

**Psychobiological aspects
of chronic pain in children
-Edited version
-Unpublished data removed**

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Chronic pain in children: Psychobiological aspects

- (1) Is chronic pain in children associated with changes in pain sensitivity (possibly due to central sensitization)?
- (2) Are children with chronic pain hypervigilant to painful sensations and do they catastrophize?
- (3) What are the consequences of early pain exposure in children?

Chronic pain in children: Psychobiological aspects

(1) Is chronic pain in children associated with changes in pain sensitivity (possibly due to central sensitization)?

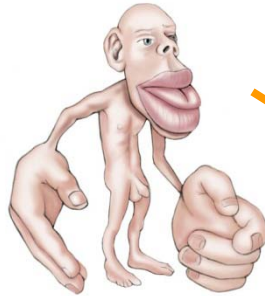
(2) Are children with chronic pain hypervigilant to painful sensations and do they catastrophize?

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Chronic Pain: Changing the gain in pain pathways

PAIN PATHWAYS

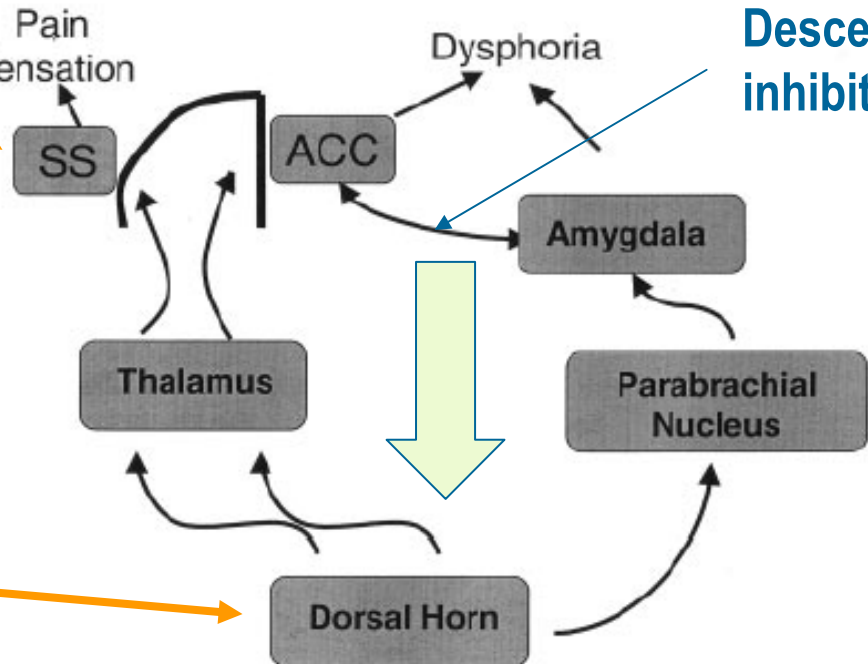
Supraspinal/
cortical plasticity



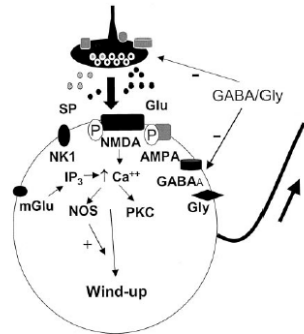
Pain
Sensation

Dysphoria

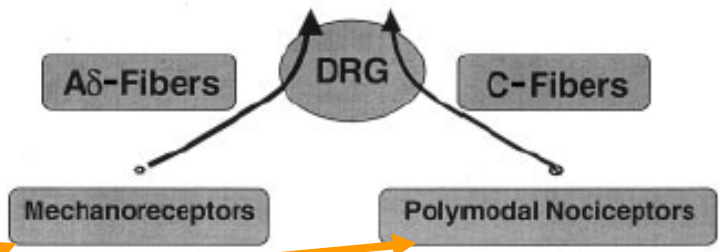
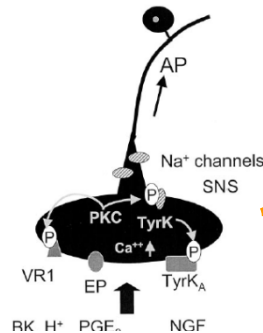
Descending
inhibition



Central
sensitization



Peripheral
sensitization



Woolf & Salter (2000)

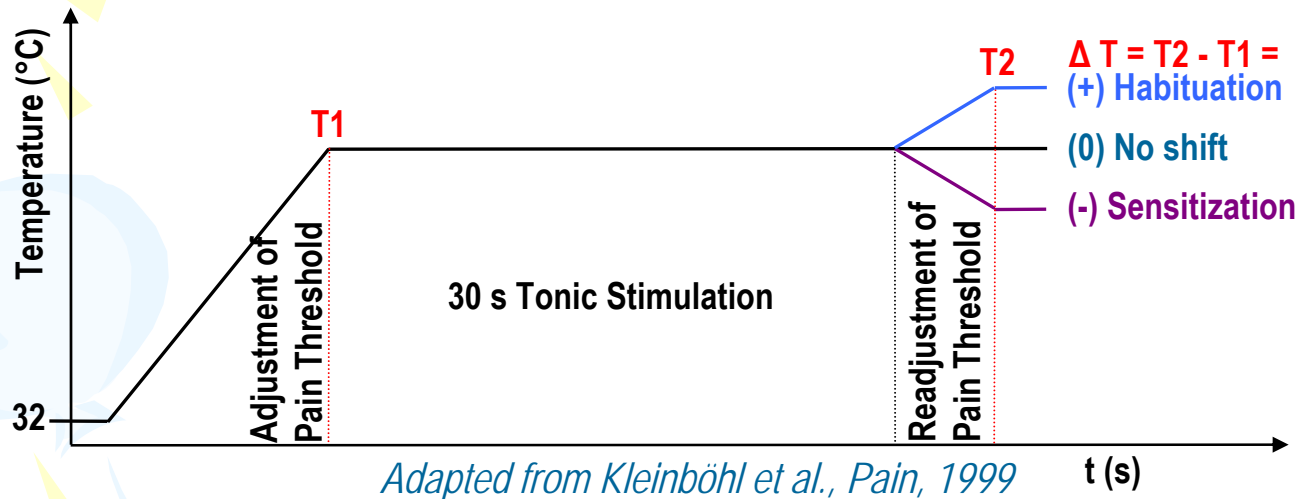
Psychophysical methods for measuring thresholds and sensitivity to pain

	Detection Threshold	Pain Threshold
Thermal (Warmth)	<i>Thermotester (Medoc)</i>	
	Heat Detection Threshold	Heat Pain Threshold
Mechanical	<i>Pinpricks (Treede et al., Mainz, 8mN - 512mN)</i>	
	Mechanical Detection Threshold	Mechanical Pain Threshold



Psychophysical methods: Measuring sensitization to pain

- Perceptual response to tonic painful heat:

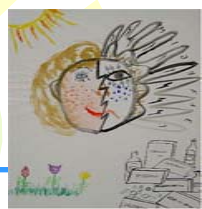


- perceptual response to repeated mechanical stimulation (pinprick nearest to pain threshold):

