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Relationship to pain, cognitive impairments, and negative appraisals

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Relationship to pain, cognitive impairments, and negative appraisals

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LUND
UNIVERSITY

DOCTORAL DISSERTATION

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Abstract

Refugees, particularly those exposed to torture and other forms of organized violence, often experience a wide range of difficulties, including posttraumatic stress disorder (PTSD), depression, and somatic disturbances, particularly pain. Multimodal treatments have been developed to target this comorbidity in refugees, with evidence suggesting they are moderately effective.

The overall aim of this thesis was to identify ways in which we might improve the efficacy of the multimodal treatment provided to tortured refugees seeking treatment for PTSD, depression, anxiety and somatic complaints. This was done by exploring the relationship between pain and PTSD in this population, at a specialist outpatient clinic in Copenhagen; DIGNITY – Danish Institute Against Torture, both at a symptom level, and at the level of two cognitive processes that had previously been shown to be important to the severity, duration, and impact of PTSD (negative trauma-related beliefs) and pain (pain catastrophizing). Another way of identify ways to improve treatment, was to find out to what extent the clients suffered from cognitive impairments based on a brief screening measured developed for this purposes (SDMT), and whether such impairments were related to traumatic brain injury (TBI), severity of PTSD, depression, anxiety, pain and overall functioning. With these aims, we hoped to help fill important informational gaps in the literature regarding the extent of pain, cognitive impairments and TBI in traumatized refugees.

Study I: The primary aim of the paper was to explore whether pain and disability levels in tortured refugees seeking treatment at DIGNITY were higher than previously estimated in a Danish validation study, and comparable to or exceeding the levels of pain and disability in mixed pain patients presenting for treatment at specialist pain services in Sweden.

Study II: The aim was to explore whether the relationship between pain and PTSD was mediated by pain catastrophizing and negative trauma-related beliefs pre-treatment, and consistent with recommendations from the literature, after controlling for the possible effects of depression on both pain and PTSD.

Study III involved an exploration of the impact of pain symptoms on PTSD, depression, and anxiety outcomes in refugees undergoing the multi-disciplinary treatment at the clinic. The primary aim was to test whether pre-treatment levels of pain predicted outcomes.

Study IV involved an exploration of the severity of cognitive impairments in refugees treated at the clinic, and their relationship to traumatic brain injury (TBI) and the severity of symptoms of PTSD, depression, anxiety, and pain at pre-treatment.

The findings add to a large body of literature suggesting a strong relationship between pain, PTSD, depression, and high levels of disability in traumatized refugees. It shows that interference from pain can lessen the effectiveness of standard multi-modal treatments for refugees. Difficulties in cognitive functioning is also shown to be a significant contributor to overall distress in tortured refugees, suggesting the need for routine screening of head trauma and cognitive impairments.

Key words Torture, trauma refugees, PTSD, pain, treatment, predictors, cognitive impairment, TBI

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To Sonja and Harry for putting everything else in perspective

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Abstract

Refugees, particularly those exposed to torture and other forms of organized violence, often experience a wide range of difficulties, including posttraumatic stress disorder (PTSD), depression, and somatic disturbances, particularly pain. Multimodal treatments have been developed to target this comorbidity in refugees, with evidence suggesting they are moderately effective.

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The findings add to a large body of literature suggesting a strong relationship between pain, PTSD, depression, and high levels of disability in traumatized refugees. It shows that interference from pain can lessen the effectiveness of standard multi-modal treatments for refugees. Difficulties in cognitive functioning is also shown to be a significant contributor to overall distress in tortured refugees, suggesting the need for routine screening of head trauma and cognitive impairments.

Summary in Swedish

Flyktingar, speciellt de som varit utsatta för tortyr och annan form av organiserat våld, upplever ofta en rad olika svårigheter, inklusive posttraumatiskt stressyndrom (PTSD), depression och somatiska symtom, särskilt smärta. Multidisciplinär behandling har utvecklats för att handskas med denna komorbiditet hos flyktingar, som har påvisat medelhöga effekter.

Det huvudsakliga syftet med denna avhandling var att undersöka och identifiera sätt att förbättra effektiviteten av multidisciplinär behandling för flyktingar som överlevt tortyr och söker behandling för PTSD, depression, ångest och somatiska symtom (t.ex. smärta). Detta utfördes genom att undersöka relationen mellan smärta och PTSD hos patienter vid en högspecialiserad öppenvårdsklinik i Köpenhamn: DIGNITY – Dansk Institut Mod Tortur. Relationen mellan smärta och PTSD studerades både på symtomnivå och genom att undersöka två typer av kognitiva processer som tidigare visats vara viktiga för svårighetsgraden, varaktigheten och inverkan av PTSD (negativa traumarelaterade kognitioner) och smärta (smärtkatastrofiering).

Ytterligare sätt att förbättra behandlingen, var att identifiera i vilken utsträckning klienterna led av kognitiv nedsättning baserat på en kort screening (SDMT) och om sådan nedsättning var relaterad till traumatisk hjärnskada (TBI), svårighetsgrad av PTSD, depression, ångest, smärta och generell funktionsnivå. Med dessa syften hoppades vi fylla viktiga kunskapsluckor i litteraturen avseende smärta, kognitiv nedsättning och TBI för traumatiserade flyktingar.

Studie I: Det primära syftet i denna studie var att undersöka om smärtnivåer och funktionsnedsättning för torterade flyktingar som söker vård på DIGNITY var större än tidigare redovisade nivåer i en liknande dansk population. Vi undersökte även huruvida smärtnivå och funktionsnedsättning var jämförbara med patienter som söker vård på specialistkliniker för smärta i Sverige.

Studie II: Syftet var att undersöka om relationen mellan smärta och PTSD medierades av negativa kognitioner (smärtkatastrofiering och negativa

traumarelaterade kognitioner). I överensstämmelse med litteraturen kontrollerades även effekten av depression på både smärta och PTSD.

Studie III utforskade hur smärtsymtom påverkar effekten av PTSD, depression och ångestsymtom på flyktingar som genomgått en multidisciplinär behandling på samma klinik. Det primära syftet var att testa om pre-nivåer av smärta predicerade behandlingsresultaten för dessa symtom.

Studie IV utforskade svårighetsgraden av kognitiva nedsättningar hos flyktingar som behandlas på kliniken och relationen mellan dessa svårigheter och traumatisk hjärnskada (TBI), graden av PTSD, depression och ångestsymtom och smärta innan behandling.

Resultaten kan adderas till en omfattande litteratur som påvisar ett starkt samband mellan smärta, PTSD, depression och höga nivåer av funktionsnedsättning hos traumatiserade flyktingar. Resultaten visar att grad av smärtpåverkan (pain interference) kan minska behandlingseffekterna i en standardiserad multidisciplinär behandling för flyktingar. Kognitiva nedsättningar visade också vara signifikant bidragande till de allmänna besvären som denna population av flyktingar med PTSD upplever, vilket antyder att det finns ett stort behov att rutinmässigt undersökta TBI och kognitiva svårigheter i populationen.

List of studies

I. Harlacher, U., Nordin, L., & Polatin, P. (2016). Torture survivors' symptom load compared to chronic pain and psychiatric in-patients. *Torture, 26*(2), 74-84. DOI: https://doi.org/10.7146/torture.v26i2.108204

II. Nordin, L., & Perrin, S. (2019). Pain and Posttraumatic Stress Disorder in refugees who survived torture: The role of pain catastrophizing and trauma-related beliefs. *Euroupean Journal of Pain*. DOI:10.1002/ejp.1415

III. Linda Nordin & Sean Perrin (2019) Pre-treatment pain predicts outcomes in multimodal treatment for tortured and traumatized refugees: a pilot investigation, *European Journal of Psychotraumatology.* 10:1. DOI: 10.1080/20008198.2019.1686807

IV: Nordin, L., Perrin, S., & Rorsman, I. Cognitive Impairment in Tortured and Traumatized Refugees with Traumatic Brain Injury. – *Manuscript in preparation.*

Abbreviations

BPI = Brief Pain Inventory

CBT = Cognitive Behavioral Therapy

CSQ-CAT = Coping Strategies Questionnaire, Catastrophizing Subscale

DIGNITY = Danish Institute Against Torture

DRI = Disability Rating Index

HADS = Hospital Anxiety and Depression Scale

HTQ = Harvard Trauma Questionnaire

HSCL-25: Hopkins Symptom Checklist-25

MCAR = Missing Completely at Random

NET – Narrative Exposure Therapy

PC = Pain Catastrophizing

PTCI = Posttraumatic Cognition Inventory

PTSD = Posttraumatic Stress Disorder

SDMT = Symbol Digit Modality Test

TBI - Traumatic Brain Injury

TRB = Trauma Related Beliefs

WHODAS = World Health Organization Disability Assessment Schedule

Introduction

One Torture Survivor's Experience

Ali [all identifying details are changed or withheld] is 38 years old but he looks much older. He walks with a limp and his shoulders are uneven. He suffers from osteoarthritis and chronic pain. He struggles to move his arms normally, and there is visible scarring (burn marks) on his hands and forearms. He is married and has one child - a daughter aged 16 years. They live together in a small, one bedroom flat in Copenhagen. Ali usually sleeps on the couch as he struggles to fall asleep until middle of the night because of pain, mainly in his shoulders. He wakes up frequently in a cold sweat from nightmares. He has lived in Denmark for 13 years but has not been able to achieve more than a basic level of Danish. He has tried repeatedly to learn the language but simply cannot concentrate on his studies. Ali has tried to hold various jobs over the years as a cleaner but struggles with constant pain and feelings of depression and anxiety.

