinal Hernia repair	10%	2- 4%
Thoracotomy	30-40%	~10% ?
Coronary bypass	30-50%	5-10%
Caesarean sectio	10%	~4%
Hip arthroplastic	20%	<5%
Craniofacial surgery	5%	

Modified from Kehlet,, Jensen, Woolf, Lancet 2006 and others

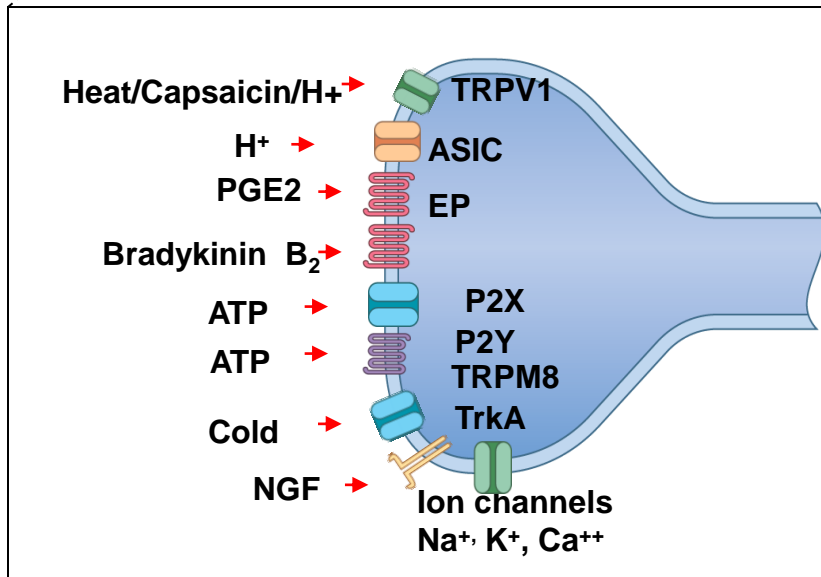
Tissue inflammation:

- Neurotransmitters
- Peptides: SP; CGRP; BK
- Prostaglandins
- Leukotrienes
- Neurotrophins
- Cytokines
- Chemokines
- Proteases
- Protons



Elements in injury sensitization:

NGF-TrkA activate signaling pathways. PLC, MAPK
NGF transport to DRG: increase in: SP, TRPV1 Nav 1.8
Cytokine release ; Il-1, Il-6 ,TNF- α
Protons act on TRPV1 and ASIC



Nerve injury

Cellular changes

Spontaneous neuronal activity at injury site and in DRG

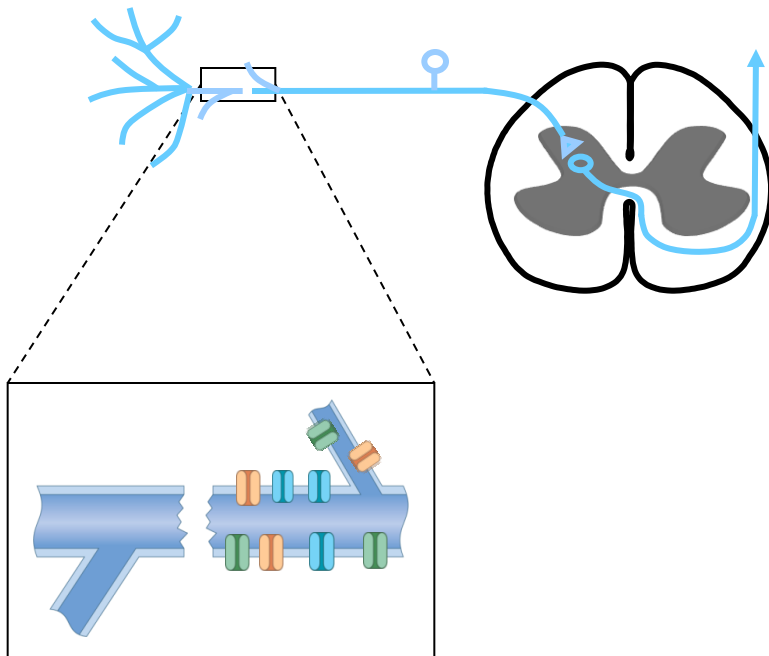
Expansion of receptive fields of DH cells

Recruitment of silent cells in DH

Increased response to suprathreshold stimuli

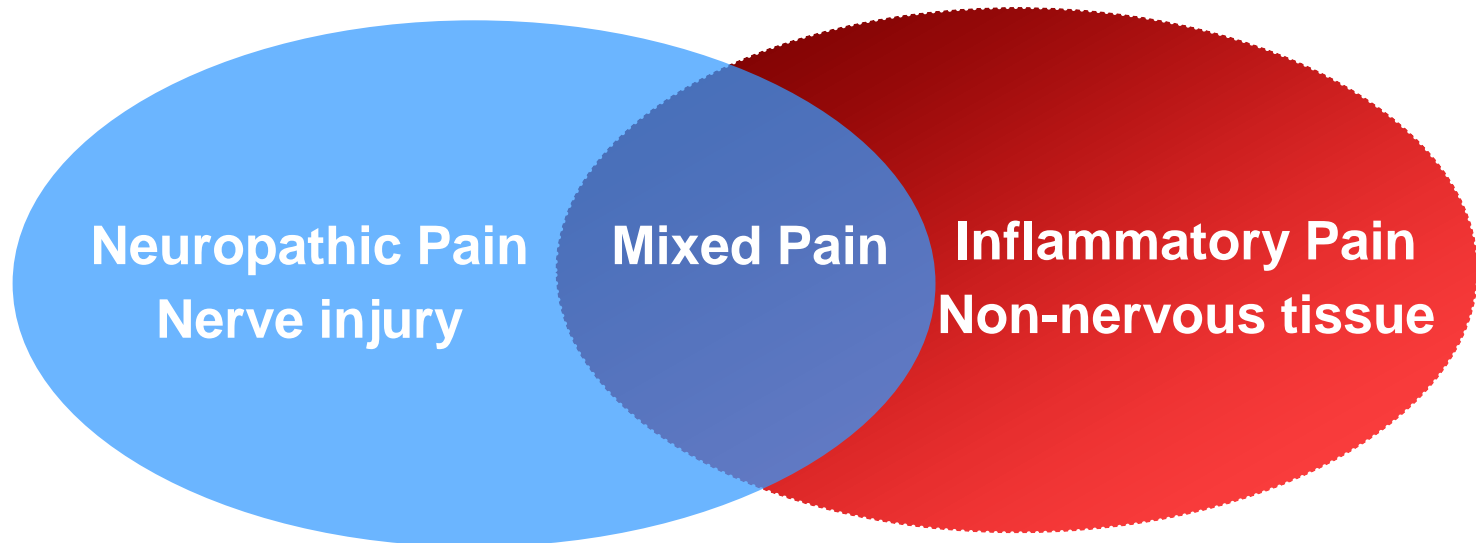
Lowering of threshold

Abnormal summation



Na ⁺ channels	TTX S/R	N. injury
Nav 1.1	S	↓
Nav 1.2	S	↓
Nav 1.3	S	↑
Nav1.4	S	↑
Nav1.5	R	↑
Nav1.6	S	↓
Nav1.7	S	↓
Nav1.8	R	↓
Nav1.9	R	↓
NaX	S	↑

Neuropathic, Inflammatory and Mixed Pain



Chronic Pain: Classification

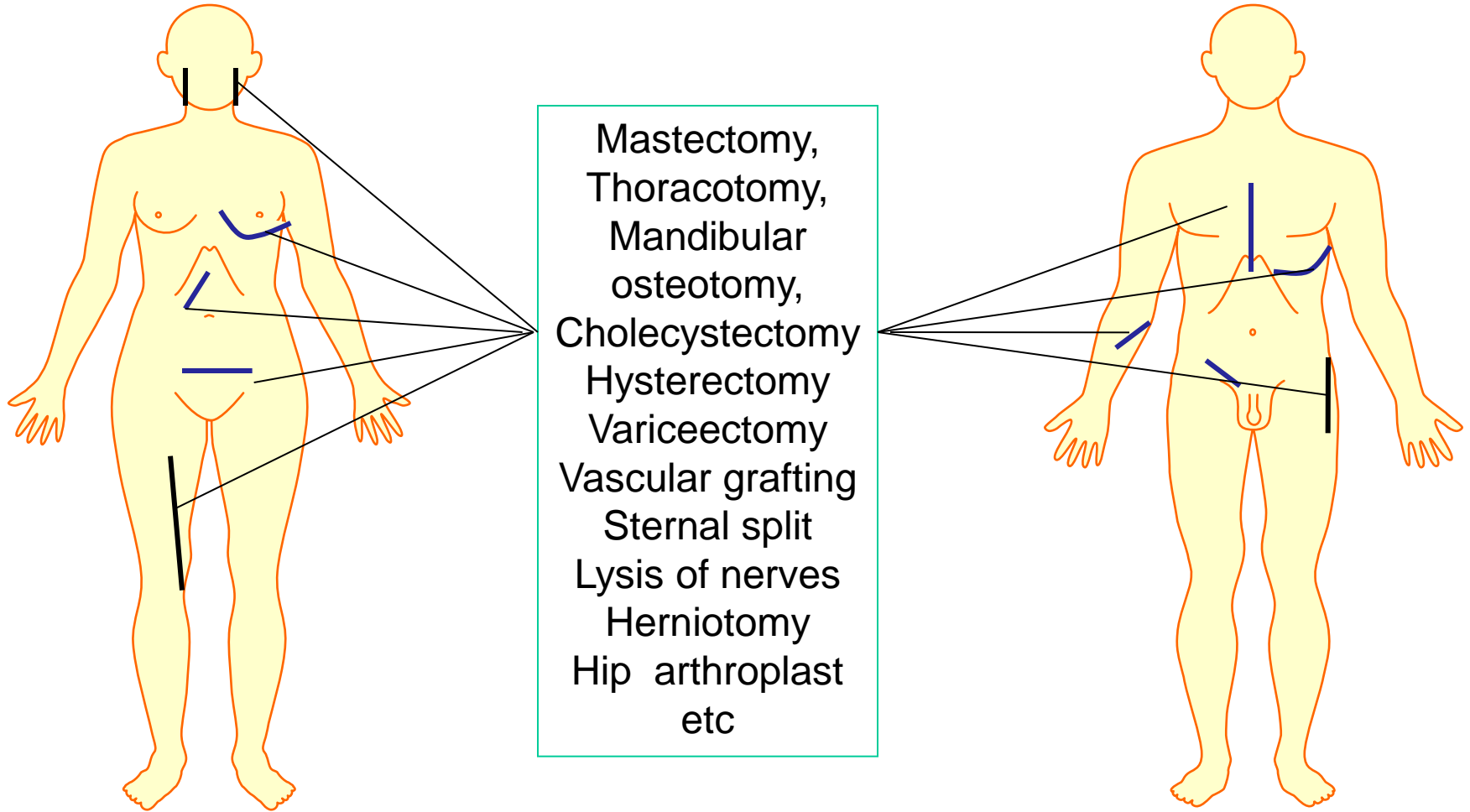
Neuropathic	Nociceptive	Mixed Pain	Idiopathic Pain
Nerve injuries	Osteoarthritis	Cancer Pain	Fibromyalgia
Amputations	Rheumatoid arthritis	Neck pain	Bodyly distress
Plexus avulsion	Postoperative pain?	Low Back pain	Whiplash injury
PHN	Colitis	Limb Pain	Irritable bowel
Trig. neuralgia	Tendinitis	Visceral pain	Interst. cystitis
Neuropathies	Myositis	Thoracic pain	
Syringomyelia	Migraine	Postoperative Pain ?	
MS	CRPS		
Spinal cord injury			
Stroke			
CRPS ?			
Postoperative pain ?			

Chronic Postoperative Pain

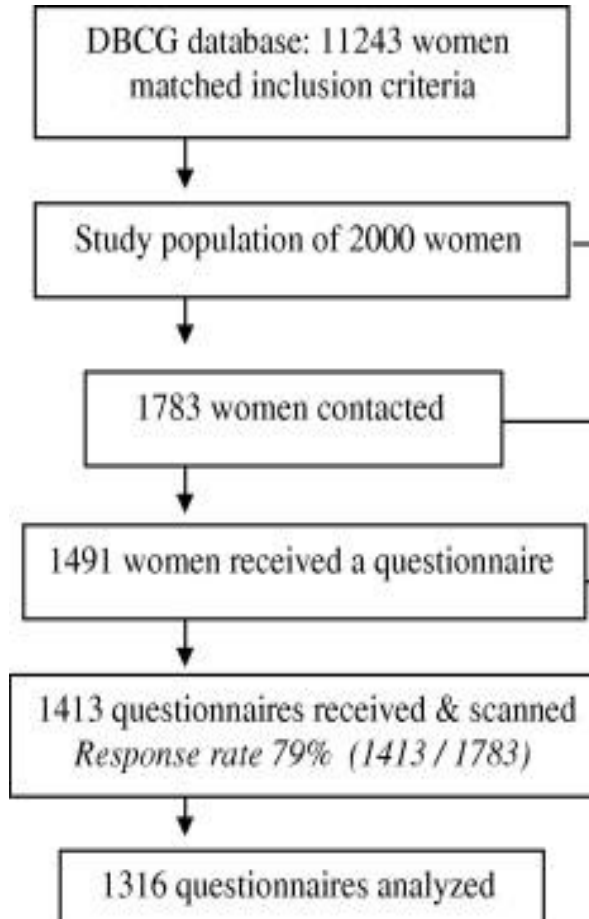
- Postoperative pain
- Neuropathic pain
- Mechanisms
- Types of operations
 - Mastectomy
 - Thoracotomy
 - Facial osteotomy
 - Herniotomy
 - Hip arthroplastic
 - Hysterectomy
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- Conclusions



Surgical procedures and chronic pain



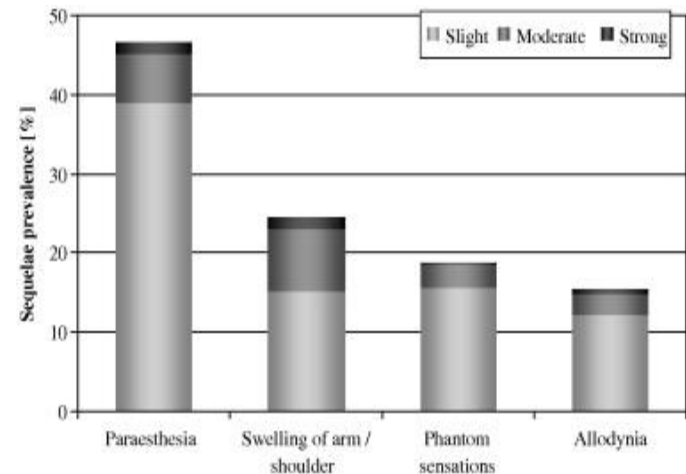
Postmastectomy Pain



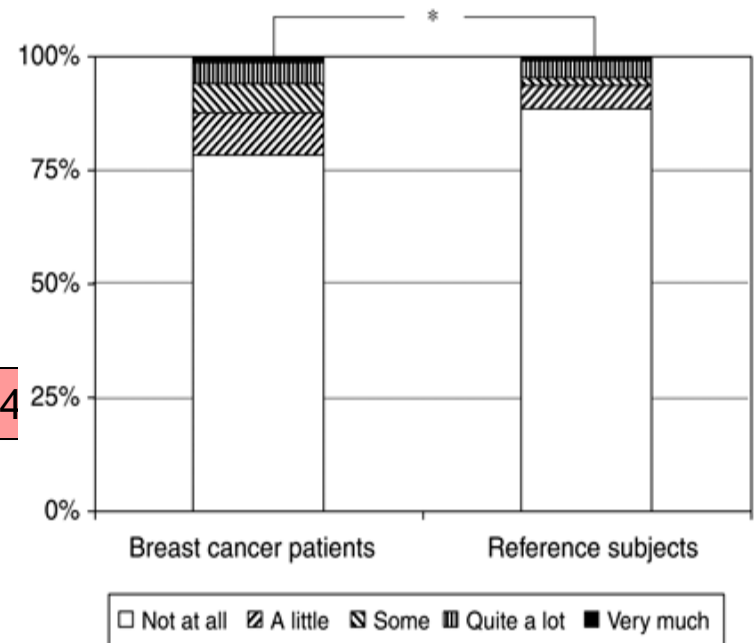
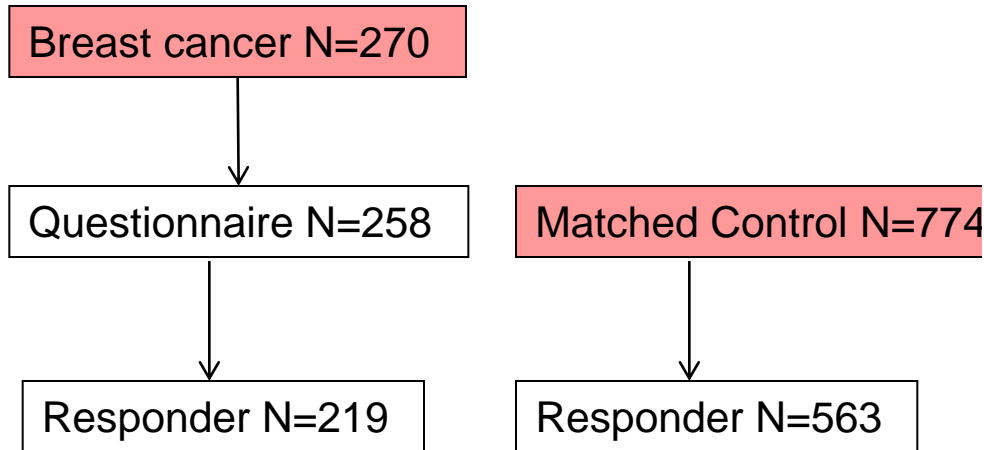
Chronic pain overall: 42%
Pain related to cancer: 29%

