KAREN PRIP

DISABILITY AMONG TORTURED REFUGEES IN RELATION TO PAIN AND SENSORY FUNCTION IN THEIR FEET

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PhD thesis

DISABILITY AMONG TORTURED REFUGEES IN RELATION TO PAIN AND SENSORY FUNCTION IN THEIR FEET

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The Institute of Public Health
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DIGNITY - Danish Institute Against Torture
2014

This PhD study was carried out during my employment at the Research Initiative in Rehabilitation, Institute of Public Health, Faculty of Health Sciences, University of Southern, Odense, Denmark, and DIGNITY - Danish Institute Against Torture in Copenhagen (the former Rehabilitation and Research Centre for Torture Victims in Copenhagen) in the period from September 2006 to December 2013

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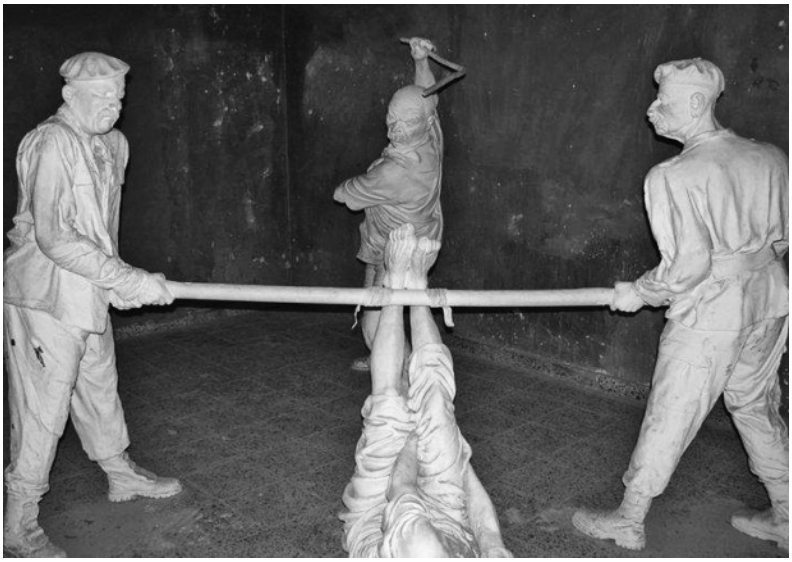
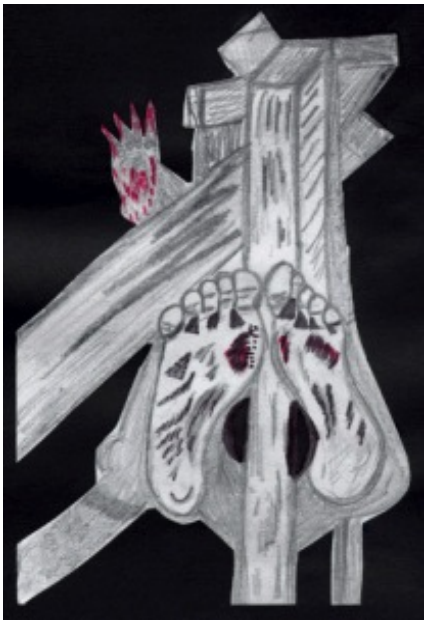


Presentation of Falanga torture
carried out during the reign of Saddam Hussein in the Amna Suraka prison,
now a museum in Sulaymaniyah, Kurdistan



Pain in the feet from falanga

Falanga
Beatings under the feet
Pushed down
the stair case
Landing lowest down in the
torture cellar
The pain is dreadful
in this black world
The pain increases day by day

by Shamal Adel Salim

Disability among tortured refugees in relation to pain and sensory function in their feet

PhD thesis

by

Karen Prip

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PREFACE

When I in 1992 was employed as chief physiotherapist at the Rehabilitation and Research Centre for Torture Victims in Copenhagen (RCT) a new door was opened for me. My assignment was to lead and develop the physiotherapy work with our patients that were torture victims with physical and mental sequaele after torture. I met a world that was filled with personal stories about torture, horror and suffering and my professional approach to physiotherapy treatment was challenged. It came to change my professional life completely.

At that time RCT was located in the University Hospital (Rigshospitalet) in Copenhagen. The centre was founded by Inge Genefke, MD, DMSc, in 1982 together with a group of Amnesty doctors (1), and has thus gained long experience of rehabilitating traumatized and tortured refugees living in Denmark. In 2012 the organisation changed its name to DIGNITY - Danish Institute Against Torture.

A group consisting of psychiatrists and physicians, a psychologist, nurses, physiotherapists, social counsellors and interpreters worked together with patients at the clinic. My earlier experience was from private practice, where my patients mainly had been referred for musculoskeletal pain, mostly neck and low-back pain.

As a trained specialist in manual therapy I felt confident that I would be capable to examine and treat our torture victims for their physical sequelae after torture. Yet, this turned out to be a great challenge, both professionally and emotionally.

The existing clinical examination procedures turned out to be more complicated than expected with these patients. Ethical and cultural considerations had to be made. To communicate with the patient using an interpreter was also a new experience. Most of all, the body pain pattern with multiple pain sites and the high pain intensity puzzled me. Some patients had, to me unfamiliar physical and psychological reactions, such as ‘flash back’, sweating and aggravation of pain, even after a gentle physical treatment. Light exercises had the same effect. Other patients that reported having pain, hardly felt when I touched their skin.

Most of the patients referred for physiotherapy had been exposed to falanga torture, beatings to the soles of the feet with a variety of instruments. During my many years working with manual therapy and teaching physiotherapists in diagnostics and treatment

of musculoskeletal disorders, I had worked together with Professor Finn Bojsen-Møller, at the Medical Faculty, University of Copenhagen. He is a specialist in foot functioning and inspired my later interest in studying the long-term consequences of falanga.

In 1995, I began working more closely with Kirstine Amris, rheumatologist at RCT. We examined pain mechanism after falanga, resulting in two publications (2, 3). With the Parker Institute we also performed MR-scanning of the feet in a group of torture victims to look for possible structural explanations for the pain experienced, resulting in one publication (4) and one publication on ultrasound scanning (5). At the same time a systematic monitoring for quality assurance of the physiotherapy work was initiated with one part focusing specifically on falanga. This led to the development and completion of the RCT 'Manual for Physiotherapy' that contained standardized examination procedures with written instructions (6).

In 2006, I was offered the opportunity to begin a PhD-fellowship at RCT, making my dream come true. I here got the possibility to document the physical consequences of torture, and to explore pain mechanisms after torture and the influence of pain on disability in tortured persons. My hope is that the knowledge gained from this thesis will help health professionals to better understand torture survivors' pain conditions, and consequently influence their choice of treatment in the future.

FINANCIAL SUPPORT AND OTHER CONFLICTS

This study was primarily supported by DIGNITY, Danish Institute against Torture (until 2012 The Rehabilitation and Research Centre for Torture Victims) in Copenhagen. Furthermore I received grants from Foundation Juchum, Kong Christian den Tiendes Fond, Lippmann Fonden, Torkil Steenbeck's Legat, Danish Physiotherapist Association, Grosserer Andreas Collstrup and his son Rudolf Collstrup's Mindelegat and Doctor Sofus Carl Emil Friis og Hustru Olga Doris Friis's Legat. The author declares that I have no personal financial interest in any commercial company or institution directly or indirectly related to this thesis.

ABBREVIATIONS

AI	Amnesty International
ANOVA	Analysis of variance
ANCOVA	Analysis of covariance
CAT	United Nations Convention Against Torture and other cruel, inhuman or degrading treatment or punishment
CDT	Cold detection threshold
ºC	Degree Celsius
CI	Confidence interval
CPT	Cold pain threshold
DESNOS	Disorders of extreme stress not otherwise specified
DRI	Disability Rating Index
F	Torture victims exposed to falanga
HADS	Hospital Anxiety and Depression Scale
Hz	Hertz
HPT	Heat pain threshold
IASP	International Association for the Study of Pain
ICF	International Classification of Functioning and Disability
kPa	kiloPascal
MDT	Mechanical detection threshold
NF	Torture victims not exposed to falanga
OR	Odds ratio
PPT	Pressure pain threshold
QST	Quantitative sensory testing
SPSS	Statistical Package for Social Sciences
SIP	Stimulus-independent foot pain
SEP	Stimulus-evoked foot pain
TP	Tender points
UN	United Nations
UNHCR	United Nations High Commissioner for Refugees
VAS	Visual Analogue Scale
WDT	Warm detection threshold
WHO	World Health Organization
WMA	World Medical Association

SUMMARY IN ENGLISH

Recent studies indicate that almost half of the 1st generation asylum seekers in Denmark have been subjected to torture. At DIGNITY - Danish Institute Against Torture in Copenhagen, tortured refugees are offered clinical assessment and multidisciplinary rehabilitation for long-term sequelae, among them pain and mobility problems. One frequent form of torture is falanga which is the term for systematic repeated application of blunt trauma to the foot soles.

The overall purpose of this thesis was to analyse the mechanisms of chronic pain and self-reported disability caused by generalized torture and falanga torture.

The most important findings concern (1) the clinical presentation of chronic pain in torture victims, (2) the pain-related disability and (3) the underlying pain mechanisms based on quantitative sensory testing (QST) results of the sensory dysfunction in their battered feet.

Paper 1, explores clinical findings in 11 men with chronic pain after falanga torture as compared with 11 controls. The torture victims had pain in their feet and lower legs and a compensated walking pattern, usually with severe pain during walking. Reduced light touch and thermal sensation, tactile dysesthesia, allodynia, and tenderness on palpation were common findings. Clinical signs of nerve injury in the feet were found indicating two neuropathic pain mechanisms, one dominated by a peripheral pain generator and the other indicating central sensitization, but a nociceptive contribution cannot be excluded. It was reasonable to assume that these changes were due to the falanga exposure.

Paper 2, describes activity limitations in tortured refugees referred for rehabilitation, particularly the impact of neuropathic pain resulting from falanga. Physiotherapists assessed 103 consecutive torture victims with a long history of sequelae after torture, among them pain and mobility problems. All had been subjected to various forms of physical and psychological torture and 71 victims had also suffered falanga. Main outcome measure was the Disability Rating Index (DRI; 12 items) to assess self-reported capacity to carry out daily activities. All torture victims perceived clear activity limitations according to the DRI. The falanga victims' feet were categorized according to the type of foot pain: stimulus-independent pain; stimulus-evoked pain; no pain. The two groups with foot pain displayed sensory dysfunction and suffered more extensive

activity limitations. After correction for confounding factors, these two groups reported significantly more activity limitations in 7 out of 12 DRI items than those who were not exposed to falanga.

In Paper 3, a new group of torture victims from the Middle East was examined. The objective was to clarify underlying pain mechanisms by quantifying sensory impairments in the feet of torture victims who had experienced both generalized torture and those who in addition had been exposed to falanga. Data from these two groups was compared with data from a separately recruited group of 14 ethnically matched controls. We employed quantitative sensory testing (QST) including thresholds for touch, cold, warmth, cold-pain, heat-pain, deep mechanical pressure pain and wind-up to cutaneous noxious stimuli in the foot soles. The investigators were blinded to whether the 32 male torture victims from the Middle East had (n=15), or had not (n=17) been exposed to falanga. Almost all falanga victims had moderate or severe pain in their feet and in twice as large an area of their foot soles as other torture victims. A comparison with normal data indicated that both tortured groups had hypoesthesia for all cutaneous sensory fibre groups except those transmitting cold and heat pain, in addition to deep mechano-nociceptive hyperalgesia. The sensory disturbances in relation to the control group are compatible with central sensitization and de-sensitization, pointing to a core role of central mechanisms. Peripheral sensitization may also play a role.

In Paper 4, the same group as in paper 3 was analysed. The purpose was to extend the group analysis into individual sensory profiles of victims' feet and to explore possible relations between external violence (torture), reported pain, sensory symptoms and QST data to help clarify the underlying mechanisms. A normality criterion, from our ethnically matched control group data, was set as the mean +/− 1.28SD, thus including 80% of all values. QST data were transformed into three categories in relation to our normality range; hypoesthesia, normoesthesia or hyperesthesia/hyperalgesia. Most patients, irrespective of having been exposed to falanga or not, reported severe pain when walking, often associated with hyperalgesia to deep mechanical pressure. Hypoesthesia to mechanical stimuli co-occurred with numbness, burning and with deep mechanical hyperalgesia more often than not, but otherwise, a hypoesthesia to cutaneous sensory modalities did not co-occur systematically to falanga, pain or sensory symptoms. We interpret these findings as a sign of changes in central sensory processing as the unifying pathological mechanism of chronic pain in these persons.