Ali has happier memories of his childhood in his home country, although these memories become harder and harder for him to recall. Everything changed when he was about 17 years of age, just after he made a single negative comment about the leader of his country to a few friends while sitting in a café. Someone at the café (or perhaps one of his friends) told the police about his negative comment and soon after the police came to his parents' house and arrested him. He was not told why he was arrested, nor was there a trial. He was placed into a tiny cell with several other adult men. The conditions were horrible and they were all given a single meal per day.

On his second night in the prison, guards entered the cell and dragged him to another room. They took turns beating him with their fists and feet. After they had beaten him, they began to ask him about his connections to the opposition. No matter what he said, they did not believe him and would beat him, then threaten to kill him and his family. Each night he was woken from his sleep and dragged into another cell and beaten. His guards soon advanced the torture and began to apply

electric shocks to the most sensitive parts of his body. They were also beating other prisoners to death in front of him and tried to force him to beat other prisoners. One night he was taken into another cell, only to find his sister tied up and crying. They again demanded information from Ali, and when he could not provide any, they beat and raped his sister.

After a few months of repeated torture, Ali was released from prison but government agents constantly watched him. His family introduced him to a woman and they eventually fell in love and married. He tried to find work but with no predictability, he would suddenly be arrested, tortured, and then released again after a month or so. His wife became pregnant with their daughter and Ali did his best to find work and support his family. However, after being arrested and then released with terrible bruises over his head and body, Ali's parents arranged to have him taken out of the country. It took their whole life-savings and borrowings from relatives. Ali did not want to leave his family behind but knew if he stayed he would be killed. His parents told him that his wife and daughter would soon follow him.

Ali left his country, hidden in the back of trucks, and then climbing over the mountains into a neighboring country. In the mountains he saw the dead bodies of women and children who had tried to flee. After several months of extreme deprivation, beatings by gangs and police, he arrived in Denmark and claimed asylum. A year later his wife and daughter escaped and the family were reunited in Denmark.

The joy of him seeing his family again was short-lived for Ali. His daughter resembled his sister who had been raped by his prison guards and looking at her could trigger terrible intrusions and worries that something would happen to his daughter. He knew he had to provide for his family but he struggled to learn Danish or to hold down a job. He was in constant pain and intrusive thoughts about his torture, and overwhelming feelings of guilt, left him feeling paralyzed. He stopped going out of the apartment and took to long periods lying in bed. His family eventually dragged him to the doctor and told about his nightmares and flashbacks, and the constant pain. The doctor referred him for multidisciplinary treatment at DIGNITY.

I was working as the psychologist in the team that treated Ali. Except for me, the team consisted of a medical doctor, physiotherapist and social counselor. We were the first mental health professionals that Ali had ever met in his life. All he knew about "shrinks" was what he'd heard from family and friends in his home country,

i.e., they were just another instrument of torture. He eventually began to trust us and his reluctance to talk about what happened to him began to ease. In psychotherapy, we focused on creating a narrative of a recurring intrusion that involved his hands being tied behind his back and his wrists being lifted in the air, and hearing his sister screaming in pain. These intrusions often triggered beliefs that he was responsible for his sister's rape because he had made a stupid comment about the regime to a friend. He believed his intrusions and nightmares were a form of punishment for his "crime" and stupidity, and the symptoms would thus never leave him.

Sometimes when Ali would describe the traumatic events in sessions, he would begin to rub his shoulder and wrists, in obvious physical discomfort. At times he would stop the exposure completely and say the physical pain he was experiencing in his shoulders and wrists was simply too intense to ignore and he could not remember what happened to him. He would say that his body had been "destroyed" by the torture and the pain made it impossible for him to be a good husband and father. He did not believe that he could live any kind of meaningful life with this chronic pain he was experiencing.

As we worked on his intrusions (exposure) and low mood (behavioral activation), it was clear that his ongoing physical pain was a serious impediment to his progress in treatment. The pain triggered traumatic intrusions and the intrusions intensified his experience of pain. His understandable but catastrophic thoughts about his pain contributed to his feelings of hopelessness and depression, as much as his guilt about his sister and his traumatic intrusions.

The physiotherapist in the team worked closely with him to cope better with his pain and his constant feelings of anxiety. The social counselor helped Ali to become a more active agent in his own life and network, and educated him in how the Danish society works. The medical doctor helped Ali with medication, to understand what kind of injuries he had gotten during torture, and referred him to a specialist for his asthma that was not properly treated.

As a team, we struggle at times with the focus of the treatment; Ali was both in so much mental and physical pain. When we worked on the PTSD the physical pain sometimes seamed to worsen, and vice versa. We know that refugees with torture experiences similar to Ali, and with chronic pain, can derive clinically meaningful benefits from trauma-focused psychotherapy and the physiotherapy offered in the clinic. However, it is difficult to predict which patients are less likely to benefit

from this approach, and thus how we might modify treatment to improve its efficacy. This program of research aimed to help address this important question.

At the end of treatment Ali was not as scared of the horrific memories anymore. He understood that they would always be there, but now he could think about them without them disturbing him as much as they had done before. Ali could not go back to work; his body couldn't manage any physical labor anymore. Ali had begun taking Danish classes again and he now spent time with family and friends. He was no longer depressed and he could again see a future for himself and his family. He could even feel joy in his life, especially when he was together with his family, something he could not when he first entered treatment.

Overview

According to the United Nations Convention 51 (UN High Commissioner for Refugees (UNHCR). 2010), a refugee is someone who is outside of their country, and unable or unwilling to return due to a well-founded fear of being persecuted for reasons of race, religion, nationality, membership of a particular social group, or political opinion. Between 2009 and 2018, the number of refugees worldwide grew from 43.3 million to 70.8 million, a record high (UN High Commissioner for Refugees (UNHCR). 2019). It is important to point out that the majority of refugees worldwide do not reach the shores of Western countries, they remain internally displaced or in neighboring countries (UNHCR, 2019).

Refugees and asylum seekers are disproportionately exposed to extreme stressors, including major losses and potentially traumatic events such as torture and war exposure, both before and during displacement, that are capable of causing severe long-term health-related difficulties, including mental health problems (Bogic et al., 2012; Priebe, Giacco, & El-Nagib, 2016). In addition, refugees encounter post-displacement stressors that can negatively impact their future mental health, including resettlement difficulties, language barriers, perceived stigma and discrimination (Kirmayer et al., 2011; Miller & Rasmussen, 2010). Meeting the health and mental health needs of refugees represents a significant challenge to host countries and individual healthcare providers (Satinsky, Fuhr, Woodward, Sondorp, & Roberts, 2019).

Torture, Trauma, and Mental Health in Refugees

Deliberate human cruelty through the infliction of physical and psychological torture, is one of the most severe traumatic experiences one can encounter (Steel et al., 2009). The most used definition of torture is Article 1 of United Nations Convention Against Torture:

"...any act by which severe pain or suffering, whether physical or mental, is intentionally inflicted on a person for such purposes 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. It does not include pain or suffering arising only from, inherent in or incidental to lawful sanctions."

- United Nations Convention Against Torture, Article 1.1 (United Nations. General Assembly, 1984).

In research on violence and refugees, this definition is often extended to include violence from unofficial members of society, i.e. as in civil conflicts (United Nations. General Assembly, 1984). It is important to note that torture does not usually consist of a single traumatic event but exposure to a series of extreme traumas with purposeful and severe impact (Steel et al., 2009). Torture survivors also report that the time spent waiting between these multiple torture episodes, when imagining the worst possible torture scenario, to be as traumatic as the torture itself (Basoglu, 2009).

Despite a worldwide ban by the United Nations, ratified by 158 countries, torture is still widely practiced by nation states and groups of individuals with nations acting in a quasi-governmental capacity. Amnesty International has identified systematic use of torture and other ill-treatments being practiced in 141 countries (Amnesty International, 2014). The prevalence of torture exposure among refugee populations differs across studies, but is generally acknowledged to be quite high (30–76%) (Masmas et al., 2008; Sigvardsdotter, Vaez, Rydholm Hedman, & Saboonchi, 2016). It is important to note that only a minority of torture survivors arrive as refugees in Western countries where they are more likely to be included in epidemiological studies; many die during torture or are simply too disabled or poor to find their way to safety (de Williams & van der Merwe, 2013).