Identified risk factors:

- Radiotherapy
- Young age
- Short education, single status



Postmastectomy Pain



Identified risk factors:

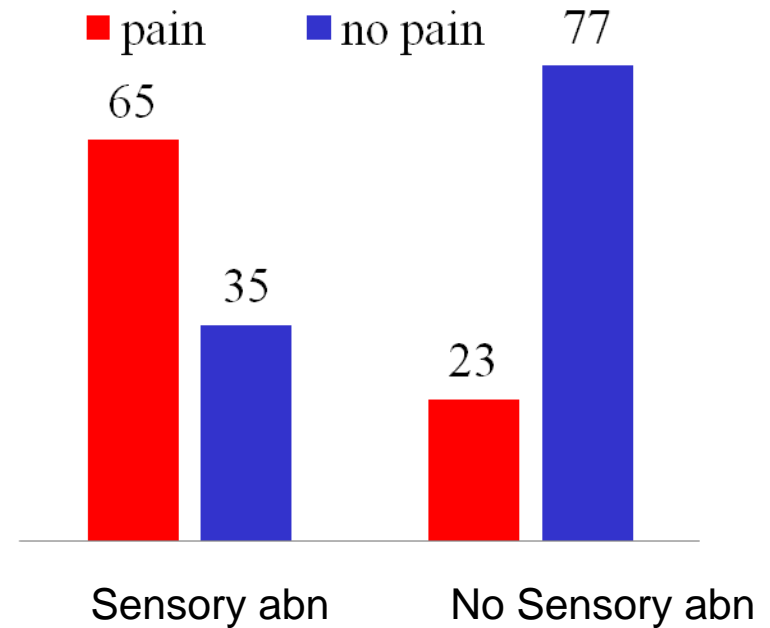
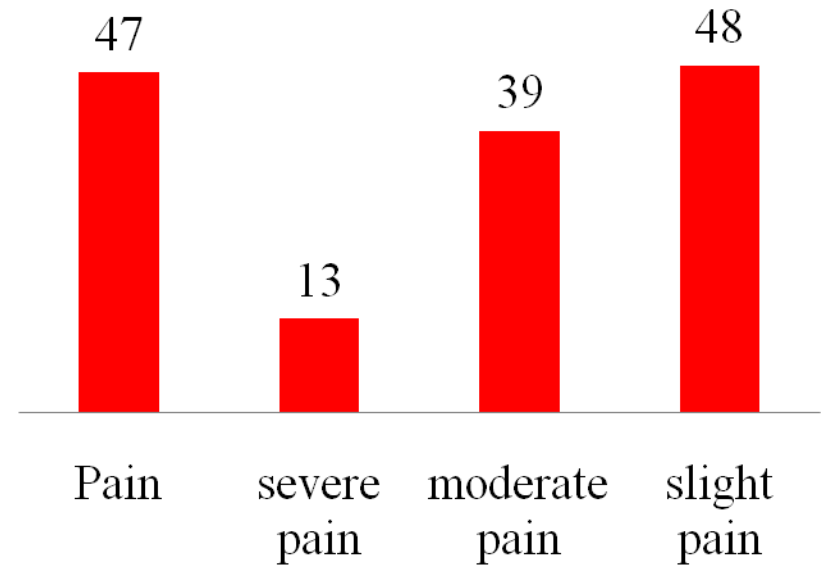
- Prior breast surgery
- Tumour in upper lateral quadrant
- Young age

Postmastectomy pain syndrome: 24%
Control: 10%

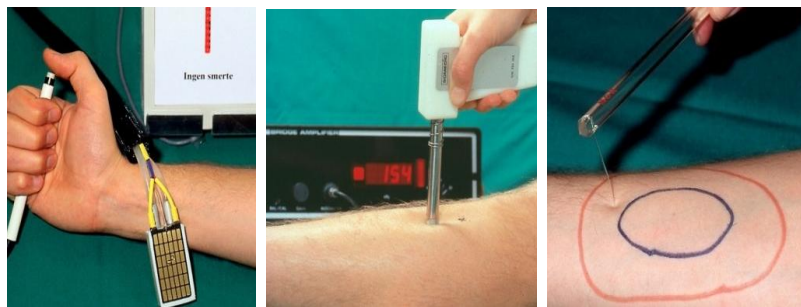
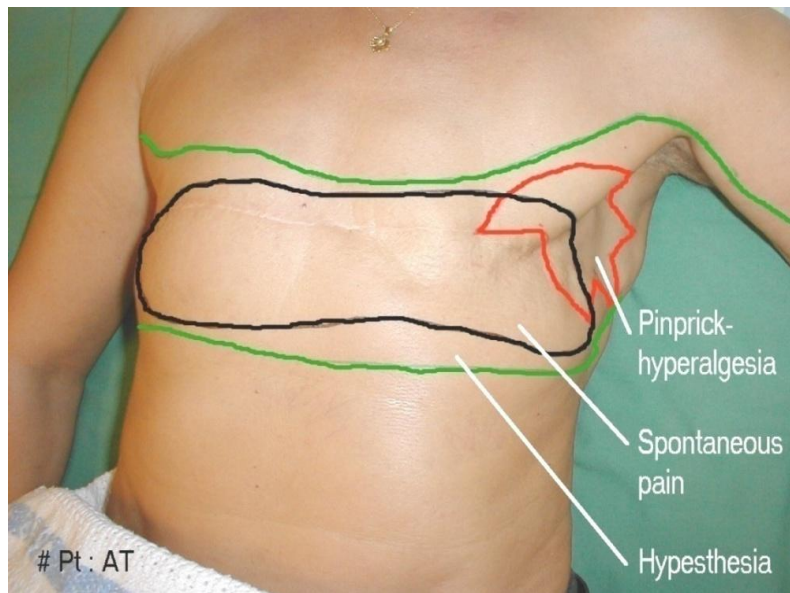
Persistent pain after breast cancer surgery

Nation wide questionnaire
3754 women operated 2005/2006
3253 responded (87%)
Pain 2-3 yrs after surgery

Pain related to young age
Pain related to radiotherapy
Pain related to sensory disturbance



Postmastectomy pain: Epidemiology



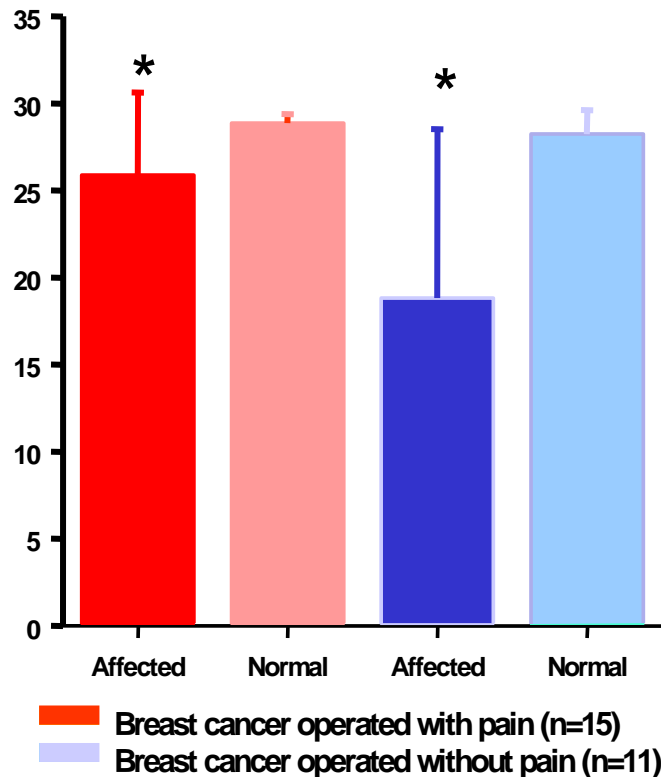
Study	N	Chest pain	Arm pain	Follow up
Chiverton et al. 1985	65	11%	26%	Not indicated
Krøner et al. 1989	110	23%	54%	12 mths
Tasmuth et al. 1995	283	-	34%	30 mths
Wallace et al. 1996	103	-	-	2-6 yrs
Carpenter et al 1998	134	27%	-	> 3mths
Smith et al. 1999	408	29%	-	6 yrs
Peuckman et al. 2000	2000	29%	20%	>5 yrs
Vilholm et al. 2008	219	24% 10% control	-	18 mths
Gärtner et al. 2009	3253	47%	-	24-36 mths

Chronic Postmastectomy Pain: Paradox sensitivity

Sensory loss:

Reduced cold sensitivity on painful and painless op. side

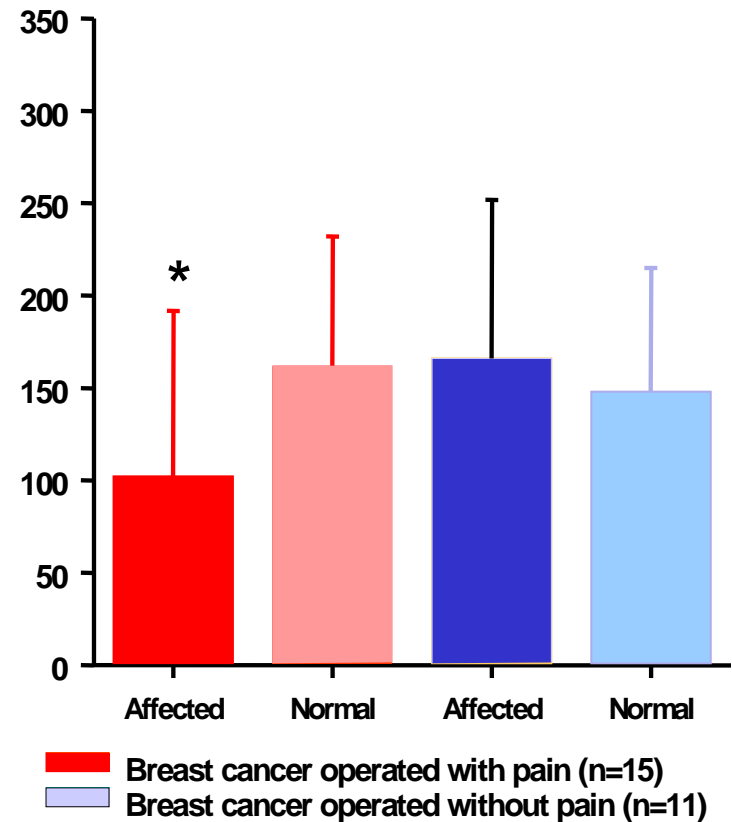
Temp °C



Hypersensitivity:

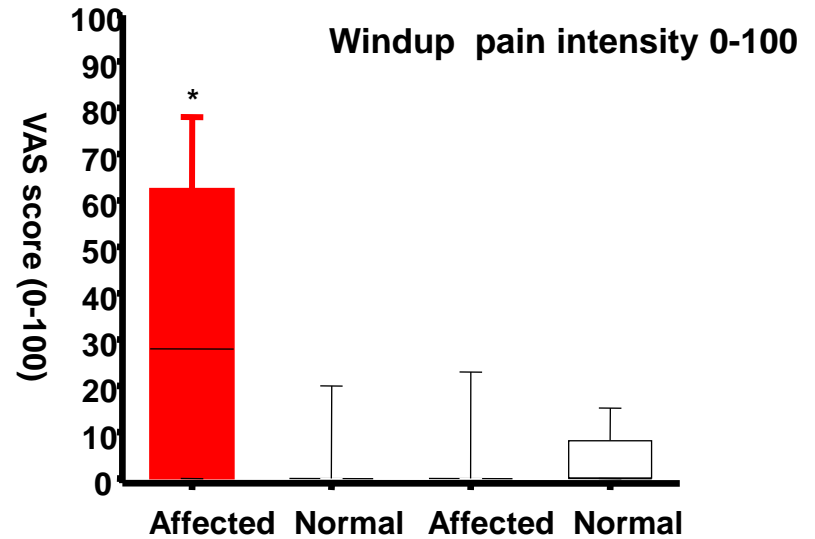
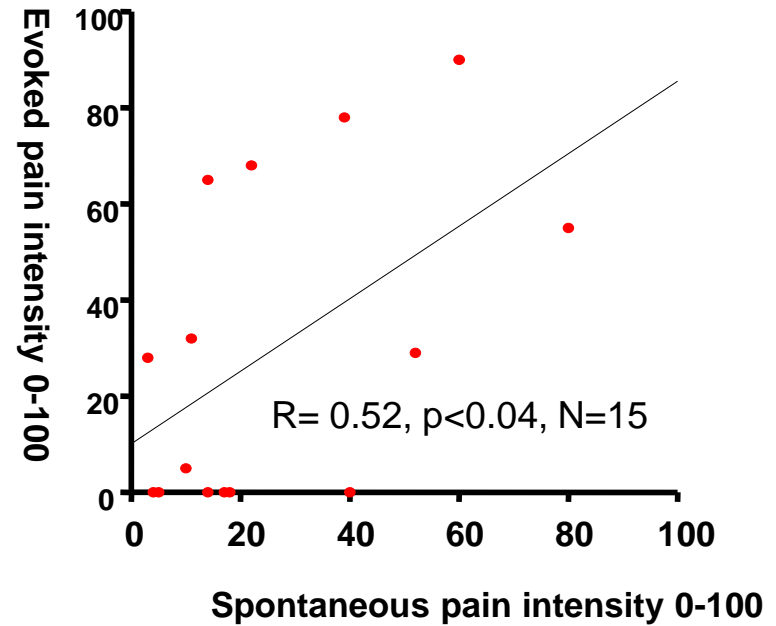
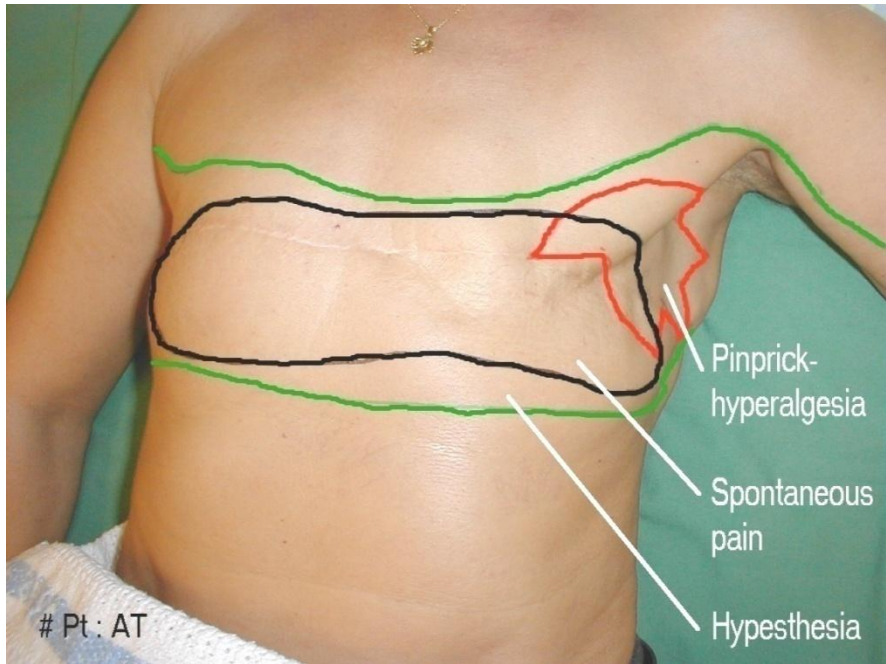
Mechanical threshold reduced on painful side

