NIH Workshop: Developing Meaningful Endpoints for Pain Clinical Trials

PAIN CLINICAL ENDPOINTS-BIOMARKERS

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IMMPACT Biomarker assessment:

- Neuroimaging
- Sensory Testing
- Skin Biopsies

Smith et al. EJP 2017

Brain-based biomarkers

For pain as the problem (=disease): obvious option - sensation of pain is a brain function

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Problematic (e.g. Davis et al. 2017; Nature Reviews Neurology)
Potential benefit: more sensitive – e.g. treatment responsiveness detected earlier (Duff et al. Science Translational Medicine 2015)

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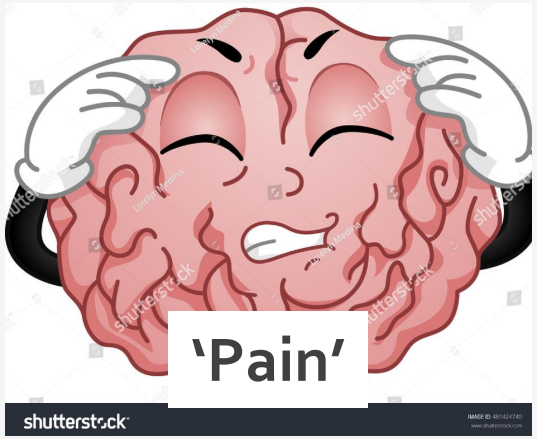
As 'mechanistic' biomarker?



Pain = 7

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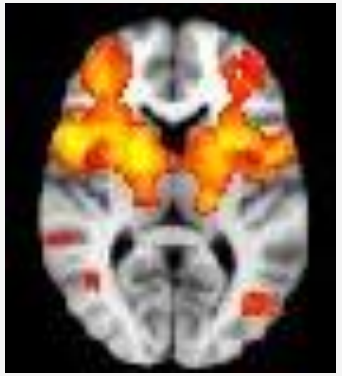
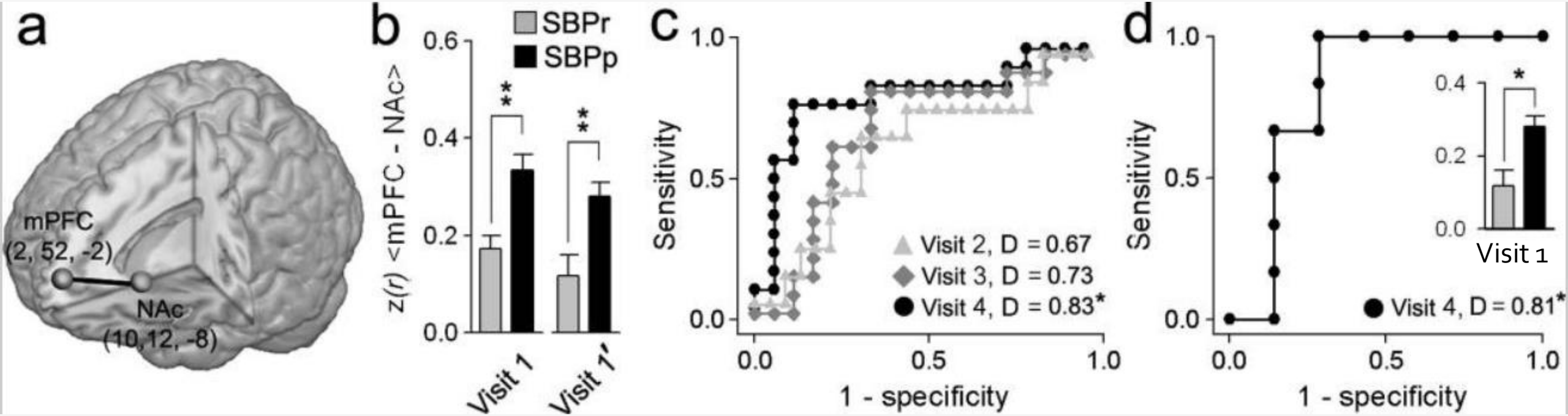


Different endophenotypes

Brain-based biomarkers

Endophenotypes as predictive/prognostic biomarker?

Validation group



Baliki et al. 2012 Nat Neurosci

Brain-based biomarkers – resting state networks

Default mode network changes: 'chronic pain seems to reorganize the dynamics of the DMN and as such reflect the maladaptive physiology of different types of chronic pain'.

	DMN-insula connectivity up	DMN-some other non-DMN region connectivity up
n=20 (505 patients)	n=10	n=9

Ceko et al. 2020, Pain

Brain-based biomarkers – resting state networks

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	DMN-insula connectivity up	DMN-some other non-DMN region connectivity up	Pain at time of study visit? Yes	Pain at time of study visit? Not reported
n=20 (505 patients)	n=10	n=9	n=10	n=5

Ceko et al. 2020, Pain

Brain-based biomarkers – resting state networks

Fibromyalgia patients: chronic widespread pain for at least 1 year with an average daily intensity of at least 4/10.