SUMMARY IN DANISH (Dansk resumé)

De nyeste undersøgelser viser, at næsten halvdelen af 1st generations asyl ansøgere i Danmark har været udsat for tortur. I DIGNITY – Dansk Institut Mod Tortur i København, får torturerede flygtninge med langtidsfølger, så som smerter og funktionsevnenedsættelse, mulighed for at blive undersøgt og gennemgå et tværfagligt rehabiliteringsforløb. En hyppig torturmetode er falanga, som er betegnelsen for systematisk gentagne slag mod fodsålerne med et stumpt instrument.
Det overordnede formål med denne afhandling er at analysere mekanismerne for kroniske smerter og selv-rapporteret funktionsevnenedsættelse forårsaget af generaliseret tortur og falanga tortur.

De vigtigste fund beror på 1) præsentation af kliniske undersøgelser af kroniske smerter hos torturofre 2) de bagvedliggende smertemekanismer, baseret på kvantitative sensoriske tests (QST) studier af sensorisk dysfunktion i torturofrenes fødder og 3) den smerte relaterede funktionsevnenedsættelse.

Artikel 1 udforsker kliniske fund hos 11 mænd fra Mellemøsten med kroniske smerter efter falanga tortur sammenlignet med 11 etnisk matchede kontrolpersoner. Torturofrerne havde smerter i deres fødder og underben og et kompenseret gang mønster, ofte med stærke smerter ved gang. Almindelige fund var nedsat reaktion ved let berøring og nedsat termisk følelse, taktil dysæstesi, allodyni, og ømhed ved palpation. Der var tydelige kliniske tegn på nerveskade i fødderne, hvilket indikerede to neuropatiske smertemekanismer, den ene domineret af en perifer smerte generator og den anden af en overfølsomhed i centralnervesystemet. En nociceptiv komponent kan dog ikke udelukkes. Det er rimeligt at antage at disse ændringer skyldes en eksponering for falanga.

Artikel 2 beskriver aktivitets begrænsninger hos torturofre henvist til rehabilitering, især betydningen af neuropatisk smerte som følge af falanga. Fysioterapeuter undersøgte løbende 103 henviste torturofre med langtidsfølger, blandt andet smerte- og mobilitetsproblemer. Alle havde været udsat for forskellige former for fysiske og psykiske tortur metoder og 71 af dem havde også været udsat for falanga. Det vigtigste måleinstrument var the Disability Rating Index (DRI: 12 aktiviteter) til måling af selv-rapporteret evne til at udføre daglige aktiviteter. Alle torturofre havde en tydelig

oplevelse af aktivitetsbegrænsninger i henhold til DRI. Falanga ofrenes fødder blev herefter kategoriseret i henhold til type af fodsmerte: 1) stimulus-uafhængig smerte 2) stimulus-afhængig smerte 3) ingen smerte. De to falanga grupper med fod smerter fremviste sensorisk dysfunktion og havde flere aktivitetsbegrænsninger. Efter at have korrigeret for confounding factors, rapporterede disse to grupper signifikant flere aktivitets begrænsninger i 7 ud af 12 DRI aktiviteter end gruppen, der ikke havde været udsat for falanga.

I artikel 3 undersøges en ny gruppe mænd (n=32) fra Mellemøsten, som havde været udsat for tortur. Formålet var, ved kvantificering af sensoriske funktionsnedsættelser i fødderne, at tydeliggøre de bagvedliggende smertemekanismer hos henholdsvis de torturofre, som havde fået generaliseret tortur og de som yderligere havde fået falanga. Data fra disse to grupper blev sammenlignet med data fra en separat rekrutteret gruppe af 14 raske etnisk matchede kontrol personer. Der blev anvendt kvantititative sensoriske tests (QST) med detektionstærskler for berøring, kulde, varme, kulde-smerte, varme-smerte, dybe mekaniske tryk og summation med kutane noxious stimuli (responset tiltager ved gentagne stimuli) i fodsålerne. Undersøgelsen var blindet, idet man ikke vidste om de 32 mandlige torturofre fra Mellemøsten, havde (n=15), eller ikke havde (n=17) været udsat for falanga. Næsten alle falanga ofre havde moderate eller stærke smerter i fødderne og i dobbelt så stort et område af fodsålerne sammenlignet med torturofre uden falanga. En sammenligning med normale data fra kontrolgruppen indikerer, at begge torturgrupper havde hypoæstesi (nedsat følelse ved stimulation) i alle kutane sensoriske fibre, undtagen de der transmitterer kulde- og varmesmerte. Endvidere havde de dyb mekano-nociceptiv hyperalgesi (overfølsomhed for nociceptive stimuli). En sammenligning af QST data fra gruppen, der havde været udsat for generaliseret tortur med data fra gruppen som yderligere havde fået falanga, viste ingen forskel på gruppeniveau. De sensoriske forstyrrelser hos de to torturgrupper sammenlignet med den raske kontrolgruppe tyder på central sensibilisering og de-sensibilisering og indikerer, at centrale mekanismer kan have stor betydning. Perifer sensibilisering kan dog også spille en rolle.

I artikel 4 bliver samme gruppe som i artikel 3 analyseret. Her var formålet at udvide gruppe analysen med individuelle sensoriske profiler af fødderne og at udforske mulige relationer mellem ydre vold (tortur), rapporteret smerte, sensoriske symptomer og QST

data for derved at tydeliggøre de bagvedliggende smertemekanismer. Normalitets kriteriet, for den etnisk matchede kontrolgruppe's data, var sat til middelværdi +/- 1.28SD, hvilket inkluderede 80% af alle værdier. QST data blev transformeret til tre kategorier i relation til normalitets intervallet: hypoesthesia (nedsat følelse ved stimulation), normoesthesia (normal følesans) og hyperesthesia/hyperalgesia (overfølsomhed for stimulation af alle slags/overfølsomhed for nociceptive stimuli). De fleste torturofre, uanset om de havde været udsat for falanga eller ej, rapporterede stærke smerter ved gang, ofte forbundet med hyperalgesi ved dyb mekanisk tryk. Hypoæstesi ved mekaniske stimuli optrådte samtidig med følelsesløshed, en brændende følelse, og mekanisk hyperalgesi. Det bør fremhæves, at hypoæstesi ved kutane sensoriske modaliteter ikke ses systematisk i forhold til falanga, smerter eller ved sensoriske symptomer. Sammenfattende tyder disse fund imidlertid på patologiske mekanismer i de sensoriske processer i centralnervesystemet hos denne gruppe af torturofre.

LIST OF PUBLICATIONS

This thesis is based on the following papers:

Paper 1

Prip K, Persson AL. Clinical findings in men with chronic pain after falanga torture. Clinical Journal of Pain 2008; 24(2):135-141.

Paper 2

Prip K, Persson AL, Sjölund BH. Self-reported activity in torture victims and the impact of neuropathic pain from falanga – a cross-sectional study. Disability & Rehabilitation 2011;33(7): 569-579.

Paper 3

Prip K, Persson AL, Sjölund BH. Sensory functions in the foot soles in victims of generalized torture, in victims also beaten under the feet (falanga) and in healthy controls. A blinded study using quantitative sensory testing. BMC International Health and Human Rights 2012;12:39: p. 1-12.

Paper 4

Prip K, Persson AL, Sjölund BH. Pain when walking: individual sensory profiles in the foot soles of torture victims - a controlled study using quantitative sensory testing. BMC International Health and Human Rights 2012;12:40: p. 1-10.

INTRODUCTION

Torture is commonly occurring in 112 out of 159 countries of the world's countries (7). Recent studies indicate that almost half of 1st generation asylum seekers in Denmark have been subjected to torture (8). However, torture often goes undetected (9) for years in spite of hospital visits for both chronic pain and mental problems. At DIGNITY - Danish Institute Against Torture, (10) formerly Rehabilitation and Research Centre for Torture Victims in Copenhagen, more than 100 tortured refugees with residence permits are treated annually, after referral from their general practitioners (11). In recent years the majority of patients referred have come from the Middle East and their traumatic experiences after for instance Saddam Hussein's regime in Iraq are massive, both as regards torture, repression and persecution.

The patients' multiple problems interact profoundly with each other; thus not reducible to a single central diagnosis or domain of suffering. Consequently the psychological, somatic and socio-economic issues are all important. DIGNITY's rehabilitation department is specialized in rehabilitating traumatized persons who have been exposed to torture, ill treatment and severely traumatizing experiences such as war and organized violence. An interdisciplinary and bio-psycho-social rehabilitation approach has been adopted as a guiding principle. DIGNITY is also recognized by the Danish National Board of Health as a national centre specializing in treatment of severely traumatized refugees. This group of well-defined patients our clinic makes systematic studies of torture victims' problems possible.

One frequently used torture method in the Middle East countries is falanga, systematic repeated application of blunt trauma to the soles of the feet (12). Falanga results in severe chronic pain in the feet, often giving lifelong walking difficulties and thereby a severe disability. For this thesis I chose to explore pain and pain mechanisms in the feet of tortured men from the Middle East in order to make the study groups as homogeneous as possible.

Since my clinical experience had led me to suspect that foot pain after falanga in torture victims had a peripheral origin from neural tissue damage caused by the beatings, I started by making clinical examinations hereof in studies 1 and 2.

When I had examined patients in the clinic, it was obvious to me, that most patients had great difficulties to carry out even small and easy every-day activities. This led to that I also investigated the possible relations between foot pain and self-reported activity limitations in paper 2. Furthermore, I wanted to more objectively try to clarify the underlying pain mechanisms in the feet of torture victims by quantifying their sensory impairments using quantitative sensory testing (QST) in papers 3 and 4.

This thesis thus aimed to provide new knowledge of both scientific and clinical relevance about chronic pain in torture victims, about the pain-related disability after torture and about the underlying pain mechanisms based on the QST results of sensory dysfunction in victims' feet.

BACKGROUND

The concept of pain and definitions

Pain is elicited by tissue-damaging (noxious) or potentially tissue-damaging stimuli, mediated by nociceptive nerve fibres that are specialized peripheral afferent fibres that react to tissue damaging stimuli. Nociception is thus the detection of such stimuli. The perception of pain has many dimensions including cognitive and affective components in addition to physiological/biological aspects (13, 14). In addition, pain is a personal experience, something we feel and communicate. The current definition of pain accepted by the International Association for the Study of Pain (IASP) reads *"An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage"* (15).

An individual's ability to experience acute pain is a survival mechanism that protects the body against threatening and actual tissue damage. It necessitates behavioural responses to keep such damage to a minimum. Acute pain is a normal common sensation, and a reaction to suddenly appearing tissue threatening damage. Chronic pain, on the contrary, is an abnormal condition (16) and a sensory dysfunction (17) where the pain continues even when there is no obvious noxious threat. Chronic pain may be considered as a continuing sensory abnormality which happens as a result of an ongoing peripheral pathology, such as chronic inflammation or autonomous reactions, even independent of the cause that started it. Alternatively, changes in the central nervous system may have become the pathology, and the pain is maladaptive as it does not offer any survival advantage (18).

Traditionally the distinction between acute and chronic pain relies upon the arbitrary interval of time from the onset (19). The IASP (15) provides a widely used definition of chronic pain that takes into account duration and "appropriateness" and defines chronic pain as *"pain without apparent biological value that has persisted beyond the normal tissue healing time (usually taken to be 3 months)"*. In the context of chronic widespread pain the following criteria, according the American College of Rheumatology (20), must be present for at least 3 months: pain in the left side of the body, pain in the right side of the body, pain above the waist and pain below the waist. In addition, axial skeletal pain (that is, pain in cervical spine, anterior chest, thoracic spine, or low back) must be present.

Chronic pain is a common symptom in western societies with a median point prevalence of 15-19 % of the adult population (21, 22). Furthermore it has been reported that chronic pain experienced from the musculoskeletal system is common in a northern European population (23). The absence of detectable illness or disease and the importance of psychosocial factors are characteristics of many of these chronic pain conditions (24-28).

Pain mechanisms

Nociceptors are nerve receptors that are categorized after their afferent fibres into unmyelinated C-fibres (group IV fibres) or thin myelinated Aδ-fibres (group III fibres). They respond to potentially tissue damaging stimuli (29). After a peripheral nerve lesion they may become abnormally sensitive and develop pathological spontaneous activity or react to mechanical or thermal stimuli (30). The larger myelinated Aβ-nerve fibres mediate stimuli to touch.

Nociceptive pain is elicited by noxious stimuli (mechanical, thermal or chemical) from peripheral nociceptors when tissue damage or potential tissue-damage occurs. Muscle and joint pain are common examples.

Peripheral sensitization may occur after inflammatory processes where healing (reparatory) mechanisms of neural tissues in response to injury, and the reactions of adjacent tissues, may lead to a state of hyper-excitability in primary afferent nociceptors. This type of sensitization is influenced by the activation of the immediate environment where chemical inflammatory substances play a vital role. The nociceptors may react with spontaneous neuronal activity and increased sensibility to touch, pressure, cold and heat because of lowered sensory thresholds. The Aδ-nociceptors normally have a high threshold but are easily sensitized after tissue damage (18, 31).