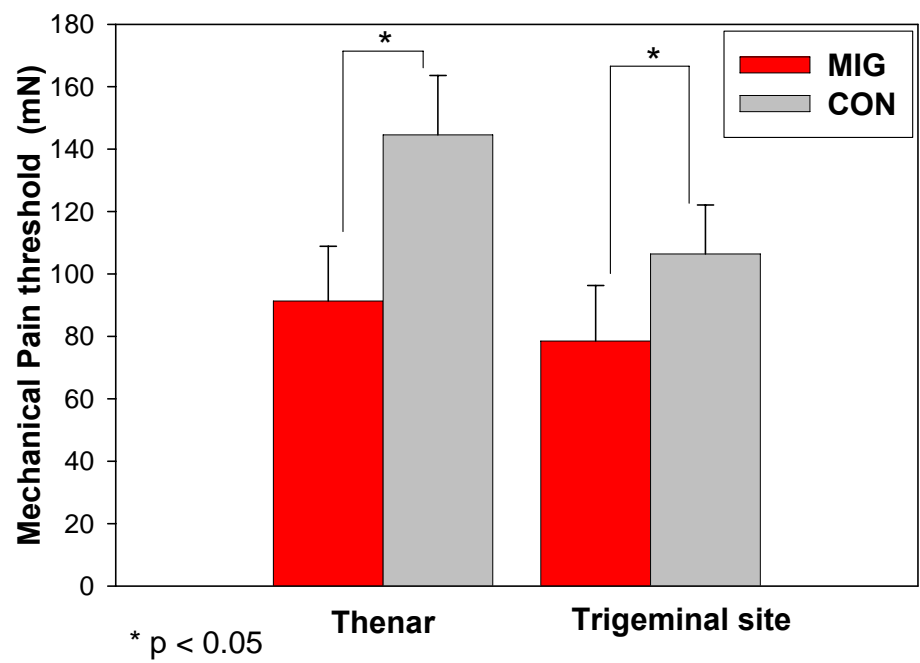
Δ intensity = intensity rating for a series of 10 stimuli – intensity of single stimulus (NRS: 0-100)



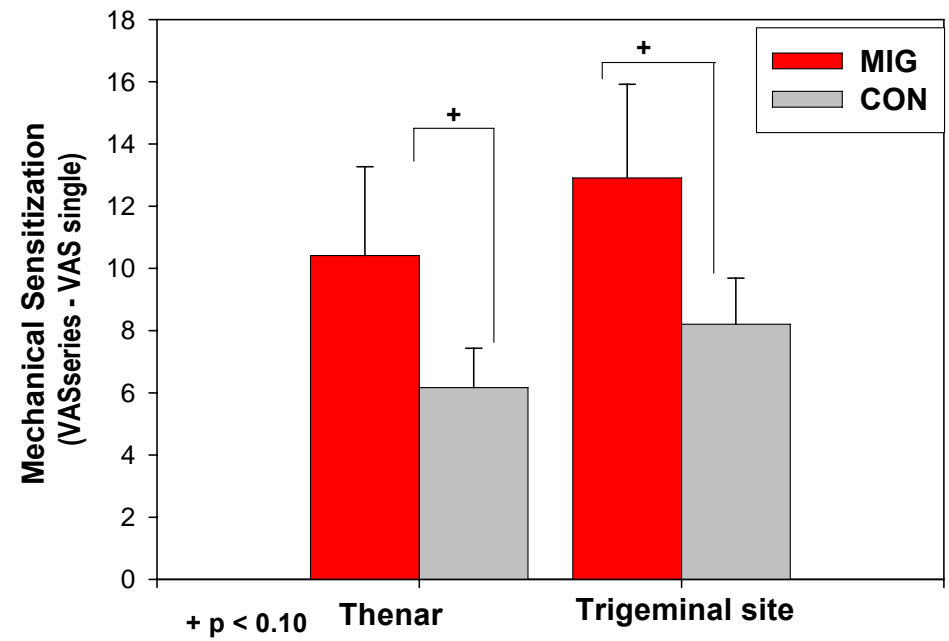
Pain sensitivity in pediatric migraine



Pain threshold



Perceptual sensitization



mechanical stimuli: lowered pain threshold and increased pain sensitization to repeated pain stimuli at reference site and pain site



Pain sensitivity in recurrent abdominal pain

=> enhanced visceral pain sensitivity

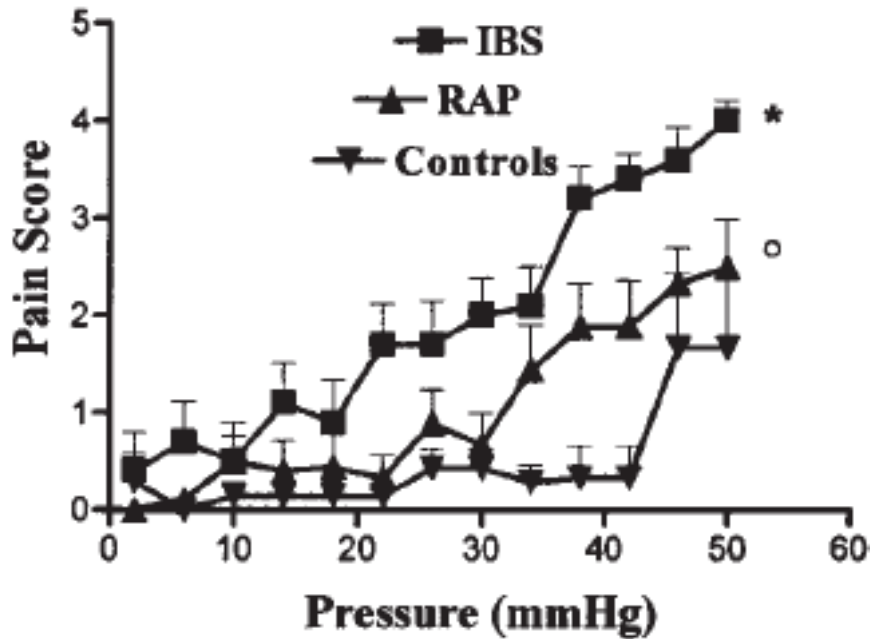


Fig 1. Rectal pain perception for study patients during barostat testing.