	Patients (n=27)	Controls (n=27)	Patients (n=16)	Controls (n=16
Age (yrs)	42	42	49	49
Pain duration (yrs)	11	n/a	12	n/a
Anxiety symptoms (HADS)	8	4	10	5
Depression symptoms (HADS)	5	2	5	2

Ceko et al. 2020, Pain

Brain-based biomarkers – resting state networks

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	Scanner pain-free cohort		Scanner pain cohort	
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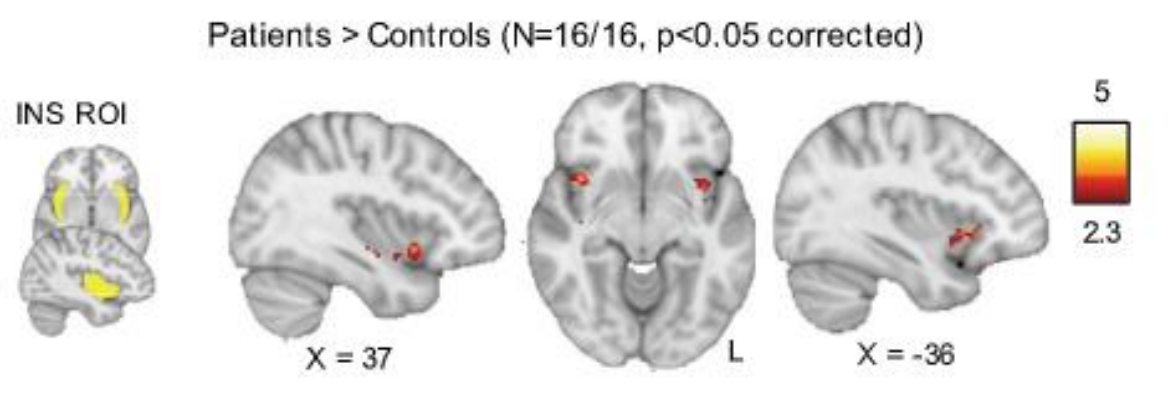
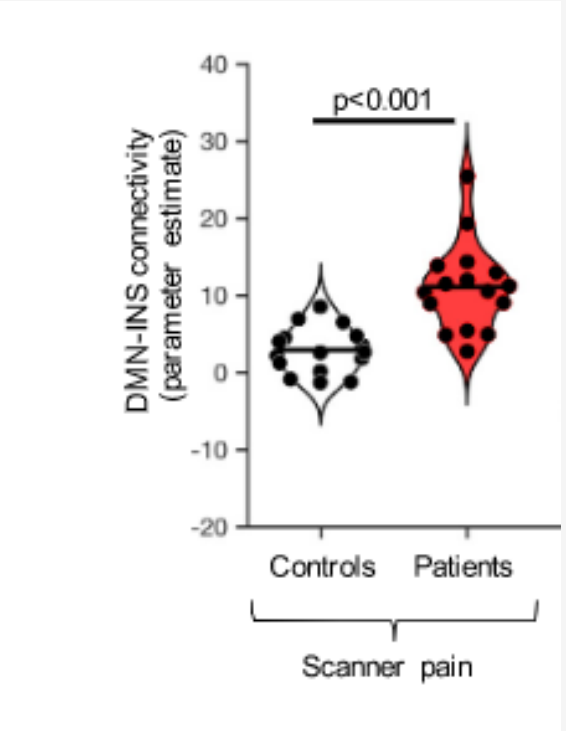
Pain duration (yrs)	11	n/a	12	n/a
Anxiety symptoms (HADS)	8	4	10	5
Depression symptoms (HADS)	5	2	5	2
Pain at the time of scan (/10)	0	0	4.4	0.05