KPa



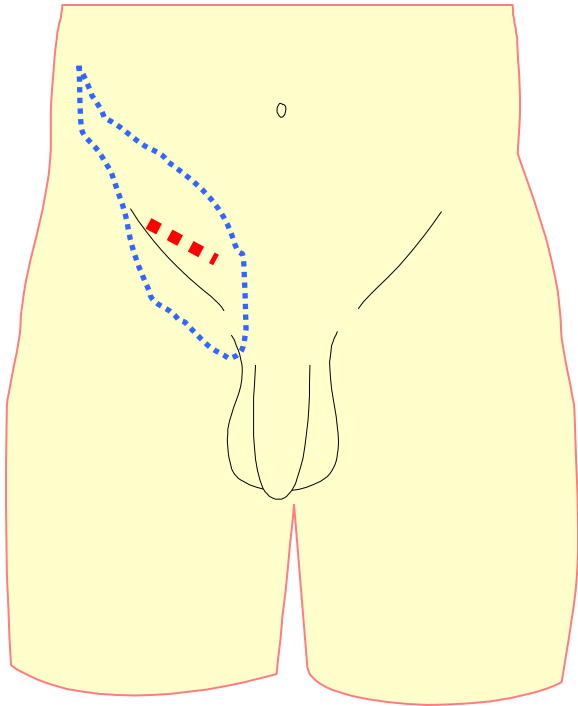
Post mastectomy Pain:

sensory loss
hypersensitivity
wind-up like pain



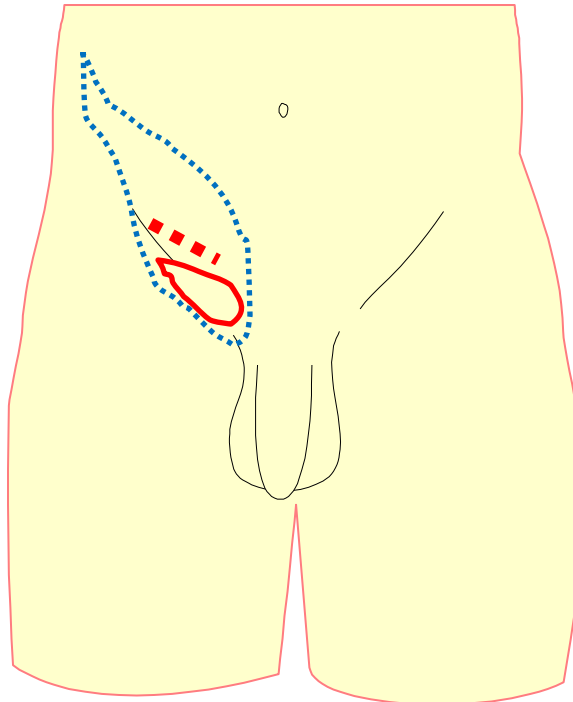
■ Breast cancer operated with pain (n=15)
□ Breast cancer operated without pain (n=11)

Sensory abnormality post-herniotomy pain



Reduced
sensitivity

Increased
sensitivity



60-yr M, healthy; 2003 inguinal
herniotomy

Fulltime work as a work
manager; active in sport

2003: Inguinal herniotomy
uncomplicated

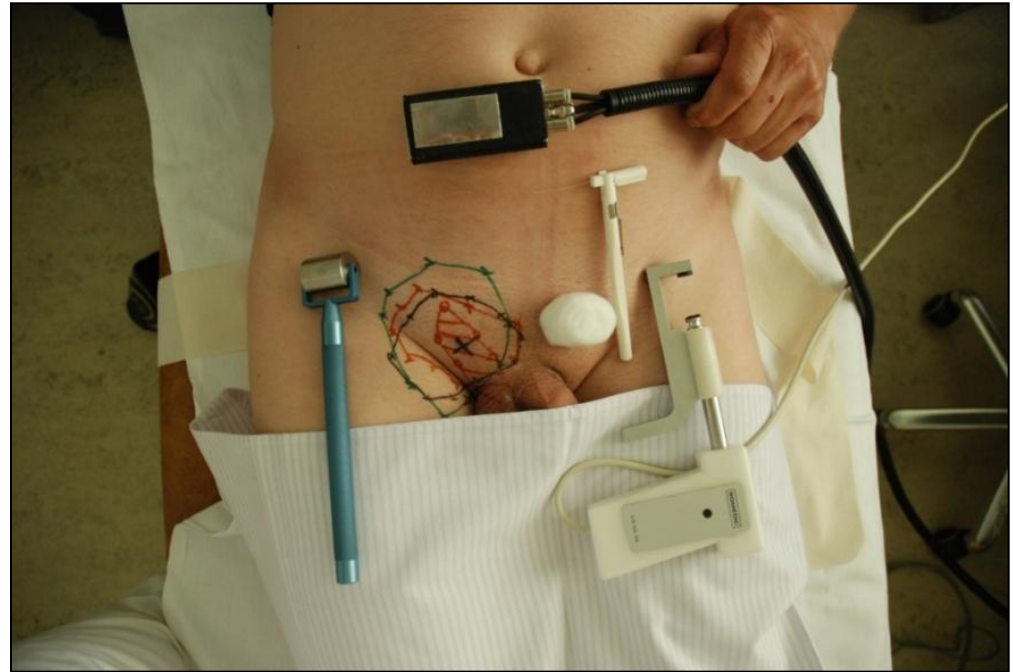
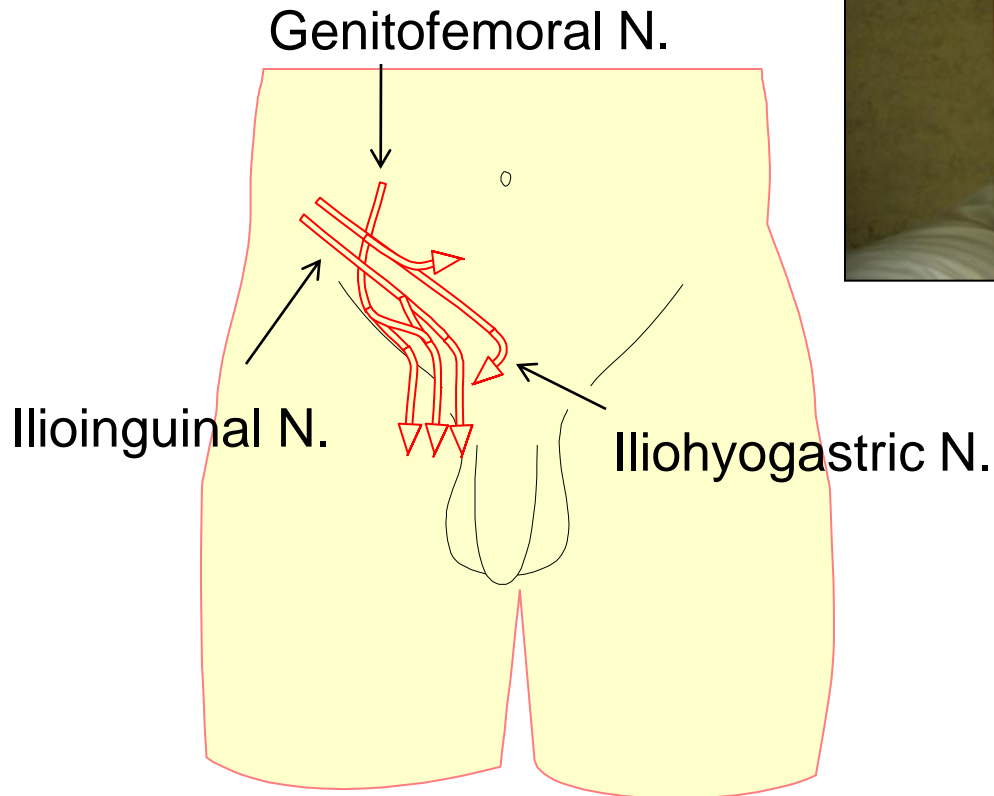
Constant pain: **VAS:2**
movement pain: **VAS:7**

Wake up 1-2 x during night
because of pain

Can't do sports, Can't walk with
his dog. Has put on 5 kg.
Sexual activity stopped

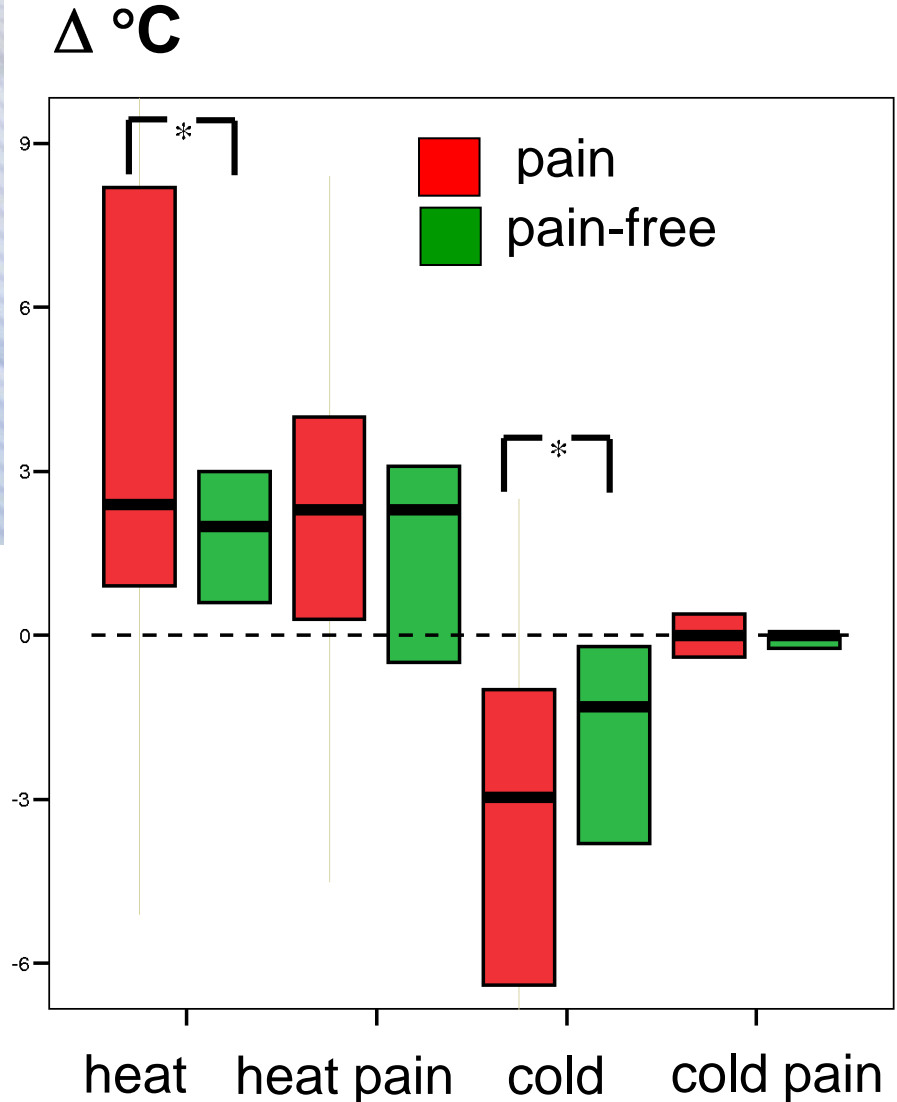
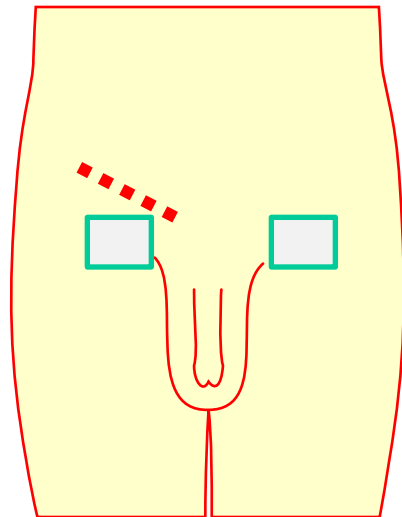
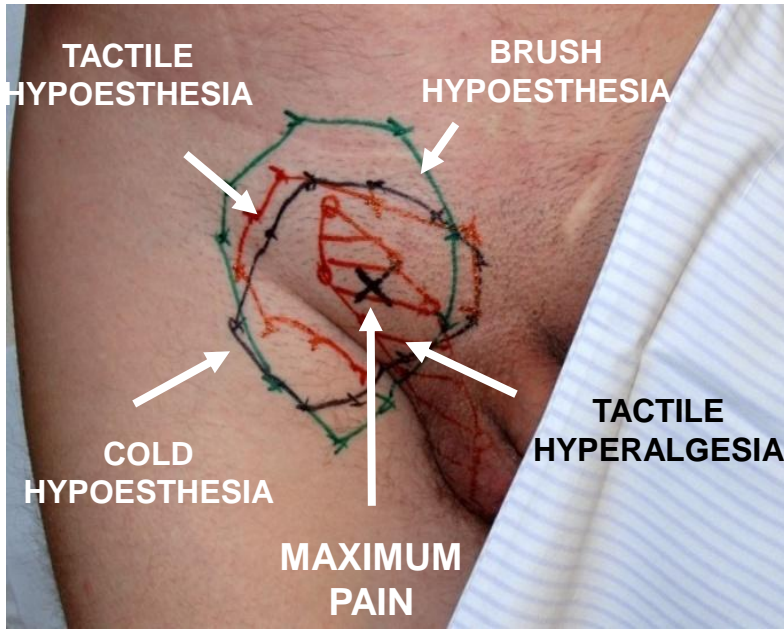
Persistent postherniotomy pain:

Sensory loss ?
Hypersensitivity ?



