**Ruprecht-Karls-Universität Heidelberg**
**Medizinische Fakultät Mannheim**
**Dissertations-Kurzfassung**

# Optimizing the utility of Quantitative Sensory Testing for individual diagnostics and development of a mechanism-based classification of neuropathic pain

Autor: Jan Vollert
Institut / Klinik: Zentrum für Biomedizin und Medizintechnik Mannheim (CBTM)
Doktorvater: Prof. Dr. R.-D. Treede

Quantitative Sensory Testing (QST) following the DFNS (German Research Network on Neuropathic Pain) protocol assesses the function of the somatosensory nervous system. Long-term aim of QST research is the establishment of a mechanism-based classification of neuropathic pain. Over the last years, a central database with QST assessments of healthy participants, healthy participants under human surrogate models of neuropathic pain, and patients suffering from neuropathic pain has been built within the European consortia IMI Europain, Neuropain and the DFNS.
Aim of this work was to show that QST assessment is comparable between the participating centers across Europe in an analysis of heterogeneity, to use unsupervised clustering methods to identify subgroups of sensory profiles appearing across etiologies of peripheral neuropathic pain and may indicate underlying mechanisms of pathophysiology, to develop an individual assignment algorithm sorting QST profiles to these subgroups, to estimate the frequency of these subgroups across the common entities of peripheral neuropathic pain diabetic polyneuropathy, peripheral nerve injury and post-herpetic neuralgia and to further validate the subgroups identified in patients in surrogate models of neuropathic pain, in which the underlying mechanisms are well described.
Heterogeneity was overall low between the 11 participating European centers and the 13 QST parameters for healthy participants, and virtually non-existing for patients suffering from polyneuropathy or peripheral nerve injury. The cluster analysis found three sensory phenotypes, which are mainly characterized by either sensory loss (SL), intact sensory function and mild thermal hyperalgesia (TH) or loss of thermal detection and mild mechanical hyperalgesia (MH). The most common phenotype in diabetic polyneuropathy was SL (83%), followed by MH (75%) and TH (34%, note that percentages are overlapping and not additive). In peripheral nerve injury, frequencies were 37%, 59% and 50%, and in post-herpetic neuralgia, 31%, 63% and 46%. Surrogate models of denervation were similar to the SL phenotype, but also showed mild pinprick hyperalgesia and paradoxical heat sensations. Peripheral sensitization models resembled the TH phenotype, while models of central sensitization showed high similarities to the MH phenotype.
These data suggest that classifying patients based on QST profiles in an approach developed hypothesis-free in patients and validated in models with well-described mechanisms may be a good strategy for mechanism-based stratification of neuropathic pain patients for future clinical trials, as encouraged by the European Medicines Agency EMA.