Ceko et al. 2020, Pain

Brain-based biomarkers – resting state networks

Scanner pain cohort





Ceko et al. 2020, Pain

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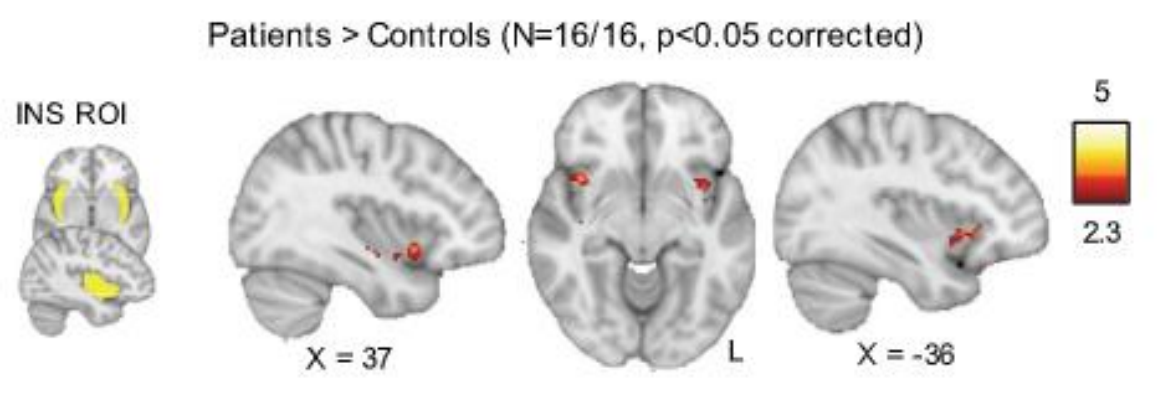
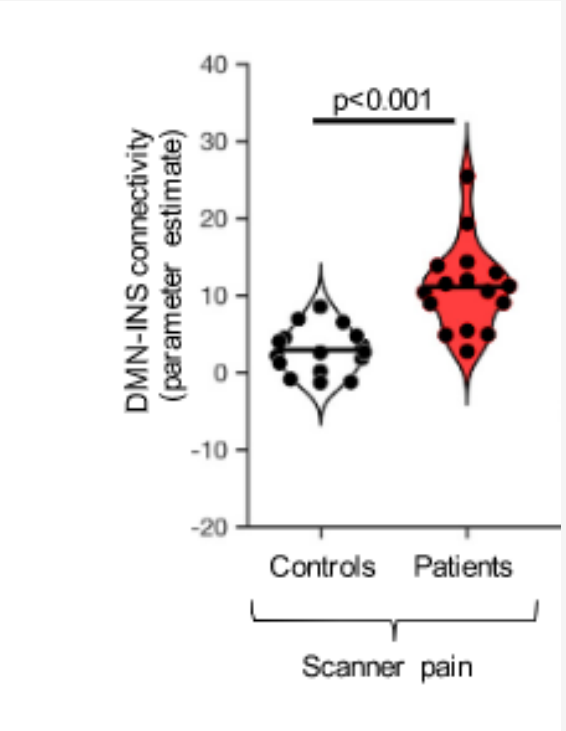
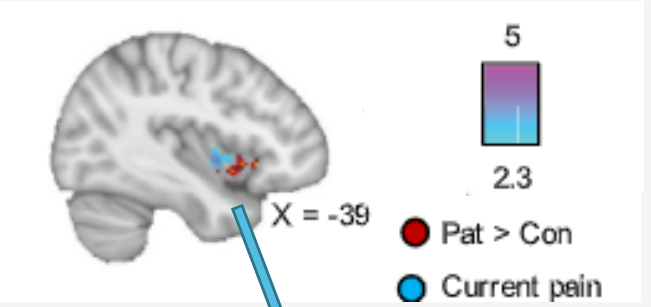
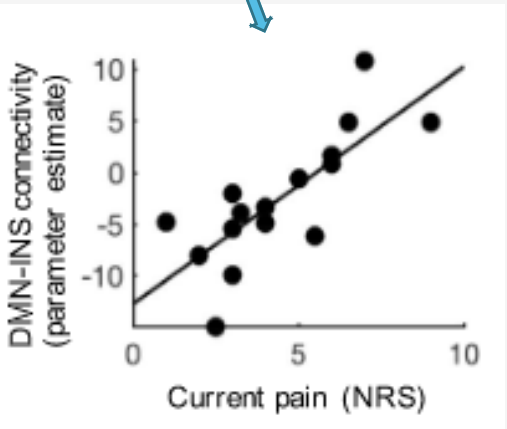