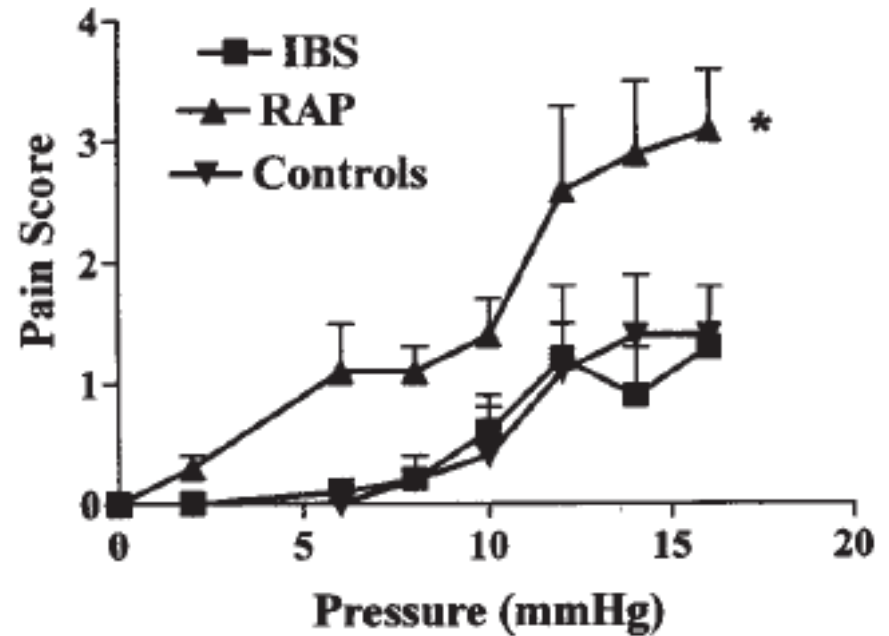
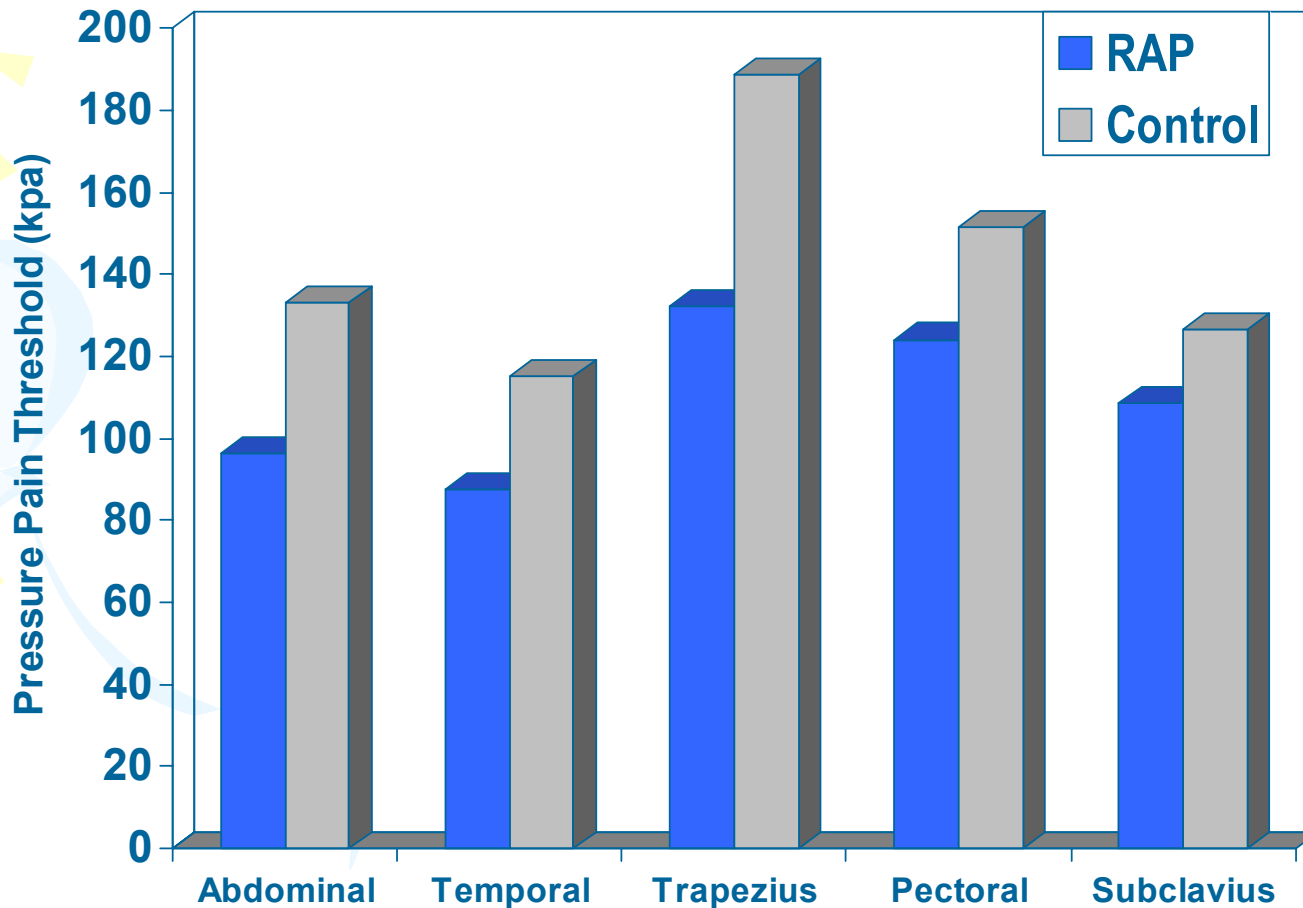


Fig 2. Gastric pain perception for study patients during barostat testing.



Pain sensitivity in recurrent abdominal pain



RAP: globally reduced pressure pain thresholds

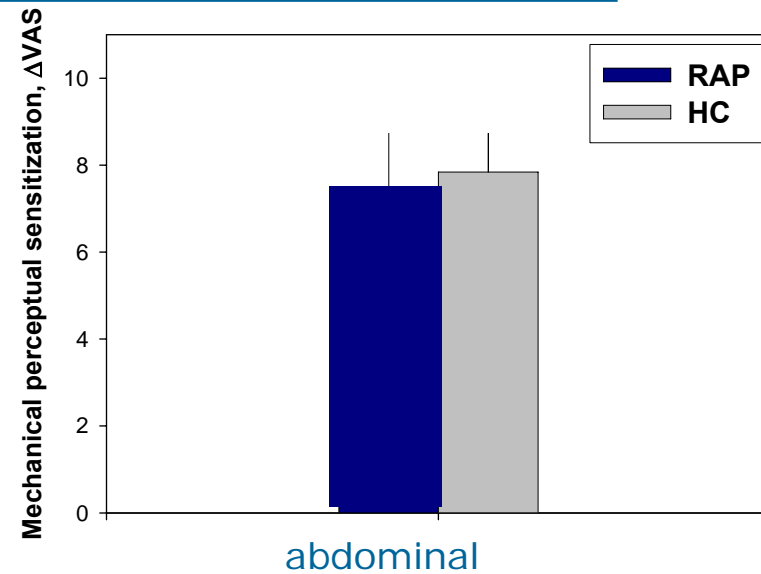
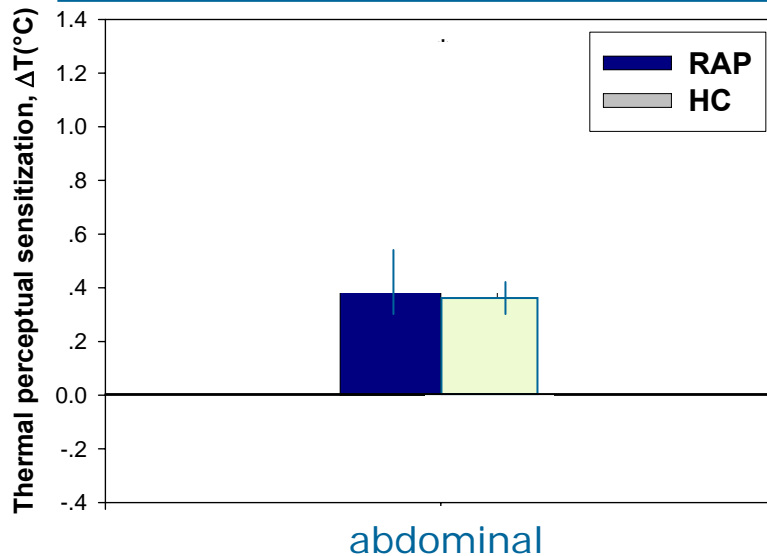


Pain sensitivity in recurrent abdominal pain



	RAP	HC
Heat pain thresholds ($^{\circ}\text{C}$, $M \pm \text{SD}$)	42.6 ± 2.7	42.2 ± 2.6
Mechanical pain thresholds (mN, $M \pm \text{SD}$)	209.9 ± 140.3	177.7 ± 113.9

ABDOMINAL



=> no evidence for altered somatic (mechanical, heat) pain sensitivity at pain site (abdomen)