It has been established that refugees in general, and torture survivors in particular, have high rates of mental and somatic health problems (discussed below). In addition, it is now increasingly acknowledged that while pre-migration experiences, including traumatic exposures (and particularly torture), significantly raises the risk of mental health problems, the prevalence of mental health problems among refugees likely reflects the cumulative effects of multiple stress exposures over a lifetime (Hollifield, Warner, Krakow, & Westermeyer, 2018; Hynie, 2018). In addition to pre-migration factors (including trauma), the act of migration can itself involve exposure to further traumas, and at the very least, extreme forms of stress. Also, the refugee faces significant stressors in their new country, including uncertainty about their asylum status, separation from family members, employment and housing difficulties, loss of status, poverty, prejudice and sometimes organized violence against refugees (Hynie, 2018). For refugees resettled in a new country, the presence of physical and mental health problems is associated with difficulties integrating into the new society (e.g., becoming language proficient and financially independent), which further contributes to overall levels of disability (Schick et al., 2016).

Mental Health Problems in Refugees

The past 15 years has seen a growing number of systematic reviews and meta-analyses of studies examining the mental health of refugees (Abu Suhaiban, Grasser, & Javanbakht, 2019; Fazel, Wheeler, & Danesh, 2005; Hollifield et al., 2018; Hynie, 2018; Morina, Akhtar, Barth, & Schnyder, 2018; Slewa-Younan, Uribe Guajardo, Heriseanu, & Hasan, 2015; Steel et al., 2009; Teodorescu et al., 2015; Turrini et al., 2017). Overall, the same range of mental health problems identified in traumatized non-refugee populations are found in refugees but the most common (and frequently studied) are posttraumatic stress disorder (PTSD), depression, anxiety, and somatic complaints (e.g., migraine and musculoskeletal pain) (Morina et al., 2018; Rometsch-Ogioun El Sount et al., 2019; Teodorescu et al., 2015; Turrini et al., 2017). It is important to note that prevalence rates for PTSD and other mental health problems in refugees vary widely across studies, and depending upon (among other issues) the method of assessment, the time-since trauma, and whether the refugee is internally or externally displaced (Morina et al., 2018).

Based on studies with the strongest methods, estimates for the prevalence for PTSD in refugees range from 9% to 36%, and for depression and anxiety disorders

between 4% and 44% (Turrini et al., 2017). In respect of PTSD in refugees who have been tortured, an early meta-analysis by Steel et al. (2009) found an average prevalence rate of approximately 31%. A more recent review by Abu Suhaiban et al. (2019) reported estimates for PTSD ranging from 23% to 88%.

Comorbidity between PTSD, depression, and anxiety at the symptom and disorder level is common (> 65%) among refugees (Close et al., 2016; Fazel et al., 2005; Lindert, Ehrenstein, Priebe, Mielck, & Brahler, 2009). Another common form of comorbidity alongside PTSD and depression in refugees is chronic pain (Carinci, Mehta, & Christo, 2010; Steel et al., 2009; Williams, Pena, & Rice, 2010). While no meta-analyses have investigated the prevalence of chronic pain conditions in refugees selected because of trauma exposure, Rometsch-Ogioun El Sount et al., (2019) carried out a meta-analysis of chronic pain in the subset of refugees seeking treatment for PTSD. Across studies, between 50% and 94% reported headaches, and 72% to 85% reported leg pain, followed by other pain localizations (pelvis, stomach, chest, and unspecified or diffuse locations).

Negative Trauma-Related Appraisals and PTSD

According to the fifth edition of the Diagnostic and Statistical Manual for Mental Disorders (American Psychiatric Association., 2013), PTSD involves (direct or indirect) exposure to a traumatic event, followed by the development of symptoms from four symptom clusters: intrusion; avoidance; negative alterations in cognitions and mood; and alterations in arousal and reactivity. The criteria are similar to those in the latest (11^{th}) edition of the International Classification of Diseases (World Health Organization., 2018). The reasons why some (but not all) individuals exposed to a traumatic event go on to develop chronic symptoms of PTSD are complex, likely involving an interaction between genes, alterations in brain functioning during and after the trauma, and a range of pre-and post-trauma psychosocial factors (Blacker, Frye, Morava, Kozicz, & Veldic, 2019; DiGangi et al., 2013; Shvil, Rusch, Sullivan, & Neria, 2013).

While not excluding the possibility of biological risk factors, psychological models of PTSD have tended to focus on the way the trauma is represented in memory, including the meaning of the event and its consequences to the individual (e.g., trauma-related beliefs) (Brewin & Holmes, 2003; Elwood, Hahn, Olatunji, & Williams, 2009). According to these models, some individuals become

preoccupied with the most vivid and distressing, sensory and emotional aspects of the event during the trauma and in its immediate aftermath. This form of "data-driven" processing is believed to interfere with encoding of contextual cues that link the traumatic event to a specific time, place, persons, actions and outcomes; contextual cues which make it less likely that the trauma memory will be inadvertently reactivated by contact with reminders (Brewin, Dalgleish, & Joseph, 1996; Ehlers & Clark, 2000; Halligan, Michael, Clark, & Ehlers, 2003).

For these individuals, subsequent reactivations of the trauma memory often involves vivid recollections of the most distressing sensory and emotional aspects of the trauma, which are again processed in a data-driven way (i.e., ignoring current contextual cues for safety), leading to a current sense of threat (Halligan et al., 2003). In turn, the intrusions trigger repeated (and usually unsuccessful) attempts at memory/emotional suppression and avoidance of traumatic reminders. These suppression/avoidance strategies prevent processing of the trauma memory, i.e., the incorporation of important contextual cues into the trauma memory, which reduces the likelihood of future traumatic intrusions.

The recurrence of intrusive recollections of the memory, despite efforts to suppress and avoid them, along with events that occur during and after the trauma, facilitate the development of negative, trauma-related appraisals. These appraisals reflect an increased sense of personal vulnerability to harm in a now more dangerous and uncaring world, and an increased sense of personal responsibility for traumatic events that have or may occur (Ehlers & Clark, 2000). Such beliefs contribute to an increased vigilance for threat cues that makes further traumatic intrusions, avoidance and other dysfunctional responses more likely, and to contribute to low mood and intense feelings of guilt, hopelessness, and isolation (Dunmore, Clark, & Ehlers, 1999, 2001; E. B. Foa, Ehlers, Clark, Tolin, & Orsillo, 1999). Systematic reviews of the literature have repeatedly found that the presence of negative trauma-related appraisals are associated with an increased risk for developing PTSD and depression in the aftermath of a trauma, and are strongly associated with the severity and duration of both disorders (Heron-Delaney, Kenardy, Charlton, & Matsuoka, 2013; LoSavio, Dillon, & Resick, 2017; Ozer, Best, Lipsey, & Weiss, 2003).

Pain Catastrophizing and Pain

The International Association for the Study of Pain has defined chronic pain as pain lasting for more than 3 months, persisting even though the initial injury is healed (Treede et al., 2019). Not everyone who develops symptoms of chronic pain has suffered an injury; the pain may be a consequence of an underlying disease process or syndrome (e.g., rheumatoid arthritis, fibromyalgia, migraine, endometriosis), of surgery or other medical interventions (e.g., cancer treatments), or reflect no disease process/injury at all (Raffaeli & Arnaudo, 2017). Pain can negatively impact every aspect of an individual's day-to-day life, including their cognitive, emotional, behavioral, family and social functioning (Duenas, Ojeda, Salazar, Mico, & Failde, 2016). Worldwide, chronic pain is identified as a significant contributor to disability, reduced quality of life, and higher healthcare costs (Rice, Smith, & Blyth, 2016). Whatever its causes, the experience of pain, and how the individual responds to pain, are both influenced by a number of different psychological factors (Linton & Shaw, 2011).

One of the first, and most studied, psychological factors in relation to the severity and impact of chronic pain is *pain catastrophizing* (Edwards, Bingham, Bathon, & Haythornthwaite, 2006; Flink, Boersma, & Linton, 2013; Linton & Shaw, 2011; Quartana, Campbell, & Edwards, 2009). Catastrophizing was first identified as a maladaptive cognitive process of importance to the development and maintenance of depression and anxiety (Beck, Rush, Shaw, & Emery, 1979). Accordingly, contact with a stressor led some individuals to focus on the most fearful/distressing aspects of the stressor, and to imagine, and then ruminate upon various 'worst-cases scenarios', leading to a heightened sense of distress, of being overwhelmed by the stressor, and other dysfunctional responses (e.g., avoidance, blame, excessive reassurance seeking) (Beck et al., 1979). Catastrophizing was thought to emerge from generalized schema involving beliefs that negative events were frequent, difficult to prevent or to cope with, and likely to have long-term negative effects for the individual (Beck et al., 1979).