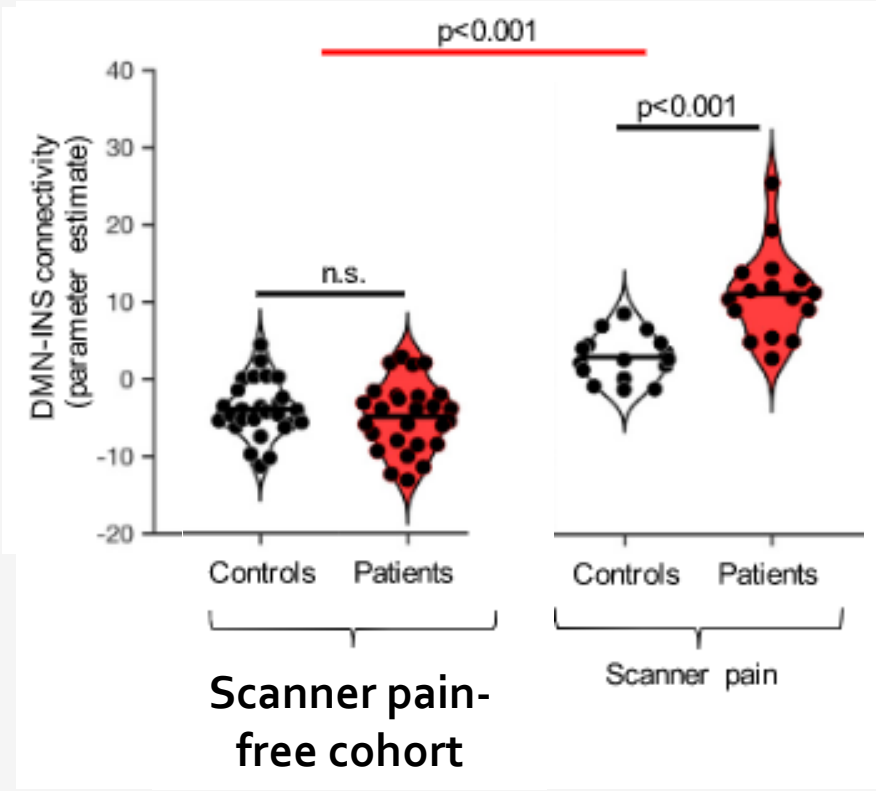






Ceko et al. 2020, Pain

Brain-based biomarkers – resting state networks



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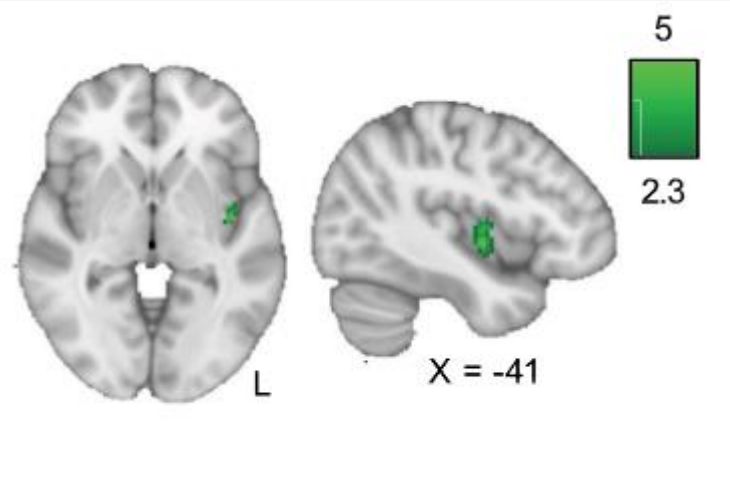
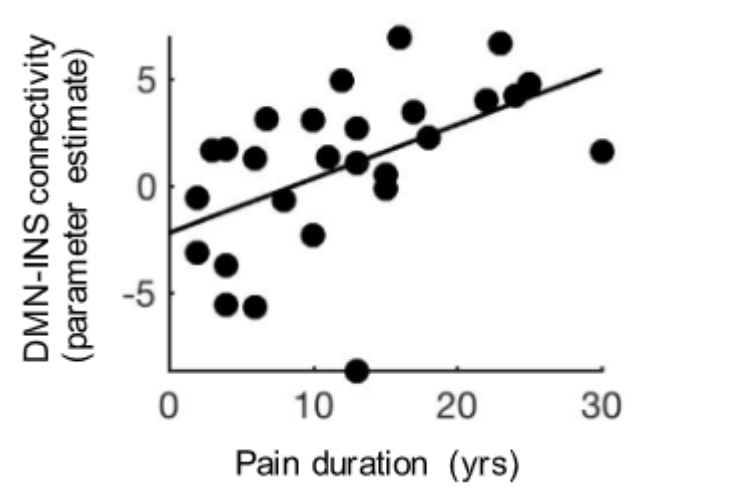
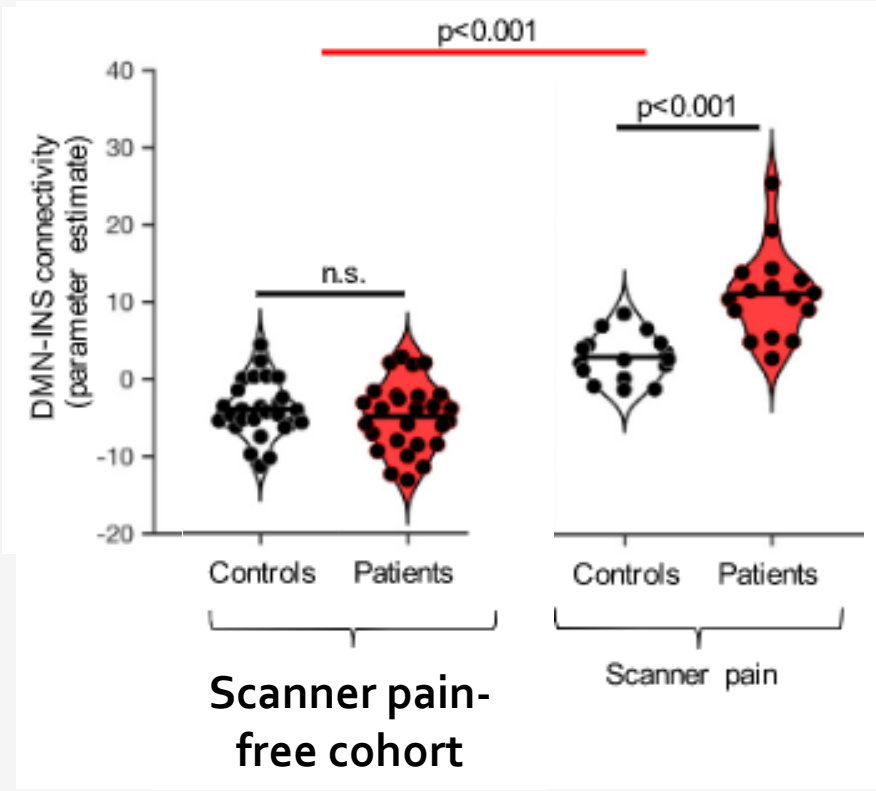