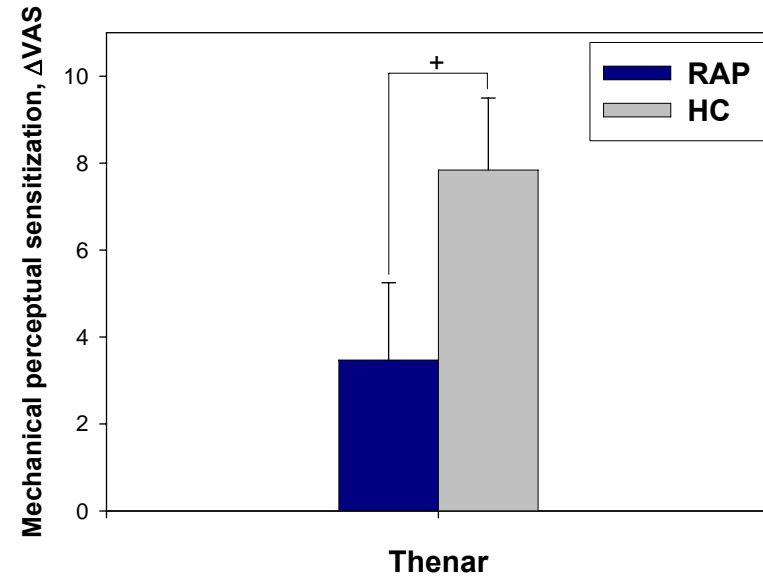
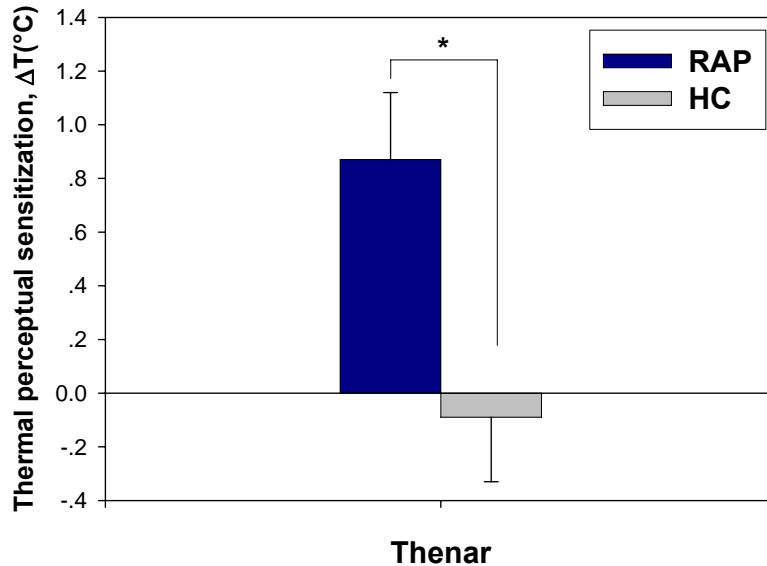


Pain sensitivity in recurrent abdominal pain



	RAP	HC
Heat pain thresholds ($^{\circ}\text{C}$, $M \pm \text{SD}$)	43.8 ± 3.8	43.2 ± 3.6
Mechanical pain thresholds (mN, $M \pm \text{SD}$)	165.2 ± 121.4	200.9 ± 118.2

THENAR



=> Same or reduced somatic (mechanical, heat) pain sensitivity at reference site (thenar)

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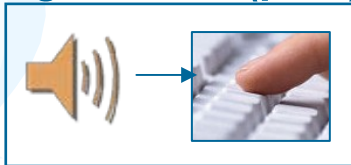
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Changes in vigilance to pain in migraine and RAP?

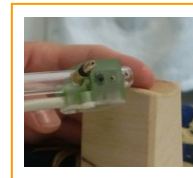
Oddball Standard Protocol:

Targets: rare ($p=.2$)



reaction time task

Standards: frequent ($p=.8$)



