What is the role of SENSORY ASSESSMENT in analgesic clinical trial design and the development of improved analgesic treatments?

Or: the sensory phenotype is important

Sektion Neurologische Schmerzforschung und Therapie

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Conflicts of interest

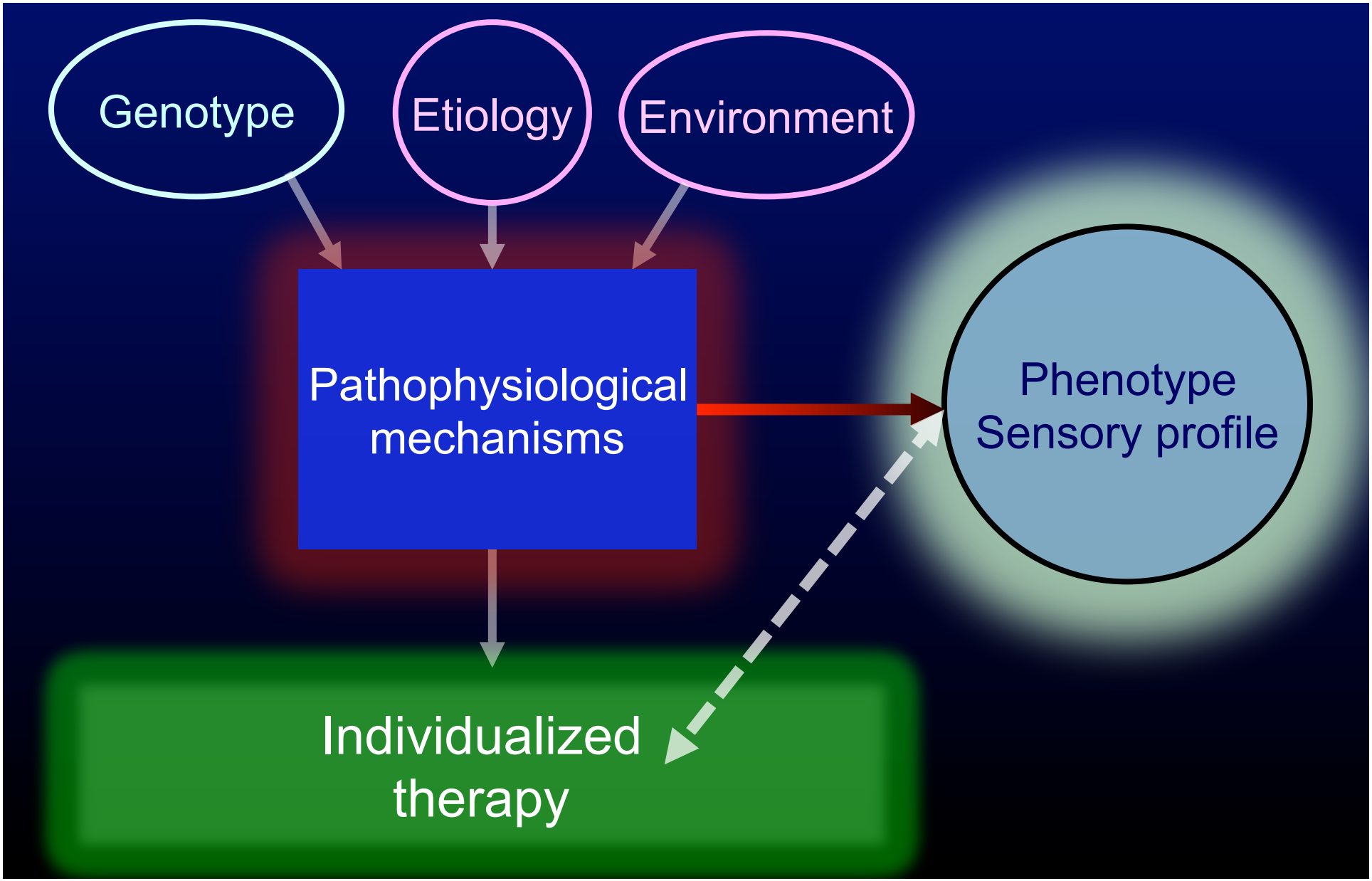
<u>Grant / Research Support:</u>
Pfizer, Genzyme, Grünenthal,
Member of the IMI „Europain“ collaboration
and industry members of this are: Astra Zeneca, Pfizer, Esteve, UCB-Pharma, Sanofi Aventis, Grünenthal, Eli Lilly, Boehringer Ingelheim
German Federal Ministry of Education and Research:
German Research Network on Neuropathic Pain (01EM0903)
Modelling Pain Switches (0315449B)
German Research Foundation (DFG): BA1921/2-2, JA240/19-1