The definition of pain catastrophizing has evolved over the years and been influenced by the development of brief self-report measures designed to assess this construct (Quartana et al., 2009). As initially described, pain catastrophizing was thought to involve a tendency to magnify or exaggerate the potential harm to the individual from the pain sensations, difficulty disengaging from these pain signals, and a general tendency to be fearful of and worried about pain (Quartana et al., 2009). Two self-report scales were developed to assess this construct, the pain

catastrophizing subscale of the Coping Style Questionnaire (CSQ-CAT; used in the present thesis) (Rosentiel & Keefe, 1983) and the Pain Catastrophizing Scale (PCS) (M. J. L. Sullivan, Bishop, & Pivik, 1995). The items of the catastrophizing subscale of the CSQ were used (together with other items) to construct the Pain Catastrophizing Scale (PCS). Factor analyses performed on the Pain Catastrophizing Scale produced (but not always) three factors reflecting (magnification, rumination and helplessness) (Sullivan et al., 2001). The pain catastrophizing items of the CSQ-CAT (included in the PCS) loaded most highly on the helplessness factor. Accordingly, when confronted with pain sensations, individuals with a tendency to catastrophe focus intently on these sensations, appraising/interpreting them as signs of serious injury/disease (magnification), then ruminating about the potential causes and consequences of the pain, with increasing feelings of helplessness in respect of their ability to reduce, manage, or cope with the pain and its consequences (Sullivan et al., 2001).

Why some individuals engage in pain catastrophizing and others do not remains uncertain (Quartana et al., 2009). A recent meta-analysis of fMRI studies found an association between the strength of pain catastrophizing (measured with standardized self-report scales) and activity in brain regions associated with pain perception and modulation (Galambos et al., 2019). There is also evidence from twin studies that pain catastrophizing may be a heritable trait that is then influenced by the individual's experiences with pain, and the way that others around the person, including the medical community, attend and respond to complaints about pain (Burri, Ogata, Rice, & Williams, 2018).

Flink et al. (2013) have argued that pain catastrophizing is essentially a dysfunctional form of problem solving, the aim of which is to minimize the negative emotions that are triggered by pain and other stimuli. In this respect, pain catastrophizing is similar to the 'rumination as problem-solving gone wrong' argument made in cognitive models of depression and anxiety (Nolen-Hoeksema, 1991; J. M. Smith & Alloy, 2009). There is a growing body of evidence suggesting that rumination (which arguably includes catastrophizing) is important to the severity and maintenance of symptoms across a wide range of disorders (Kim & Eaton, 2015; Nolen-Hoeksema & Watkins, 2011).

It is important to point out that in current psychological models of chronic pain, including the fear-avoidance (Vlaeyen & Linton, 2000, 2012) and psychological flexibility models (McCracken & Vowles, 2014), pain catastrophizing is only one of a number of different psychological processes thought to contribute to the

severity, duration, and functional impact of chronic pain symptoms. Nevertheless, systematic reviews of the literature routinely find that scores on self-report measures of pain catastrophizing are strongly associated with the severity and chronicity of pain symptoms, and with pain-related disability, in both healthy individuals and those with a diverse range of health conditions (Edwards et al., 2006; Keefe, Rumble, Scipio, Giordano, & Perri, 2004; Lewis, Rice, McNair, & Kluger, 2015; Quartana et al., 2009; Sullivan et al., 2001). However, and despite the high prevalence of chronic pain in refugees, particularly survivors of torture, relatively few studies have examined pain catastrophizing in this population.

Relationship Between PTSD and Pain in Refugees

As noted above, among the various forms of comorbidity found alongside PTSD and depression in traumatized refugees, recurrent symptoms of pain are among the most common (Carinci et al., 2010; Steel et al., 2009; Williams et al., 2010). These findings of comorbidity in refugees are consistent with the broader literature on mental health difficulties in trauma-exposed populations. For example, approximately 50% of people injured because of combat or motor vehicle accidents develop both PTSD and chronic pain (Fishbain, Pulikal, Lewis, & Gao, 2017). In refugees, it appears that comorbid pain symptoms have impacts on functioning and quality of life that are separable from and additive to those of PTSD and depression (Buhman et al., 2014; Carinci et al., 2010; Olsen, Montgomery, Bojholm, & Foldspang, 2007). Furthermore, when refugees report both PTSD and chronic pain, the severity, duration, and functional impact of the two conditions tends to be increased (Ruiz-Parraga & Lopez-Martinez, 2014).

Such observations have led to the development of theoretical models that aim to help explain the high degrees of comorbidity between PTSD and chronic pain (for an example, see Figure 1.) (Asmundson, Coons, Taylor, & Katz, 2002; Asmundson & Katz, 2009; Norton & Asmundson, 2003; Otis, Keane, & Kerns, 2003; Sharp & Harvey, 2001). What these models share is the argument that there probably exists a number of different personal vulnerabilities (both biological and psychological) that increase the likelihood of an individual developing PTSD and chronic pain in the aftermath of a trauma, and/or shared vulnerabilities which exacerbate and prolong both conditions once they develop (Otis et al., 2003).

As mentioned above, in cognitive models of PTSD, negative trauma-related beliefs are viewed as a trauma-specific form of cognitive bias that arises partly because of a biased attention to and misinterpretation of threat cues, particularly but not exclusively traumatic reminders (Elwood et al., 2009). In the fear-avoidance model of pain (Vlaeyen & Linton, 2000), pain catastrophizing plays an important role in the development of a heightened fear of pain, vigilance to pain signals, avoidance and disability. Both negative trauma-related beliefs and pain catastrophizing can be viewed as disorder-specific instances of cognitive bias. This is interesting since among the various personal characteristics identified in the shared vulnerability and mutual maintenance models of PTSD and pain, cognitive biases are common to all of them. Specifically, the different models suggest that a heightened awareness of (and attention to) potential threat cues, including bodily sensations involved in anxiety and pain, combined with a tendency to misinterpret (exaggerate) the degree of harm/injury signaled by these cues, may increase the risk for and severity and duration of both PTSD and chronic pain (Otis et al., 2003).

Both pain catastrophizing and negative trauma-related beliefs are understudied constructs in refugee populations. This is unfortunate given accumulating evidence from accident victims that catastrophizing, and pain catastrophizing in particular, mediates the relationship between pain intensity and PTSD (Andersen, Karstoft, Brink, & Elklit, 2016; Carriere, Martel, Meints, Cornelius, & Edwards, 2019; Pedler, Kamper, & Sterling, 2016). Likewise, there is a large body of evidence that negative trauma-related beliefs there are associated with increased PTSD severity, comorbidity, and functional impairment in trauma-exposed individuals (Heron-Delaney et al., 2013; Ozer et al., 2003). Identification of factors that contribute to both the severity and duration of PTSD and pain in refugees holds the promise of improving the efficacy of current treatments for this population.

The studies in this thesis focus on different aspects of this shared vulnerability between PTSD and pain (Figure 1). The figure is used below to describe which of the parts in the model that each study focuses on.

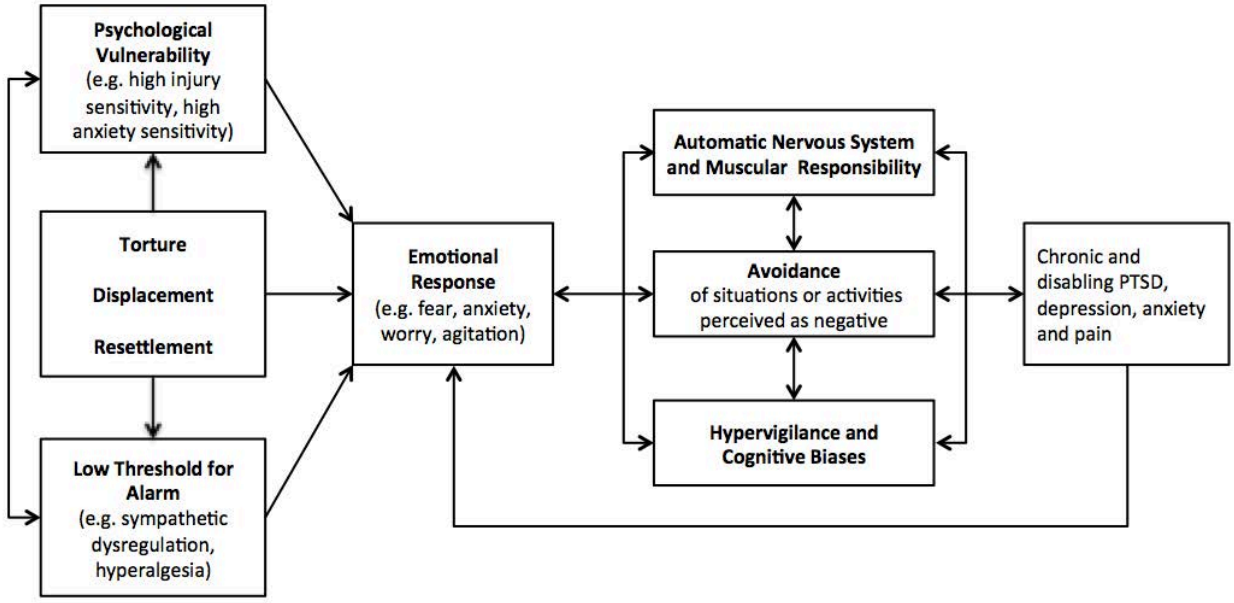

Figure 1. Shared Vulnerability Model (Asmundson & Katz, 2009)