Chronic postherniotomy pain: Thermal

Reduced thermal sensitivity =
Loss of function

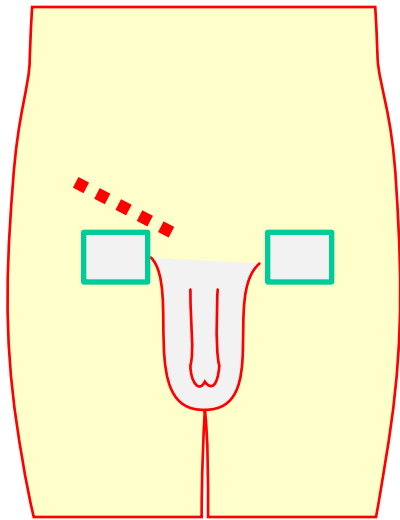


Chronic postherniotomy pain: Pressure

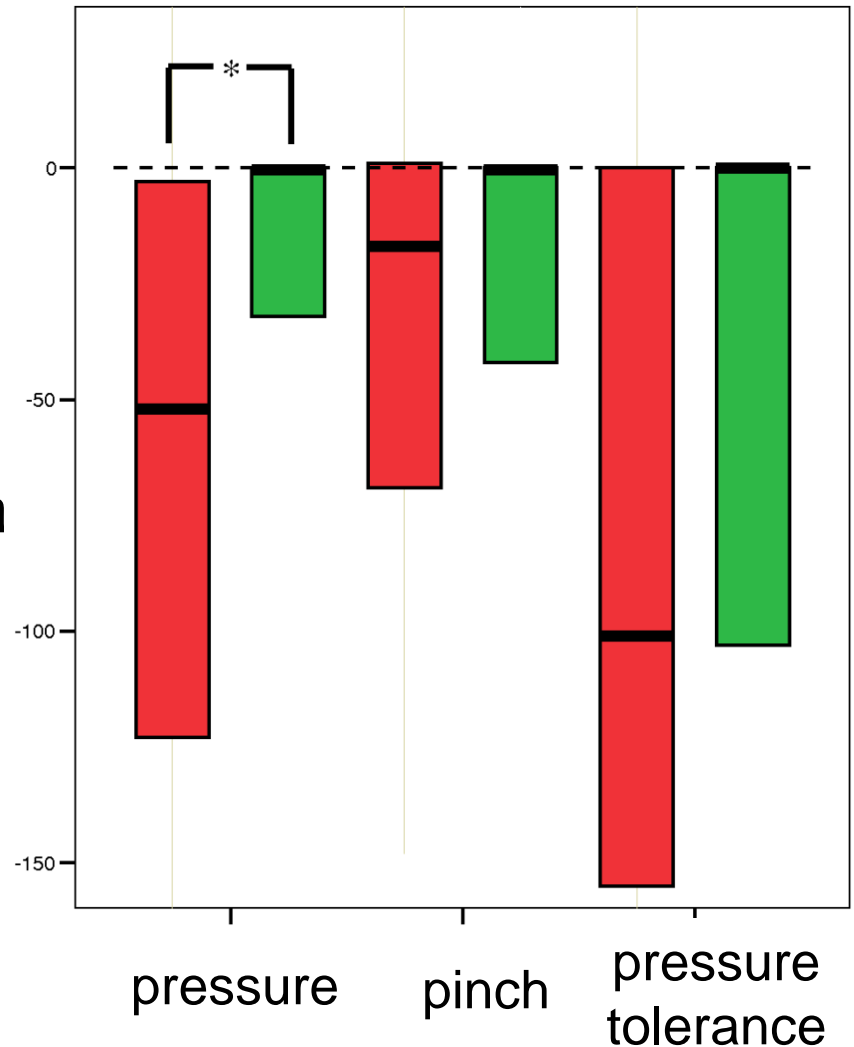
Δ pressure pain threshold = operated side – contralateral side

Reduced pain threshold = Hyperexcitability

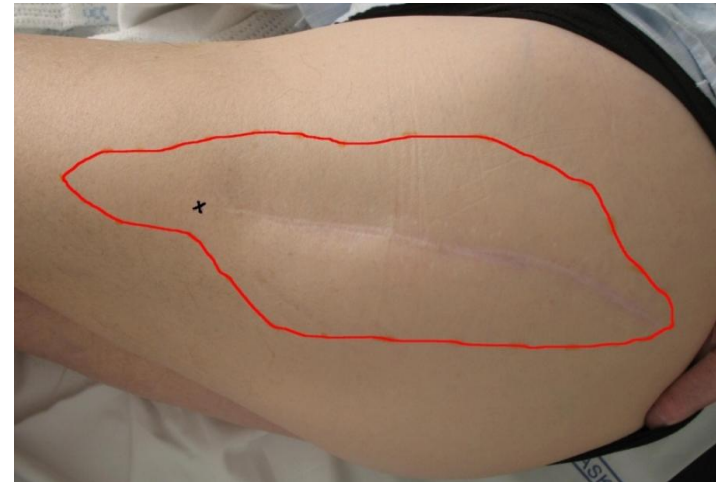
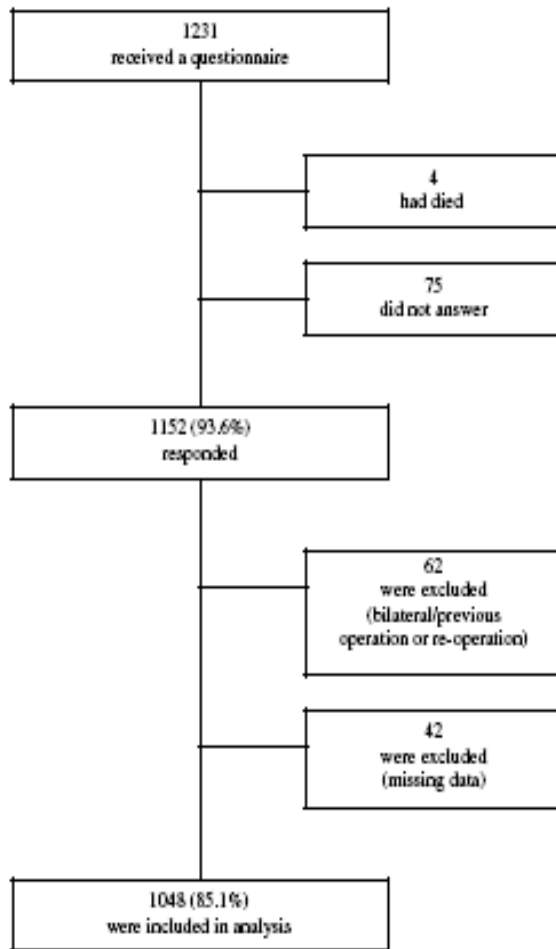
■ pain
■ pain-free



Aasvang et al. 2007



Chronic pain: Hip arthroplasty

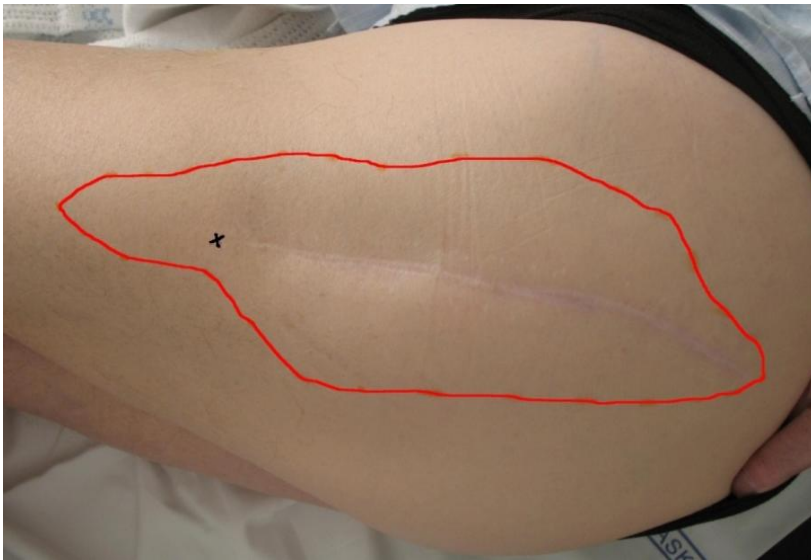


Danish Hip Arthroplast database www.dhr.dk
12 31 Q's to Danish patients operated
between March 1 and Oct 31, 2003

Follow-up 1- 1½ yr:
294 (22%) had pain
124 (12%) daily pain
53 (5%) moderate to severe pain

Sensory examination: Hip arthroplasty

None had sensory loss
Hypersensitivity was localised



Nikolajsen et al.2009

Material:

51 pts with daily pain > 3

18 Pain pts examined

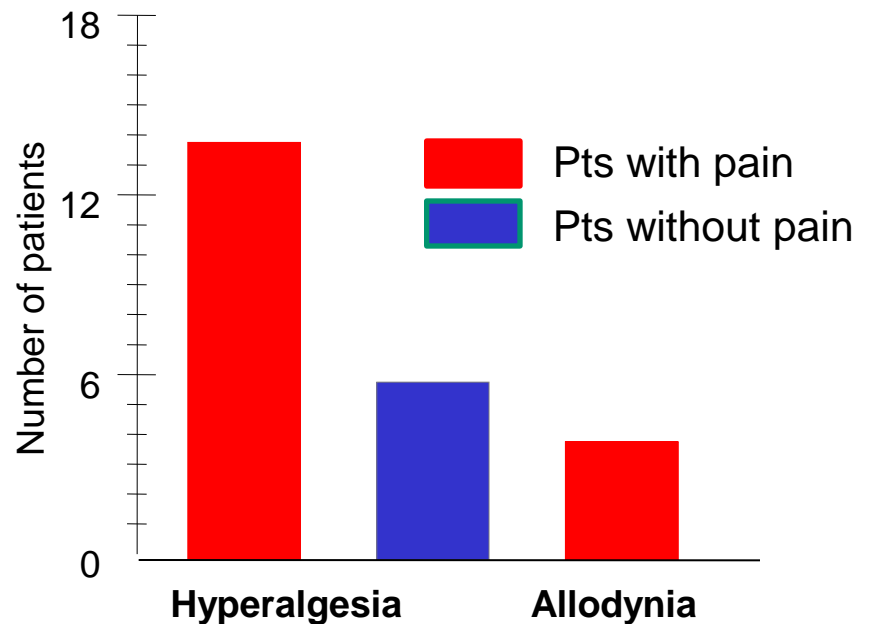
18 matched controls examined

Sensory examination:

Tactile (TDT, TPT)

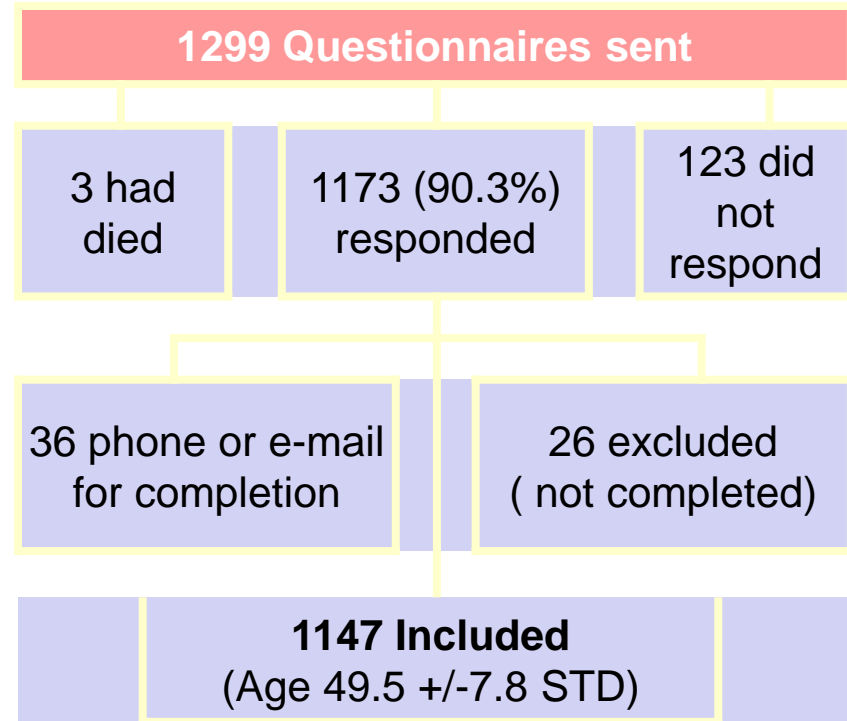
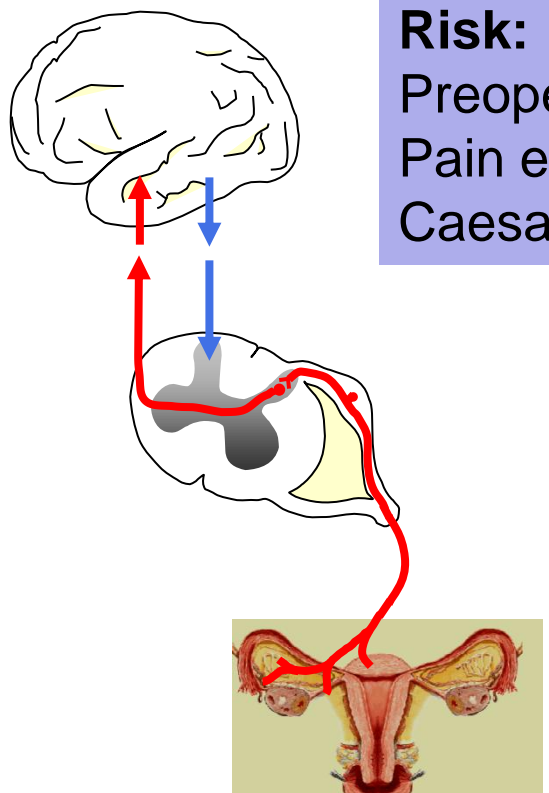
Pressure (PPT, PTT)

Thermal (CDT; CPT, WDT, WPT)



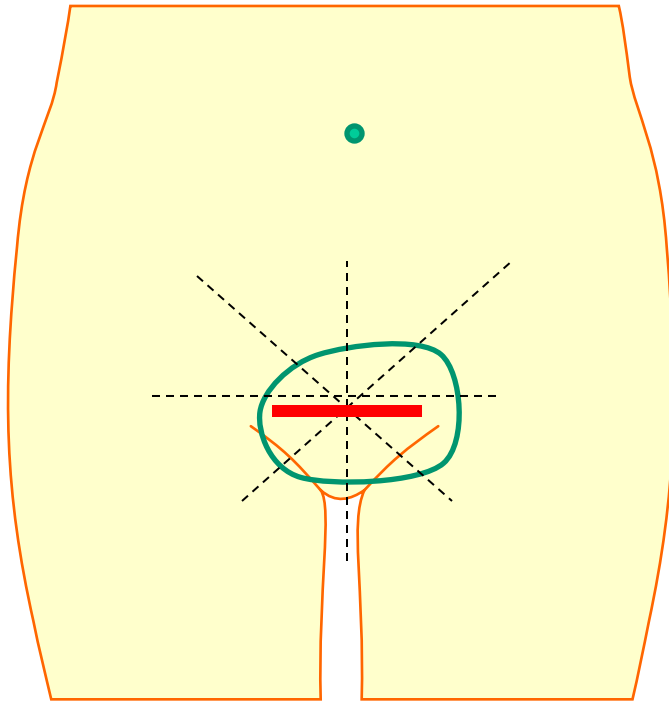
Pain after hysterectomy: 1 yr. follow-up

Risk:
Preoperative pain
Pain elsewhere
Caesarean section



Pain after hysterectomy: N=1135; Preop pain: 61.9%; Postop pain >12 mths: 31.9%

Hysterectomy: Skin hypersensitivity (N=90)

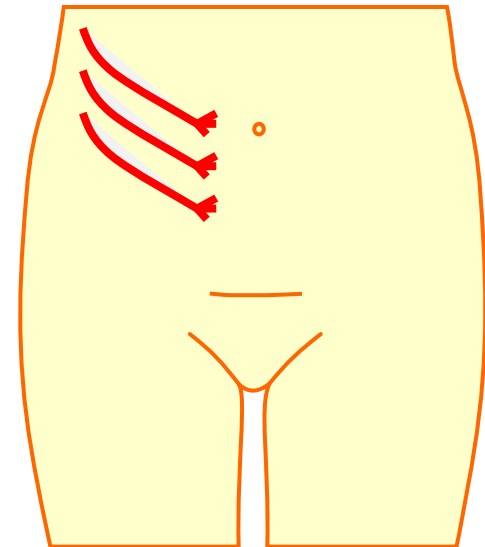
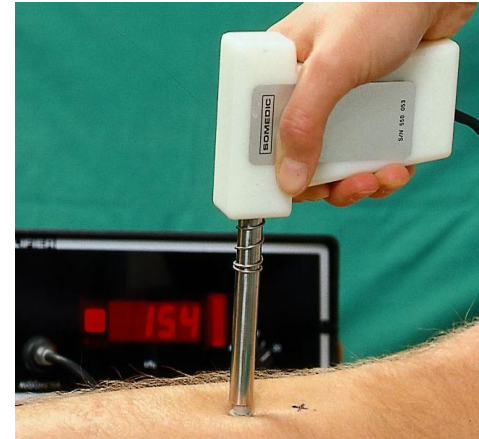
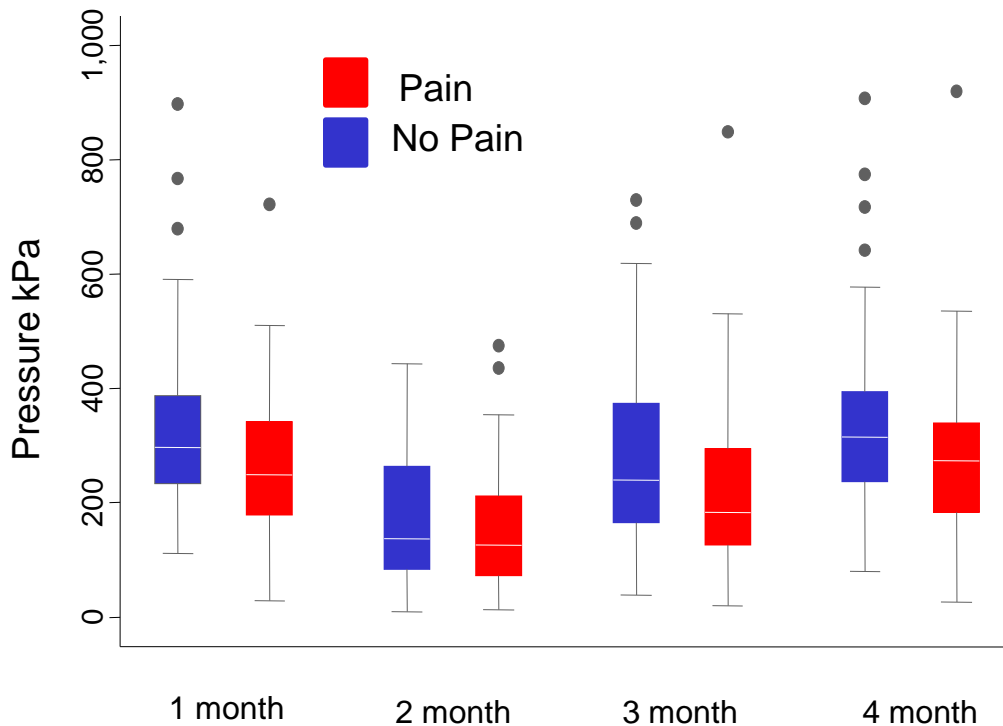


