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A More Pessimistic Life Orientation Is Associated With Experimental Inducibility of a Neuropathy-like Pain Pattern in Healthy Individuals

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Abstract: **The clinical pattern of neuropathic pain, diagnosed using the quantitative sensory testing (QST) battery (German Research Network on Neuropathic Pain), could be partly mimicked in healthy volunteers after topical capsaicin application. However, similar to clinical neuropathic pain that develops in only a subgroup of patients who have a neurologic lesion, this attempt to mimick a neuropathic pain pattern succeeded only in a small fraction (18%) of healthy individuals. In the present assessment, we pursued the hypothesis that the inducible subgroup differed from the other healthy participants with respect to their psychological phenotype. Therefore, in an observational study, participants were assessed using a comprehensive set of psychological variables comprising general psychological and pain-related cognitive-emotional mechanisms. The sum scores of the questionnaires were significantly linearly correlated with each other. Principal component analysis indicated that a major source of variance (46%) could be attributed to dispositional optimism examined via the Life Orientation Test (LOT). The LOT score significantly differed between the groups of participants, either those in whom a neuropathy-like pattern of pain assessed via QST could be partly (50–60% of the 11 QST parameters) induced (n = 20) or not (n = 90; *P* = .0375). It emerged again as the main selection criterion in a classification and regression tree predicting a participant's group assignment (inducible neuropathy-like QST pattern versus noninducible neuropathy-like QST pattern) at a cross-validated accuracy of 95.5 ± 2.1%. Thus, the few participants in a random sample of healthy volunteers who, after topical capsaicin application, partly resemble (to a degree of about 60%) the clinical pattern of neuropathic pain in the QST test battery, are preselectable on the basis of psychological factors, with a particular emphasis on pessimistic life attitudes.**

Perspective: ***In a small fraction of 18% of healthy volunteers, topical capsaicin application resulted in a neuropathy-like pattern in 50 to 60% of the components of a clinical test battery. These individuals displayed a more pessimistic life attitude as assessed by means of the LOT.***

Key words: *Dispositional optimism, quantitative sensory testing, catastrophizing, experimental pain, healthy individuals.*

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Neuropathic pain develops as a result of lesions of the peripheral or central somatosensory nervous system,[1] although not in every individual. In addition to the main causal factors such as morphological damage, further factors need to trigger its development.[69] Among these, psychological factors have been highlighted. They contribute to interindividual differences in the sensitivity[15,22,25] to pain and its chronification.[34,37,48,52] For instance, pain anxiety and catastrophizing contribute negatively to neuropathic pain and its treatment.[43,51,59,61,65] Pain vigilance, ie, a tendency to focus on pain-related bodily sensations, was also related to the development of chronic pain.[35,36] Moreover, general positive psychological attitudes such as dispositional optimism have been linked to lower pain intensity and better coping with pain.[6,18,19,21,34] By contrast, negative affectivity and distress, comprising mood, somatization, and anxiety, have been positively linked to the development of chronic pain.[10,13,62,64]

We have recently shown that the clinical pattern resembling neuropathic pain can be partly mimicked (60–70% of 11 standardly measured quantitative sensory testing [QST] parameters) in a few healthy volunteers after topical capsaicin application.[40] However, similar to clinical neuropathic pain, in this previous study, only a few of the participants, 18%, displayed neuropathy-like symptoms. Identifying those individuals in whom neuropathic pain will develop after a triggering incident is an active research topic and has already led to the association of various factors with this clinical course.[5] Considering the contribution of psychological factors to the development of neuropathic pain, in the present analysis, we tested the hypothesis that healthy individuals in whom a pattern of neuropathic pain can be experimentally induced differ with respect to psychological factors from those in whom this was not possible. To this end, the psychological phenotypes of the participants of that study[40] were described using a set of psychological variables comprising catastrophizing, pain anxiety and pain vigilance, dispositional optimism, mood, somatization, and state anxiety. These psychological factors have been selected to include a comprehensive set of risk factors as well as dispositional optimism representing a resilience factor that were evidently related to chronic pain.

Methods

Participants, Study Design, and Pain Data

The study followed the Declaration of Helsinki on Biomedical Research Involving Human Subjects and was approved by the Ethics Committee of the Medical Faculty of the Goethe University, Frankfurt am Main, Germany. Informed written consent was obtained from each participant. The present assessment is a secondary analysis of a recently published study.[40] The assessments were performed in the same random sample of healthy individuals of Caucasian ethnicity by self-assignment (N = 110, aged 18–36 years, 46 men),[40] mostly medical students in the local faculty. The ethics vote included coverage of the present psychological assessments. The participants' health was ascertained by medical history and physical examination, including vital signs.

This report focuses on psychological factors that had been acquired as an add-on during a previous investigation and had not been reported before.[40] In this previous study, we assessed the degree to which a pattern of neuropathic pain can be induced in healthy volunteers in reaction to experimentally induced pain. In this study, experimental hyperalgesia was obtained by applying 150 mg capsaicin cream (.2%, manufactured by the local hospital pharmacy) onto a 3 × 3 cm^2 skin area and covering it with plaster for 30 minutes before testing.[49] The body area to be tested was randomly assigned to the participants; possible sites were the dorsal sides of the hand in the dermatome of the nervus radialis (n = 61) or of the foot in the dermatome of the nervus fibularis profundus (n = 49). The resemblance of clinical neuropathic pain after application of the well-established experimental pain model of capsaicin sensitization[49] was assessed using a standardized clinical test battery[56] for neuropathic pain (QST), developed by the German Research Network on Neuropathic Pain.[56,57] QST uses the administration of thermal and mechanical stimuli grouped into 7 tests that result in 13 different parameters of sensory perception and pain. The detailed methodology was reported in the previous study.[40] Detection and pain thresholds to thermal cold and warm stimuli were assessed on a 9-cm^2 skin area using a thermode at a baseline temperature of 32°C and increasing or decreasing the temperature by 1°C/s (TSA 2001-II; Medoc, Ramat Yishai, Israel). The thermal sensory limen (TSL) was assessed using alternating applications of cold and warmth. If during this procedure the participant indicated a sensation of warmth or heat pain during administration of a cooling temperature, a paradoxical heat sensation was noted. The mechanical detection threshold was assessed by applying 10 punctate stimuli using von Frey hairs at strengths of .25 to 512 mN (Optihair2-set; Marstock Nervtest, Schriesheim, Germany). The mechanical pain threshold was measured using 10 pinprick stimuli at 8 to 512 mN (The Pin-Prick; MRC Systems, Heidelberg, Germany). The mechanical pain sensitivity and dynamic mechanical allodynia were determined using pinprick stimulus intensities of 8 to 512 mN applied concomitantly with stimuli of light touch. The participant rated how painful each stimulus was on a numerical rating scale ranging from 0 ("no pain") to 100 ("strongest pain imaginable"). The wind-up ratio was measured in 5 runs, starting with a single stimulus of 256 mN followed by series of 10 stimuli of the same intensity (application frequency 1 Hz, skin area of application 1 cm^2). The vibration detection threshold was obtained by applying a Rydel-Seiffer tuning fork (64 Hz, 8/8 scale) on the processus styloideus radii for the hand area or the malleolus medialis for the foot area. The pressure pain threshold was assessed by applying blunt pressure stimuli at the musculus thenar or the musculus abductor hallucis (Commander Algometer; JTECH Medical, Midvale, UT). The QST tests were