Traumatic Brain Injury and Cognitive Impairment

The available literature suggests that exposure to torture is one of the single strongest determinants of PTSD and chronic pain in refugees (Abu Suhaiban et al., 2019; Rometsch-Ogioun El Sount et al., 2019; Steel et al., 2009). Another potential contributor to both of these conditions is a history of head injuries and/or exposure to other types of events capable of causing brain injury (e.g., explosive blasts, asphyxiation, and whiplash) (Nampiaparampil, 2008; Perry et al., 2016). Refugees are more likely than the general population to have experienced physical assaults, injuries and/or torture but relatively few studies have investigated the prevalence or consequences of traumatic brain injuries (TBIs) in this population (McPherson, 2019). This is unfortunate because the types of injuries sustained during torture are themselves associated with a higher incidence of neurological sequelae, including impairments in various aspects of executive functioning (e.g., attention, memory, cognitive control) suggestive of TBI (Keatley, Ashman, Im, & Rasmussen, 2013; Moreno & Grodin, 2002). Likewise, exposure to traumatic events in general, which is elevated among refugees, is associated with an increased risk of head injuries or experiences known to produce TBI's and cognitive impairments (e.g., suffocation, inhalation of toxic substances, rapid acceleration of the head) (Bradley & Tawfiq, 2006; Keatley et al., 2013).

Definitions of TBI vary but they are generally described in the literature as an "alteration in brain function, or other evidence of brain pathology, caused by an external force" (Menon et al., 2010). The severity of TBIs are usually graded mild, moderate or severe based on scores from the Glasgow Coma Scale and the duration of loss of consciousness and posttraumatic amnesia (McKee & Daneshvar, 2015). The relationship between these severity categories of TBI, neuropathology and functional outcomes are all three grades of TBI are capable of producing significant and long-lasting impacts on all aspects of day-to-day functioning (Tsyben et al., 2018)

Again, and despite the high rate of exposure to events capable of producing TBIs, relatively few studies have reported upon TBIs in refugees (McPherson, 2019). Similar to other conditions, prevalence estimates for TBIs in refugees vary widely based on characteristics of the sample and the methods by which head injury and TBIs are assessed. A study of refugees seeking treatment for mental health problems at a specialist clinic for torture survivors in the USA found that 69% reported at least one significant blow to the head with half of these individuals losing consciousness as a result (Keatley et al., 2013). A study of Vietnamese torture survivors resettled in Boston found that 78% had experienced a TBI as a direct consequence of their torture experiences (Mollica et al., 2014). A study of UK refugees presenting for treatment at a community clinic for traumatized individuals found 51% to have had a TBI, with half of these individual's TBI being directly tied to their experience of torture (Doherty, Craig, Gardani, & McMillan, 2016).

There is a large body of evidence that finds cognitive impairments to be common among individuals who have suffered from mild, moderate or severe TBIs (Karr, Areshenkoff, & Garcia-Barrera, 2014; Ruttan, Martin, Liu, Colella, & Green, 2008) including combat veterans (Karr, Areshenkoff, Duggan, & Garcia-Barrera, 2014). Likewise, cognitive impairments, including alterations in attentional control, task-shifting, inhibition, information processing speed, working- and long-term memory have been identified in trauma-exposed populations with PTSD and depression who have not had a TBI (Olff, Polak, Witteveen, & Denys, 2014; Parlar et al., 2017). It is important to point out that TBIs at the less severe end of the spectrum can produce changes in cognitive functioning similar to those found in individuals with PTSD alone (Cicerone et al., 2011). However, very few studies have reported upon cognitive impairments or their relationship to TBIs, PTSD, and depression in refugees (Ainamani, Elbert, Olema, & Hecker, 2017; Kivling-Boden & Sundbom, 2003).

This is unfortunate because there is now a growing body of evidence, based primarily on studies of combat veterans and individuals involved in road traffic accidents, with trauma-exposed comparison groups with no history of TBI, that have found a history of TBI (irrespective of cognitive impairments) is associated with a significantly increased risk of psychiatric disorder, including PTSD (Carlson et al., 2011; Perry et al., 2016). Also, the available evidence suggests that trauma-exposed individuals with TBIs and PTSD/depression have greater impairments in cognitive functioning (Nelson, Yoash-Gantz, Pickett, & Campbell, 2009) and poorer functional outcomes than those with TBIs or PTSD/depression alone (Pietrzak, Johnson, Goldstein, Malley, & Southwick, 2009; Polusny et al., 2011).

With respect to the relationship between TBIs and chronic pain, an early meta-analysis by Nampiaparampil (2008) found that 52% of civilians and 43% of combat veterans exposed to a TBI reported a chronic pain condition (primarily headaches), with individuals experiencing mild TBIs at greatest risk. The authors also found that the relationship between pain severity and TBIs was independent of the relationship between pain and PTSD/depression across studies. A recent US study involving 116,813 combat veterans found a similar prevalence (57%) for chronic pain conditions (Seal et al., 2017). When compared to combat veterans with no TBI, PTSD, or depression, the risk for chronic pain was elevated in veterans with mild TBIs, with the highest risk found for those with moderate to severe TBIs. However, and in contrast to the findings of the earlier meta-analysis, the authors found that the risk for chronic pain and pain-related disability was highest among combat veterans who had a TBI and both PTSD and depression. In a recent review of the available literature on the relationship between TBIs and chronic pain, Irvine and Clark (2018) concluded that while there was a strong association between the two conditions, the underlying mechanisms were poorly understood and further studies were needed of trauma-exposed populations other than combat veterans. To date, the relationship between TBIs, PTSD, and chronic pain in refugees has not been explored.

Treatment of Mental Health Problems in Refugees

In contrast to a large evidence base for the treatment of PTSD, depression, and anxiety in non-refugee, trauma-exposed populations (Bisson, Roberts, Andrew, Cooper, & Lewis, 2013; Kline, Cooper, Rytwinksi, & Feeny, 2018), relatively few randomized controlled trials have been carried out specifically with traumatized refugees. The existing studies focus either on trauma-focused monotherapies or

multimodal interventions targeting mental, physical, and social difficulties (Drozdek, 2015; Nickerson, Bryant, Silove, & Steel, 2011). Multimodal treatment programs are the most common for refugees and are designed to address the broad array of problems found in this population, including psychiatric disturbance and somatic complaints, social adaptation, and broader psychosocial difficulties (Drozdek, 2015). A recent meta-analysis found that the two most evaluated mono-therapies for PTSD in refugees are trauma-focused CBT and narrative exposure therapy (NET), both of which yield significant reductions in symptoms of PTSD (largely in comparison with no treatment controls) in resettled refugees (Nose et al., 2017).

The evidence base in respect of multimodal treatments is small with significant heterogeneity across studies making it difficult to draw firm conclusions about their comparative efficacy for PTSD, depression, and somatic complaints. The available studies suggest that a combination of multimodal and trauma-focused treatments in specialized clinics for refugees, including those exposed to torture, produces small to moderate reductions in PTSD, depression, and anxiety (Drozdek, Kamperman, Bolwerk, Tol, & Kleber, 2012; Drozdek, Kamperman, Tol, Knipscheer, & Kleber, 2014). Very few studies have reported on the effects of trauma-focused and multidisciplinary treatment on chronic pain outcomes in traumatized refugees (Baird, Williams, Hearn, & Amris, 2017; Rometsch-Ogioun El Sount et al., 2019).

Across all forms of treatment for PTSD in refugees, there is evidence, albeit limited, that the presence of comorbid difficulties including psychiatric and health-related conditions, employment/financial difficulties, offender status, and unresolved asylum claims, are associated with poorer outcomes (Haagen, Ter Heide, Mooren, Knipscheer, & Kleber, 2017; Porter & Haslam, 2005; Raghavan, 2013; Sonne et al., 2016; Stammel et al., 2017; Stenmark, Guzey, Elbert, & Holen, 2014). As noted above, recurrent pain is one of the most common comorbid complaints in refugees with PTSD and depression, with separable impacts on daily functioning. However, the impact of pain on PTSD and depression outcomes in treatment for refugees is understudied (Baird et al., 2017). A recent study by Sonne et al. (2016) found that pain severity predicted poorer depression, but not PTSD outcomes in a multimodal treatment for tortured refugees resettled in Denmark. Finally, the extent to which trauma-related beliefs and pain catastrophizing mediate the relationship between pain and PTSD in refugees, and their relationship to outcomes in mono and multimodal therapies for refugees with PTSD, depression, and/or chronic pain has not been examined.