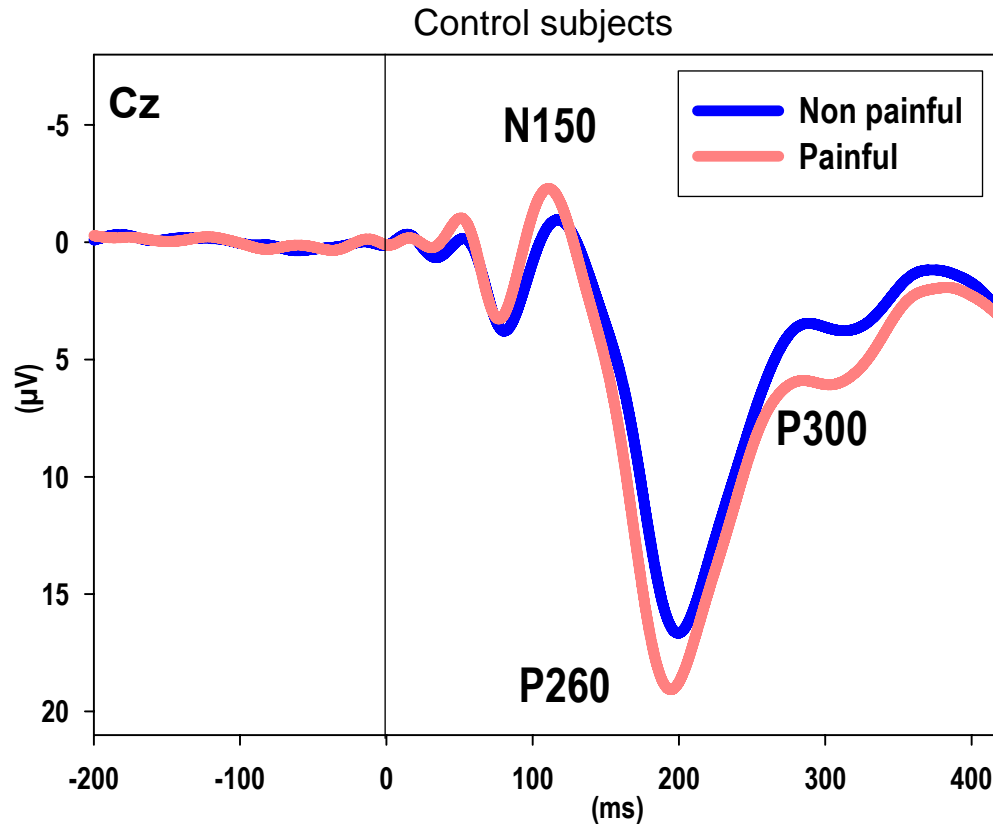
no response required

- ▶ allows to measure:
 - somatosensory processing
 - attentional modulation

Block 1,3,5:
painful

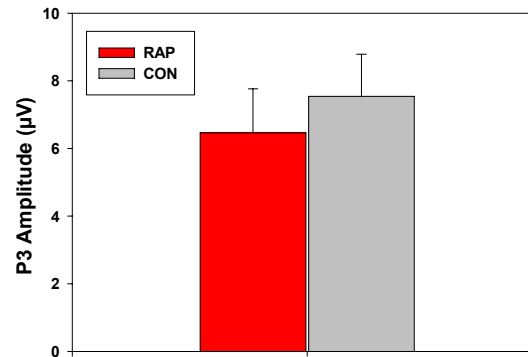
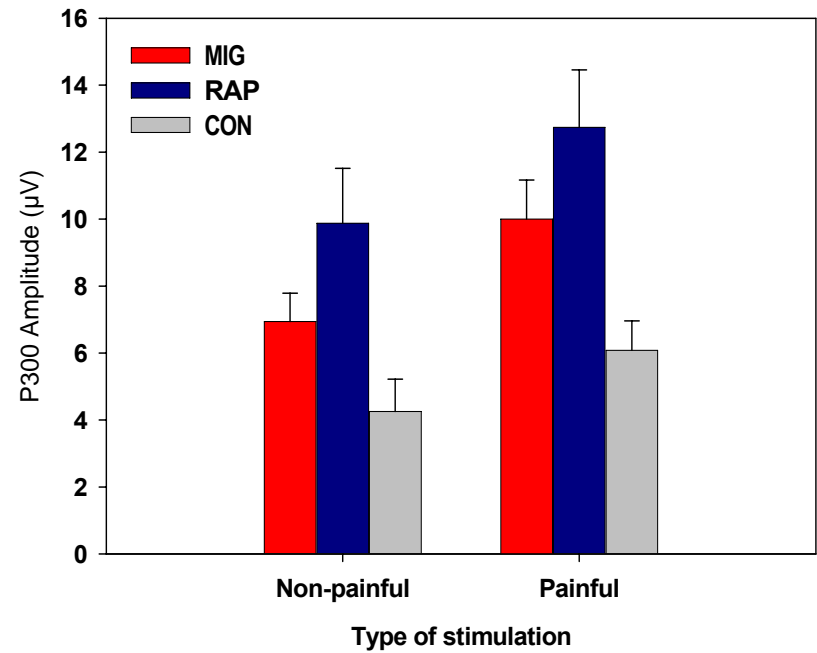
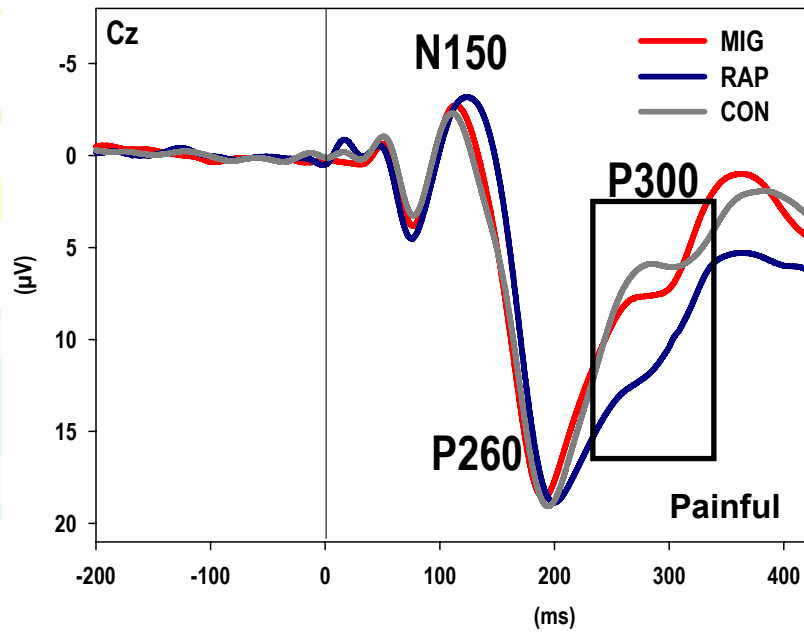
Block 2,4,6:
non painful

Somatosensory evoked potentials in children with migraine and RAP



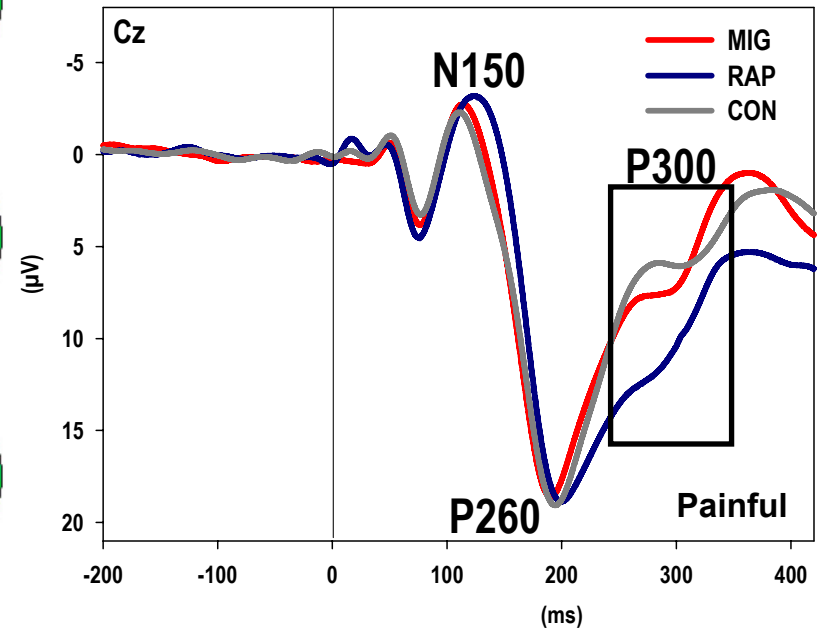
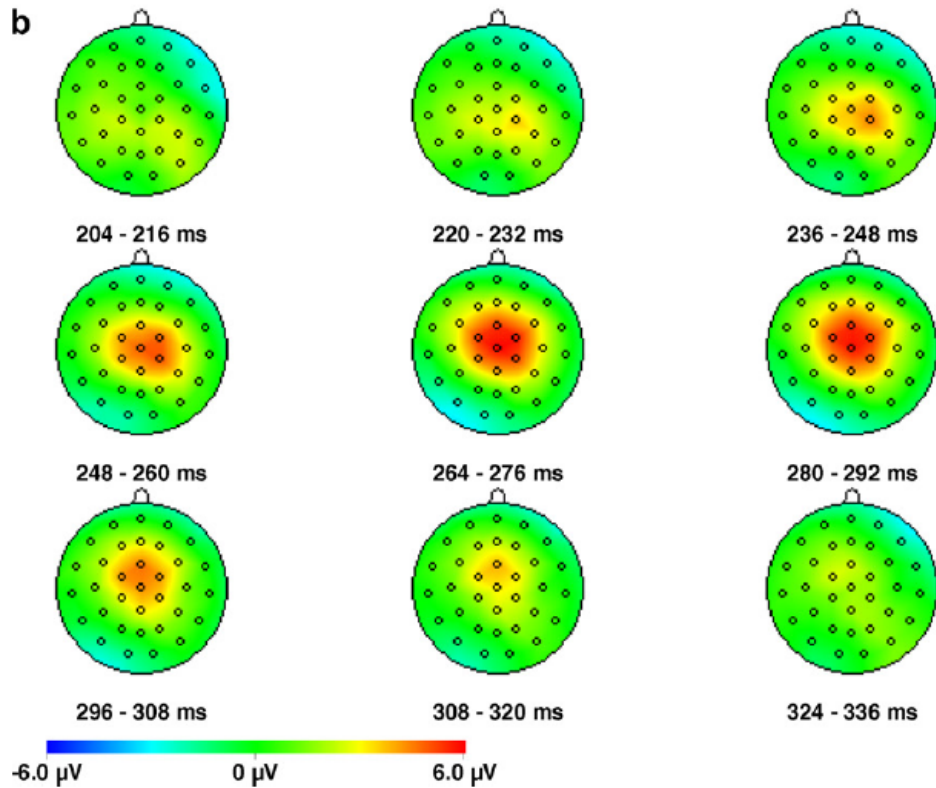
N150-P260: CON = RAP = MIG

Changes in vigilance to pain in migraine and RAP?