Hyperalgesia		Before	4 months
Brush	N, %	16 (17.8)	3 (3.3)
	Area, cm ²		
	Median (range)	40 (20-60)	30 (22-60)
Pinprick	N, %	20 (22.2)	5 (5.6)
	Area, cm ²		
	Median (range)	39 (5-60)	22 (13-60)

Pain following hysterectomy:

Prospective study: N= 97

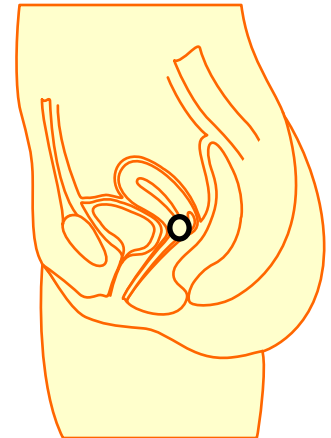
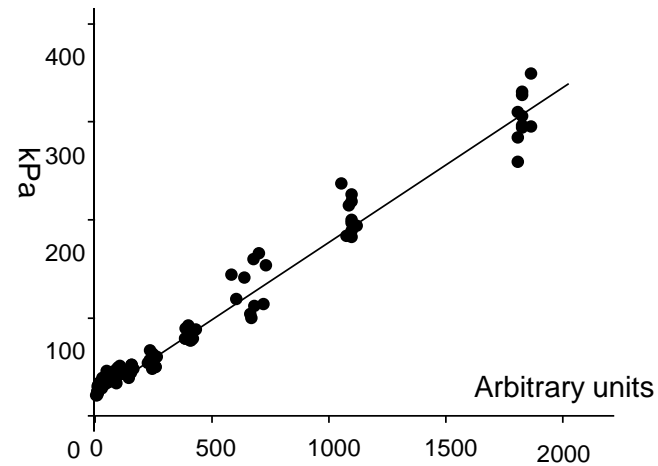
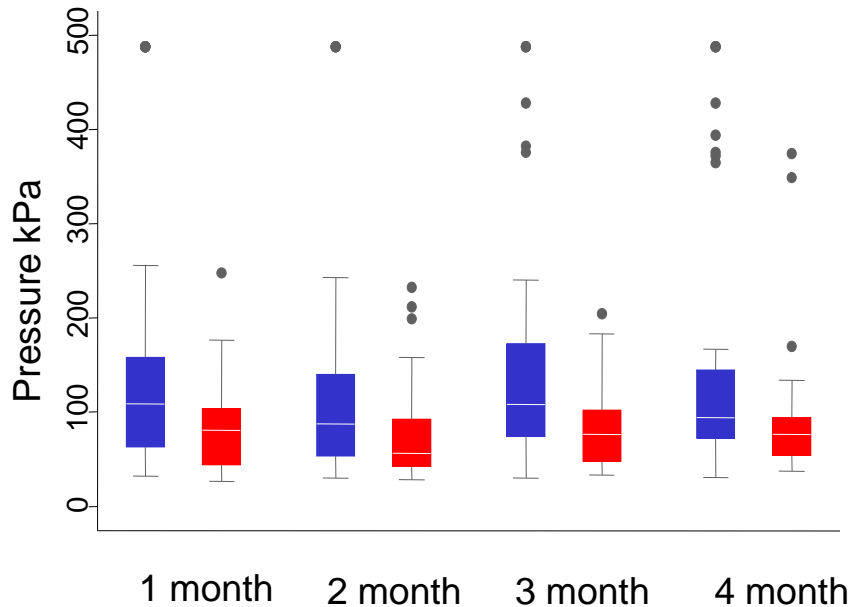
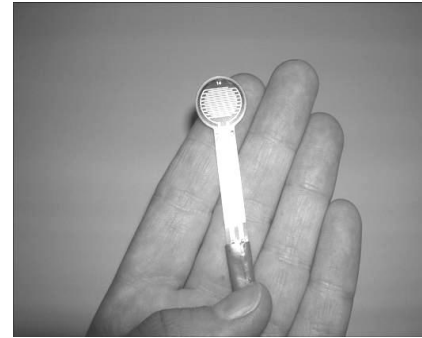
Pain tolerance threshold
in women with and without
pain **before** hysterectomy.



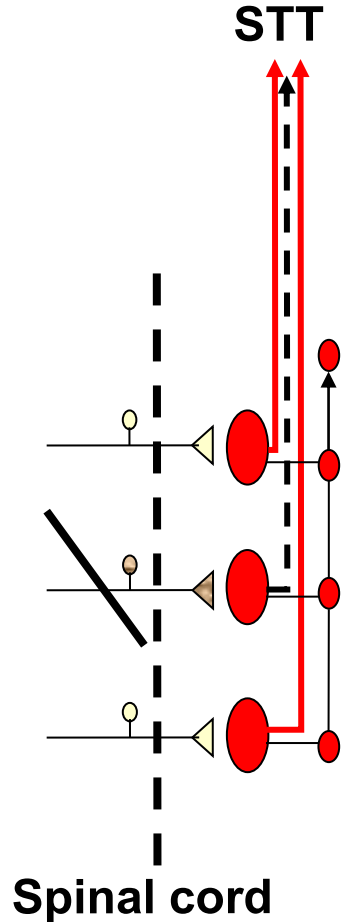
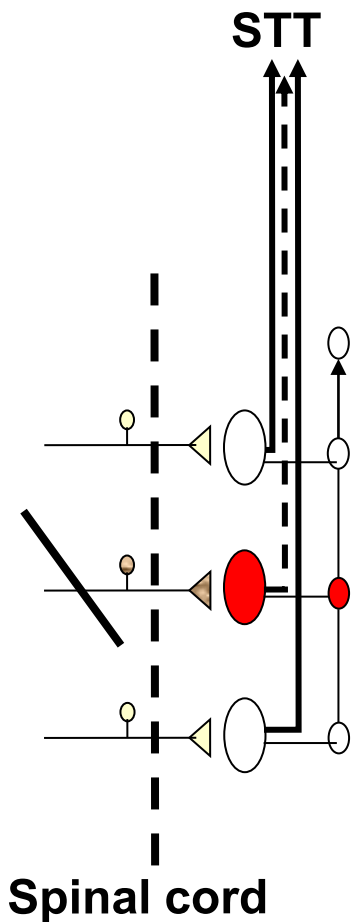
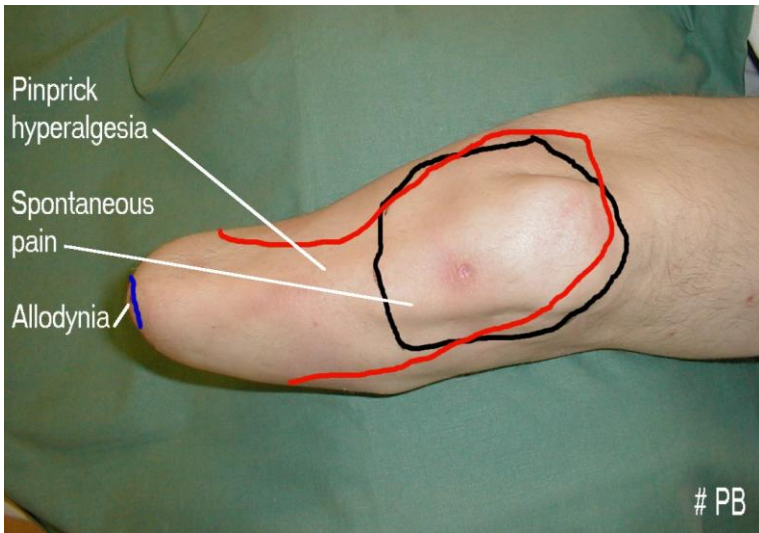
Pain following hysterectomy:

Prospective study: N= 97

Vaginal pain threshold
in women with and without
pain **before** hysterectomy.



Postamputation pain



Phantom Pain Mechanisms:

Peripheral

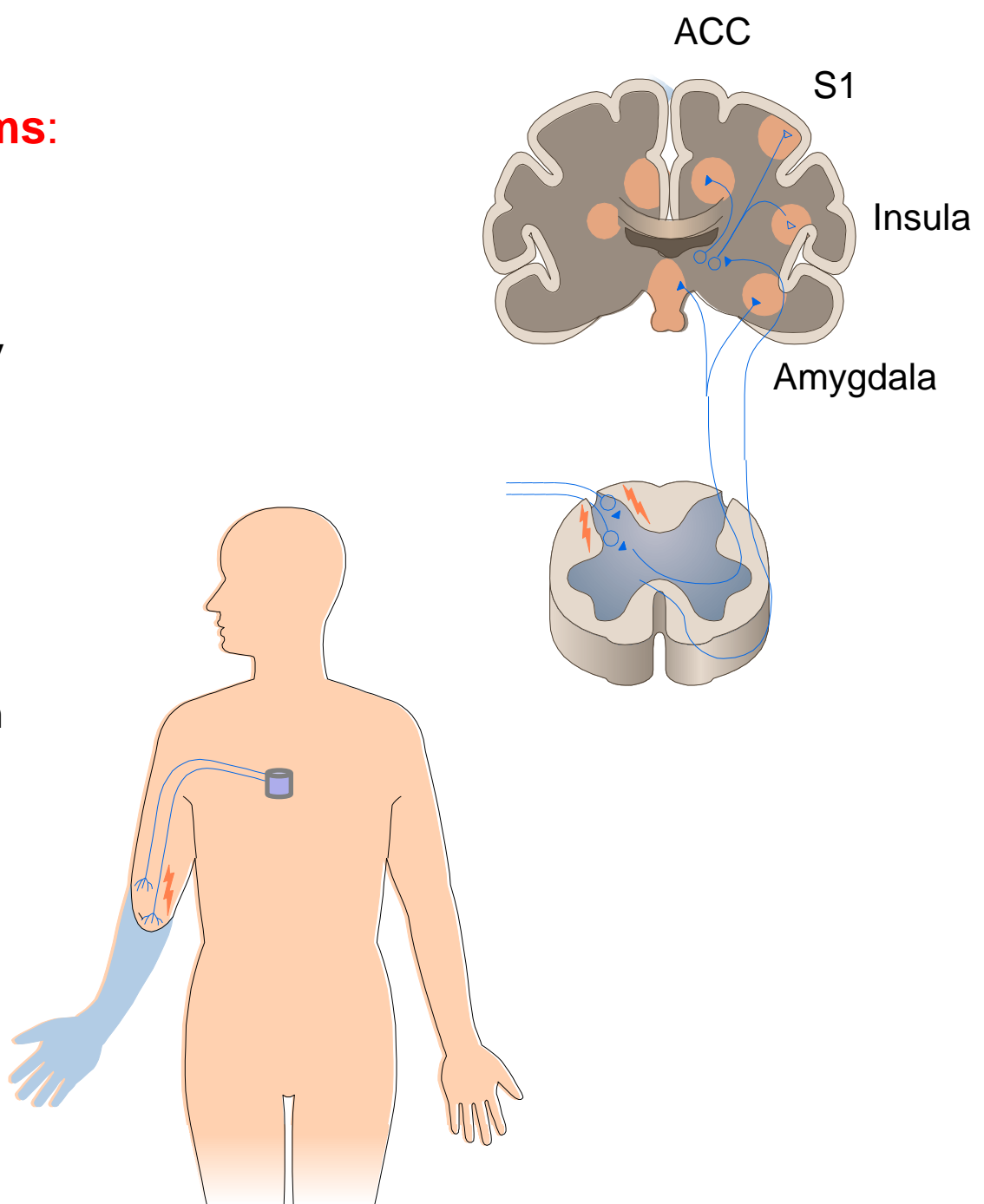
- Peripheral sensitisation
- Spontaneous neuronal activity
- DRG abnormal activity

Spinal

- Central sensitization
- Spontaneous neuronal activity
- Wind up like pain
- Spread of central sensitisation

Supraspinal

- Cortical reorganisation
- Anxiety
- Catastrophising



Neuroplasticity in amputation:

24 pts with postamputation pain

14 High Phantom pain intensity (mean VAS: 6.4)

10 Low Phantom Pain intensity (mean VAS: 1.7)

Measures:

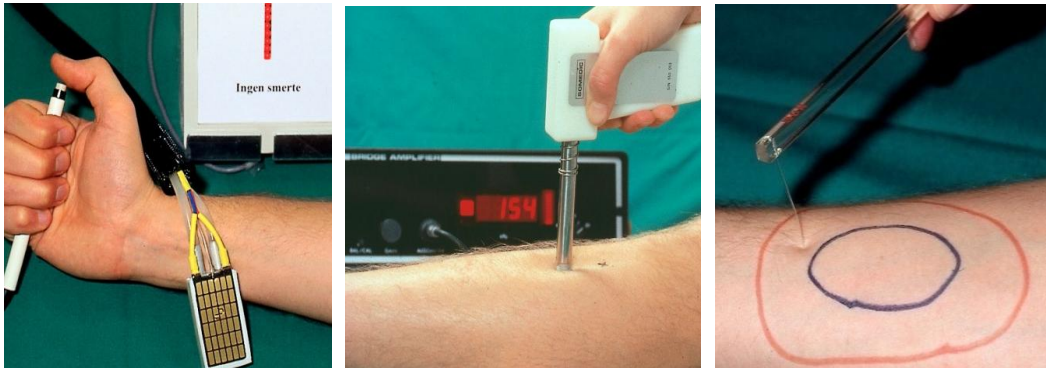
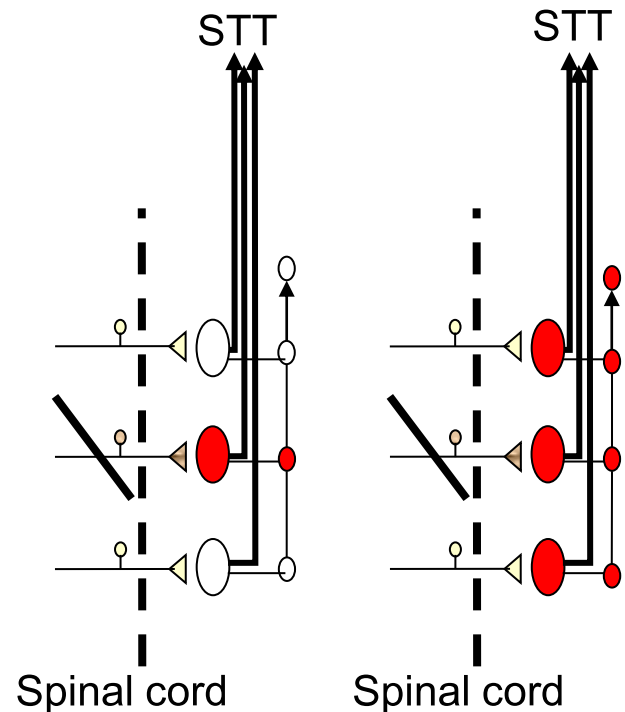
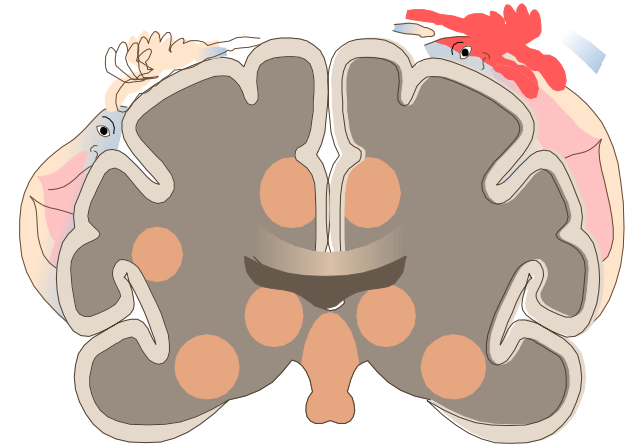
Mechano sensitivity