<u>Consultant / Speakers Bureau:</u>
Pfizer, Genzyme, Grünenthal, Mundipharma, Allergan, Sanofi Pasteur, Medtronic, Eisai, UCB BioSciences, Eli Lilly, Boehringer Ingelheim, Astellas, Novartis, Biogen Idec, Astra Zeneca, Bristol-Myers Squibb

Individualized pain therapy

- Research on a network level – large cohorts
- A new classification with modern diagnostic tools and biomarkers
  - No therapy based on etiological entities
  - Therapy addressing sensory phenotypes and potentially mechanisms

Hypothesis: mechanism-based therapy



Sensory phenotype – indirect clinical assessment

- Predictive clinical assessment (pain mechanisms)
- Stratification tool

- Efficacy-response (surrogate endpoint)
- Outcome measure tool

Sensory phenotype – indirect clinical assessment

- The sensory phenotype allows to subgroup patients
- Sensory phenotypes reveal the mechanism of pain
- Sensory phenotypes reveal novel “drugable” targets
- Sensory phenotypes can be assessed in clinical practice
- Sensory phenotypes show predictive validity in treatment trials
- Discussion:
  Do regulatory bodies accept approval in subgroups?

Agenda

The sensory phenotype allows to subgroup patients

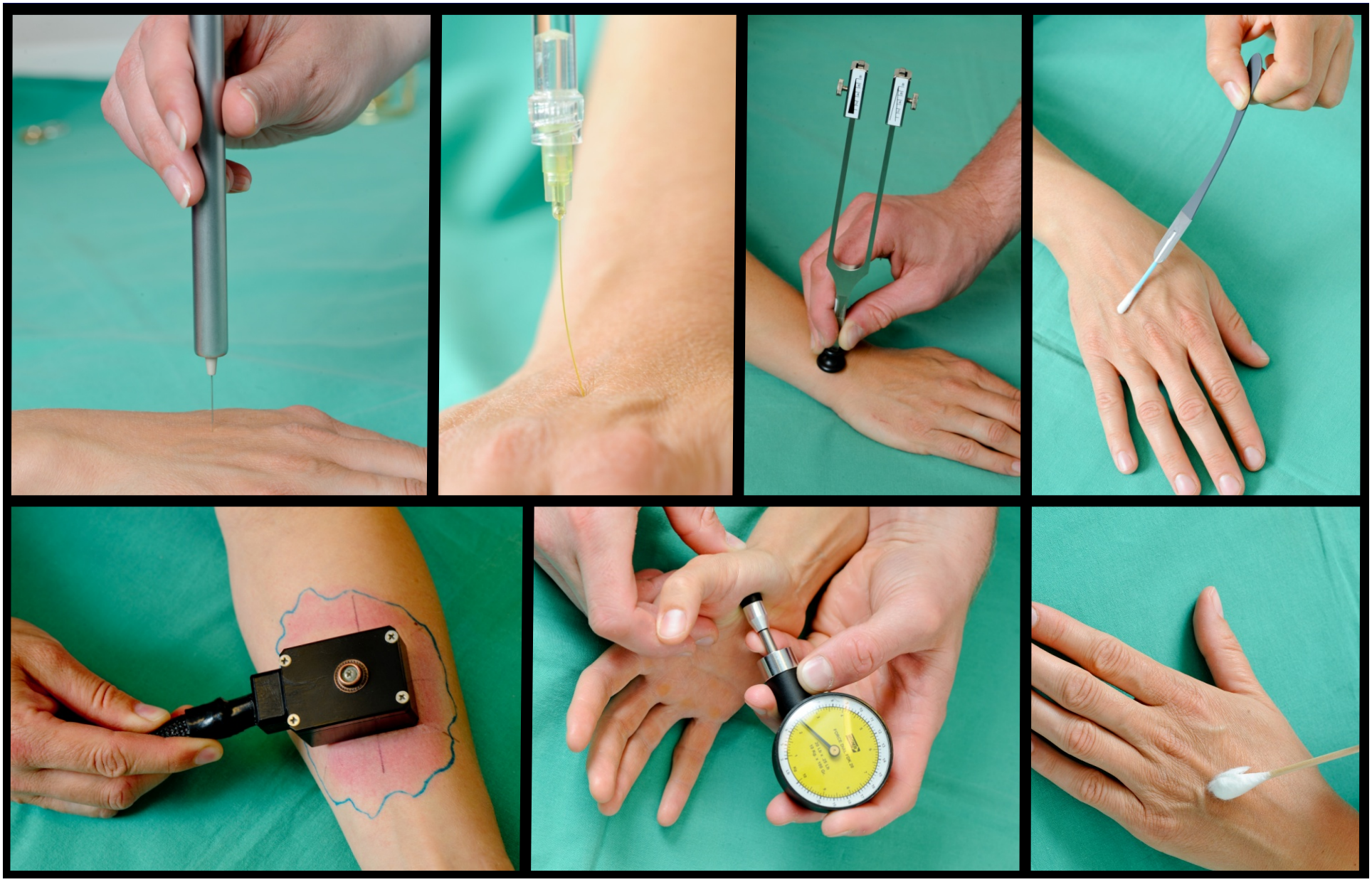
Segmentation methods to subgroup patients using QST

AT BASELINE

The German Network on Neuropathic Pain (DFNS)