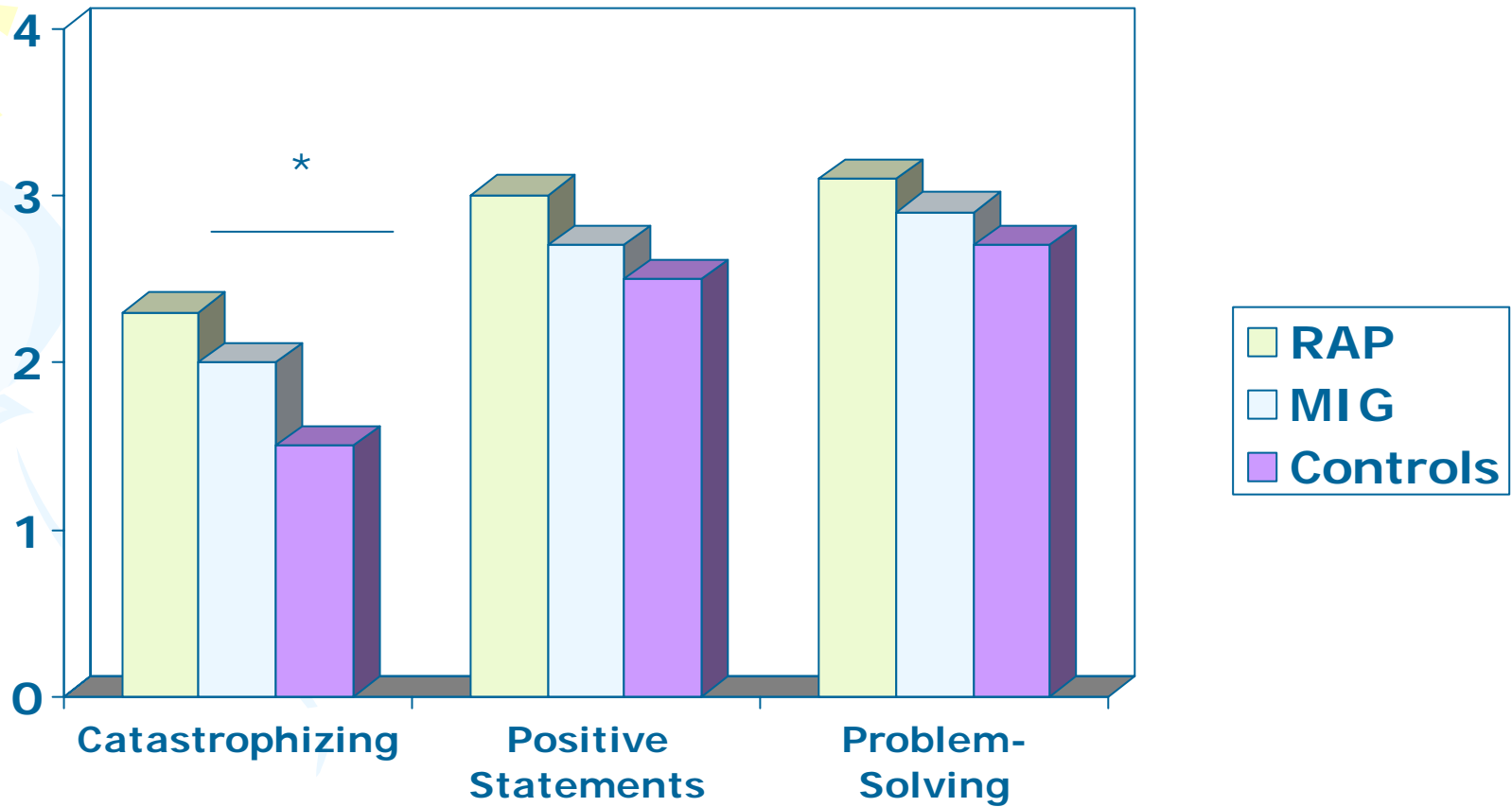
But:
P300 to auditory targets is unaltered

Somatosensory evoked potentials in children with migraine and RAP



SEP difference map: RAP vs. CON for nociceptive stimuli

Pain-related Cognitions



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Development of pain pathways in humans and rats

Human (postconceptional week)	Rat (day of embryonal development)	System
7.-8.	E15	Reflex movements to stimulation, spontaneous movements
10.-11.	E16	Sensory innervation of hand / paws
13.-14.	E17	Complete sensory innervation of body surface, receptive fields
26.	E19	Withdrawal reflex to nociceptive stimulation
22.-34.	starting E19	Development of projections from thalamus to primary sensory cortex
26.-31.	not applicable	Facial responses to noxious stimulation
postnatal period	postnatal week 2-3	Functional maturation of descending pain inhibitory mechanisms

* Rats are born after 20 days of embryonal development.

Differences between adults and neonates:

- neonates: A β and C-fibers terminate both in lamina I, II
- activation of A β -fibers can induce central sensitization in neonates, but not adults
- neonates:
 - larger receptive fields
 - pain-inhibiting mechanisms not fully developed