Neuropathic pain is always associated with nerve injury. The criteria for neuropathic pain are: a) history indicating injury or disturbance of the nervous system; b) projected pain, that is in the area innervated by the injured nerve and; c) disturbed sensory function in the painful area. If a mixed peripheral nerve with a cutaneous branch or a central somatosensory pathway is involved, there is almost always an area of abnormal

sensation and the patient's maximum pain is coextensive with or within an area of sensory deficit. The sensory deficit is usually related to noxious and thermal stimuli, indicating damage to small diameter afferent fibres. The key characteristics for neuropathic pain are well-described by several authors (30, 32, 33).

Central sensitization occurs when central neurons, innervated by nociceptive fibres, undergo dramatic functional changes, including a state of hyper-excitability. These sensitization phenomena normally disappear as the tissue heals and the inflammation subsides. However, when primary afferent function is altered in a permanent way by injury or disease of the nervous system, these processes persist (34, 35). In neuropathic pain, central sensitization is a prominent feature, manifested as hyperalgesia (an increased pain reaction to a noxious stimulus) and/or allodynia (pain provoked by a stimulus that does not normally evoke pain). Typical disturbances of sensory function are also increased or decreased sensitivity as well as unpleasant, abnormal sensations.

Clinically, neuropathic pain symptoms are characterized by the lack of apparent signs of tissue damage and often by a delayed development (36, 37). It varies in intensity, but the pain may increase upon repeated stimulation (so called wind-up) (38) and there is sometimes an after-sensation of persistent pain lasting long after the stimulation has ceased. In addition, there may be signs of hyperactivity of the sympathetic nervous system, for example increased sweating, change of skin temperature, and trophic or colour changes of the skin (39).

Furthermore, a distinction in neuropathic pain should be made between spontaneous pain and pain evoked by a stimulus. Spontaneous pain (stimulus-independent pain) can be described as constant or intermittent (or paroxysmal) and most patients describe having both (e.g. constant 'burning' pain plus intermittent pain experienced as 'shooting' or 'electric shock-like'). In addition, spontaneous paresthesia and dysesthesia are distinct abnormal sensations, sometimes including sensations such as that of crawling, numbness, itching and tingling. Stimulus-evoked pain may be elicited by everyday environmental stimuli such as the gentle touch and pressure of clothing, wind, hot or cold temperature and body movements such as daily activities, walking or driving a car (37).

Recently, the definition of neuropathic pain has been revised by the Task Force on Taxonomy of the International Association for the Study of Pain: *"pain caused by a lesion or disease of the somatosensory nervous system* (15, 40), and a grading system of "definite", "probable", and "possible" neuropathic pain has also been introduced (33). Hence, the term neuropathic pain is a clinical description, and not a diagnosis, which demands a demonstrable lesion or a disease that satisfies and/or is in accordance with established neurological diagnostic criteria.

It should be noted that the presence of symptoms or signs alone does not justify the use of the term neuropathic. Where possible, neuropathic pain should be divided into peripheral or central neuropathic pain based on the anatomic location of the lesion or disease. The characterization of pain as neuropathic or not depends on the application of the usual, careful neurologic diagnostic process. In this respect, the presence of a single positive or negative finding on examination is often not diagnostic.

Assessment of pain and sensory function

Measurement of pain relies on recording the patient's report because pain is a personal experience and there are no objective ways to measure pain directly. There are some instruments and methods for assessing pain and tenderness semi-objectively. The most common is the visual analogue scale (VAS; (41)). Furthermore, pain drawings (42) and quantitative sensory testing (QST; (43)) are used as part of the assessment for patients in chronic pain.

Quantitative sensory testing (QST) was introduced in pain research by Lindblom et al (44, 45) to quantify sensory disturbances in particular pain conditions. The rationale behind QST is to test for patterns of sensory loss (small and large nerve fibre function) or sensory gain (hyperalgesia, allodynia, hyperpathia) and to assess cutaneous and deep mechanical nociception (46, 47). It is a semi-objective psycho-physical method demanding full attention and collaboration from the patient.

The concept of disability

Disability is an umbrella term, covering impairments, activity limitations, and participation restrictions and is thus not just a health problem. United Nations Convention on the Rights of Persons with Disabilities (CRPD; (48)) acknowledges that

disability is '*an evolving concept' but also stresses that 'disability results from the interaction between persons with impairments and attitudinal and environmental barriers that hinder their full and effective participation in society on an equal basis with others*'.

The phenomenon is complex and reflects the interaction between functions of a person's body and functions of the society in which he or she lives (49). Disability has therefore great impact on an individual's health functioning in daily life. A method to classify health and health related domains, is to use the 'International Classification of Functioning, disability and health', more commonly known as the ICF (50). It provides a standard language and a framework for describing an individual's health condition. In ICF, the term functioning refers to all body functions, activities and participation, and denotes the positive aspects of the interaction between an individual (with a certain level of health) and that individual's contextual and personal factors. The health and health related domains are classified from the individual perspective and from the societal perspective using two lists: one list for body functions and structures, and one list for the level of activity and participation. Since an individual's functioning and disability is related to his/her chosen context, ICF also includes a list of environmental factors that influences the health condition (51, 52).

Regarding the health condition of tortured refugees, family support and relationships (acquaintances, peers, colleagues, neighbours) in the near community context all have an influence. According to the ICF attitudes, values, norms, factual beliefs and religious beliefs in the environment all influence the individual's behaviour and social life, and originate from people external to the person whose situation is being described. Thus, they are not those of the person themselves (50).

Persons with disabilities are diverse and heterogeneous. Some stereotypical views of disability emphasize wheelchair users and a few other 'classic' groups such as blind and deaf people. Disability encompasses for instance the soldier who loses his leg to a landmine or more invisible health conditions such as mental dysfunction. Generalization about 'disability' or 'people with disabilities' can be misleading. Personal factors such as gender, age, socioeconomic status, sexuality, ethnicity, and cultural heritage differ in

disabled people. Each has his or her personal preferences and responses to disability (49).

In the ICF, the term 'functioning' is an umbrella term for body function, body structures, activities and participation. In contrast, 'disability' is an umbrella term for impairments, activity limitations and participation restrictions that denotes the negative aspects of the interaction between the individual and the individual's contextual factors (environmental and personal factors). These factors interact with the individual's health condition and determine the level and extent of the individual's functioning and disability.

A pain related disability may arise in a patient with the sensory impairment chronic pain living in a context that can include physical obstacles, stress, degrading attitudes, and lack of societal support, that all limit the patient's level of activity and participation (53). Disability may also include more complex aspects such as avoidance behaviours (54), leading to the detrimental consequences of long-term inactivity.

There are few reports of disability after torture (55-57). However, among tortured prisoners of war, there were more long-term symptoms and diagnoses than in controls. Low physical function and an impact on quality of life were also reported (58-60). In a population of Bosnian refugees who had recently fled from the war in Bosnia and Herzegovina Mollica et al (55) found that psychiatric comorbidity was associated with disability independent of the effects of age, trauma, and health status. Former Bosnian refugees who stayed in the region continued to exhibit psychiatric disorders and disability three years after the initial assessment (56). Hunt et al (57) investigated late life disability in former prisoners of war. They found that conditions of captivity and health concerns or emotional distress during captivity may contribute to long-term adverse health outcomes as measured by late life disabilities. However, tortured prisoners of war showed more long term symptoms and diagnoses than the controls. The high levels of disability from torture in the few existing reports (55, 61, 62) may be due not only to the victims' high perceived pain intensity and mental state but also to their previous pain experiences of torture and fear that the pain will increase permanently if they are physically active, leading to fear avoidance reactions (cf. (54, 63)). Additionally, the falanga victims who have difficulties in walking and use a

compensatory gait pattern (64, 65) show signs of functional limitations and they may be considered disabled rather than ill (11).

Chronic pain implies not only the perception of pain, but also suffering, namely a negative affective response in higher nervous centres generated by pain, and having influence on the disability. Other negative events that torture victims often have experienced such as disappearance or loss of loved ones also have influence (49). In addition to suffering some individuals also develop pain behaviours, which are all forms of behaviour presented by the individual to express their pain and that are commonly understood by those nearby (13, 66). These include both verbal and non-verbal behaviours, e.g. simple facial and verbal expressions, such as grimaces or frowns, holding, guarding, or touching body parts affected by pain. The person beliefs that certain activities, identified as "dangerous" or "threatening", will induce further pain and suffering, and this often results in hyper-vigilance and catastrophizing thoughts regarding bodily sensations and avoidance behaviour (17, 53, 54, 63, 67-69)

Torture

Torture is often used as a political instrument to break down an individual's personality. Often, methods that do not create permanent, visible damage are used in order to make it difficult to document torture (12, 70).

The United Nations' (UN) 'Convention against torture and other cruel, inhuman or degrading treatment or punishment' (71) is ratified by 147 states of the current 192 member states of the UN. However, according to Amnesty International Annual report 'The state of the world's human rights', 101 countries of the world used torture or other ill-treatment in 2011 (7).

In article 1 of the CAT (71) torture is defined as: "…*any act by which severe pain or suffering, whether physical or mental is intentionally inflicted on a person for such purpose as obtaining from him or a third person information or a confession, punishing him for an act he or a third person has committed, or is suspected of having committed, or intimidating or coercing him or a third person, or for any reason based on discrimination of any kind, when such pain or suffering is inflicted by, or at the*

instigation of, or with the consent or acquiescence of, a public official or other person acting in an official capacity……".

Prevalence of torture

Although there are no global estimates, several studies report the prevalence of torture within specific countries or territories, for example in countries that are or have been at war or in countries where torture is known to occur. Wang et al (72) conducted a survey in Kosovo in 2008 (after the war) and found that 493 (6.8%) individuals from (their sample of) 341 families reported torture experiences in northern Kosovo. Cardozo et al (73) performed a national population-based mental health survey in Afghanistan, a territory which has been under an on-going conflict for more than 2 decades. They found that 10% of a non-disabled population and 10% of a disabled population had been tortured and 31% and 32%, respectively, had been beaten by members of the Taliban or by other groups. De Jong et al (74) undertook household surveys in two districts of the Indian part of Kashmir where there is an on-going conflict. He found that 66.9% had witnessed torture, 16.9% had been tortured and 24.9% had been sexually violated. In Bangladesh, a country that is at peace but where torture still occurs, Wang et al (75) screened 1,101 households (with a population of 4,870) and found that 31% reported torture or other cruel, inhuman or degrading treatment or punishment.

Furthermore, specific ethnic groups of refugees have been surveyed. The UN's High Commissioner for Refugees (76) conducted a survey on 754 Iraqi refugees in Syria. Among those interviewed, 31% suffered from physical disabilities, 17% from mental disabilities and 25% had other mobility problems. The respondents were also asked about torture. Of the 120 (16%) surveyed persons who reported having been tortured the majority reported that they had been beaten with fists or other objects (61% and 58%, respectively). Electric shocks, objects placed under their nails, burns, rape and seeing family members being raped were also reported.

In western countries torture usually does not occur, but great numbers of refugees have obtained asylum there, and among these are many torture victims. Recent studies indicate that almost half of the 1st generation asylum seekers in Denmark have been subjected to torture (8, 77). In the United Kingdom, Frank et al (9) found that more than half of those seeking health care for pain conditions and born in a foreign country had

been subjected to torture. Torture often goes undetected (9) for years in spite of hospital visits for both chronic pain and mental problems. Williams et al (78) estimated that around 30% of asylum applicants to the UK had suffered torture. Tortured refugees, with all their physical, psychological and social problems, may thus turn up as patients for health care all over the world. Thus, persons with torture sequelae are common in countries other than the ones identified by Amnesty International, and also in countries of exile.

Regardless of numerous international declarations and conventions that prohibit ill and degrading treatment and torture, torture continues to be a critical problem. After 9/11, the fight against terrorism has increased and torture and ill-treatment have become accepted even in countries that have signed declarations and conventions to prevent torture.

Torture methods

Torture methods are often described in terms of psychological or physical methods (12, 79, 80). However, it has been assumed that all methods have both psychological and physical dimensions and affect the mind as well as the body, as recently demonstrated by Basoglu and his group (70). Some frequently used psychological methods are mock executions, being forced to watch family and friends being tortured, sexual abuse, sleep deprivation and solitary confinement. The most frequent physical methods reported are unsystematic beatings and general abuse of the entire body (often described as generalized torture) with different instruments, or being tied up for long periods in contorted, painful body positions including stress and coercion techniques (12, 65, 81, 82).