> 2500 patients with many neuropathic etiologies

13 QST parameters to assess sensory signs



Agenda

The sensory phenotype reveal the mechanism of pain

Segmentation methods identify different mechanisms

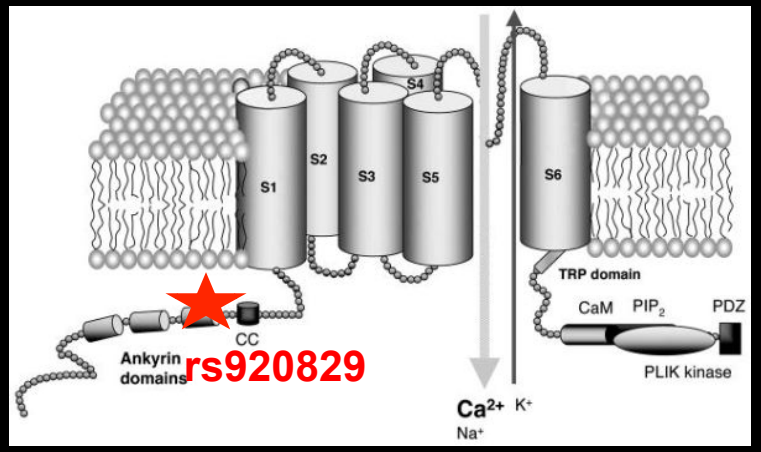
Agenda

Sensory phenotypes reveal new “drugable” targets

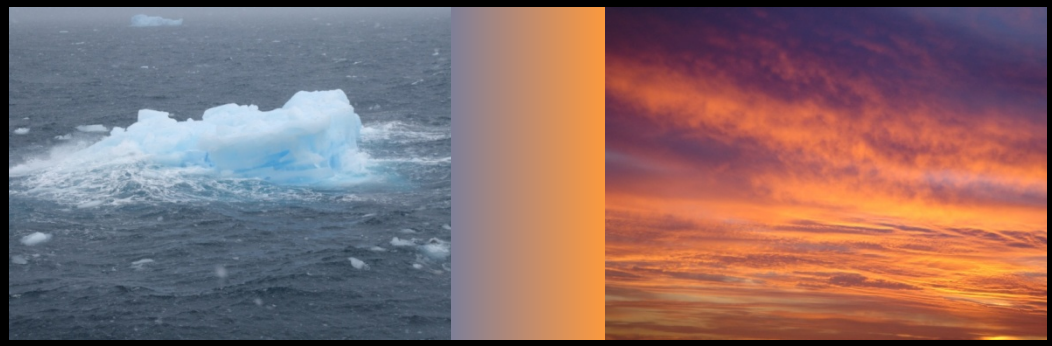
Example:

Genotyping of TRPA1

Genes and paradoxical heat – TRP A1

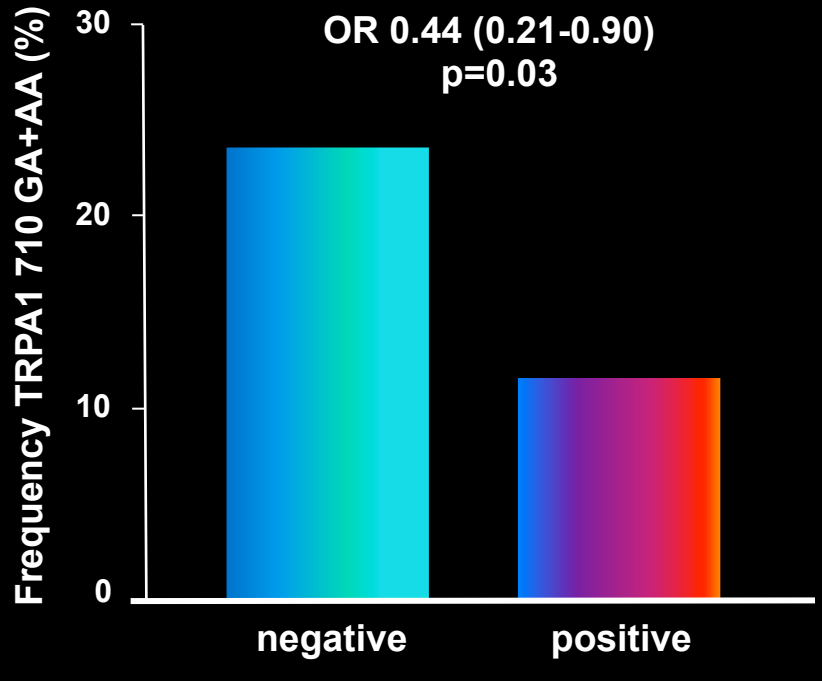


Paradoxical heat



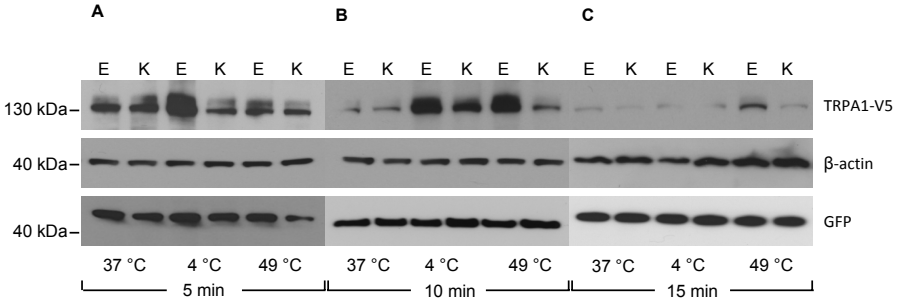
80% GG polymorphism

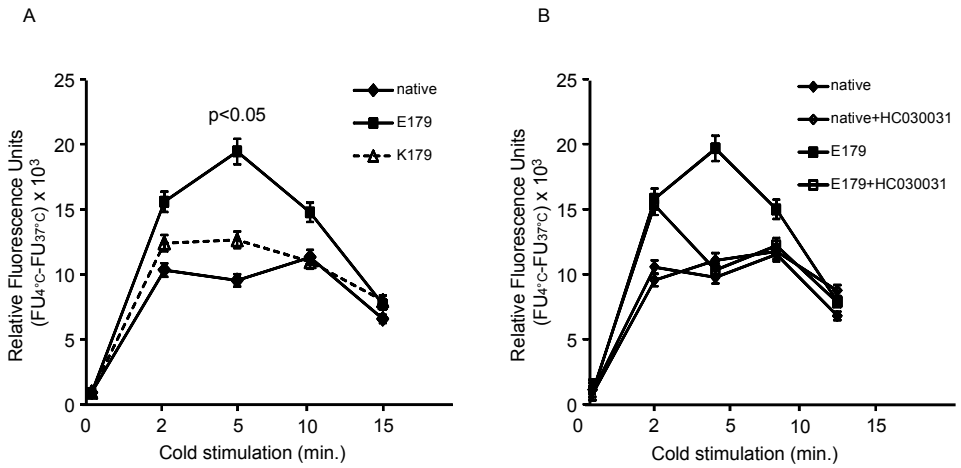
20% AA/GA polymorphism (protecting factor)