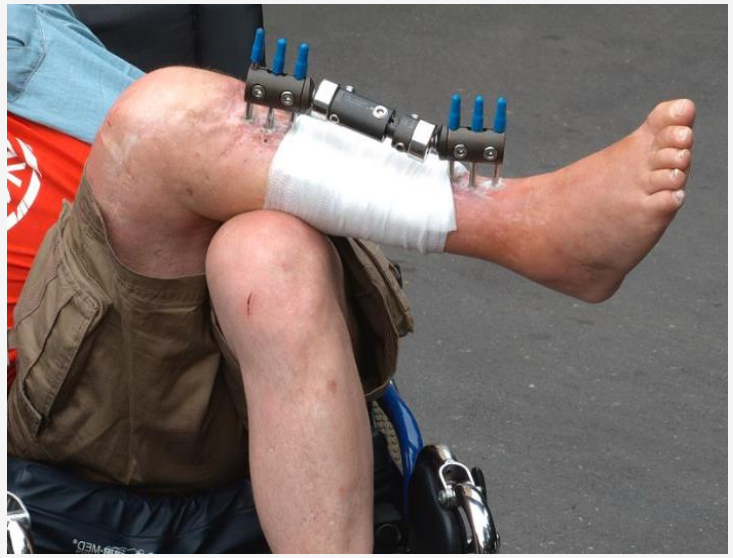


Scanner pain-free cohort

Ceko et al. 2020, Pain

Brain-based biomarkers

Pain as a symptom



https://www.gazette-news.co.uk/news/17911072.footballers-help-injured-player-suffered-broken-leg/
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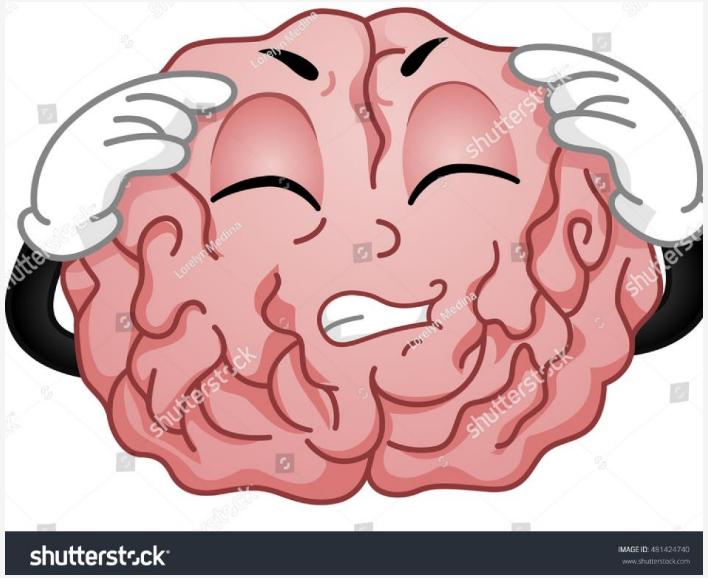
Brain-based biomarkers



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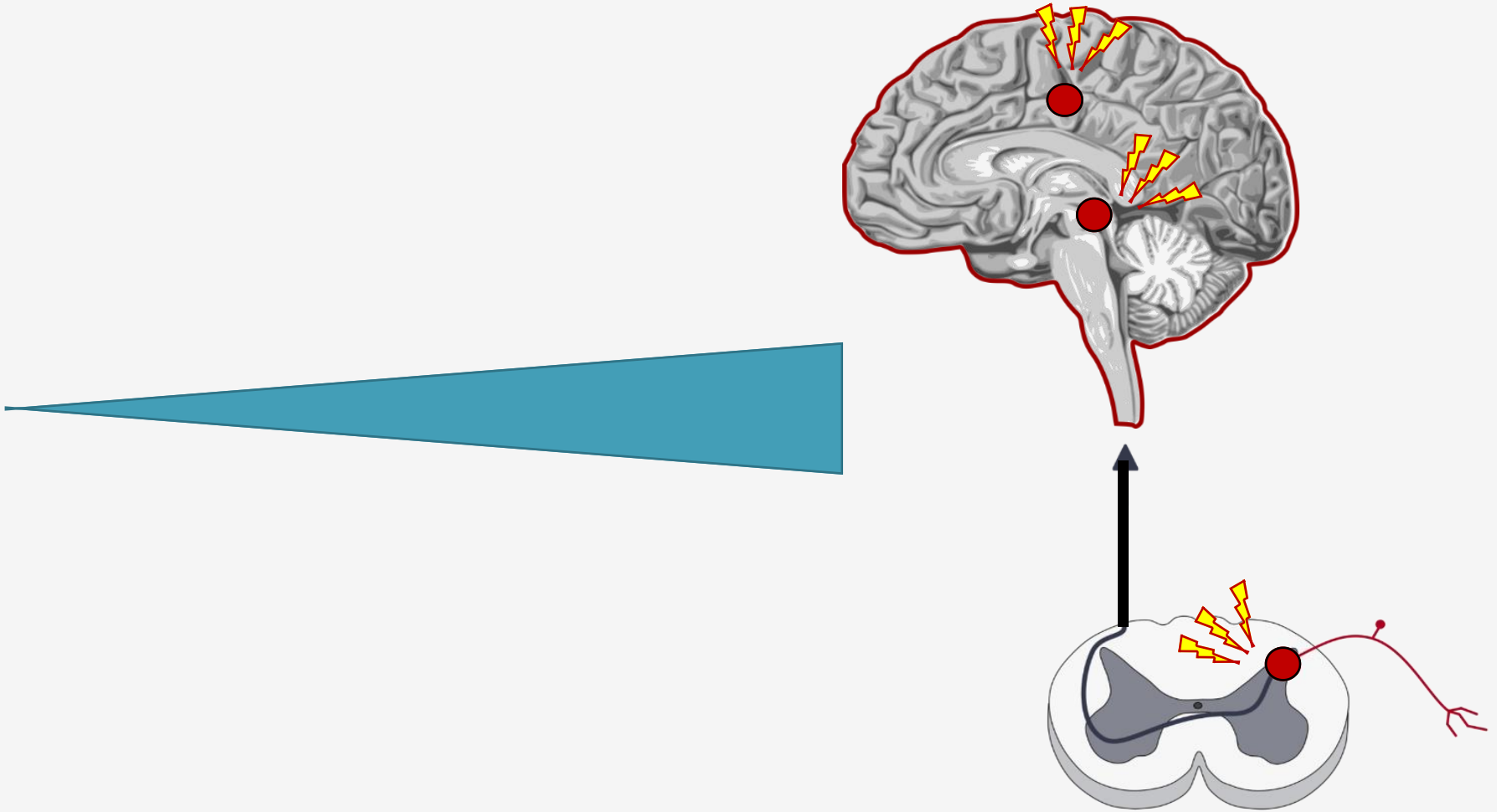
Biomarkers