Falanga (also called falaka and bastionade in Arabic and Spanish language respectively) is the term used to describe systematic repeated applications of blunt trauma to the soles of the feet – an ancient physical torture method which is widely practiced especially in the Middle East countries, but has now spread to other continents. The torture victim is beaten with wooden implements, iron bars or other instruments and is often tied up during the torture, placed lying on the floor with legs suspended or lying on a table, sitting in a chair or suspended by the legs (12). Some victims have their feet placed in

cold water after the torture, or they may be forced to walk around in between or after the blows, to increase the impact of the mistreatment (6, 83).

Long-term consequences of torture

Tortured refugees referred to our rehabilitation centre in Copenhagen exhibit multiple problems like chronic pain, post-traumatic stress disorder (PTSD), depression, anxiety, poverty, isolation, inactivity, unemployment and various other social distress factors (11, 81, 82, 84, 85). The victims may have suffered many traumatic events, and isolating a single traumatic event as the cause of the current symptoms is hardly ever appropriate.

PTSD is one of the most frequently reported mental health conditions after torture (11, 35, 84, 86-88). The diagnosis includes symptoms such as anxiety, intrusive recollections, avoidant/numbing symptoms and hyper-arousal symptoms. The mental diagnosis PTSD has, however, been criticized for being too narrowly focused on psychological symptoms and thereby not adequately reflecting the overall situation of persons suffering from intense symptoms after extreme traumas. In order to grasp the complexity of the condition a new diagnostic category has been brought forward, known as Disorder after Extreme Stress not Otherwise Specified (DESNOS; (89, 90)), the diagnosis for which requires alterations in 6 areas of functioning: 1) regulation of affect and impulse; 2) attention or consciousness; 3) self-perception; 4) relations with others; 5) somatization; and 6) systems of meaning, without specifying the degree of change in functioning. The long term sequeale of torture have been described as being dependent on the magnitude as well as the torture method (55). Adding to the overall impaired health condition, emotional distress seems to be chronic for the majority of a sample of refugee victims in Denmark (85).

Many of the symptoms and problems presented by tortured refugees are results not only of repeated traumas but also of long-lasting hardship, such as the loss of family members and friends, poverty, migration and the exile situation with its lack of social networks, almost a defining feature of the western world.

Among torture victims, almost all persons suffer from chronic pain. Usually they present widespread pain and high pain intensity (81, 82). However, it has recently been

demonstrated that different torture methods leave chronic pain conditions in different body regions (78, 81, 82, 85, 91). The most frequently reported regional pain conditions are headache and pain in the back, lower limbs, shoulders and upper limbs. Thomsen et al (92) found a high prevalence of neuropathy with pain in patients exposed to beating under the feet (81%) and partial brachial plexus injury in 64% following suspension by the arms.

Chronic pain implies not only the perception of pain, but also suffering, that is, a negative affective response to pain generated in higher nervous centres by pain and other negative events such as loss of loved ones, stress, anxiety, and so on. In addition, some individuals also develop pain behaviours, which are all forms of behaviour generated by the individual that are commonly understood to reflect their pain (13, 66). Beliefs that certain activities, identified as 'dangerous' or 'threatening', will induce further pain and suffering, probably leading to hyper-vigilance and catastrophizing thinking regarding bodily sensations and avoidance behaviour (17, 53, 54, 63, 67-69).

PTSD subjects have been reported to have 5- to 8-fold higher rates of chronic pain than the general population, with somatization as one possible mechanism (22, 93). Defrin et al found pain in PTSD subjects to be twice as common as in subjects with anxiety disorders (94). Furthermore, this pain was significantly more intense, widespread and complex than in subjects with anxiety disorders. The somatosensory tests performed by the same authors (94) revealed a paradoxical profile, in that supra threshold noxious heat and mechanical stimuli produced more intense ratings but, unexpectedly, the PTSD subjects were less sensitive to threshold stimuli. This combination of hyper-responsiveness to supra-threshold noxious stimuli and hyposensitivity to threshold stimuli is contrary to what chronic pain subjects usually exhibit, namely hyper-responsiveness with hyper-sensitivity to pain. This paradoxical pain profile may be explained by an altered sensory processing of pain signals, producing a state of hyperpathia, a syndrome characterized by an abnormally painful reaction to a stimulus, especially a repetitive stimulus, but increased pain thresholds (15).

Consequences of falanga torture

The immediate effect of falanga torture is acute pain, bleeding and oedema in the soft tissues of the feet. The swelling may progress up the lower legs (65, 95). In many cases

the condition develops into chronic pain and may occur as a result of an ongoing peripheral pathological process, but the pain can also be due to pathological changes in the nervous system (33, 37, 39, 96).

In clinical practice, often many years after falanga, the victims describe their chronic pain as a deep, dull cramping pain in the feet, which intensifies with weight bearing and muscle activity and sometimes with pain spreading up the lower legs (65, 95). Other pain symptoms are a superficial burning or stinging pain in the soles which appears spontaneously or is stimulus-evoked, and often accompanied by sensory disturbances such as tingling, pins and needles and numbness. Frequent complaints are feelings of tiredness and heaviness in the lower legs and thighs, pain in the knee and ankle joints, muscle cramps and lumbar pain when walking and standing. Often the feet are perceived as alternating between being very hot or cold and can have a tendency of increased sweating, suggesting autonomic hyperactivity. When lying down at night the victims report burning sensations in the feet.

Some authors (64) have suggested that pain in the feet after falanga resembles the symptoms of chronic compartment syndrome in the legs. The fascia plantaris of the foot has been described as another possible source for pain after falanga. The fascia has been described as thickened with an uneven surface which may be due to formation of scar tissue (4). On palpation, the fascia is sore and painful along its whole length (97). A previous claim that specific changes can be detected (‘smashed heel pads’) has not been confirmed in an Magnetic Resonance Imaging study by Savnik et al (4), who found only an unspecific thickening of the aponeurosis plantaris in feet of the falanga victims. A recent ultrasound study of the microcirculation in the planta did not find any signs of chronic compartment syndrome or other structural differences between falanga victims and controls (5).

Impaired walking is one disability in falanga victims and deviation from a normal gait pattern is frequent. They often develop a compensatory gait pattern involving a short stride, avoidance of heel strike, phase off over the lateral border of the foot and abnormal push-off of the first toe. Furthermore, they are usually only able to walk short distances (64, 65).

Rehabilitation

The WHO's current definition of rehabilitation is: *"Rehabilitation of people with disabilities is a process aimed at enabling them to reach and maintain their optimal physical, sensory, intellectual, psychological and social functional levels. In this way rehabilitation provides disabled people with the tools they need to attain independence and self-determination"* (50). Thus, the end goal of rehabilitation is to facilitate personal empowerment of the disabled person. Presently, there is consensus and evidence that rehabilitation is best accomplished by interdisciplinary teams, working together with agreed aims, agreement and understanding on how best to achieve the aims, through assessments, planning and reaching the rehabilitation goals in cooperation with the patient (98).

When assessing a disabled person to evaluate whether rehabilitation is necessary, it may be much more meaningful and true to describe a traumatized person using the ICF approach, rather than speculating whether a particular organ system is affected with an uncertain aetiology and adding symptom diagnoses or an empirical psychological categorization (11). The indications for rehabilitation may be adequately derived from the ICF approach, assessing the impairments, the activity limitations and participation restrictions in the context at hand and focusing rehabilitation to those who are distinctly limited or restricted in their life situation.

AIMS

The overall purpose of this thesis was to analyse the mechanisms of chronic pain and the self-reported disability caused by generalized torture and falanga torture.

Four studies were carried out in three different populations of torture victims with the following aims:

Paper 1: to explore clinical, structural and sensory findings in persons with chronic pain after falanga torture as compared to matched controls, and to describe the pain types present.

Paper 2: to examine self-reported limitations of daily activities in a group of torture victims with long term sequelae including chronic pain; to describe sensory disturbances and clinical findings in the feet of torture victims exposed to falanga; and to analyse a possible relation between foot pain in the group exposed to falanga and self- reported activity limitations.

Paper 3: to help clarifying the underlying pain mechanisms by extending the analysis into quantifying sensory impairments in the feet of torture victims who had experienced both generalized torture and those who had been exposed to falanga in addition; to compare the data between these two groups and to a separately recruited group of healthy men with no experience of torture from the Middle East.

Paper 4: to extend the group analysis of the QST data from paper 3 into individual sensory profiles of victims' feet to explore possible relations between external violence (torture), reported pain, sensory symptoms and QST data to help clarify the underlying pain mechanisms.

METHODS

Participants

Patients and methods are described in detail in the separate papers 1-4. The patients who participated in the four studies (Table 1) were traumatised and tortured refugees, who had been granted asylum in Denmark. They were referred by their general practitioner to DIGNITY – Danish Institute Against Torture in Copenhagen, Denmark for interdisciplinary treatment because of extensive psychological, physical and social needs. In addition, healthy controls from the Middle East community in Copenhagen were used in three of the studies.

Table 1. The total numbers, mean age, gender and country of origin of the participants included in the four studies

Paper	Participants	Mean age (range) years	Country of origin
1	Torture victims n=11 men	43 (34-54)	Iraq n=8, Iran n=3
	Healthy controls n=11 men	40 (30-52)	Iraq n=9, Syria n=1, Tunisia n=1
2	Torture victims n=87 men	40 (19-59)	Iraq n=48, Iran n=13, Afghanistan n=7, Palestine n=4, Turkey n=3, India n=2, Kosovo=2, Azerbaijan n=1, Chile n=1, Colombia n=1, Lebanon n=1, Pakistan n=1, Somalia n=1, Sudan n=1, Syria n=1
	Torture victims n=16 women	41 (30-55)	Iraq n=5, Iran n=3, Albania n=1, Burundi n=1, Lebanon n=1, Pakistan n=1, Palestine n=1, Rwanda n=1, Sri Lanka n=1, Uruguay n=1
3 and 4	Torture victims n= 32 men	45 (34-63)	Iraq n=23, Lebanon n=3, Afghanistan n=2, Iran n=2, Palestine n=1, Syria n=1
3 and 4	Healthy controls n=14	37 (21-55)	Iraq n=10, Afghanistan n=2, Lebanon n=1, Palestine n=1

All patients suffered from long term sequelae from various types of torture that they had been subjected to several years earlier in their homeland. The time elapsed since being exposed to torture was between 5 and 30 years. Papers 1, 2 and 3/4 included three separate populations. The total number of participants in this thesis was 171. All communication with the patients was performed via professional interpreters.

Prior to the four studies included in this thesis, all patients were screened by an assessment team consisting of physician, psychologist, physiotherapist, social worker, with reference to the centre's admission criteria: 1) torture victim with asylum in Denmark; 2) physical, psychological and social needs; 3) no overt psychosis: 4) no drug or alcohol abuse; and 5) available treatment capacity.

In paper 1 the 11 patients had all been exposed to falanga torture and had previously completed an interdisciplinary rehabilitation program at the institute. The 11 controls, matched on age, gender and ethnicity, with no history of torture, were recruited by the 'snowball method'; the sampling relied on referrals from initial subjects to generate additional subjects among volunteers from first generation immigrants in the Arabic community of Copenhagen.

In paper 2, 120 consecutive victims of torture who had chronic pain symptoms and mobility problems were assessed by physiotherapists. Data could not be collected from 17 out of the 120 as three refused, seven participated in single brief interventions, four were not mentally fit and data from three were lost. Thus, the results here are based on 103 torture victims (87 men; 16 women).

In papers 3 and 4, 79 consecutively referred male tortured refugees were identified via the electronic patient records of our institute. Twenty-seven persons could not be included because they did not fulfil the inclusion criteria. The remaining 52 patients were invited to participate in the study, 17 turned down the offer, and three others started but dropped out during the test sessions. Thus, the results here are based on 32 patients. To form a control group we also managed to recruit 14 ethnically and age matched healthy men from the Middle East community in Copenhagen by the 'snowball method'.

To avoid drop-outs I scheduled a meeting with each patient while they were at the clinic for other reasons and informed them about the project. This personal contact before the actual test sessions turned out to be a good approach. Furthermore, not to get too many drop outs, we found a feasible and for all parts acceptable solution, which was to send a message to the patient's mobile phone two hours before each assessment, as a reminder.

Ethical considerations

In papers 1, 3 and 4, all patients and controls received verbal and written information about the respective studies and in their native language (Arabic or Farsi and Danish) following the guidelines concerning participation in medical research issued by the Danish Ethical Committee. They also signed a written consent before assessment. The studies were approved by the Research Ethics Committee in Region Copenhagen, Denmark, and registered in the Danish Data Protection Agency.

In paper 2 the collected data constituted part of the routine medical file and patient monitoring system at our clinic. The patients were informed that they could withdraw from the study at any time without consequences for their rehabilitation programme. The assessments comply with the Helsinki II Declaration and the data were registered in the Danish Data Protection Agency.