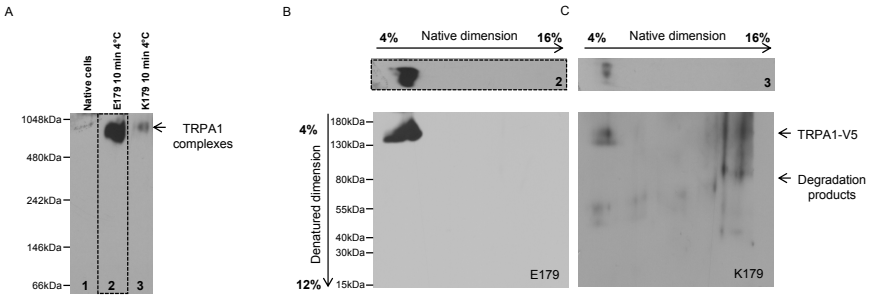


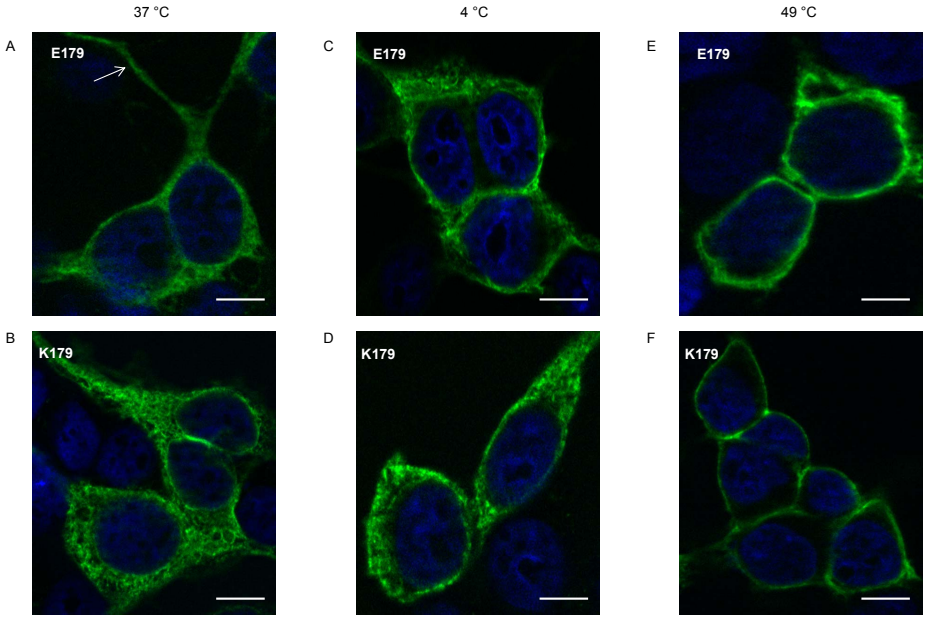
Binder et al. 2011

The SNP is functional









May et al. 2012

Agenda

Sensory profiles can be assessed in clinical practice

Easy to use questionnaires

Identification of patient subgroups

painDETECT SCHMERZ-FRAGEBOGEN

Datum: Patient: Name: Vorname:

Wie würden Sie Ihren Schmerz **jetzt** im Augenblick einschätzen?

0 1 2 3 4 5 6 7 8 9 10

kein max

Wie stark war der **stärkste** Schmerz in den letzten 4 Wochen?

0 1 2 3 4 5 6 7 8 9 10

kein max

Wie stark war der Schmerz in den letzten 4 Wochen im **Durchschnitt**?

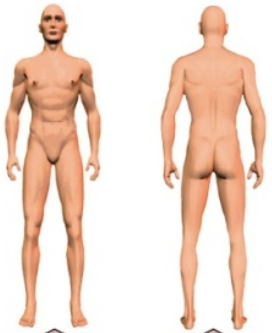
0 1 2 3 4 5 6 7 8 9 10

kein max

Kreuzen Sie das Bild an, welches Ihren Schmerzverlauf am besten beschreibt:

- Dauerschmerzen mit leichten Schwankungen ☐
- Dauerschmerzen mit Schmerzattacken ☐
- Schmerzattacken dazwischen schmerzfrei ☐
- Schmerzattacken dazwischen Schmerzen ☐

Bitte kennzeichnen Sie Ihren **Hauptsschmerzbereich**