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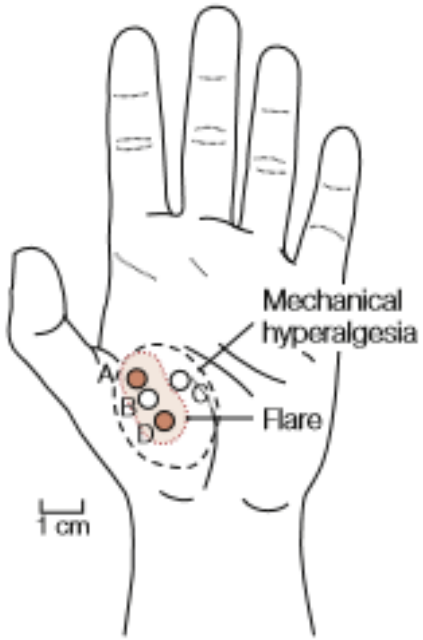
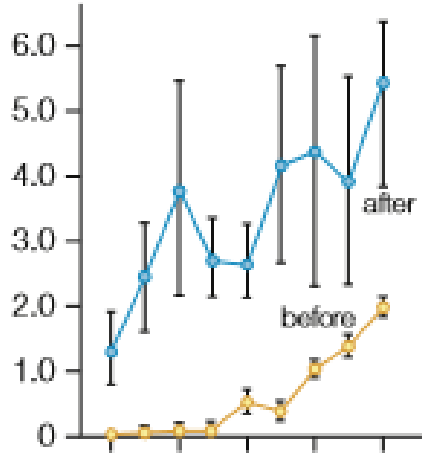
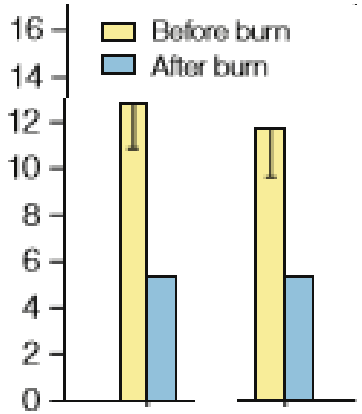