General and Specific Aims

My overall aim at the start of this Ph.D. was to identify ways in which we might improve the efficacy of the multimodal treatment we provide to tortured refugees in the specialist outpatient clinic in Copenhagen (DIGNITY – Danish Institute Against Torture). My role in the clinic has been to provide individual, trauma-focused, cognitive behavioral therapy (CBT) focused on PTSD, depression, and anxiety. However, most of the refugees seen in the clinic report recurrent symptoms of pain, often linked to their experiences of torture, and involving blows to the head, violent shaking, and asphyxiation. They also report more general problems involving concentration and memory difficulties, which given the nature of their traumas could be evidence of a TBI.

In addition to individual trauma-focused psychotherapy, all of the patients at the clinic are offered weekly individual sessions with a physiotherapist to address pain and other somatic complaints, as well as input from a social worker to help with integration into society, and from a medical doctor to discuss health, medication (including pain medications) and referral to other specialist services (if needed). This multimodal, multidisciplinary approach is the most common form of treatment offered to refugees in specialist treatment centers across Europe and elsewhere (Drozdek, 2015).

I was aware of a growing literature suggesting that a mutually maintaining relationship might exist between pain and PTSD, and that better targeting of the variables that contributed to this relationship might improve outcomes in treatment for patients with both conditions. However, this research was still largely in an exploratory stage and the studies did not involve refugees. Finally, I was aware of research that found that cognitive impairments were common in individuals with TBIs and PTSD, but again few of these studies had been carried out with refugees. We were aware that many clients were reporting possible cognitive impairments but no formal methods were in place to investigate this aspect of functioning.

DIGNITY is not just a Copenhagen-based clinic for tortured and traumatized refugees, it is also a center for research on the effects of torture and treatment of torture survivors in Denmark and abroad. DIGNITY also carries out work and research in prevention of torture in urban areas and in detentions centers. At any one time, there are numerous research projects ongoing, and as a result, the refugees seen at the Copenhagen clinic have a high assessment burden. With this this in mind, I was able to add a standardized self-report measure of trauma-related

beliefs, pain catastrophizing and a brief, standardized measure to screen for cognitive impairments (Symbol Digit Modalities Test – SDMT) to the standard assessment protocol. Were it feasible, I would have added other measures identified in the literature as potential contributors to the relationship between pain and PTSD (e.g., arousal/reactivity, behavioral/cognitive avoidance, anxiety sensitivity, self-efficacy).

Thus, the primary research aim of my theses was to explore the relationship between pain and PTSD in this sample of tortured refugees seeking treatment for PTSD, depression, anxiety and somatic complaints. This was to be done at a symptom level, and at the level of two cognitive processes that had previously been shown to be important to the severity, duration, and impact of PTSD (negative trauma-related beliefs) and pain (pain catastrophizing). A secondary aim was to explore the extent to which the clients suffered from cognitive impairments based on a brief screening measured developed for this purposes (SDMT), and whether such impairments were related to traumatic brain injury (TBI), the severity of PTSD, depression, anxiety, pain and overall functioning. With these aims, we hoped to help fill important informational gaps in the literature regarding the extent of pain, TBI and cognitive impairments in traumatized refugees, particularly those who have been tortured, and how pain relates to the severity of PTSD (and related conditions) and outcomes in treatment for tortured refugees.

Study I involved a comparison of data on pain related disability, depression and anxiety, and disability in refugees treated at DIGNITY (previously RCT), with published data obtained from: 1) a validation study of the disability measure, involving the same data collected from another refugee treatment center and a psychiatric inpatient unit, both based in Denmark; and 2) the Swedish National Register for Pain Rehabilitation. The primary aim of the paper was to explore whether pain and disability levels in tortured refugees were higher than previously estimated in the Danish validation study, and comparable to or exceeding the levels of pain and disability in mixed pain patients presenting for treatment at specialist pain services in Sweden.

Study II involved an exploration of the relationship between pain and PTSD symptoms at pre-treatment in refugees seen at the clinic. The aim was to explore whether the relationship between pain and PTSD was mediated by pain catastrophizing and negative trauma-related beliefs, and consistent with recommendations from the literature, after controlling for the possible effects of depression on both pain and PTSD.

Study III involved an exploration of the impact of pain symptoms on PTSD, depression, and anxiety outcomes in refugees undergoing the multi-disciplinary treatment at the clinic. The primary aim was to test whether pre-treatment levels of pain predicted outcomes.

Study IV involved an exploration of the severity of cognitive impairments in refugees treated at the clinic, and their relationship to the severity of symptoms of PTSD, depression, anxiety, and pain at pre-treatment. It also aimed at evaluating whether those with a history of head injury and loss of consciousness (TBI) would report more severe cognitive impairments, PTSD, depression, anxiety, pain, and health-related disability than those with a history of head injury and no loss of consciousness.

Method

Design and Settings

The Danish Institute Against Torture (DIGNITY) is a self-governing institution with a government-funded clinic that provides inter-disciplinary, multi-modal treatment targeting PTSD, depression, social and health problems in refugees who are survivors of torture or other organized violence. There have been previous studies carried out with patients from this clinic reporting on PTSD, pain, general functioning and quality of life (Carlsson, Mortensen, & Kastrup, 2006; Carlsson, Olsen, Kastrup, & Mortensen, 2010; Olsen, Montgomery, Bojholm, & Foldspang, 2006; Olsen et al., 2007).

Participants

Participants in the four studies were adult refugees who survived torture or other organized violence referred to the rehabilitation department at DIGNITY. Study I used pre-treatment data collected between 2006 and 2011 (n =197). Study II used pre-treatment data collected between 2012 and 2014 (n=197). Study III used all available data (n = 276) from the four assessments (referral, pre-treatment, post-treatment, and 9-month follow-up for all patients registered in the clinic between 2012 and 2014. Study IV used all available data from clients who had been screened for Symbol Digit Modality Test (SDMT) at pre-treatment between 2012 and 2014 (n=141).

Inclusion and Exclusion Criteria

Patients were assessed by the therapists at the clinic at four points of assessment, at referral, start of treatment, end of treatment and nine-month follow up. Inclusion criteria for the treatment program are: 1) aged 18 years or older; 2) came to

Denmark as a refugee; 3) exposure to torture or organized violence; 4) permanent right to remain (asylum) in Denmark; 5) the ability to self-finance transportation to the clinic; 6) the presence of both primary psychiatric and somatic symptoms requiring treatment; 7) no current alcohol or drug-dependency; and 8) not currently suffering from psychosis.

Intervention

Participants are referred to the clinic by their general practitioner or psychiatrist and undergo an assessment. The majority are then placed on a treatment waitlist and reassessed when treatment commences. The average waitlist time was 7.4 months (SD = 4.5). The average number of months in treatment was 12.2 (SD = 6.5) with an average of 72.8 treatment sessions (SD = 44.3; range = 17-208 sessions).

The treatment program given by the rehabilitation department at DIGNITY follows a multidisciplinary approach delivered by teams of four professionals (medical doctor, clinical psychologist, physiotherapist, and social counselor), individualized according to patient needs. The treatment program intended to help the patients to reduce the symptom load but also helping with integration and setting goals in life to be a more active agent. The overall description of the rehabilitation program was to be “the bridge back into society”. The average treatment program includes: 1) weekly, individual trauma-focused psychotherapy aimed at PTSD, anxiety, and depression (exposure-based interventions, behavioral activation) provided by a clinical psychologist; 2) weekly sessions with a physiotherapist involving coping with pain/somatic difficulties, initiating physical exercise routines (strengthening, stabilization, and flexibility), training in body awareness, and relaxation exercises; 3) sessions (as needed) with a physician focused on management of pain, sleep and psychotropic medications, and where necessary, screening and referral for other medical conditions (e.g., asthma, diabetes, arthritis); and 4) sessions (as needed) with a social counselor addressing social difficulties and focusing on helping the client to become a more active and integrated agent in his/her social network and society. Sessions with the medical doctor and social counselor are normally more frequent at the beginning of the program. Each client had individual appointments where an individualized rehabilitation plan was formulated and then followed during treatment. Each client has approximately 4-6 such planning appointments. Twenty-five percent of the clients also had psycho-educational group sessions, in addition to the

individualized treatment. Twenty-five percent of the clients were referred as a family unit, and the spouse and/or the children received family counseling. Only data from refugees who had been tortured (or exposed to organized violence) and who participated in the multidisciplinary treatment program (including the individual trauma-focused treatment) were used in the four studies.