Strahlt Ihr Schmerz in weitere Körperregionen aus? ja ☐ nein ☐

wenn ja, dann zeichnen Sie bitte die Richtung ein, wohin der Schmerz ausstrahlt.

Leiden Sie in den eingezeichneten Bereichen an einem Brenngefühl (z.B. Brennnesseln)?

nie ☐ kaum ☐ gering ☐ mittel ☐ stark ☐ sehr stark ☐

Haben Sie im Bereich Ihrer Schmerzen ein Kribbel- oder Prickelgefühl (wie Ameisenlaufen, Stromkribbeln)?

nie ☐ kaum ☐ gering ☐ mittel ☐ stark ☐ sehr stark ☐

Ist leichte Berührung (Kleidung, Bettdecke) in diesem Bereich schmerzhaft?

nie ☐ kaum ☐ gering ☐ mittel ☐ stark ☐ sehr stark ☐

Haben Sie im Bereich Ihrer Schmerzen blitzartig, elektrisierende Schmerzattacken?

nie ☐ kaum ☐ gering ☐ mittel ☐ stark ☐ sehr stark ☐

Ist Kälte oder Wärme (Badewannenwasser) in diesem Bereich gelegentlich schmerzhaft?

nie ☐ kaum ☐ gering ☐ mittel ☐ stark ☐ sehr stark ☐

Leiden Sie in den von Ihnen eingezeichneten Bereichen unter Taubheitsgefühl?

nie ☐ kaum ☐ gering ☐ mittel ☐ stark ☐ sehr stark ☐

Löst ein leichter Druck z.B. mit dem Finger in diesem Bereich Schmerzen aus?