Thermal sensitivity

Wind-up like pain

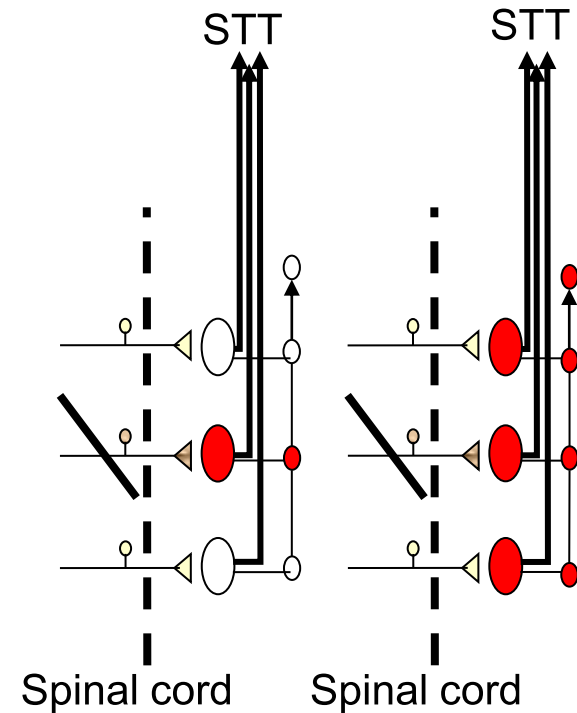
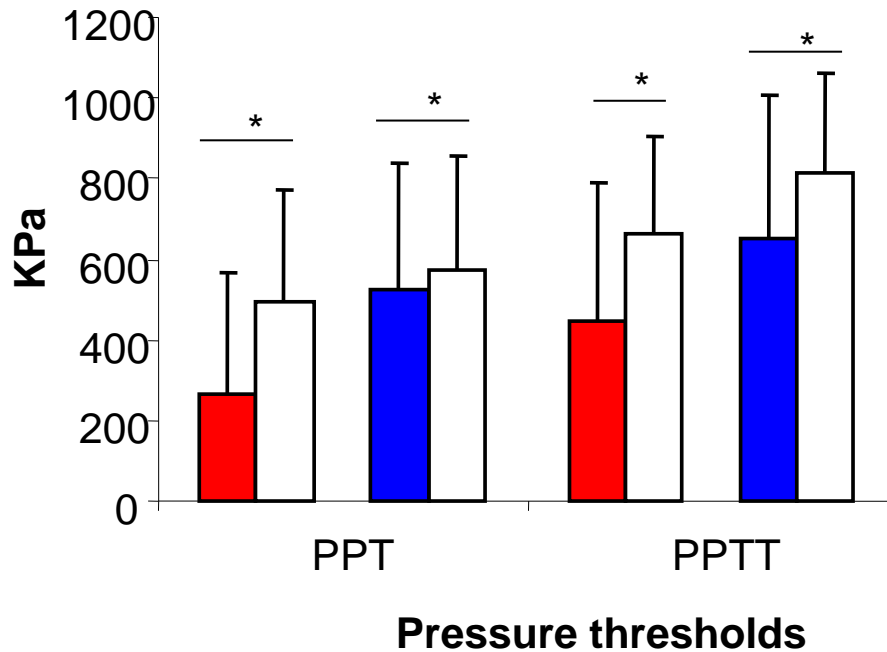
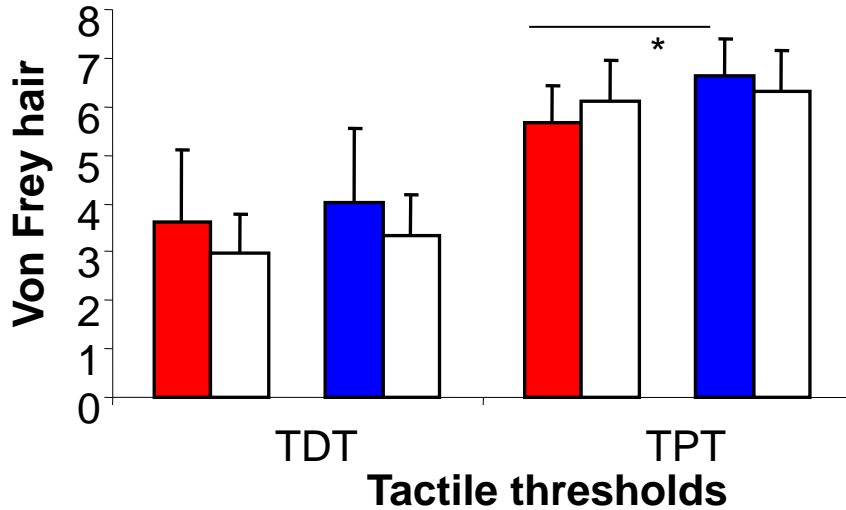
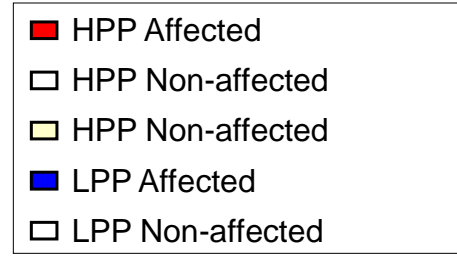
Referred pains

Catastrophizing



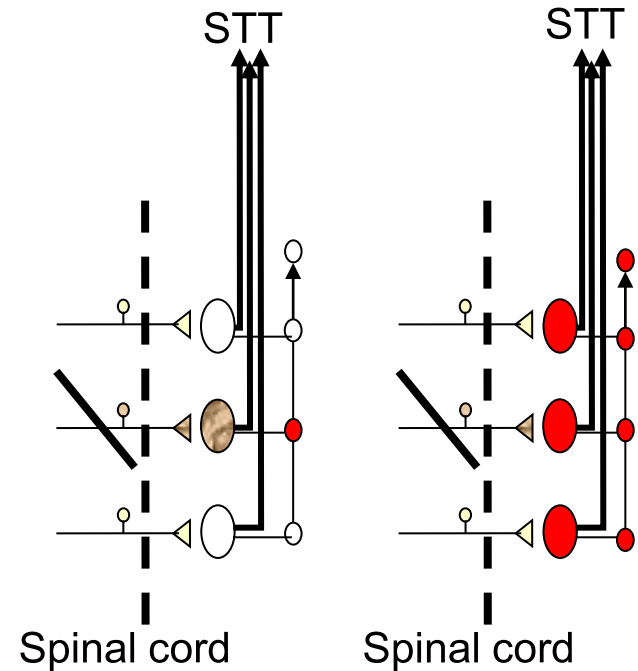
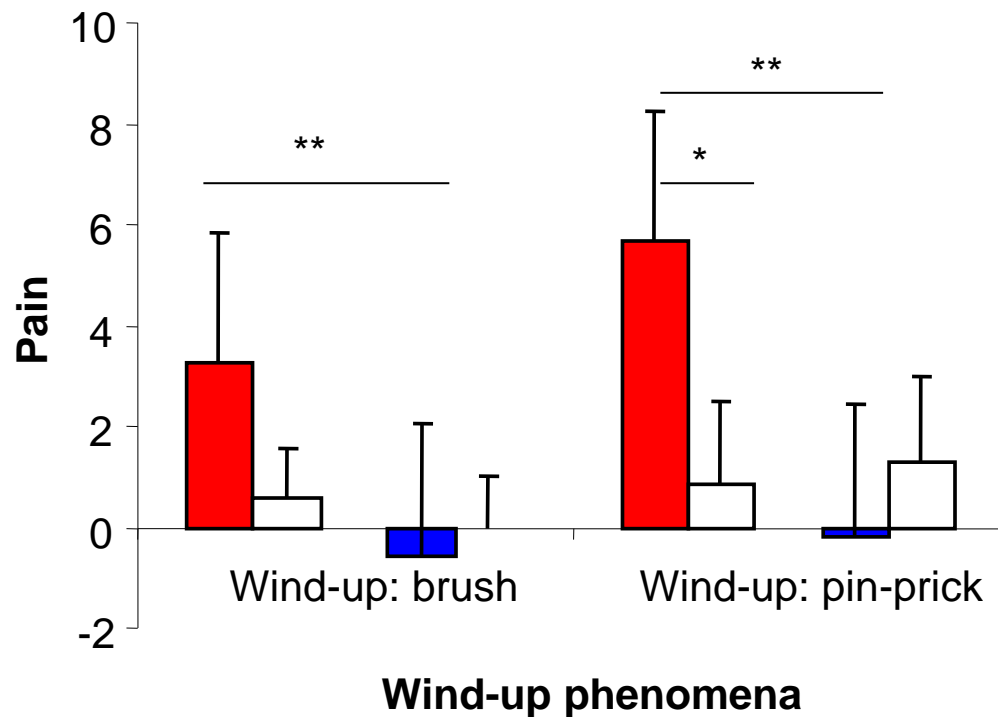
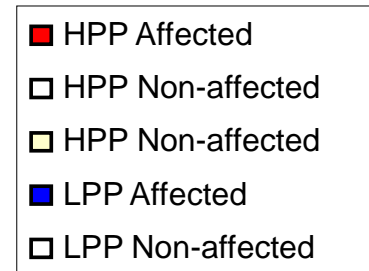
Amputation: 14 HPP, 10 LPP

Mechanical hypersensitivity



Amputation: 14 HPP, 10 LPP

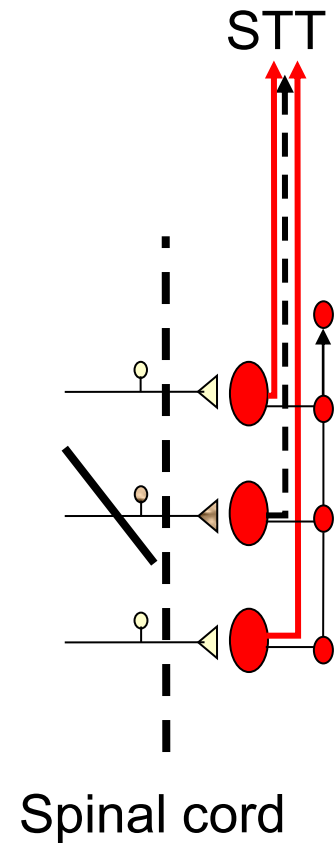
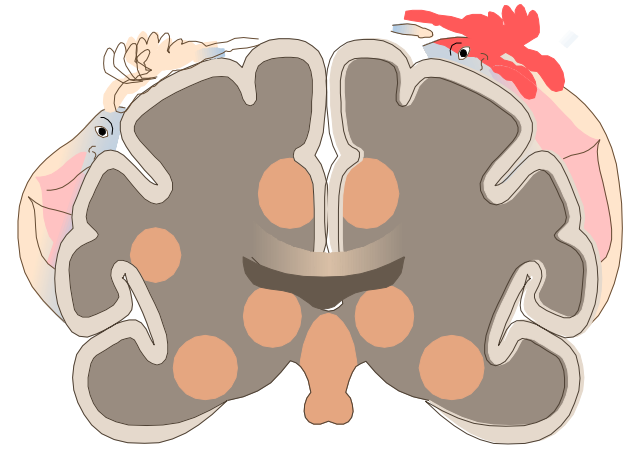
Central sensitization: wind-up



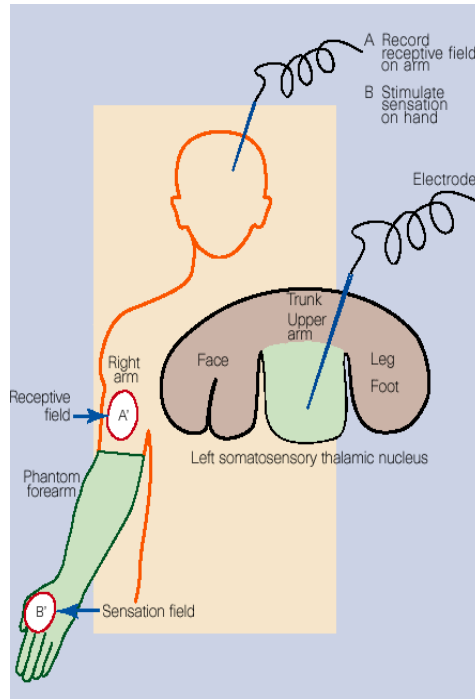
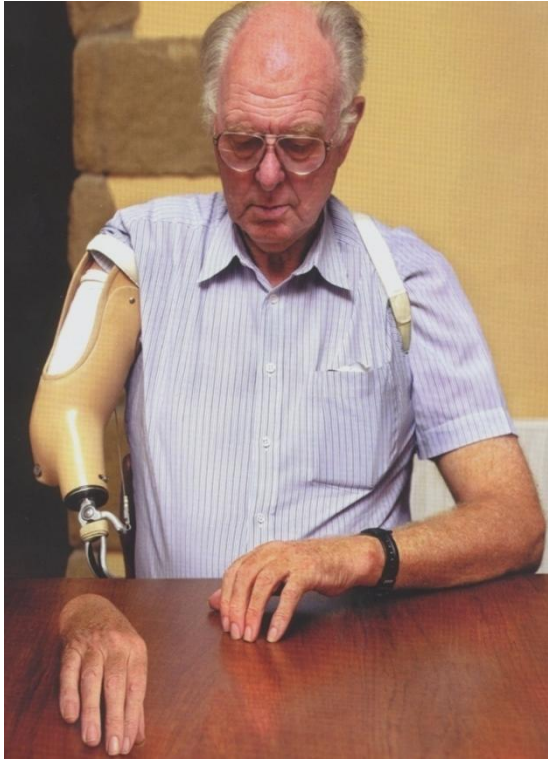
Postamputation Pain