Heat pain ratings

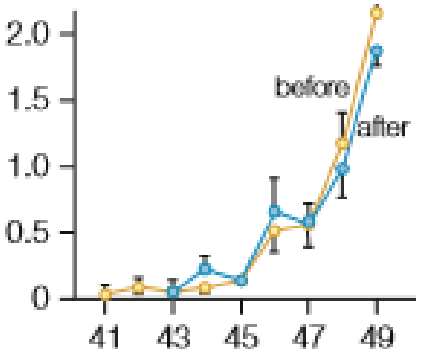
Injury site



Mechanical pain threshold

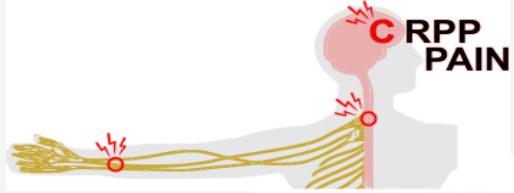


Outside injury



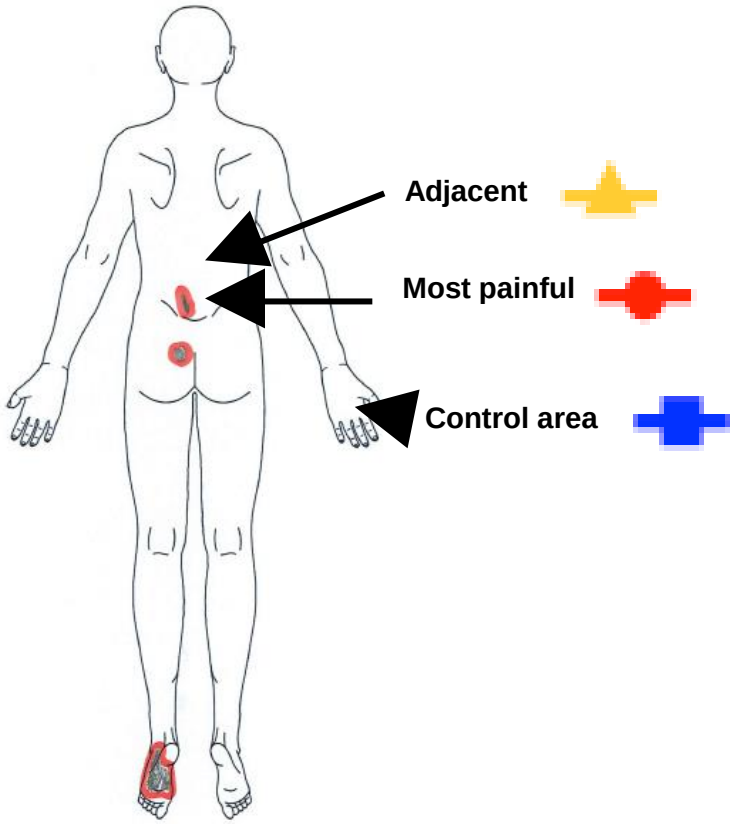
Stimulus temperature (°C)

Adapted from the Textbook of Pain 2013



Name Pat.: _____

Untersucher: _____ Pat. ID: _____



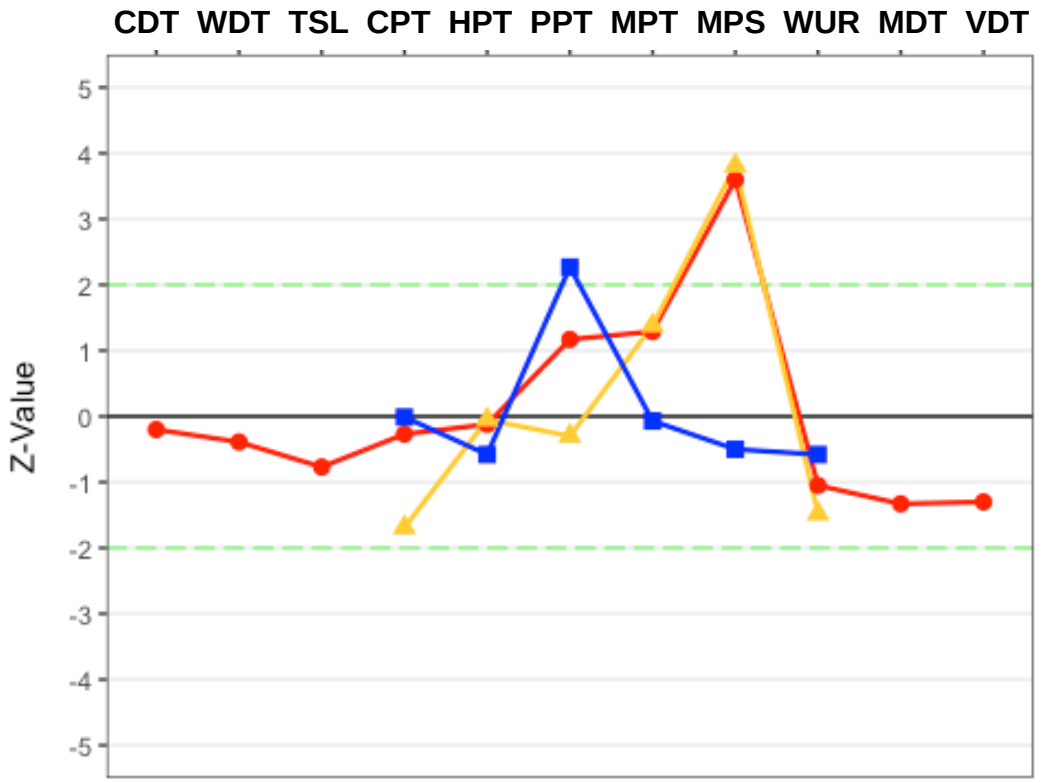
Intensität

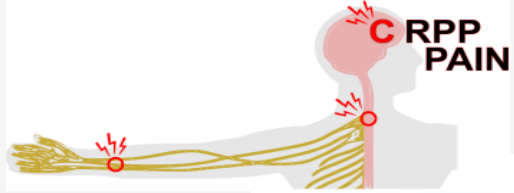
Kein Schmerz 0 1 2 3 4 5 6 7 8 9 10 Stärkste vorstellbare Schmerzen