nie ☐ kaum ☐ gering ☐ mittel ☐ stark ☐ sehr stark ☐

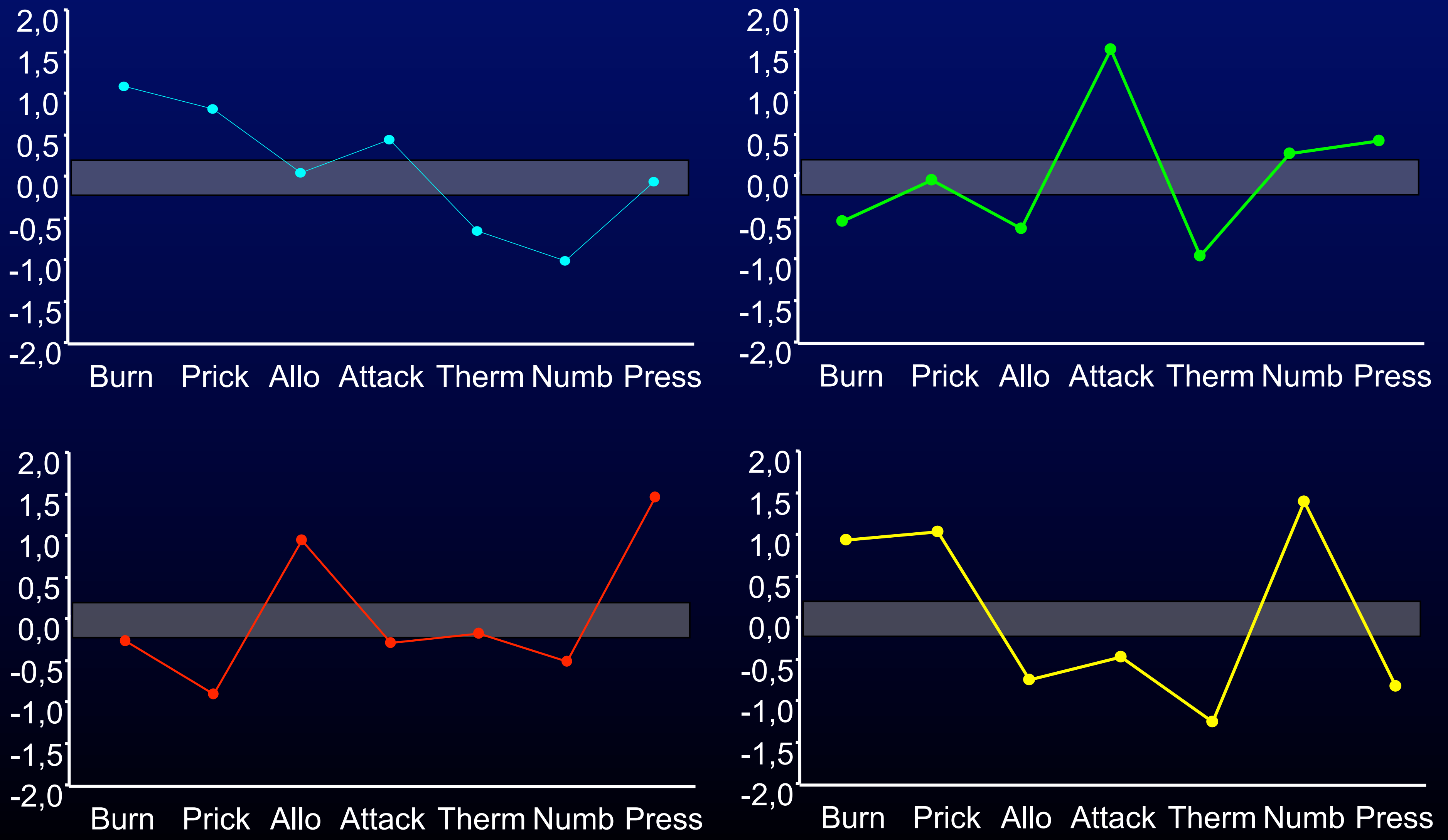
(vom Arzt auszufüllen)