Procedures

In paper 1 we explored clinical findings in 11 men with chronic pain after falanga torture as compared with 11 controls. All participants were interviewed regarding pain characteristics in the feet and lower legs at rest and when walking. Structural changes and motor and sensory function were clinically assessed according to a standardized protocol (6). The walking pattern was observed for compensatory gait patterns.

In paper 2 five physiotherapists assessed 103 consecutively referred torture victims with a long history of sequelae, among them pain and mobility problems. All had been subjected to various forms of physical and psychological torture and 71 victims reported in addition having been exposed to falanga. The assessments included a medical history, a comprehensive examination of musculoskeletal functioning and for falanga victims, a specific foot assessment of sensory function in the feet. The main outcome measure

used was: the Disability Rating Index (DRI; 12 items; (99)) to assess self-reported capacity to carry out daily activities.

In papers 3 and 4 we employed interviews asking about pain intensity, pain area, sensory symptoms and stimulus dependence to characterize the pain. Quantitative Sensory Testing (QST; (46)) was performed by investigators blinded with regard to patient history, diagnosis and whether the patients, 32 male torture victims from the Middle East, had (n=15), or had not (n=17) been exposed to falanga.

QST included thresholds for touch, cold, warmth, cold-pain, heat-pain, deep pressure pain and wind-up to cutaneous noxious stimuli in the foot soles. All assessments took place in the research laboratory in our institute. The time for the assessment sessions was scheduled for 3x2 hours within a two-week period with the aim of causing minimal discomfort to the patients. The examinations took place in a quiet room with a stable temperature of 22-24 ºC. During all foot examinations, the patients lay on a couch with a special soft mattress. The examiner stood at the foot end of the couch while the interpreter sat beside the patient. Individual needs were met to avoid painful positions and to make the patient feel as comfortable as possible. A research assistant was present at all procedures.

Clinical data on anxiety and depression were retrieved from the medical records. An ethnically matched control group was available. The normality criterion, from our control group data, was set as the mean +/− 1.28SD, thus including 80% of all values. QST data were transformed into three categories in relation to our normality range; hypoesthesia, normoesthesia or hyperesthesia/hyperalgesia.

Assessment of subjective symptoms

Questionnaires (papers 1-4)

In papers 1, 3 and 4 the patients were interviewed by KP using Danish questionnaires translated into Arabic or Farsi by the interpreter (see Appendices). The golden rule was to keep communication short and concise, in an easy-to-understand language. The same two interpreters were employed throughout the study and had been given firm and consistent instructions. Both interpreters had more than 10 years of experience of translation in interdisciplinary clinical practice for torture victims. They had also

previously volunteered for being tested and were thus familiar with the examination techniques.

Pain drawings (papers 2, 3 and 4)

In paper 2 a pain drawings was used to assess pain locations. The physiotherapist asked the patient to shade in the location of their pain on the surface of a body chart depicting the front and back of a human body (100). The locations were quantified by using a body chart, divided into 44 areas, on a transparent sheet of paper (42). Two neck areas were excluded because they crossed the midline of the body and thus did not divide the body into two sides (right and left), which could be done with all the remaining areas, thus leaving 42 areas. The number of painful areas for each victim was registered by placing the transparent sheet over the body charts and if the victim had pain in ≥ 31 areas (75% of the 42 areas) this was registered. The areas were dichotomized < 31 and ≥ 31.

In papers 3 and 4 the examiner (KP) asked the patients to shade in their painful areas on a body chart (the same chart as used in paper 2) and their painful feet areas on a special foot chart (separate views of right and left foot soles) (101). The shaded-in areas on the pain drawings were measured in square millimetres and calculated as a percentage of the total foot sole area using a commercial software programme (Quantify One; K:L:O:N:K, Denmark), a method that has been shown to be reliable (102, 103) for quantifying pain drawings.

Body and foot pain intensity (papers 2, 3 and 4)

In paper 2, the body pain intensity was assessed using a paper Visual Analogue Scale (VAS) (37, 41). Patients were instructed to mark their pain during the past 14 days with reference to the most painful area of the body on a VAS with the anchor points no pain=0 and worst imaginable pain=100. The results were dichotomized at 0-48 mm=slight to moderate pain and at 49-100 mm=severe pain.

In papers 3 and 4, the victims were instructed to mark their current pain with reference to the most painful area of the body by marking with a vertical line “your pain now” with the same anchor points as above. In addition current pain intensity in the right and left foot soles was also registered.

Psychological function (paper 3)

The Hospital Anxiety and Depression Scale (HADS) (104) was part of the psychological clinical pre-assessment at our clinic. Patients were instructed to complete the questionnaire in order to record how they had felt during the past week. Each question was read by the psychologist in Danish and translated by the interpreter according to the Arabic or Farsi HADS version, as required, and the response marked with an X on the relevant 0-3 Likert-scale.

HADS is a self-assessment mood scale, specifically designed for use in non-psychiatric hospital departments as a screening tool (104), but subsequent use has shown that it is a useful and reliable instrument in other settings too (105). It was also designed as an aid for the clinician for guidance as to probable therapeutic intervention. HADS consists of 14 statements that include two subscales. Seven questions are related to anxiety and seven to depression, each with a score range of 0-21. Scores 0-7 are regarded as normal and scores 8-10 are regarded as borderline cases (mild anxiety and depression) whereas scores above 11-14 (moderate) and 15-21 (severe) both indicate anxiety and/or depression.

Clinical examination

Structural changes in the feet (paper 1)

Structural changes in the feet were clinically examined according to a standardized protocol. Manual palpation was used to assess soft tissues. To assess if the heel pads had reduced elasticity the examiner applied a light pressure over the tuberosity of the calcaneum and registered on a 3-point Likert scale if it was, normal = 0, slightly/moderately reduced = 1, or markedly reduced = 2. The answers were dichotomized (normal/reduced). The fascia plantaris was examined by passively extending the first three toes and in so doing stretching the fascia. Structural changes, thickened and/or uneven, were registered on palpation and any scars on the feet were noted.

Sensory function in the feet (papers 1 and 2)

In papers 1 and 2, examination of the sensibility in the foot was performed in accordance with normal clinical bedside practice to identify neurological signs. Light

touch was examined with a cotton swab that gently touched the skin. A comparison was made with the sensibility on the other side and eventually with more proximal skin areas. Thermal sensation was examined with the forks of a tuning fork, where one fork was heated in the palm of the hand or under warm water while the other remained at normal room temperature. It was registered if the client could, with eyes closed, distinguish the hot fork from the cold fork when it touched the skin. Dysesthesia, an unpleasant abnormal sensation, spontaneous or provoked, was registered if light touch or light pressure induced pain. Allodynia or pain provoked by a stimulus that does not normally evoke pain, was registered if light touch or light pressure induced it.

Screening for tenderness on manual palpation (papers 1-4)

The definition of tenderness is given as "abnormal sensitiveness to touch or pressure" in Dorland's Illustrated Medical Dictionary (106). According to Bonica (19), the clinical examination of deep tenderness is best elicited by digital palpation exerting firm deep pressure on the painful site, whereas cutaneous tenderness is said to be present when pain and discomfort are elicited by moderate pressure applied to the skin. Tender sites in muscles and soft tissues are commonly called tender or trigger points (100, 107).

A pressure of 4 kg was applied with the thumb or the 2nd or 3rd fingers and the response was registered on a 4-point Likert scale (0 = no tenderness, 1 = slight tenderness (tenderness on request), 2 = moderate tenderness (spontaneous verbal response or flinch) and 3 = severe tenderness (jump reaction). The answers were dichotomized as no = no/slight tenderness, and yes = moderate/severe tenderness.

In papers 1-4, tenderness on palpation in the whole fascia of the foot and localized tenderness at the fascia spring on the tuber calcanei under the heel was registered.

In paper 1, in addition, the abductor hallucis muscles (located at the medial foot-border at the talo/navicular joint), the tibialis anterior muscles (10 cm caudally of the patella apex) and the soleus muscles (10 cm proximally of the calcaneum) were similarly examined for tender points as a sign of increased excitability in deep sensory systems.

In paper 2, the patient's body was screened for local tenderness (tender points). A finding of 11 out of 18 positive tender points was registered as positive, following the fibromyalgia criteria used by Wolfe et al (20).

Quantitative sensory testing in the foot soles

Quantitative sensory testing (QST) was introduced in pain research by Lindblom et al (44, 45) to quantify sensory disturbances in particular pain conditions. The rationale behind QST is to test for patterns of sensory loss (small and large nerve fibre function) or sensory gain (hyperalgesia, allodynia, hyperpathia) and to assess cutaneous and deep mechanical nociception (46, 47). The German research network on neuropathic pain introduced a comprehensive QST protocol using well established tests for most aspects of somatosensation. Frequently used methods are cutaneous mechanical detection thresholds, thermal tests, algometry, and wind-up tests. We chose to apply some of their protocol relevant for our research in paper 3 and 4, as we wanted to investigate for possible lesions of Aβ, Aδ and C-nerve fibres and central sensitization.

All thresholds were determined using the method of limits (108), where the intensity of the sensory stimulus is increased until the participant perceives the specified sensation and immediately reacts by indicating the stimulus detection, by pressing a push button, at the same time also terminating the stimulus. This method has the advantage of simple instructions and short test times and has additionally been described as a reliable tool for evaluation of human small nerve fibre function (109). It is a semi-objective psycho-physical method demanding full attention and collaboration from the patient. Since verbal instructions are an important for QST outcome and to ensure that all participants received the exact same instructions, we used standardized scripts for the translating interpreters.

A. Mechanical detection thresholds (papers 3 and 4)

Tactile sensitivity (light touch) is mediated by large myelinated Aβ-nerve fibres. The tactile sensitivity was assessed on the foot soles bilaterally by measuring the mechanical detection threshold (MDT) to light touch with Semmes-Weinstein monofilaments (North Coast Medical, Inc.) (94, 110). We used 17 out of the 20 available monofilaments, from size 2.83 (target force 0.07 g) through to size 6.65 (target force 300 g). The detection threshold was defined as the least target force that elicited a

sensation of touch. The monofilament was applied at 90° angle against the skin until it bowed, during 1.5 s, held for 1.5 s and slowly released during 1.5 s (111-113). The exact threshold was found by performing three repetitive tests with ascending fibre sizes, until one monofilament elicited at least one out of three responses (the patient saying 'yes'). The next larger filament size was applied to confirm this threshold. The detection thresholds were registered for all five sites, bilaterally. In the controls it was only registered in the arch of the foot, bilaterally. The filament size registered was converted into target force in gram (g) according to a standardized conversion table.

B. Brush test (papers 3 and 4)

Dynamic mechanical allodynia/hyperalgesia is a painful or unpleasant sensation evoked by cutaneous mechanical stimulus which does not normally evoke pain. To examine this phenomenon we used the so called brush test, a qualitative test with light strokes with a soft brush (SENSELab^{tm} – Brush-05; Somedic, Hörby, Sweden). The patients were carefully familiarized with the procedure by brushing the skin on a non-sensitive non-hairy area, for example, the volar surface of the forearm or the volar surface of the hand. Three consecutive strokes were applied with the brush to the skin in the arch of both foot soles over a 60 mm long distance and the patient indicated if the stimulus was unpleasant or painful (114).

C. Thermal thresholds (papers 3 and 4)

Thermal testing (44) is used to examine un-myelinated C-fibres (mediating warmth stimuli) and thinly myelinated Aδ-fibres (mediating cold stimuli) function. Additionally, the thresholds of the nociceptors in the foot soles can be tested by potentially tissue damaging heat and intense cold stimuli.

A low baseline temperature results in higher (hypo-) thermal thresholds and therefore the skin temperature should be measured in the same area and prior to thermal thresholds (44). Thus the skin temperature was measured bilaterally in the arch of the foot soles immediately prior to the thermal tests using a hand-held laser FLUKE 62 mini IR thermometer at a distance of approximately 5 mm to the skin.

The thermal tests (44, 46, 108, 115) were performed to assess cold and warm detection thresholds (CDT and WDT) and cold and heat pain thresholds (CPT and HPT) using a

TSA 2001 Peltier stimulator (MEDOC Inc., Israel). The Peltier thermode, size 3x3cm, was placed on the arch of the foot sole and attached with full contact to the skin using an elastic Velcro tape. We used the method of limits (108) and a baseline temperature of 32°C. The stimulator's cut-off temperatures were set to 0°C for the cold and 50°C for the warmth assessments, respectively. If the participant did not respond to the stimulus before the cut-off limit was reached, this was the value registered. The CDT and WDT were each measured by 4 ramped stimuli (1°C/s; return rate 1°C/s) and an inter-stimulus interval of 15 s. The CPT and HPT were each measured by 4 ramped stimuli (1.5°C/s; return rate 10°C/s) and an inter-stimulus interval of 30 s. The detection thresholds used in the analyses were the mean values of the 4 stimuli for CDT, WDT, CPT and HPT, respectively.