after Benrath & Sandkühler, 2000

Pain sensitivity in children with NICU experience

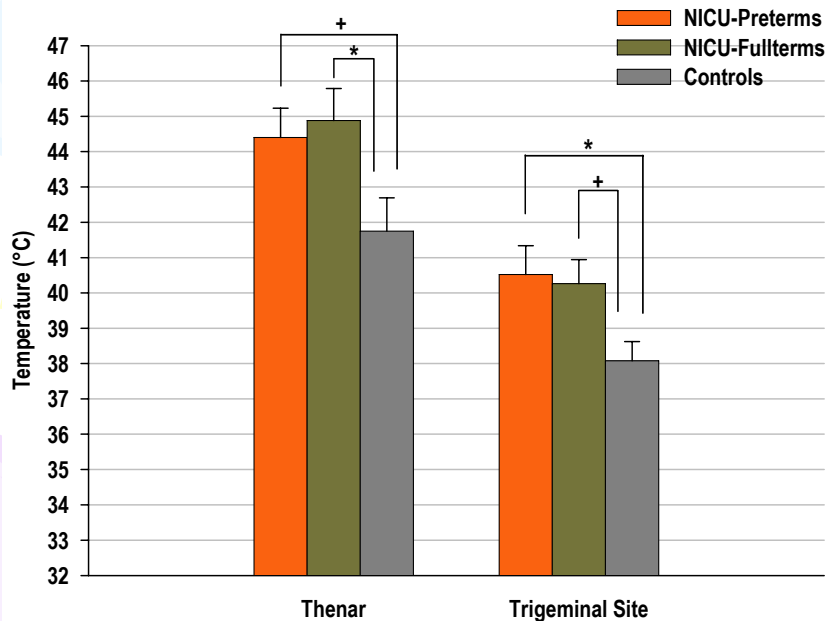
Amplification of descending inhibition

Central sensitization of pain pathways

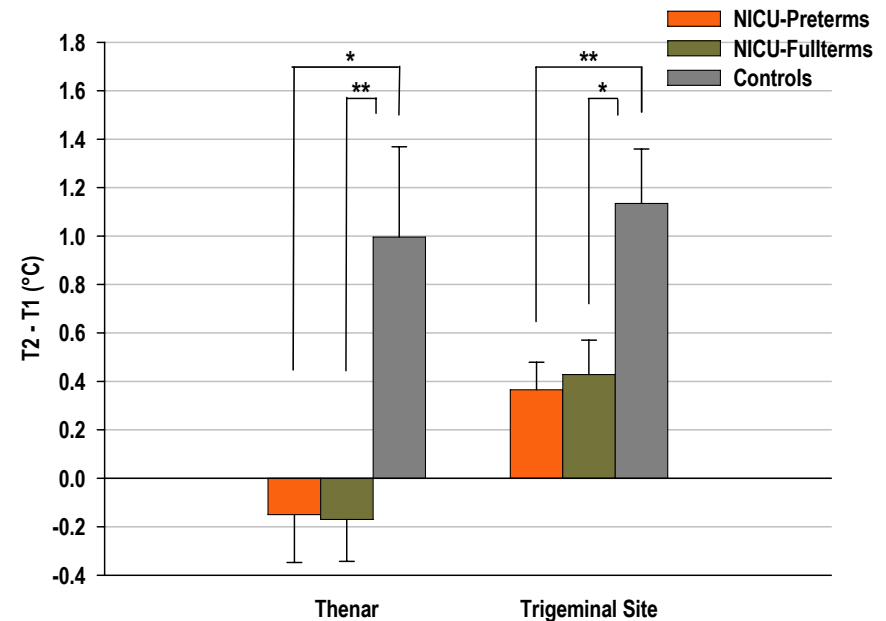
minor nociceptive input

Ren et al., 04

Heat Pain Thresholds:
Hypoalgesia



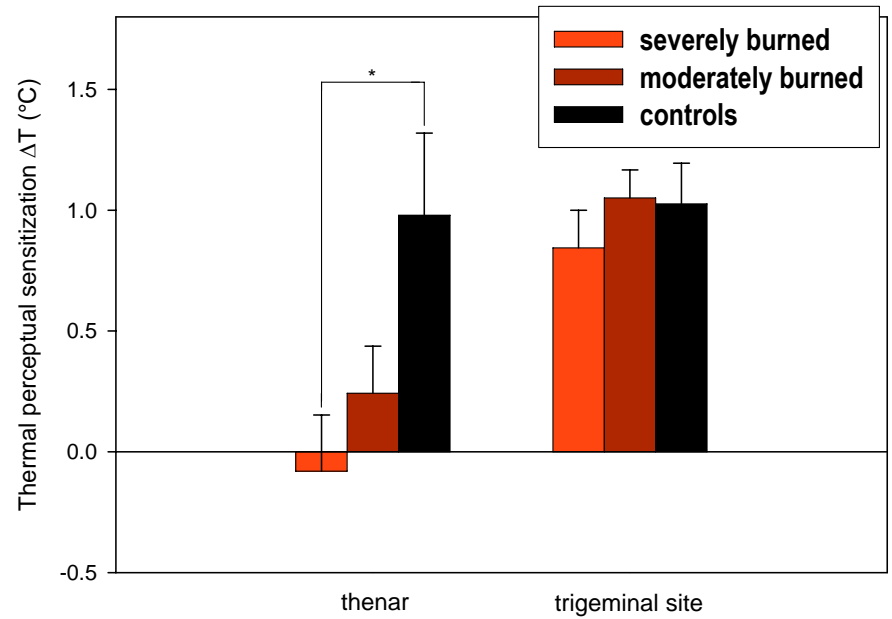
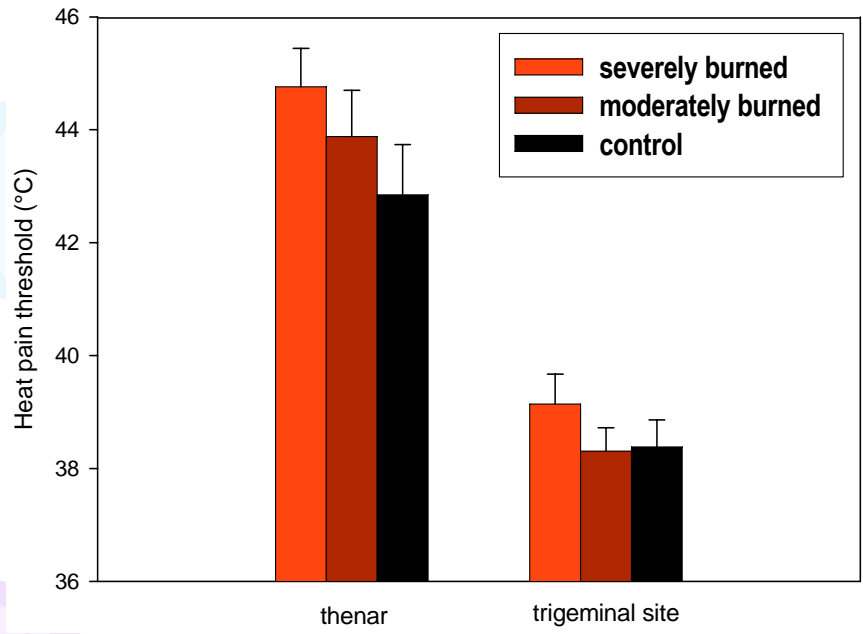
Tonic Painful Heat:
Hyperalgesia



Small thermode (16x16mm)

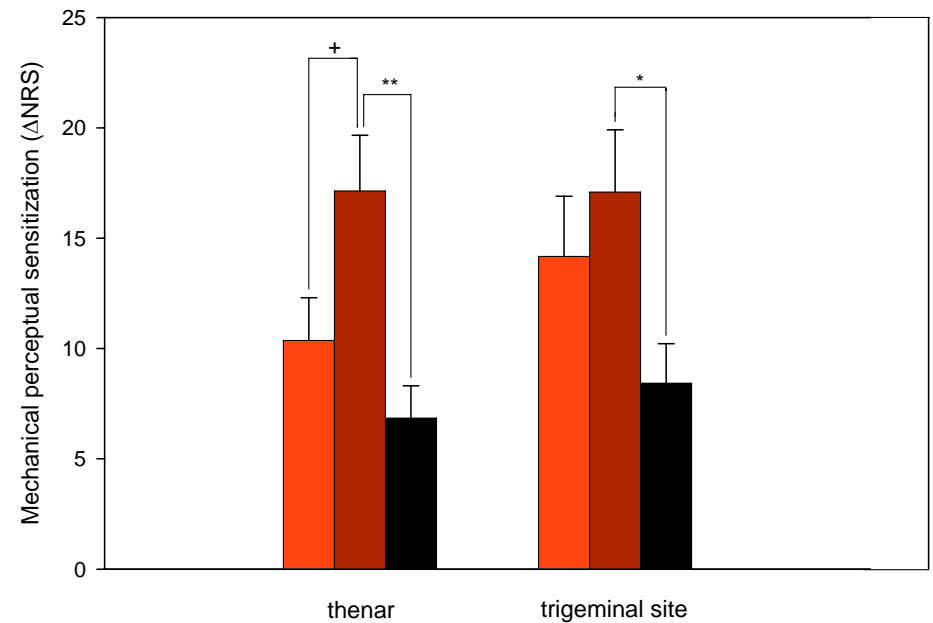
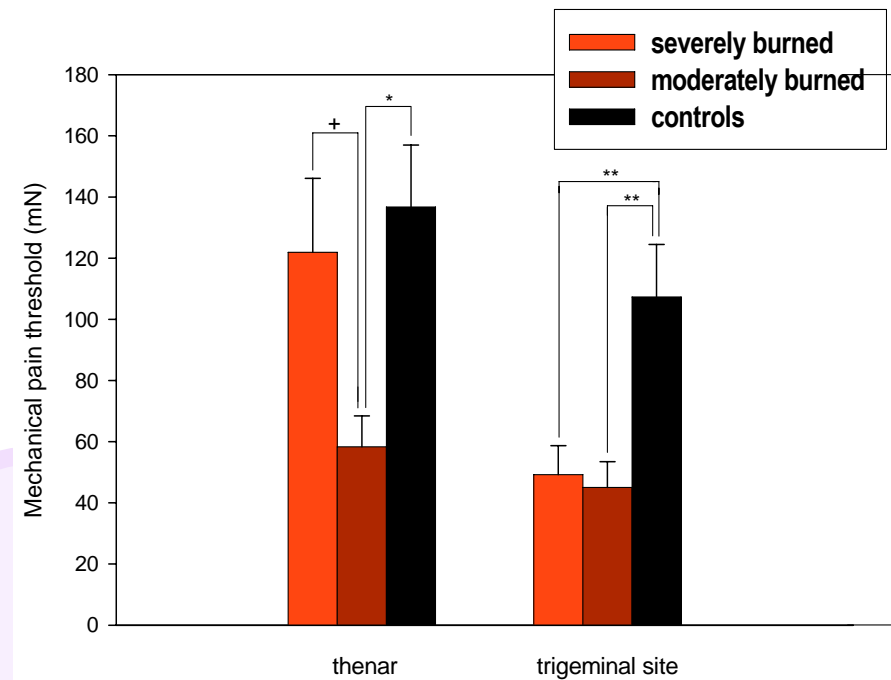
Burn injuries during infancy and their consequences