☐ x 0 = 0 | ☐ x 1 = ☐ | ☐ x 2 = ☐☐ | ☐ x 3 = ☐☐ | ☐ x 4 = ☐☐ | ☐ x 5 = ☐☐

Score - Gesamtsumme ☐☐ **von 35**

Baron et al. 2009

Questionnaire profiles – subgroups



Baron et al. 2009

Cluster analysis – % of clusters

Cluster	1	2	3	4	5
PNP	13	16	37	9	26
PHN	34	11	25	25	5

Agenda

The sensory phenotype shows predictive validity in treatment trials

Segmentation methods identify differential response

Pregabalin in HIV-neuropathy

Randomized, double-blind, placebo-controlled trial

– Pain difference: VAS -0.25, P = 0.4

Severe pinprick hyperalgesia at baseline (1/3)

- Pain difference VAS -2.14 (P<0.01)

– Low-to-moderate pinprick hyperalgesia

- Pain differende VAS -0.06 (P=0.88)

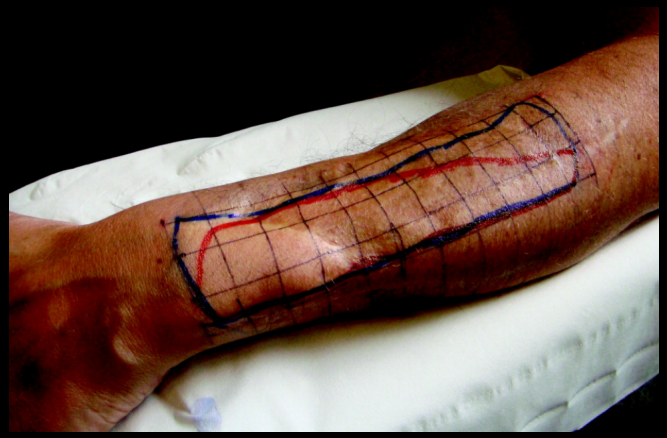
Simpson et al. 2008

Evidence

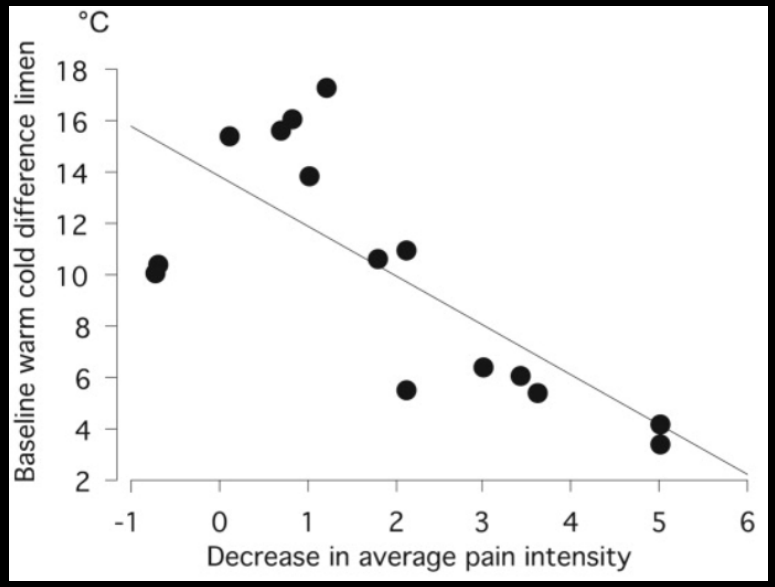
Neuropathic pain trial:

Botulinum toxin in peripheral sensitization

Botulinum toxin



Predictor:
temperature sensitivity
in affected skin



Ranoux et al. 2008

Conclusion

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