Ethics

Data are kept in the accordance with Danish law about personal data protection and the study was reported to the Danish Data Protection Agency. The study was approved by the Danish Patient Safety Authority and according to the Danish National Committee on Health Research Ethics, no further ethics approvals was required for this study.

Measures

In addition to information about socio-demographic characteristics and traumatic exposure, all clients complete standardized measures of mental and physical health (described below) at the time of referral (Time 0), just prior to treatment (Time 1), at post-treatment (Time 2), and again a 9-month, post-treatment follow-up (Time 3). The post-treatment measurement was carried out approximately 2-3 weeks prior to the final treatment session. Wherever possible or necessary, the standardized questionnaires were in the preferred language of the patient. Where necessary, an interpreter was present to assist the participant in completing all measures. Approximately 2/3 (67%) needed help from an interpreter during assessment and treatment.

Harvard Trauma Questionnaire (HTQ)

Parts 1, 3 and 4 of the Harvard Trauma Questionnaire (HTQ) (Mollica et al., 1992) was used to assess Trauma and PTSD in study II-IV and head injury in study IV. Part 1 assesses (lifetime) exposure (yes/no) to 46 different types of traumatic events. Part 3 (5 items) assesses history of possible brain injury either through direct injury to the head or experiences that increase the risk of brain damage (e.g., suffocation, near-drowning, prolonged starvation). Part 4 (16 items) assesses the

symptoms of PTSD as listed in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition Revised (American Psychiatric Association., 2000) which overlap with the criteria for PTSD in the latest edition (11th) of the International Classification of Diseases (World Health Organization., 2018). For Part 4, respondents rate how much each PTSD symptom has bothered them over the past seven days using a 4-point scale (1 = Not at all, 4 = Extremely). A mean score at the item level is generated for Part 4, with a suggested cut-off score for a current DSM-IV diagnosis of PTSD of 2.5 (Gerritsen et al., 2004; Lie, 2002; Mollica et al., 1992). Part 4 of the HTQ has shown to be a valid and sensitive measure of PTSD in traumatized refugee populations (Kleijn, Hovens, & Rodenburg, 2001; Shoeb, Weinstein, & Mollica, 2007; Silove et al., 2007; Wind, 2017). Study II and III uses part 1 and part 4 of the HTQ, while study IV uses all three parts of the HTQ measured (part 1, 3 and 4).

Hospital Anxiety and Depression Scale (HADS)

Study I used the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983) to assess anxiety and depression. HADS consists of 14 items, seven items measuring anxiety and seven measuring depression. Each item is scored on a 0-3 severity scale. After adjusting for six items that are reversed scored, all responses are summed to obtain total scores for the two subscales. Recommended cut-off scores are 8–10 for doubtful clinical cases and ≥ 11 for definite clinical cases (Bjelland, Dahl, Haug, & Neckelmann, 2002; Zigmond & Snaith, 1983). To achieve a high level of specificity, a cut-off score of ≥ 11 was chosen for both subscales in Study I. Previous studies have concluded that the HADS is a reliable and valid instrument for assessing the severity of anxiety and depression in the general population and in patients in primary care, hospital, and psychiatric settings, and has been validated in multiple languages (Bjelland et al., 2002; Herrmann, 1997; Mykletun, Stordal, & Dahl, 2001; Spinhoven et al., 1997). The HADS has been found to be sensitive to the effects of trauma-focused CBT for PTSD in refugees (Paunovic & Ost, 2001).

Hopkins Symptom Checklist (HSCL-25)

The 25-item Hopkins Symptom Checklist (HSCL-25) (Mollica, Wyshak, de Marneffe, Khuon, & Lavelle, 1987) was used in study II-IV to assess both anxiety and depression. Respondents rate how much each symptom has bothered them

over the past seven days using a 4-point scale (1 = Not at all, 4 = Extremely). A total score is calculated based on the mean rating for all 25 items, as well as subscale scores based on the mean ratings for anxiety (10 items) and depression (15 items). Suggested cut-off scores both the depression and anxiety subscales are 1.75 (Lavik, Laake, Hauff, & Solberg, 1999; Mollica et al., 1987). The HSCL-25 has high levels of internal reliability, construct and criterion validity, including in trauma-exposed refugees (Kleijn et al., 2001; Tinghog & Carstensen, 2010; Wind, 2017).

World Health Organization Disability Assessment Schedule (WHODAS 2.0)

The 36-item WHO Disability Assessment Schedule (WHODAS 2.0; (Ustun et al., 2010) was used to asses health related disability in study II-IV. The WHODAS 2.0 assesses the impact of physical and psychiatric difficulties across six domains of functioning (6-items per domain): understanding and communicating; mobility; self-care; getting along with others; life activities; and participation in society. For each item, respondents rate the degree to which they have experienced difficulty in that area of functioning over the past 30 days on a 5-point scale (1 = None; 5 = Extreme or Cannot Do). An overall disability score is calculated using an algorithm that differentially weights individual items and the levels of severity and converts the total score to a 0-100 scale. Possible scores range from 0 to 100, with higher scores denoting greater disability. Normative data are available but there are no widely agreed clinical cut-offs for the scale (Konecky, Meyer, Marx, Kimbrel, & Morissette, 2014). A recent study of US combat veterans applying for PTSD-related disability benefits suggested a cut-off score $\geq$ 40 reflects clinically-significant, functional impairment (Marx et al., 2015); a score that would put the individual in the top 10% of individuals reporting health-related disability according to published norms (Üstün, 2010). The WHODAS 2.0 has been found to have good psychometric properties, with validated versions in 47 different languages, and is considered to be valid for use in different cultural contexts and with people in the general population and those suffering from physical and mental health problems (including schizophrenia and substance use disorders) (Ustun et al., 2010). The WHODAS 2.0 has been found to be sensitive to the extent of traumatic exposure, and the severity of PTSD and depression in refugees (Rasmussen et al., 2010).

Brief Pain Inventory (BPI)

The 9-item short-form version of the Brief Pain Inventory (BPI) (Cleeland & Ryan, 1994) was used to assess pain severity and pain interference in study II-IV. The first item asks whether the person has experienced any non-minor pain over the past week. They are then presented with a two-dimensional representation of the human body (front and rear projections) and asked to shade in areas where they experience pain, making it possible to assess the total number of shaded areas. The next four items assess the worst, least, average, and current pain interference (0 = No Pain, 10 = Worst Pain Imaginable). Two items assess medication use and the degree of relief from pain when using the medication (0% = No relief, 100% = Complete relief). On the last item, respondents rate the degree of interference (0 = No interference, 10 = Complete interference) in seven different areas (general activity, mood, mobility, work, relations with others, sleep, and enjoyment of life). Pain Severity (4 items) and Pain Interference (7 items) scores are the mean of the 0-10 ratings for their respective items. The BPI interference and severity scales are used in these studies. The BPI is one of the most widely-used self-report measures of pain, and has been found to have good psychometric properties and to be valid for use in medical and psychiatric populations in more than 20 languages and across cultures (Cleeland & Ryan, 1994; Mendoza, Mayne, Rublee, & Cleeland, 2006; Tan, Jensen, Thornby, & Shanti, 2004; Turk et al., 2003). The BPI has been found to be sensitive to the effects of trauma- and pain-focused interventions in trauma-exposed and tortured refugees (Carinci et al., 2010; Nordbrandt, Carlsson, Lindberg, Sandahl, & Mortensen, 2015; Williams et al., 2010).

Pain Drawing Instrument

Number of pain locations was assessed using the Pain Drawing Instrument (Margolis, Tait, & Krause, 1986) in study III. Participants are presented with a pre-printed body diagram and asked to use a pencil to shade body parts where they currently experience pain. The number of locations are then calculated. In experimental and clinical research with pain patients, including refugees, the Pain Drawing Instruments has been found to possess acceptable levels of reliability, construct and criterion validity (Barbero et al., 2015; Margolis, Chibnall, & Tait, 1988; Rometsch-Ogioun El Sount et al., 2019).

Coping Strategies Questionnaire, Catastrophizing Subscale (CSQ-CAT)

Pain Catastrophizing was assessed using the 6-item pain catastrophizing subscale of the 50-item Coping Strategies Questionnaire (CSQ-CAT; (Harland, 2003) and used in study II. The CSQ possess good psychometric properties and has been validated for use in different patient groups (Robinson et al., 1997; Swartzman, Gwadry, Shapiro, & Teasell, 1994). The pain catastrophizing subscale of the CSQ possesses high levels of internal reliability (Stoffel, Reis, Schwarz, & Schroder, 2013) and has been shown to possess adequate levels of construct and criterion validity (Geisser, Robinson, & Henson, 1994; Martin et al., 1996; Parker & Wright, 1995; Quartana et al., 2009). The CSQ-CAT was translated into Danish for the purposes of this study following published guidelines on the translation of measures (Beaton, Bombardier, Guillemin, & Ferraz, 2000) and using the validated Swedish-language version as a template/comparison (Jensen, 1993). No previous studies have reported upon the psychometric properties of the CSQ-CAT in refugees.