Peripheral mechanisms

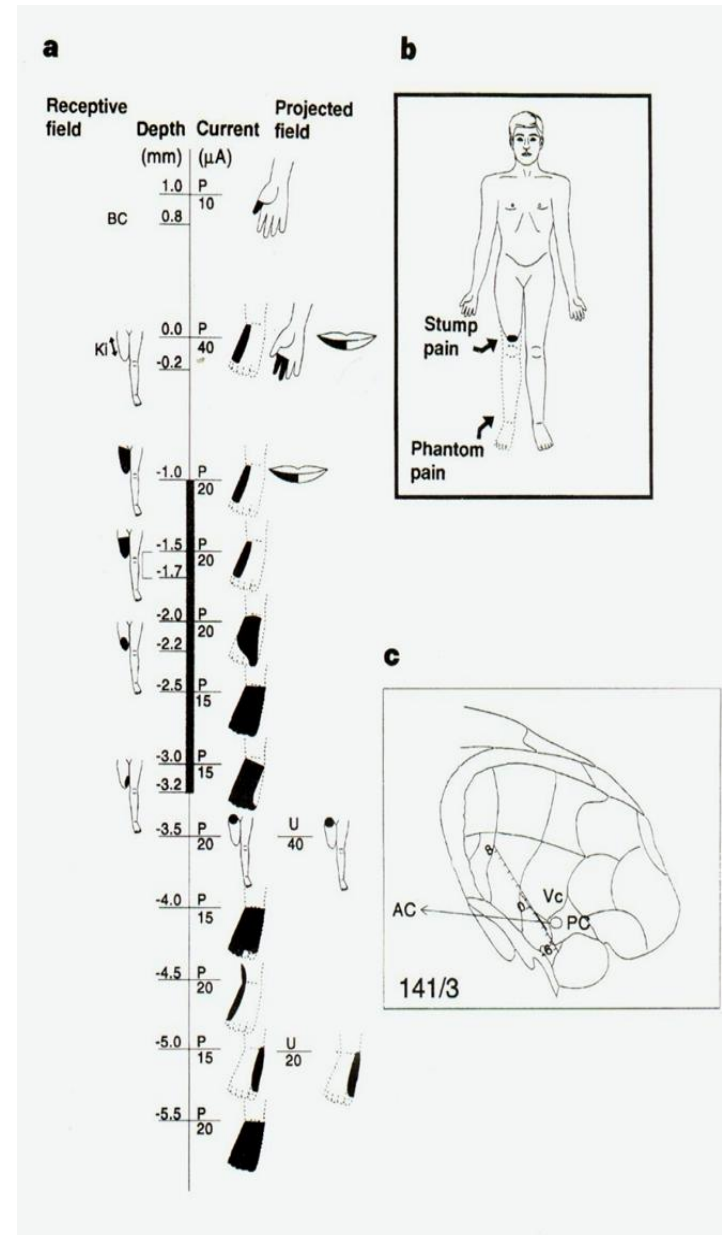
Supra-spinal mechanisms



Phantom Pain: Supraspinal mechanisms



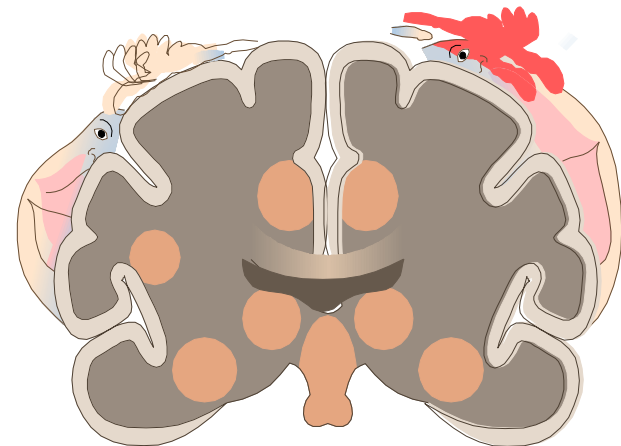
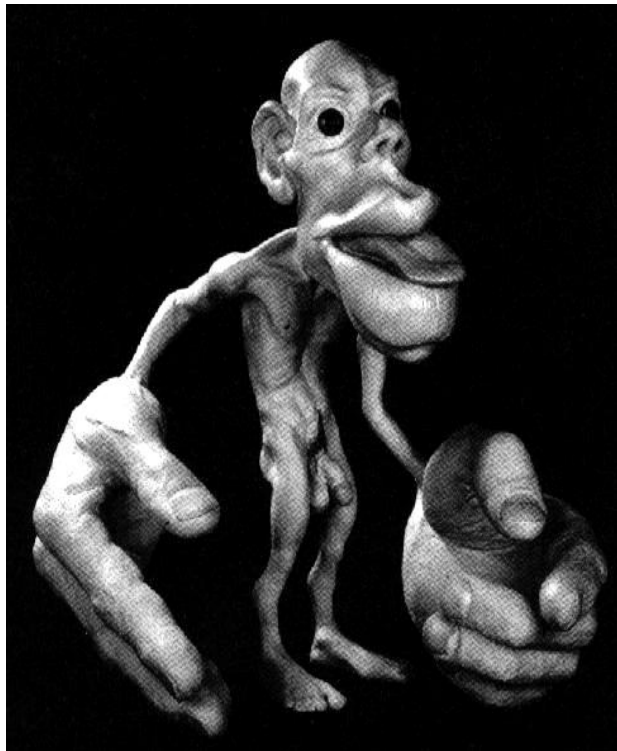
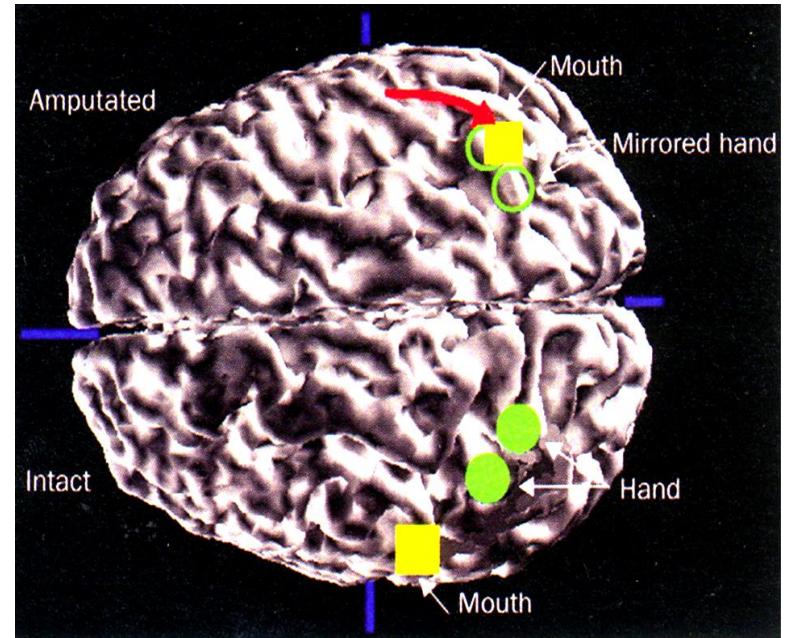
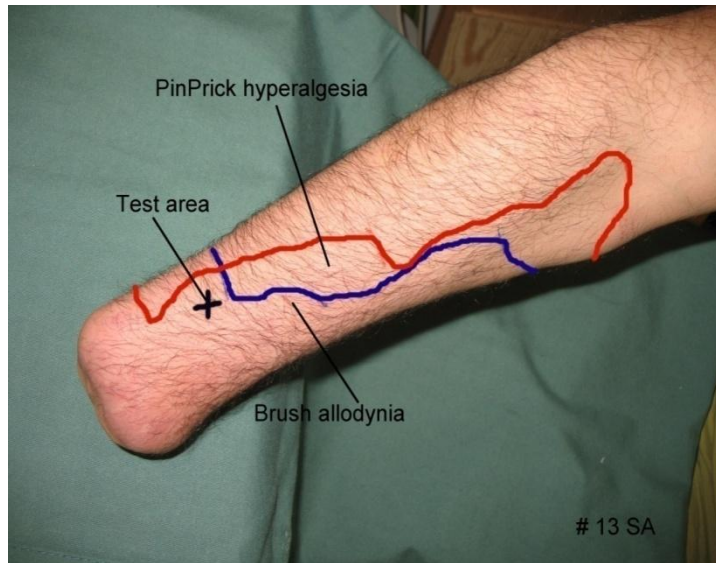
Microneurography:
Cell recording
Cell stimulation



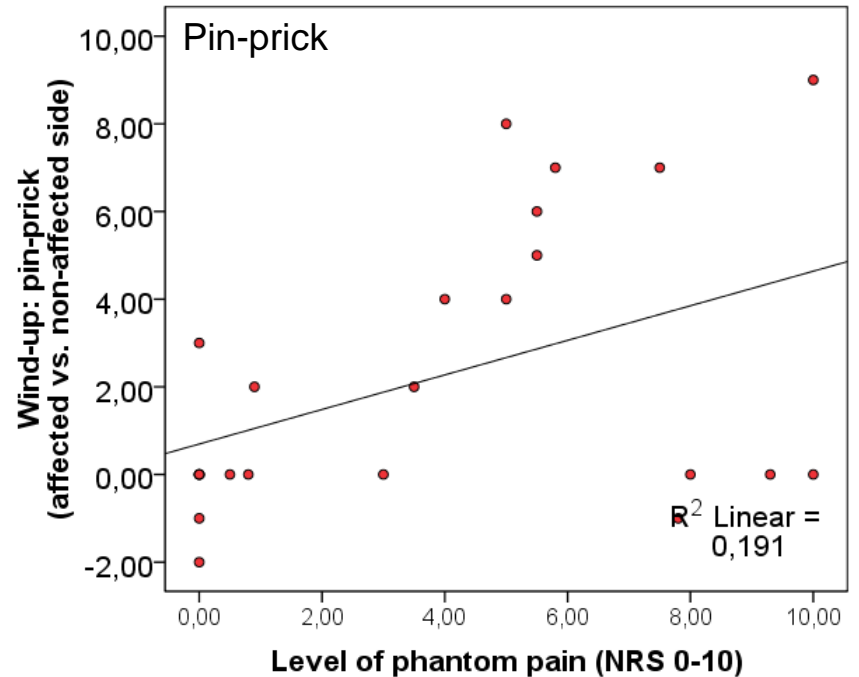
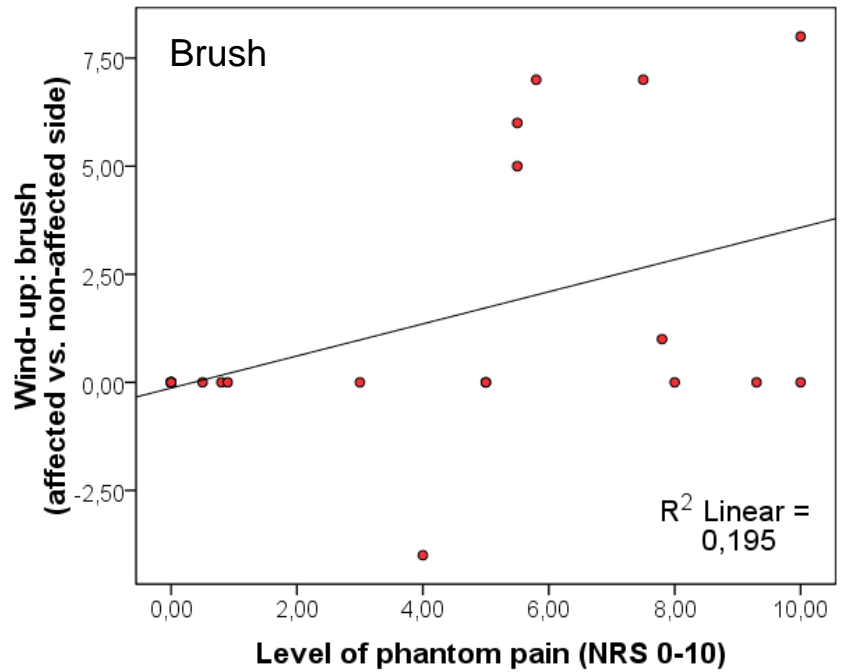
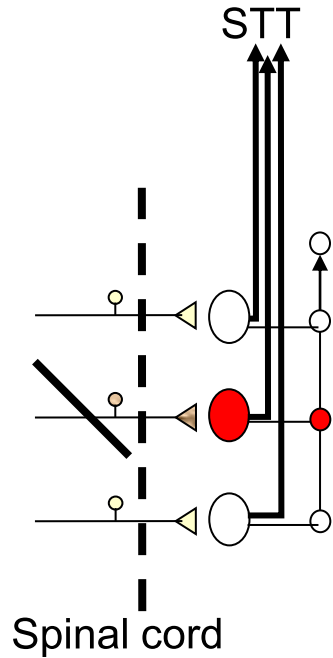
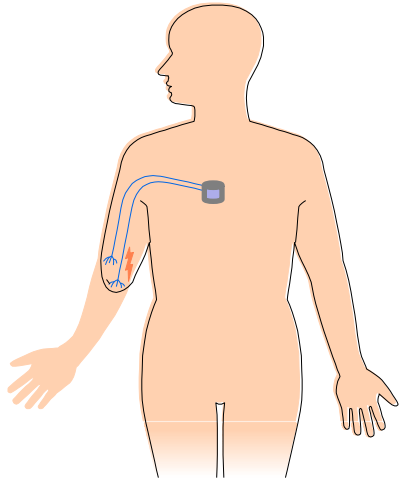
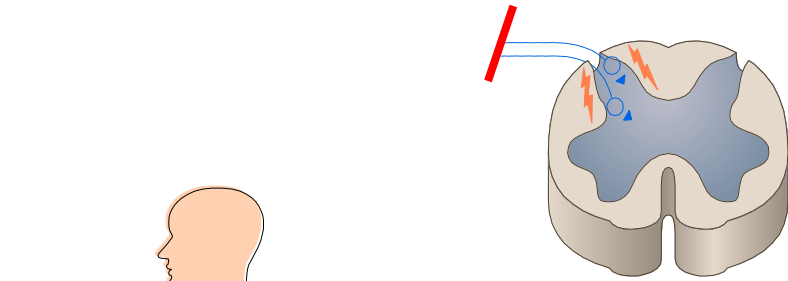
Lancet Neurol.

Davis et al. Nature 1995.

Reorganisation after deafferentation: Cortical changes?



Amputation and wind-up: Phantom pain and wind up



Amputation:

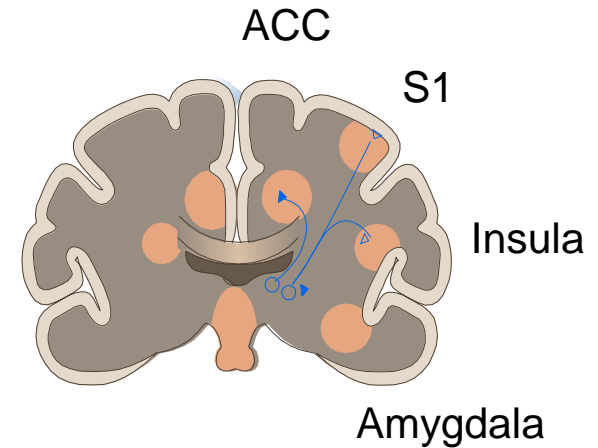
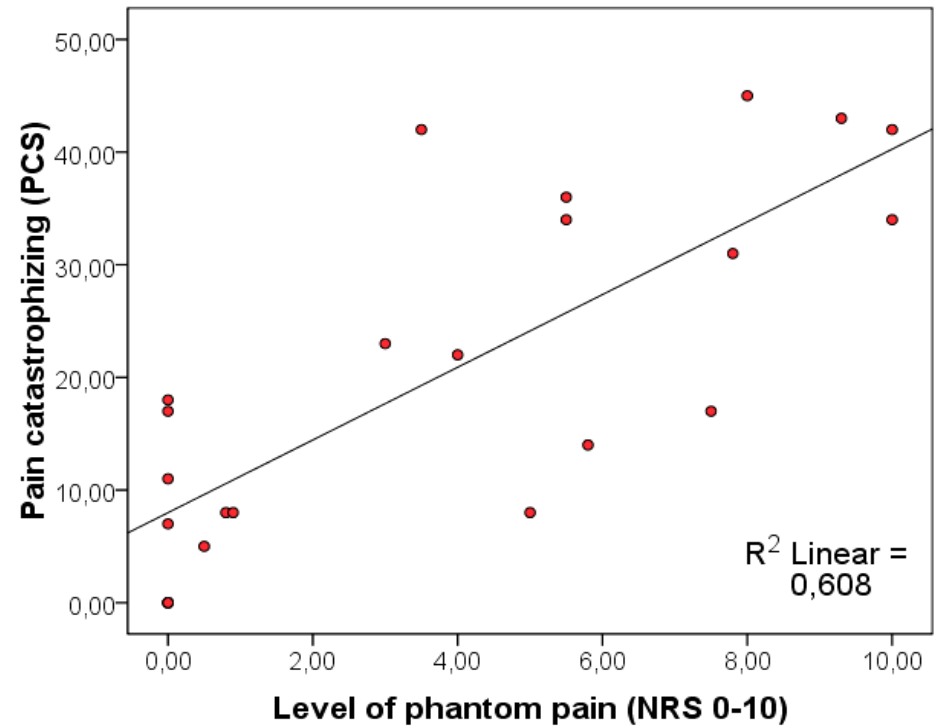
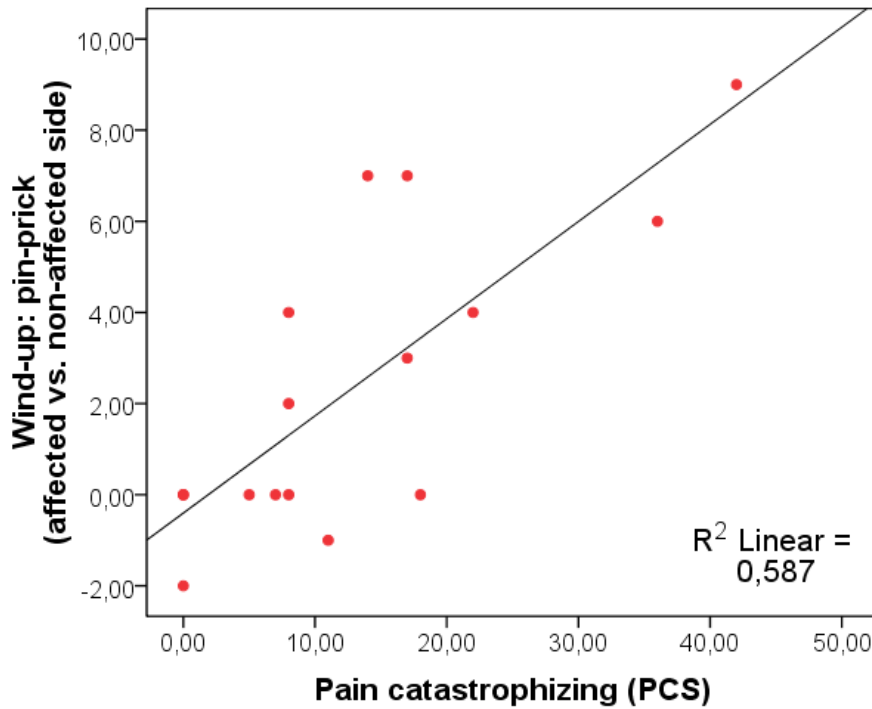
Phantom pain and catastrophizing