The participants were carefully instructed about the procedures. The following summarized instructions accompanying the MEDOC equipment were used. Just before each of the 16 stimuli the examiner (KP) said: "The next stimulus will start now."

For sensory detection thresholds (CDT and WDT) the instructions were:

- The device attached to your foot will first gradually cool down. The test also involves increasing the temperature in this thermode from a neutral temperature of 32º C. It is important that you press the button at the absolute first moment you detect the temperature change. Please stay alert and concentrate throughout the test. Do not press the button until you are confident that you have felt the stimuli. The temperature does not reach below 0 ºC or above 50 ºC. Pressing the button will turn the thermal device off and the temperature will return to 32 ºC. We will repeat the procedure four times.

For pain thresholds (CPT and HPT) the instructions were:

- In this test, we are interested in your perception of pain. The test involves decreasing the temperature in this thermode from a neutral temperature of 32 ºC. Wait until the temperature becomes painful. Press either of the two buttons the instant you decide the temperature has reached a painful point. It is important that you press the button at the absolute first instance your feel pain. This is not a test of how long you can endure the pain. We want to know the instant you decide the sensation is painful. The temperature will not reach below at 0 ºC or

above 50 ºC. Pressing the button will turn the thermal device off and the temperature will return to 32 ºC. We will repeat the procedure four times.

D. Pressure pain thresholds (papers 3 and 4)

The reliability of manual palpation is influenced by the mode of application and the training and experience of the examiner. A semi-objective method for measuring deep tenderness in muscles and for quantifying localized pain is to measure pressure pain thresholds (PPTs) using an algometer. Algometry literally means measurement of pain, and in practice, measurement of tenderness in response to a pressure applied vertically to the skin (29).

Pressure algometry has a long history in medicine. Mechanical algometers have been tested for reliability (116) and recommended as a clinical tool (117). I used an electronic pressure algometer (Somedic, Höör, Sweden; (46, 118-120) to detect deep mechanical nociception by applying pressure to the five sites on the right and left foot sole respectively, and for the control group in the arch of the foot soles. The algometer probe contact area was 10 mm and covered with 2 mm rubber. In order to obtain reliable measures the instrument was calibrated to a zero level before each session. This technique has previously been found reliable in healthy women, provided that the first measurement in a series is excluded (121).

A pre-test was performed bilaterally on the radio-humeral extensor muscle group approximately 10 cm distal to the radio-humeral joint to familiarize the patient with the procedures. The most painful area reported in the foot soles was measured last in each series to avoid evoking discomfort. The examiner applied alternating series of three measurements on the five sites, always starting with the right foot sole. A gradual pressure was applied and increased at a speed of 40kPa/s controlled via monitoring on a display. The inter-stimulus interval was 30 s, and the inter-series interval 5 min. A cut-off was set at 900 kPa/s to avoid tissue damage (121). The participant was instructed to press the push button when a sensation of pain or discomfort was perceived and the pressure ceased immediately.

E. Temporal summation of mechano-nociceptive stimuli (wind-up pain; papers 3-4)

Temporal summation or wind-up pain (38, 53, 122-124) refers to central pain sensitization caused by repeated painful stimulation of peripheral nerves at sufficient intensity to stimulate C-fibres, leading to progressively increasing response in the corresponding spinal posterior horn neurons. For this measure the thickest available Semmes-Weinstein monofilament was applied (size 6.65) (94, 125). At 0.3 Hz the examiner applied the filament four consecutive times to the skin in the arch of each foot sole. The patients were asked to rate the pain intensity on a VAS after the 1st and 4th stimulus. A 5-minute pause followed. Thereafter, to produce a more intense stimulation, 10 consecutive stimuli were applied at the rate of 1.0 Hz. The patients rated their pain after the 1st and 10th stimulus. If the VAS difference between the 1st and last stimulus was positive, a temporal summation (wind-up) had occurred. An exaggerated wind-up pain reflects central sensitization of the central nervous system (126).

Disability assessments

Observed walking pattern (paper 1 and 2)

In paper 1, we observed the patients when walking for compensatory walking patterns and for abnormal foot loading, such as walking on the lateral border of the foot; walking on the medial border of the foot; using abnormal push-off of the first toe; and capacity to walk and stand on tip-toes.

Self-reported activity limitation (Disability Rating Index; paper 2)

The DRI is an established and practical clinical and research instrument with good reliability for assessment of disability caused by limitations of common motor activities (99). Validity tests have demonstrated that the instrument discriminated well between different diagnostic categories, shows sensibility for small age and gender differences, and the compliance is high. The DRI was primarily designed for low back pain, but it is also applicable when measuring disability of patients with neck/shoulder pain, knee, hip and chronic pain (127).

In paper 2, the Disability Rating Index (DRI) was used to obtain the victims perceived capacity to perform daily activities (99). The DRI questionnaire covering 12 items concerning physical function on the activity level is constructed as a self-administered questionnaire where the patient marks a 100-mm Visual Analogue Scale in accordance

to his/her presumed ability to perform the daily physical activities in question. The 12 items are divided into three sections arranged in an increasing order of physical demand, particularly with reference to low back pain: 1-4, common basic activities of daily life; 5-8, more demanding daily physical activities; and 9-12, work-related or more vigorous activities.

To help the patient understand the meaning, a description of each item was used as a guideline (128). Answering the question 'How do you manage the following activities?' the patient marked his perceived capacity regarding each item on the 100mm VAS. The score on VAS was the distance from the zero point to the marking in mm. The anchor points were 0 = perform without difficulty and 100 = not at all able to perform. Each item was presented in Danish by the physiotherapist and translated for the victim by the interpreter.

Statistics

In paper 1, the data were presented as descriptive dichotomized categorical variables (yes/no) for the individual's right and left feet.

In paper 2, Student's independent sample t-test and Fisher's exact test were employed for comparisons between groups. To detect differences for each DRI item we chose to dichotomize the relevant variables age, pain areas, tender points – and analysed them using VAS and univariate ANOVA's and a post-hoc Tukey analysis. Further statistical analyses were conducted in two steps. First, a univariate ANOVA was done for each DRI item between the groups: stimulus-independent foot pain, stimulus-evoked foot pain; not exposed to falanga. In a second stage, a stepwise analysis of covariance (ANCOVA) was performed to adjust for possible influences of age, pain distribution and number of tender points.

In papers 3 and 4, we chose to analyse data from the right and left feet separately, even if they may share common analysis mechanisms in the central nervous system, The mean, SD, 95% CI, median, and range were calculated for all QST variables as were the correlations between both feet. Student's t-test or Fisher-s exact test was used to test for differences between sides. To detect differences between the three groups: victims not exposed to falanga, victims exposed to falanga, and to the controls we used univariate

ANOVA's test. A post hoc Tukey analysis was performed to indicate the differences between data in the respective groups. Acceptable p-values were set to ≤ 0.05.

The data were analysed with SPSS software (Statistical Package for Social Sciences, version 15.0 in papers 1 and 2, and version 18.0 in papers 3 and 4).

SUMMARY OF RESULTS

Paper 1

Compared to the controls, the 11 torture victims had pain in their feet and lower legs and a compensated gait pattern, usually with severe pain during walking. The severe pain was combined with a reduced sense of light touch and of thermal sensation. Tactile dysesthesia, allodynia, and tenderness on palpation in the fascia plantaris or under the heel were common findings. These clinical findings were non-existent or only rarely seen in the controls. The observations of individually reported pain characteristics of torture victims' feet were divided into three groups: no reported pain; chronic pain in the feet appearing spontaneously, that is, stimulus-independent pain; and pain evoked by activity, stimulus-evoked pain, where pain appears in response to a stimulus for example physical activity such as walking. The latter was more common. Structural changes in the feet were found in more than half of the victims, but did not correlate with pain reports.

Paper 2

All 103 included torture victims had been subjected to various forms of physical and psychological torture. Seventy-one had also been exposed to falanga. The mean body pain intensity (VAS) was 71 mm (95% CI, 67–75 mm). Fifteen had slight/moderate pain (intensity below 49 mm), and 82 victims had severe pain (VAS 50-100 mm). Significantly more falanga victims than other torture victims reported severe pain intensity in the body. Body pain drawings showed that 19 victims had marked ≥31 of the 42 areas of the body as painful, whereas 80 victims had marked less than 31 areas. Positive tender points in at least 11 out of 18 palpated locations in all body regions were present in 31 victims, meeting the palpation criterion for fibromyalgia. Of the 31 patients with tender points, 25 were falanga victims and 6 had not been exposed to falanga.

All the torture victims perceived clear activity limitations according to the DRI. The falanga victims' feet were categorised according to the type of foot pain: stimulus-independent pain; stimulus-evoked pain or no pain. The two falanga groups with foot pain (stimulus-independent and stimulus-evoked) had even more extensive activity limitations than the falanga group with no foot pain and the group not exposed to falanga. This held for the majority of the DRI items, mostly the items that involved high

dynamic foot loads such as ‘climbing stairs’, ‘standing bent over a sink’, ‘lifting a bag’, ‘making a bed’, ‘running’, ‘heavy work’, ‘lifting heavy objects’ and ‘participating in exercises or sport’. The odds ratio for the risk of foot pain after falanga compared to other forms of torture was 3.54 (CI 1.86-6.73). After correction for confounding factors, these two groups (stimulus-independent and stimulus-evoked) reported significantly more activity limitations in 7 out of 12 DRI items than those who were not exposed to falanga.

Paper 3

When breaking the blinding, it turned out that 17 patients had not been exposed to falanga (NF) and 15 had been exposed to falanga (F). All 32 patients reported pain in many parts of the body. The most common reported painful regions were the neck, shoulder and the low-back. The mean body pain area was larger and the current body pain intensity was higher in the falanga group, however not statistically significant. Data on anxiety and depression from HADS forms in the medical records indicated severe anxiety and depression in both the NF and the F group.

Since we could collect data from 64 feet but the central pain processing occurred in 32 persons, we examined whether QST data from the two sides of a single individual corresponded. The Pearson correlation coefficient from the right versus left data of the torture victims was generally high and the t-test did not show any significant difference between the sides. The same held for the control data. Almost all falanga victims had moderate or strong pain in their feet and in twice as large an area of their foot soles as other torture victims. However, both torture groups reported sensory dysfunctions such as numbness, cold sensations, burning, pricking sensations, dysesthesia and allodynia in the feet. Thus, there were no obvious differences between those exposed to falanga or not regarding irritative phenomena.

One-third of those not exposed to falanga had no pain in their feet and many reported slight pain; in spite of this, there were no differences in foot sole QST data between the tortured groups. A comparison with normal data indicated that both tortured groups had hypoesthesia for all cutaneous sensory fibre groups except those transmitting cold and heat pain, in addition to deep mechano-nociceptive hyperalgesia. A comparison of the QST data between victims having been exposed to generalized torture and victims who

in addition had been exposed to falanga, showed no differences on the group level. However, in relation to our data from controls, there was significant hypoesthesia for mechanical thresholds and hyperalgesia for deep mechanical nociception. We found equal temporal summation (wind-up pain) in both torture groups after repeated cutaneous mechanical stimulation. The wind-up effect was about the same in the feet of the controls as in the falanga group.

Paper 4

The results are presented as individual sensory profiles of victims' feet to explore possible relations between external violence (torture), reported pain, sensory symptoms and QST data to help clarify the underlying mechanisms. Since the Pearson correlation coefficient from the right versus left data was generally high and the t-test did not show any significant difference between the sides, only data from the left foot are presented.

The results from measuring sensory modalities with QST have varying denominations. We therefore transformed the QST data into three categories in relation to the normality range from our matched controls: hypoesthesia, normoesthesia and hyperesthesia/hyperalgesia. The normality criterion, from our control group data, was set as the mean +/− 1.28SD, thus including 80% of all values.

Most patients, irrespective of having been exposed to falanga or not, reported severe pain when walking. Such severe pain was often accompanied by sensory symptoms like burning or pricking and sometimes with dysesthesia also at rest often associated with hyperalgesia to deep mechanical pressure. Hypoesthesia to mechanical stimuli co-occurred with numbness, burning and with deep mechanical hyperalgesia more often than not, but otherwise, a hypoesthesia to cutaneous sensory modalities did not co-occur systematically to foot trauma (falanga), pain or sensory symptoms. Moreover, an exaggerated wind-up reaction was rare in these patients.

GENERAL DISCUSSION

The most important findings in this thesis concern (1) the clinical presentation of chronic pain in torture victims, (2) their pain-related disability and (3) possible underlying pain mechanisms, based on QST studies of sensory dysfunction in their battered feet.

Clinical presentation of chronic pain in torture victims

Paper 1 was an exploratory study where bedside neurological and structural data on the clinical presentation of foot pain in falanga victims was collected. Data on physical functioning was also collected. All findings were compared to a non-tortured control group. This had to our knowledge not been attempted before and is, as such, of importance for the clinical work with torture victims worldwide. The clinical examination is also an essential part of the diagnostic process of neuropathic pain. Neurological bedside examination is the most important part of this examination and includes testing of touch, vibration, pinprick, cold and warmth (129).