Heat pain

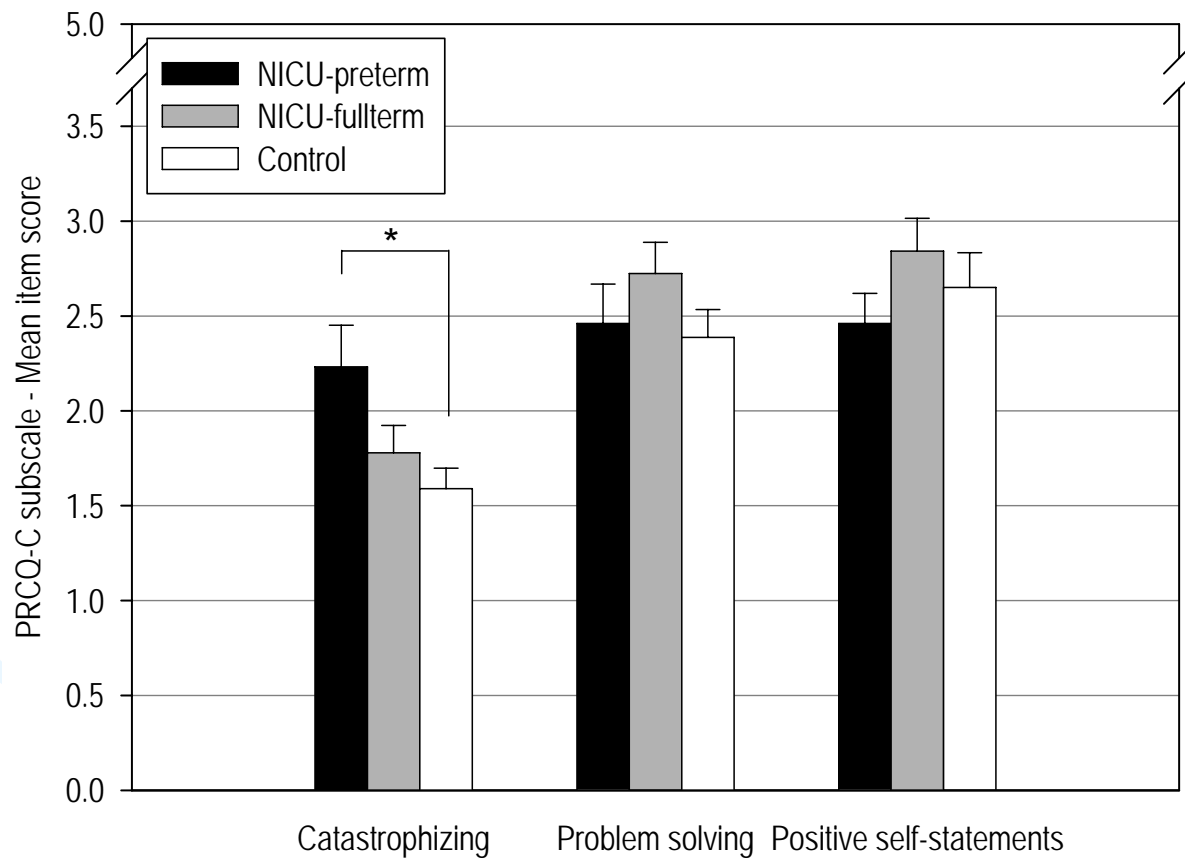


Burn injuries during infancy and their consequences

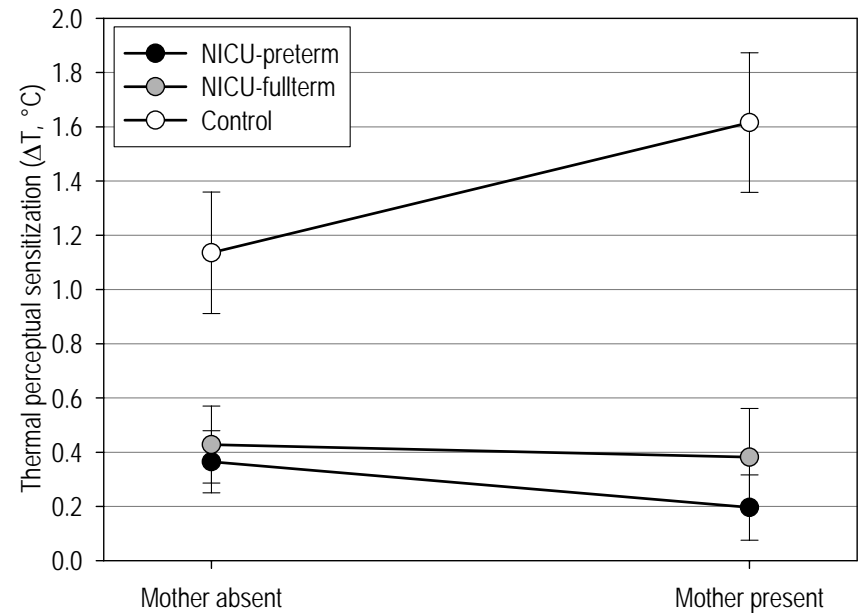
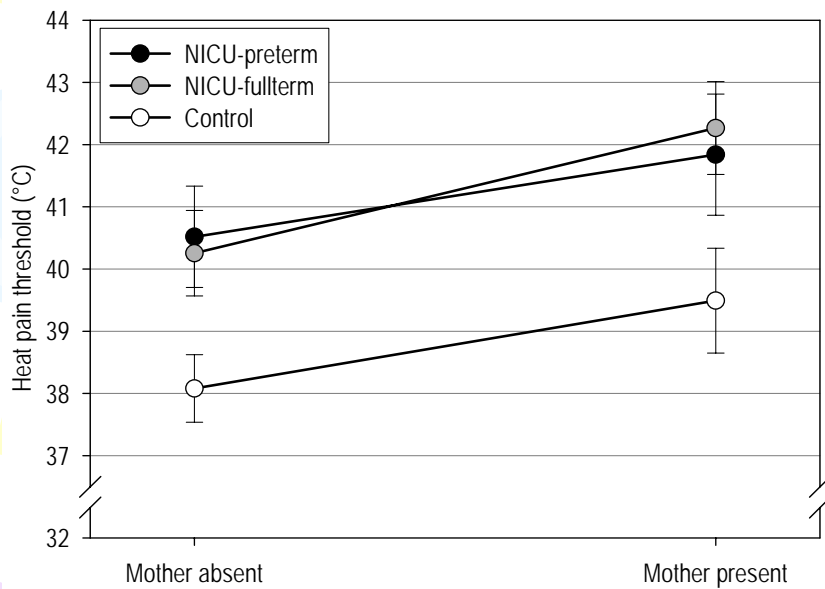
Mechanical pain



Pain-related Cognitions



Pain Sensitivity in the Presence and Absence of the Mother



Summary & Conclusions

- ✓ recurrent migraine or abdominal pain in children and adolescents is associated with altered pain sensitivity with RAP showing more local and modality-specific changes than MIG
- ✓ children and adolescents with recurrent migraine and abdominal pain are hypervigilant to painful and non-painful (somatic) stimuli and catastrophize with RAP > MIG
- ✓ exposure to painful experiences during the neonatal period (especially as a preterm) and during early infancy can result in long-term alterations (at age 9-14 yr) of pain sensitivity, stress reactivity, cognitive coping and parent response to pain and may predispose to chronic pain

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