Pain Catastrophizing (Sullivan 1995)

Helplessness

Magnification

Rumination



Phantom Pain Mechanisms:

Peripheral

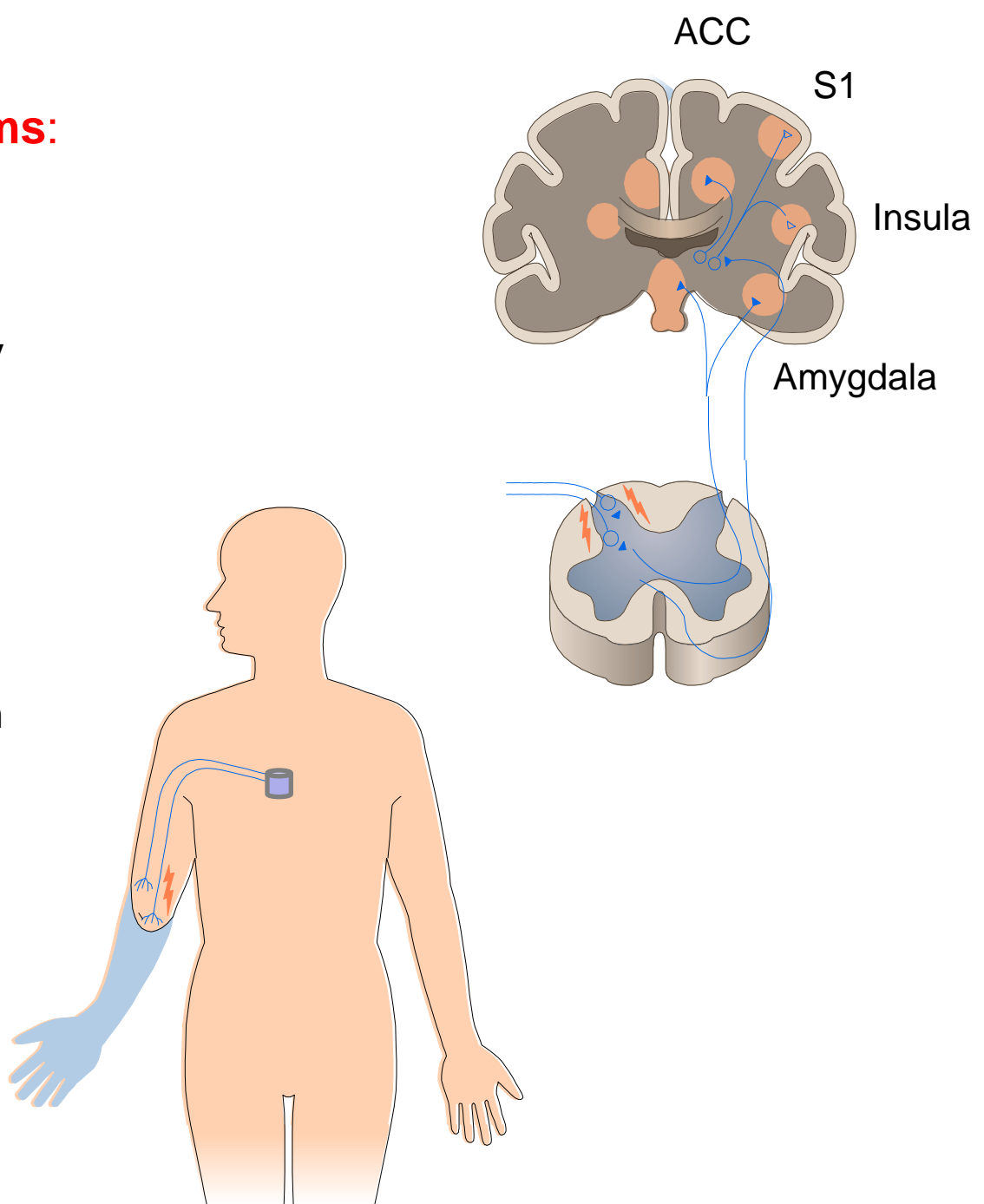
- Peripheral sensitisation
- Spontaneous neuronal activity
- DRG abnormal activity

Spinal

- Central sensitization
- Spontaneous neuronal activity
- Wind up like pain
- Spread of central sensitisation

Supraspinal

- Cortical reorganisation
- Anxiety
- Catastrophising



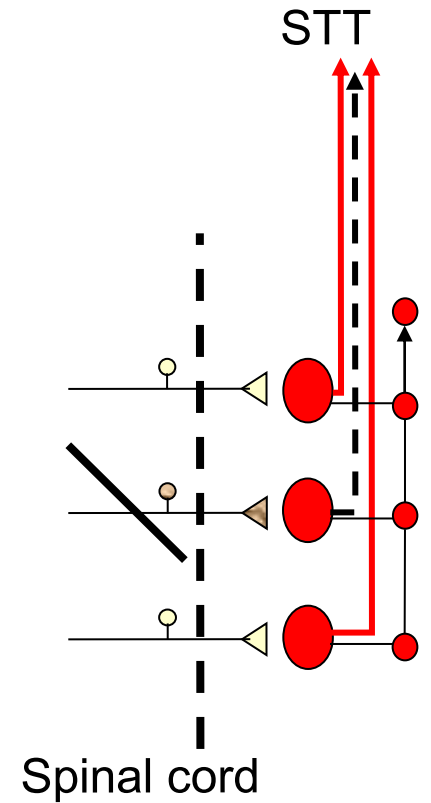
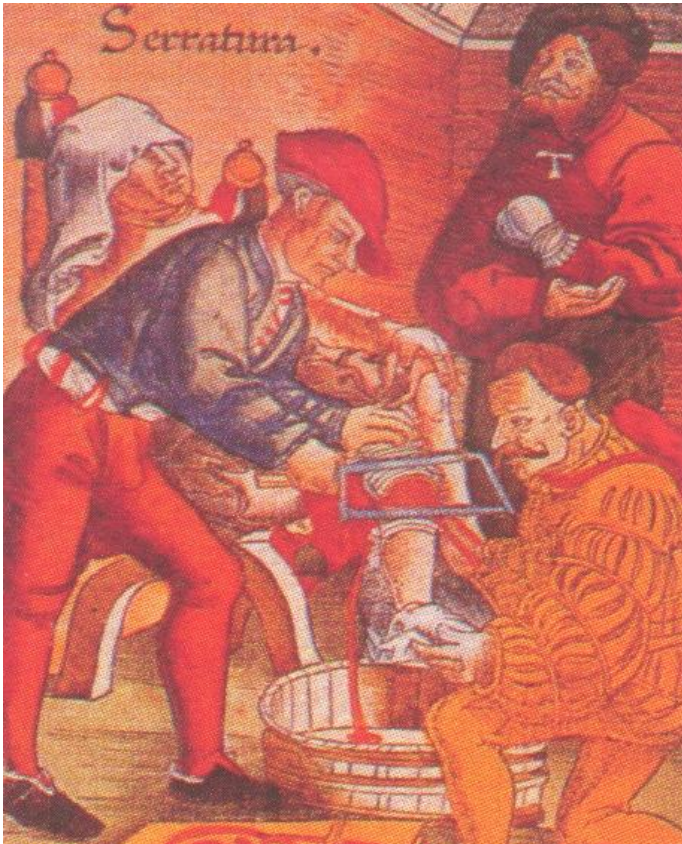
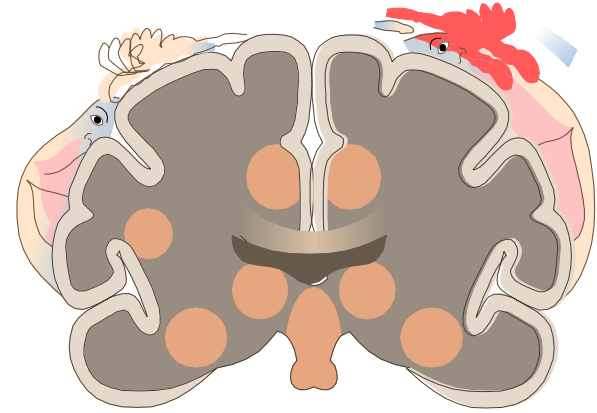
Postamputation Pain

Interaction between:

Peripheral mechanisms

Spinal mechanisms

Supra-spinal mechanisms



**Surgical procedures
with nerve injury pain**

CABG

Hernia

Nerve lysis

Mastectomy

Thoracotomy

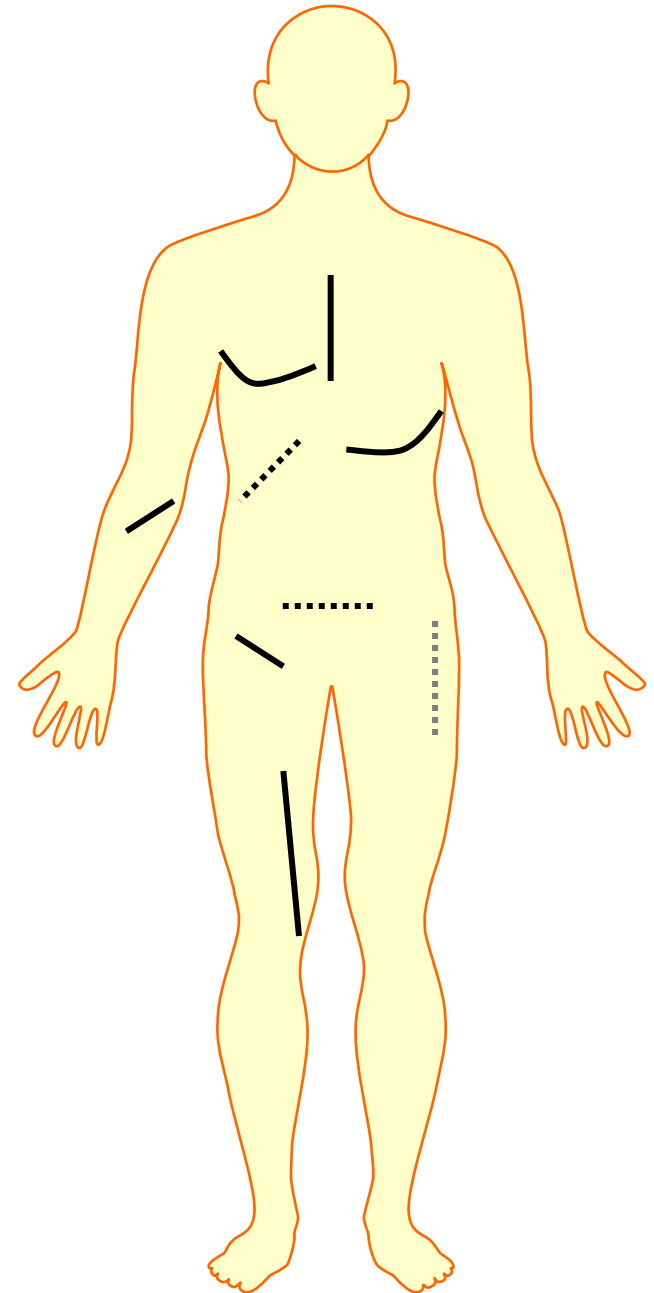
Vascular graft

**Surgical procedures
without nerve injury pain**

Hip arthroplasty

Hysterectomy

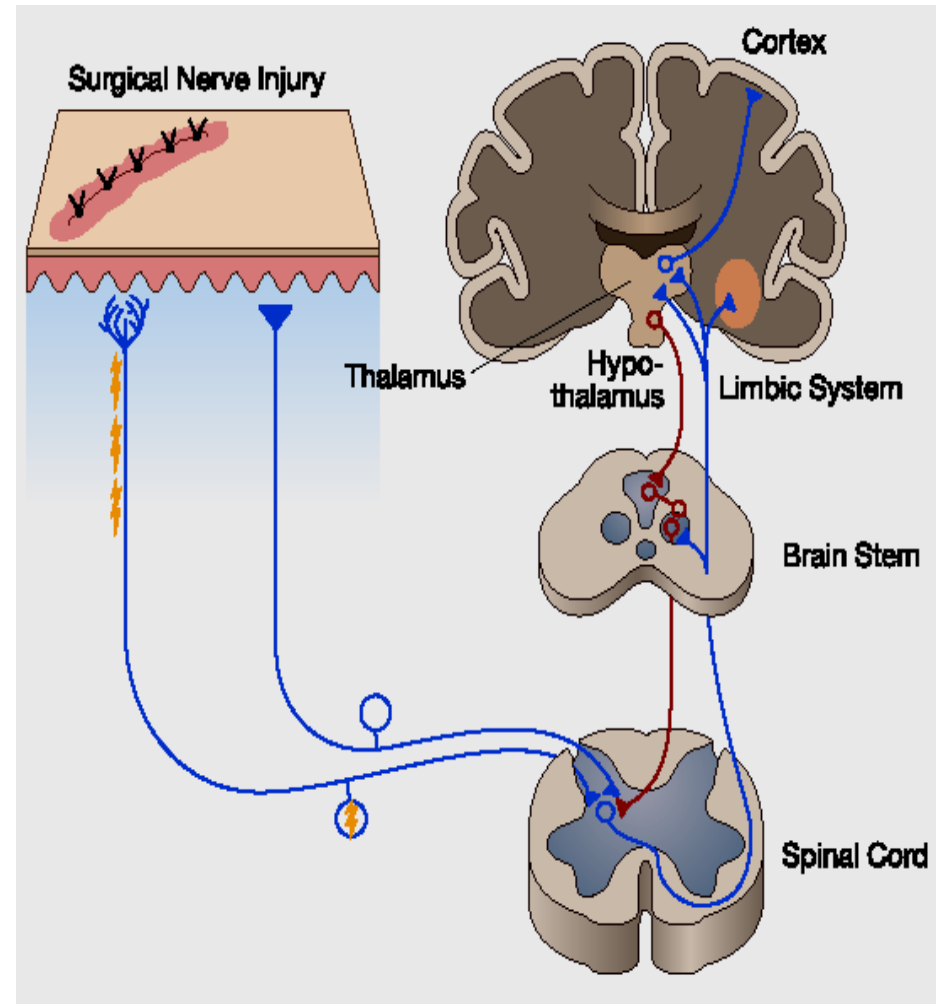
Cholecystectomy ?



Conclusion:

Postoperative nerve injury pain

- Injury to nerves a risk factor for chronic pain after surgery
- Postsurgery changes mimick sometimes those seen after nerve injury
- Chronic postoperative pain can be modulated by agents acting on neuronal hyperexcitability
- Future studies need to clarify the role of early aggressive treatment and preventive measures





Collaborators at DPRC:



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