Additionally, from the bedside examination and the falanga victims self-reported pain characteristics we gained new knowledge about their pain distribution and sensory function in the feet and lower legs. The mean pain intensity experienced by most of the tortured refugees in my studies was high and similar to that in other patients disabled by chronic pain (130). Furthermore, all the victims had chronic pain in several parts of the body, pointing at a disturbed pain modulation, also reported by Defrin et al (94) and confirming earlier observations (91).

It should be remembered that the torture episodes occurred in the previous home countries of the victims, more than 5 years earlier, which makes it extremely unlikely that soft or hard tissue injuries had not healed at the time of our examination. However, several, but not all, of the victims examined in paper1 had structural changes in the tortured areas of the feet that were not seen in the age-matched controls (131). Hence, these changes, and the walking difficulties of the victims, may contribute to a nociceptive component in their chronic pain conditions (96). On the other hand, since the extent of these structural changes did not correlate to the pain reports it is unlikely that they are responsible for the severe foot pain experienced by most of the victims examined in this study.

The frequent occurrence of sensory symptoms and signs in the feet among the torture victims along with the anamnestic reports that beatings under the foot soles had indeed occurred, are indicative of, but do not prove that neuropathic pain contribute to these pain conditions.

In papers 1 and 2 the severe pain in the foot soles could be divided into two chronic pain conditions: one appearing spontaneously, stimulus-independent foot pain and the other evoked by activity, stimulus-evoked foot pain. In these studies the foot pain was clearly evoked by walking, a mechanical stimulus.

In addition, as evident from paper 3, screening for mental problems indicated high levels of both anxiety and depression in most of the torture victims examined. It is possible that psychogenic pain conditions also contribute to the complex clinical presentation here, even if there was only a weak relation between HADS scores for anxiety/depression and pain intensity in the feet.

Pain related disability

The old bio-medical model (132) assumes that all pain has a distinct pathophysiological cause and that clinicians should be able to find and treat that physiological problem only. However, for the treatment of chronic pain in torture victims, the biomedical model is inadequate due to its limited scope.

I have used the bio-psycho-social model (133) that views the patient's whole situation from another perspective as being an interaction between biological, psychological, and socio-cultural aspects. As demonstrated, the very complex web of bio-psycho-social problems that our patients have, including a high level both of anxiety and of depression (HADS in papers 3 and 4), disability (128) in addition to chronic pain (131, 134, 135), all inevitably have implications for the individual's ability to interact with other people, to involve themselves in societal activities, or even to enter the labour market.

Loeser (13, 14) suggests 'suffering', as a state of emotional distress that is associated with events threatening the biological and psycho-social integrity of the individual. He describes suffering as the negative affective response produced by pain, a state of

depression, anxiety, or fear and that suffering often is related to severe pain. However, suffering may also occur with pain that is less severe, or in conditions that do not produce pain at all. This explains that pain and suffering are two separate phenomena that often interact or supplement each other (136, 137). In the literature victims of torture are described to suffer from feelings of guilt for being a silent witness to the torture and the death of others, guilt for being forced to participate in the torture of loved ones, guilt for surviving while others disappeared or guilt for not being able to talk about the experience in a way that could help others (138).

The results in paper 2 where the activity patterns were specifically characterized in relation to the foot pain condition present showed that this group of torture victims, consisting mostly of young men, were highly disabled. Furthermore, the high mean body pain intensity reported may be an important explanatory factor for the activity limitations that can be interpreted as a fear-avoidance or kinesiofobia like reaction (54). Following the ICF concept (53) , that the impairment pain has influence on a person's activity level, most of the participants in paper 2 perceived extensive limitations to perform daily activities, as indicated by the DRI scores. This is consistent with the findings of Basoglu et al (70), that irrespective of torture method, many victims suffer severe sequelae. Interestingly, the presence of chronic widespread pain seems to predict inactivity also in the general population (139).

Another important aspect was that, in this particular sample of torture victims, it was possible to examine activity differences between victims exposed to and victims not exposed to falanga. In 9 out of 12 DRI items, the falanga victims reported more pronounced activity limitations, usually for activities involving foot load. Thus, foot pain after falanga seems to be the cardinal impairment reducing the victim's ability to perform even simple daily physical tasks.

The focus in paper 2 was to examine the individual's perceived activity level and analyse a possible relation between foot pain and self-reported activity limitation. This extends earlier research on victims of torture and prisoners of war where mostly surveys and retrospective cross-sectional studies focusing on long-term mental health, symptoms and diseases after torture were used. (55-61, 140).

Possible pain mechanisms

As commented previously, the mean pain intensity experienced by most of the tortured refugees was high (128) and similar to that in other patients disabled by chronic pain (130). Furthermore, all the victims had chronic pain in several parts of the body and tenderness at the same locations as in fibromyalgia (141), pointing at a disturbed pain modulation, also reported by Defrin et al (94).

The majority of the torture victims in papers 1, 3 and 4 reported severe stimulus-evoked pain in the feet. In papers 3 and 4 the foot pain area was much larger in the falanga victims, but surprisingly the qualitative descriptors like numbness, pricking sensation and cold or burning sensations in the feet were similar in both groups (exposed and not exposed to falanga).

A tentative explanation for the stimulus-independent pain in the patients can be that mechanical torture against the foot soles may give rise to spontaneous activity, evoked peripherally in nociceptive afferents due to permanent mechanical injury of nerve bundles in the foot soles proper, as described by Baron (30). In the feet with stimulus-evoked pain described in paper 1 the clinical sensory findings were dominated by dysesthesia and deep mechanical hyperalgesia. Thus, the foot pain in this group may be more related to central sensitization.

However, it should be noted that the presence of symptoms or signs alone does not justify the use of the term neuropathic. Where possible, neuropathic pain should be divided into peripheral or central neuropathic pain based on the anatomic location of the lesion or disease. The characterization of pain as neuropathic or not depends on the application of the usual, careful neurologic diagnostic process. In this respect, the presence of a single positive or negative finding on examination is often not diagnostic. In 2008, Treede et al (33) proposed a grading system for neuropathic pain. It was intended to be used to decide on the level of certainty with which the presence or absence of neuropathic pain can be determined in an individual patient.

The grading system mentioned above (33), relates to that the pain distribution should be found in the area that is typical for the underlying disorder (first criterion). In all studies intense, often activity related pain was found in the feet of falanga victims which

usually, when examined in detail in paper 4, occurred also in the victims not exposed to falanga. In addition, pain was abundant in other parts of the body in all the torture victims. This may be due to a generalized central sensitization in these persons. Central sensitization is also one of the mechanisms that contribute to neuropathic pain and extends its symptoms outside the innervation territories of the injured nerve areas, which was taken into account when making the conclusions.

The second criterion relates to establishing a relation between history in these studies generalized torture or falanga in addition, and the reported pain distribution. Most clearly the patients who were exposed to falanga had pain in their feet at rest and when walking. Thus, to qualify for causing neuropathic pain the lesion should affect the somatosensory system, which could be inferred from the patients' reports. Moreover, all victims examined here had been exposed to other forms of torture in addition, beatings being the most common (82). This wide-spread pain may either be due to a loss of central inhibition, like in fibromyalgia, or at least partly due to minute nerve injuries at the beaten body (81).

The third criterion is dependent on the clinical examination with demonstration of negative or positive sensory signs that support the presence of a lesion in accordance with the distribution of pain. Such sensory disturbances were found in the painful traumatized foot soles in papers 1, 3 and 4. However, the picture is muddled by the fact that such disturbances were also present in victims not reporting falanga.

The fourth criterion relates to diagnostic tests, such as nerve biopsies, which were not applicable here. However, the QST findings in papers 3 and 4 strongly indicate the presence of relevant disturbances affecting the somatosensory system.

Following the clinical sensory findings in papers 1 and 2, we suspected that there would be differences between falanga and no falanga, but surprisingly in paper 3, no significant QST findings were detected between the two groups. Instead we found significant hypoesthesia for all cutaneous sensory fibre groups except those transmitting cold and heat pain and in addition hyperalgesia for deep mechanical nociception in the feet of both falanga-exposed and unexposed victims compared to the control group, with little positive evidence of increased cutaneous excitability. Whereas the cutaneous

hypoestesia may be due to extensive nerve injury in the falanga victims, the corresponding finding in the victims not exposed to falanga can only be explained by a central desensitization. It is interesting to note that Giertmülen et al recently found that sensory gain is highly prevalent in peripheral nerve injury which is compatible with the deep mechanical hyperalgesia found here (142). On the individual level, many complex and diverse combinations of sensory findings were found.

To be able to participate in QST tests as in papers 3 and 4 demands an intellectual process by which one becomes aware of, perceives, or comprehends the instructions. It involves all aspects of perception, thinking, reasoning, and remembering. In spite of the participants' psychological and physical conditions, it is noteworthy how the patients were able to steadily pay attention, answer questions and participate in QST. Thus, the results were reproducible between feet in the same patient and also between repeated tests. Our patients, however, were easily fatigued and had more pauses during the test situation than scheduled. This increased time consumption must be taken into consideration in future research planning.

The magnitude of torture and the trauma intensity between individual patients was not known in detail. Information about if they had been subjected to other forms of injury to the nervous system or to the head was inconsistent but when found at the clinical entry assessment, such patients were excluded. In addition, the findings that the brains of tortured persons may undergo atrophic changes (88, 143), and may show plastic changes, sometimes partly reversible [see (144, 145)]. Such changes may have prevented adequate sensory detection, thus also making the interpretation of our QST results difficult. On the other hand, Basoglu et al (146) investigated the relationship between various torture events and long-term psychological status, and found no correlation between reports of head trauma (beating or blows on the head) and psychological symptoms.

During the QST warm and cold threshold measurements some of the patients reached the cut-off temperature values (warmth 50°C; cold 0°C) without the patient pressing the signal button, indicating severe loss of sensation. It is unlikely that the phenomenon was due to lack of understanding since there were no unexpected reactions.

The QST findings on the group level comply in some sense well with the results of researchers studying other neuropathic pain conditions, which have been found to comprise a complex web of different pain and sensory characteristics (147-152) rather than consistent findings related to a particular causative factor, here a repetitive mechanical trauma.

Since no differences on the group level were found, we continued the QST analyses producing individual profiles as is the case in the clinical situation with torture victims (paper 4). It has been recommended by several authors, to find each person's sensory profile as various sensory symptoms differ between individuals (33, 35, 46, 47, 153-155).

This analysis showed that most patients, irrespective of having been exposed to falanga or not, reported severe pain when walking (paper 4, table 3), which was often associated with hyperalgesia to deep mechanical pressure and hypoesthesia to mechanical stimuli.

Defrin et al (94) who studied persons with PTSD likewise found elevated sensory thresholds for tactile and thermal stimuli, but did not test for mechano-nociception. They also examined the effect of supra threshold stimuli finding an increased reactivity similar to that in hyperpathia. Taken together, these findings indicate an altered sensory processing in patients with PTSD. Most of the patients in papers 3 and 4 had PTSD, with severe anxiety and depression HADS scores, but no correlations were seen between HADS and QST variables.

Study limitations

Recruitment of participants

The patients in the studies comprising this thesis were tortured refugees with residence permits in Denmark. All were referred by their general practitioner to our specialized centre for rehabilitation of torture victims in Copenhagen because they experienced physical, psychological as well as social sequelae from torture. Consequently they were vulnerable and thus may have other problems in daily life. From clinical experience and from other studies from our centre (85), we know that other factors such as the victims traumatic experiences, the level of education and socio economic conditions have

differed among my participants and probably had an influence on their chronic pain and disability.

Approximately 80% of the referred patients are men and 20% are women. Therefore, I chose to examine men from the Middle East in all papers in order to form a homogeneous group with similar cultural background. Thus, in paper 2, the 16 tortured women were not included in the main analyses.

A large effort and repeated attempts were needed before I succeeded in recruiting both torture victims and controls in papers 1, 3 and 4. In paper 1, 30 victims, who had earlier completed a lengthy interdisciplinary rehabilitation program, and who had been exposed to falanga, were contacted by mail or telephone. Eleven torture victims were included. The 11 control persons were recruited using the so called snowball method.

In paper 2, out of the 152 consecutively referred patients to physiotherapy, complete data from 103 physiotherapy records could be retrieved. The data in paper 2 would have been more complete if all participants, not only torture victims exposed to falanga had been foot examined, but for historical reasons these data were not available. However in the blinded papers 3 and 4 all feet were examined, and today all assessed patients reporting foot pain are specifically examined in our clinic.