x = schmerzhafteste Stelle

Kommentare

Quantitative Sensory Testing profiles





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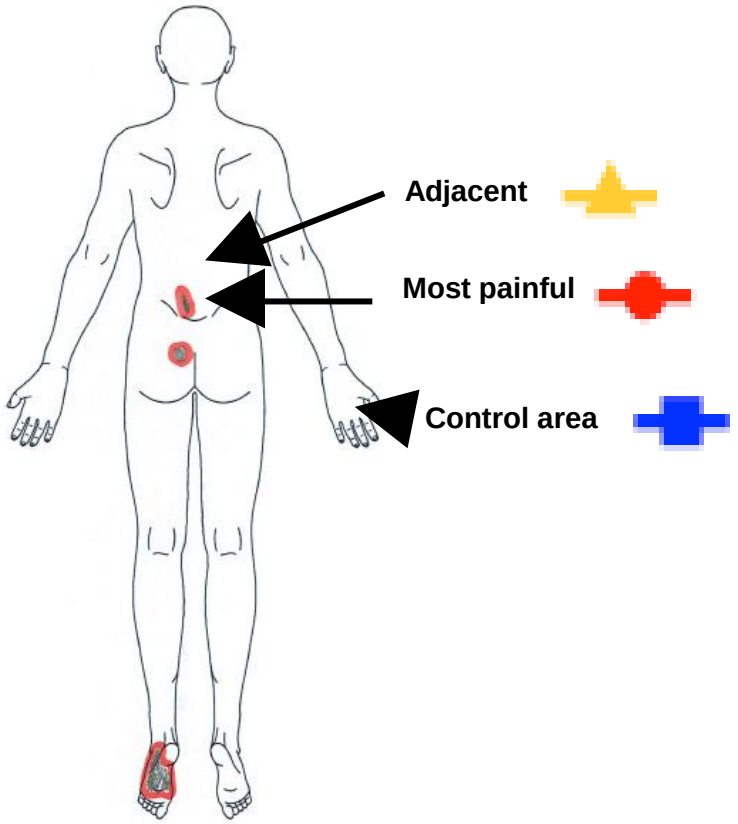

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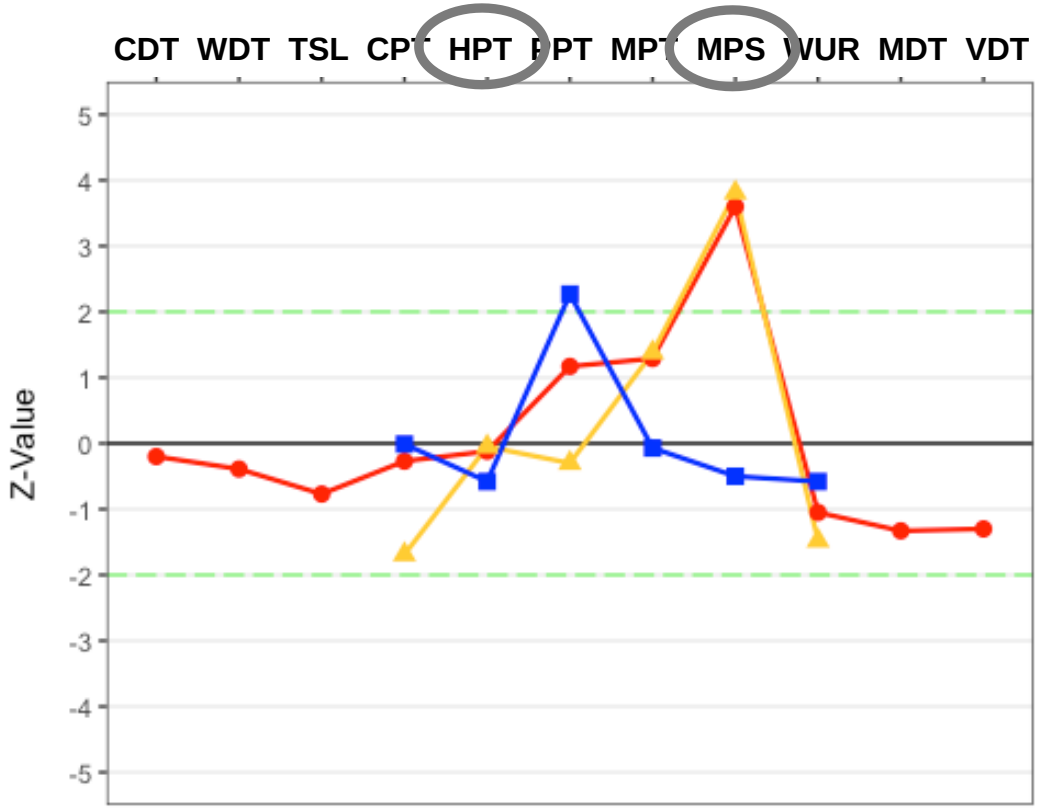

Take home messages

- The biomarker to choose / aim to develop depends very much on the purpose
- A suitable biomarker for pain might depend on the underlying condition, even in the instance of chronic pain
- It is difficult but not hopeless!

Integrative Spinal Research

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