In papers 3 and 4, the recruitment of new patients entirely depended on the admittance to the clinic. Eventually 79 screened patient records resulted in that 32 patients accepted to participate. The reason for the low number might be that the patients were in the pre-admission phase and were not yet accepted for treatment at the time of recruitment. The 14 control persons were recruited by the 'snowball' method. The number of persons in papers 1, 3 and 4 are relatively few, and the study results would have been strengthened if a larger number had been included. One other point I would draw attention to is that my sample is highly selected and thus may not be representative for all victims of torture.

Choice of assessment instruments

The Physiotherapy Manual, developed and used in our clinic since 2000 (6), included both the interview questions and the foot assessment protocol used in all 4 papers, but

these had not been validated. An important issue that was not included was the magnitude, the extent and the exact site of the beatings. This would have been valuable information but is difficult to obtain since questions about these matters may provoke flashbacks. However, the answers gave other important information, for example if the pain was stimulus-independent or stimulus-evoked. According to the recent recommendations in the guidelines concerning neuropathic pain assessment (129) it would have been valuable if we additionally had included screening tools such as the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) (156). Such data might have further supported our interpretation of whether or not the findings suggestive of neuropathic pain components really contributed to the overall foot pain in paper 1.

To assess pain characteristics however, common validated and reliable instruments were used, for pain intensity VAS (37, 41), for pain location (pain drawing; (42) and for psychological function HADS; (104) and for perceived functional capacity DRI; (99).

In papers 3 and 4 some self-constructed questionnaires from papers 1 and 2 were used. Including a questionnaire developed for assessing neuropathic pain was also considered. However, we judged that adding more questionnaires would have been too time-consuming and the risk of patients dropping out would increase. In addition, neither of these instruments has been validated in the relevant languages.

To reach the criteria for clinical classification of suspected neuropathic pain (157) we could also have added measures of abnormal nerve function by nerve conduction studies which would have contributed to the validity of the results in the conclusion that part of the pain condition was neuropathic. However, to carry out more detailed nerve conduction studies with electrical or painful stimulation of peripheral nerves in these patients should be avoided for obvious reasons in persons who have previously been tortured. Stable examinations of ‘evoked potentials’ from C-fibres are also technically difficult to perform.

Instead, we proceeded to quantitative sensory testing in papers 3 and 4. These tests demonstrated that all torture victims (falanga victims and those not exposed to falanga) had sensory disturbances in the feet. Comparing the two groups we had expected that

there would be substantial differences in sensory function. However, this was unexpectedly not the case.

In paper 2, I found the DRI a useful instrument that was easy to administer, supported as it is by clear guidelines. It is a short self-report instrument and covers 12 activities that concern normal daily activities. However, it should be remembered that the instrument evaluates perceived rather than actual limitations and that a performance measure might have yielded a different picture. During the 10 years that it has been used in our clinic it has been found useful for describing the victims' level of disability in terms of physical functioning. Moreover, when communicating with authorities it is a strong indicator for describing the individuals' disability. In adapted versions, the DRI has also been introduced in rehabilitation settings for torture survivors in Sri Lanka, Bangladesh, Cambodia, Zimbabwe, South Africa and Sierra Leone together with DIGNITY's international partners.

Communicating with torture victims

The traumatic background of torture victims and the physical, psychological and social consequences are often missed by health professionals (158, 159). In spite of the recommendations to include knowledge about torture and the consequences of torture in their curriculums, little or no efforts have been made to comply with the recommendations on examination of torture victims given in the Istanbul protocol (101). Our experience is also that the patients do not mention their earlier traumatic events first hand. They often regard there torture experiences as shameful and full of feelings of guilt. It is, for instance, a prerequisite to create an atmosphere of trust and respect and establish a high level of confidentiality.

Various declarations, in particular the Tokyo Declaration of 1975 for medical doctors, the Position Statement on nurses and torture of 1989, and the Guidelines for physiotherapists of 1995, state that health professionals must know about torture, including its methods, consequences and possibilities for rehabilitation. Nevertheless, this is not easily done since the health professionals must ask for the information of the traumatic events, and rely on their capacity to deal with it.

Many years of clinical experience has shown that it is extremely difficult to collect data on the extent and magnitude of the beatings of the soles. This information would have been valuable but not possible. The victims often become unconscious during the torture act and cannot account for how severely and how many times they were beaten. There is also the risk of provoking flashbacks and other psychological reactions during the interview, with no psychologist at hand. Thus, for both scientific and ethical reasons we avoided this topic.

In the Arab culture the foot soles can be used to show disrespect for another person but showing the soles of the feet to another person is not 'Haram' (forbidden by the Muslim religion). In this context, however, it was different as the focus was health related.

Generally, all interpreting is based on a relationship of trust. In our institute the golden rule for our interpreters therefore to respect a pledge of secrecy and discretion, a fact which was made clear to all involved, including the patient, at the beginning of the assessments (160). The interpreters must also be aware of their responsibility. An empathic approach to the patients' situation is valuable. The interpreter translates everything that is said, preferably with the linguistic nuances. It is not the interpreter's duty to judge that something is not worth translating.

I was aware that there is a risk of misunderstandings to occur when communicating through a third person. From many years of experience in communicating through interpreters I did my best to secure dynamic communication and statements were limited to a few sentences at a time. A direct translation of what I said, supported by a more detailed explanation, turned out to be the best way of conveying the true meaning.

A common view in western societies today is that people from other cultures, especially from the Middle East, are difficult to approach and to offer health care. A common belief is that men from the Arabic cultures feel uncomfortable to be treated by or even touched by a female western health professional. However, I have more than 20 years of experience from treatment of torture victims from all over the world and this has never been an issue. Nevertheless, ethical and cultural concerns are important and should always be considered.

QST-related considerations

In papers 3 and 4 we chose as test site the location reported as most painful by the majority of subjects as the test site for all QST tests since this is recommended in the literature (46, 47). Ideally, we could have included a non-affected test location for comparison between groups (161) which in many cases, however, can be difficult to find in these patients. In addition, we did not want to exhaust the patients further by including more sites.

When using the methods of limits for QST, the patients need to consciously perceive the stimulus processing and the information given and at the same time generate an action to indicate a response. During the period of information processing, the stimulus continues to increase, which might have led to a small error in the threshold measurements here (46, 47, 162). Moreover, slight variations in the examiner or the interpreter's facial expression, and the examiner's selection of words may affect the results. The same holds for the patient's attitude and expectations to the test situations. Quantitative sensory testing therefore needs close cooperation with the patient.

I first tried to make comparisons with normal values from the literature, but since I found few normal QST values from the foot soles, I found it necessary to collect normal data. Thus, the normal QST values used for comparisons in papers 3 and 4 were calculated from the 14 matched healthy controls. Moreover, according to Shy et al (162) normal values from one system cannot easily be transposed to other systems. I fully agree with them in their conclusion that QST is a potentially useful tool for measuring sensory impairment, but QST results should not be the sole criteria used to diagnose pathology because many factors can influence the test results.

Repetitive electrical stimulation is often used to produce temporal summation. Regarding my participants, however, I find this method unsuitable, since it may recall the torture situation and everything it entails. I therefore decided to use a superficial mechano-nociceptive stimulus from the thickest (no 6.65) Semmens-Weinstein monofilament available (94, 125) for producing wind-up pain with two different frequencies (papers 3 and 4).

When using QST in this group of tortured refugees I found that the patients were able to act in accordance with my given instructions translated into their respective language. The patients were consciously signalling when they felt their thresholds of a given stimulus and participated actively in the process through three assessments lasting six hours. Most important, however, was the high side-to side correlation of all QST tests in the feet.

Perspectives and recommendations

In this thesis the main object has been to in depth examine foot pain and sensory disturbances in tortured refugees. When rehabilitating patients with multiple problems, it is often wise to employ ICF related reasoning (52, 53), starting by stabilizing the platform for rehabilitation with treatment at the impairment level. Foot assessment is only a small part of the clinical examination at our institute, but as I have found with large impact on self-reported disability regarding common daily activities in tortured refugees. Therefore rehabilitation of torture victims should include interdisciplinary assessments in order to reveal each individual's critical impairments, activity limitations, participation restrictions and contextual problems at hand (11). Coordination with primary care and social institutions is another prerequisite for successful rehabilitation.

An analysis with QST as performed in papers 3 and 4 made it possible to quantify and give more detailed information about the sensory function in the victims' foot soles. The results surprisingly showed no significant QST differences between those exposed to falanga and those not exposed. However, in relation to the control group values there was significant hypoesthesia for all cutaneous sensory fibre groups except those transmitting cold and heat pain and in addition hyperalgesia for deep mechanical nociception whether exposed to falanga or not. These findings have resulted in new procedures in the Rehabilitation Department at DIGNITY with the aim that all torture victims with pain in the feet should be assessed specifically for pain characteristics and sensory disturbances.

Assistive technology should be tried out, such as shock absorbing shoe inlays and/or shoes with a thick shock absorbing sole, like ordinary sport shoes. The patient is

recommended to use these at all times. Sometimes special individually measured shoes and shock absorbing foot orthotics may be considered.

Including QST as an additional diagnostic tool in the assessment procedure as we did in papers 3 and 4 is complex and time consuming and thus not possible in everyday clinical practice. On the other hand, in papers 1 and 2 we used normal bedside examination, including most of the tests in a protocol recommended by Jensen et al (37). I agree with, several authors that recently have suggested that a bedside assessment of neuropathic pain should involve a series of systematic steps (35, 129, 157, 163), and if this had been possible in papers 1 and 2 these studies would have been strengthened. Clinical practice must include examinations performed within a reasonable period of time which is possible by using simple bedside equipment.

Future research

Chronic pain is in itself a severe sensory impairment that may have a serious impact on activities and participation in daily life as I found in paper 2. Since there may be differences between self-reported and observed activities I am now in the process of finalizing a study, including the same participants as in paper 2, with the aim to study self-reported limitations of daily activities and the level of disability observed by a physiotherapist when asked to perform the same activities.

In papers 3 and 4 I found no differences in sensory function of the foot soles using QST comparing groups of torture victims with or without exposure to falanga. Pain when walking was often associated with hyperalgesia to deep mechanical pressure and cutaneous hypoesthesia. I am now exploring possible relations between walking speed and pain in the same sample to determine activity related changes in foot pain.

Recent literature suggests a correlation between chronic pain and PSTD (94). PTSD or DESNOS contribute to the suffering of torture-related pain conditions. The most reliable knowledge about how a given effort or treatment works originates from results of randomized controlled trials. The studies regarding the effect of rehabilitation of torture survivors and other traumatized refugees are few. Randomized controlled studies of the effect of treatment and rehabilitation of torture survivors and other traumatized refugees are warranted.

In addition to injury to the body, torture may have affected the victims' cognitive functioning. To investigate possible relations between cognitive impairments and pain conditions due to torture could increase the understanding of this group with multifaceted problems. It would also be interesting to analyse the relations between mental state (PTSD, anxiety and depression) with activity limitations and participation restrictions. The influence of environmental factors on pain characteristics is another interesting field for future studies including torture victims in exile.

CONCLUSIONS

Clinical presentation of chronic pain

1. The torture victims reported high levels of pain intensity and chronic pain in several parts of the body including the foot soles.
2. Almost all the falanga victims had moderate or severe pain in their feet and in twice as large an area of their foot soles as those torture victims not exposed to falanga. One third of the latter did not report pain in their feet at all and many reported only slight pain.
3. Screening for fibromyalgia-like tender points showed no significant differences between victims exposed to and not exposed to falanga, indicating that this, when present, may be a sign of central sensitization after all forms of torture.
4. Chronic pain in the feet after falanga can be divided into 1) stimulus-independent pain (pain appearing spontaneously) and 2) stimulus-evoked pain (pain evoked by activity). The stimulus-evoked pain was predominant.

Pain-related disability

1. The torture victims perceived extensive activity limitations according to the Disability Rating Index over a wide range of daily activities compared to the normal population.
2. Falanga victims with chronic pain in the feet were more disabled than victims with no foot pain after falanga and victims exposed to other forms of torture.
3. The activity limitations were usually more pronounced in the activities that involved foot load.
4. When examined, anxiety and depression were found in all the torture victims, whether exposed to falanga or not.

Possible pain mechanisms as detected by Quantitative Sensory Testing

1. Compared to the normal data available, all cutaneous sensory fibre groups (Aβ, Aδ and C-fibres) from torture victims' feet except those transmitting cold pain and heat pain were less sensitive to external stimuli. Since this occurred also in victims not exposed to falanga a central desensitisation must be postulated.
2. Most victims displayed deep mechanical hyperalgesia, irrespective of whether having been exposed to falanga or to other forms of torture. This indicates that

central sensitization may be a general phenomenon after torture. Peripheral sensitization may also play a role.

3. Taken together, it is likely that the predominating pain type in the victims' feet is neuropathic and of a post-traumatic nature.

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