Posttraumatic Cognition Inventory (PTCI)

Trauma-Related Beliefs were assessed using the 33-item Posttraumatic Cognition Inventory (PTCI; (E. B. Foa, Ehlers, A., Clark ,D.M., Tolin, D.F., Orsillo, S.M., 1999) and used in study II. Respondents rate their level of agreement with each item a seven-point scale (1 = Totally disagree, 7 = Totally agree). Three subscales scores are computed: Negative Cognitions About the Self (PTCI-Self; 21 items); Negative Cognitions About the World (PTCI-World; 7 items); and Self-Blame (PTCI-Blame; 5 items). The PTCI has good psychometric qualities and in trauma-exposed samples, including refugees, has been found to possess high levels of construct and criterion validity (J. G. Beck et al., 2004; Hussain & Bhushan, 2009; Ssenyongaa, Owens, & Olema, 2013).

Disability Rating Index (DRI)

The Disability Rating Index (DRI) (Salen, Spangfort, Nygren, & Nordemar, 1994), was used to measure physical disability of respondents in study I. The DRI evaluates a respondent's disability by assessing activity and participation limitations. It consists of 12 items, addressing reduced functioning in everyday life situations that are answered on a visual analog scale (VAS) ranging between 0 = no difficulty, and 100 = complete difficulty. A summarizing index is computed for the average of all 12 items. The DRI has good psychometric properties (Salen et

al., 1994). The DRI has been found to possess high levels of internal reliability, and acceptable levels of construct and criterion validity, including in refugee populations (Palic, Kappel, Nielsen, Carlsson, & Bech, 2014; Persson & Gard, 2013; Rometsch-Ogioun El Sount et al., 2019).

Symbol Digit Modality Test (SDMT)

Participants were screened for neuropsychological difficulties in study IV with the Symbol Digit Modality Test (SDMT) (A. Smith, 1982). The SDMT was designed as a brief, screening measure of associative memory, visual scanning, and information processing speed. In the written format used, participants are presented a coded key matching nine abstract symbols paired with numerical digits. Below the key is a random list of the abstract symbols, each with a blank space underneath for filling in the matching number. After 10 practice items, testing commences and the final score is the correct number of substitutions in 90 seconds; scores range between 0 and 110. The written format version is assumed to be relatively free from cultural bias and a useful screen for individuals who are not fluent in the testing language (O'Bryant, Humphreys, Bauer, McCaffrey, & Hilsabeck, 2007). The SDMT possess good psychometric properties and has been shown to be sensitive to the presence of cognitive impairments (and decline) in a range of disorders (Lezak, 2012), including PTSD where effect sizes generally have been medium to strong (Qureshi et al., 2011).

Data Analysis

Attrition Analysis

For all four studies, when questionnaire data was available for a participant the percentage of missing data at the item level for each questionnaire was extremely low (< 3%), except the WHODAS 2.0, where two subscales had 10.3% and 15% items missing (self-care and getting along with people). Analyses revealed that items on individual questionnaires that were missing, were missing completely at random (MCAR) (Little et al., 2012), and the missing items were imputed using the Expectation Maximization Algorithm (Schafer & Graham, 2002). Studies I, II, and IV were cross-sectional, with individual analyses excluding participants who were missing the analyzed variables (e.g., pairwise deletion).

Study III involved a longitudinal design, wherein changes in symptoms from pre-treatment to post-treatment to 9-month follow were estimated using all available data from participants who were "active" cases (either on wait-list, in-treatment, or waiting to be followed-up) in the clinic between the start of 2012 and the end of 2014. So depending upon when the patient began treatment, either before data collection began (i.e. prior to 2012), or at the end of study period (late 2014), only one or two assessment points were available. Thus, data that were missing for assessments that occurred outside the bounds of the study period were censored by design, and by definition were missing completely at random. In consultation with a statistician, the decision was taken to estimate change scores for all participants registered in the study period, even if data were available only from one assessment (pre-treatment, post-treatment, or follow-up), to maximize the available N and to reduce the risk of biased parameter estimates in the multi-level model of change.

Statistical Analysis

To evaluate differences within and between groups, different parametric analyses were used. Descriptive statistics were produced to present demographic and clinical characteristics within the treatment group at pre- treatment and outcome at post-treatment and nine-month follow-up. Effect sizes for the between-group effects, were calculated as follows (Cohen, 1988):

Cohen's $d = M_1 - M_2 / SD_{pooled}$

Study I: Descriptive statistics were compared to two external samples.

Pearson correlations, t-tests were applied for parametric group comparisons and chi2-tests for categorical/ordinal data.

Study II: In addition to descriptive statistics on the symptom and possible mediator measures, pairwise correlations and multiple regression analyses were carried out to investigate the contribution of depression, pain severity, pain catastrophizing (PC), and trauma-related beliefs (TRBs) to the severity of PTSD symptoms. Mediational analyses were undertaken using version 3 of the PROCESS Macro (Model 4) for SPSS (available online: http://www.processmacro.org/index.html) following the procedures outlined by Hayes (Hayes, 2013).

Study III: The SPSS Linear Mixed Models (MLM) procedure was used to analyze the data according to the methods described in (Heck, Thomas, & Tabata, 2014). Unlike traditional models for repeated measures, multilevel models can effectively manage unequal numbers of observations and missing data in the repeated measure (Kwok et al., 2008).

Study IV: Pairwise correlations and multiple linear regressions were calculated. Subgroup analyses were undertaken wherein participants who reported a head trauma injury with or without a loss of consciousness were compared on the measures via one-way analysis of variance (ANOVA).

Research studies

Study I - Torture survivors' symptom load compared to chronic pain and psychiatric in-patients

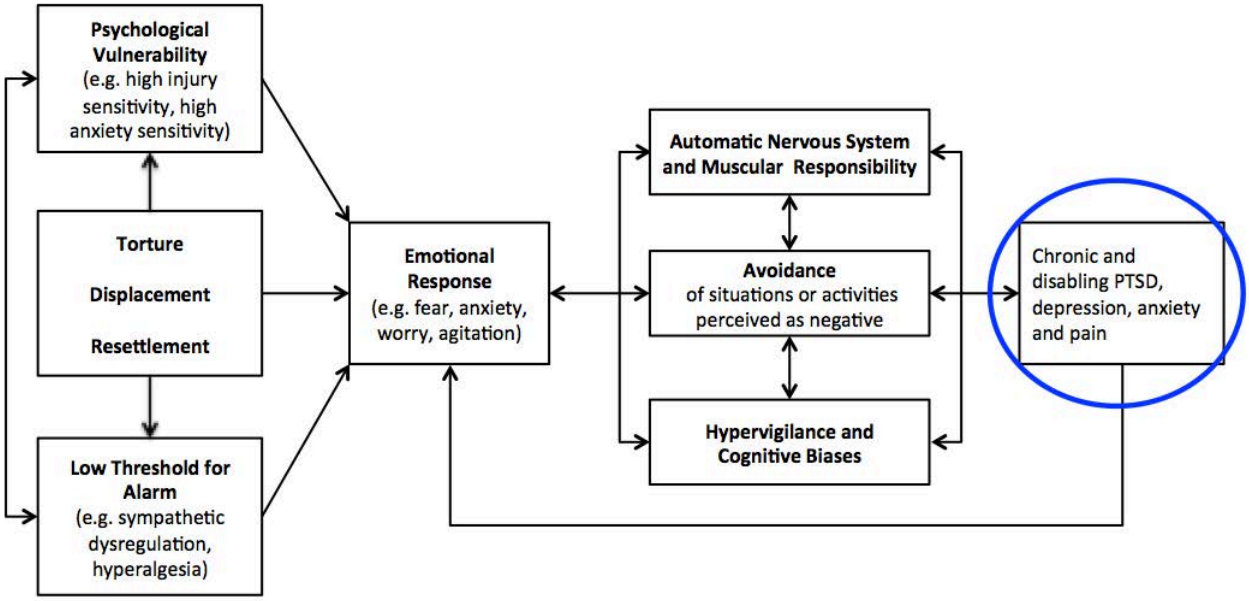

Figure 1. Shared Vulnerability Model (Asmundson & Katz, 2009)

Introduction

This study focuses on the far right box in the shared vulnerability model, circled (figure 1). The purpose of this study was to compare, the pre-treatment Disability Rating Index (DRI) and Hospital Anxiety and Depression Scale (HADS) scores of tortured and traumatized refugees referred to outpatient treatment at DIGNITY (in this study called RCT) with other patient-groups. The study also investigates whether there might be a presumptive underestimation of psychiatric disability in another similar study of a Danish refugee-sample (Palic et al., 2014). Information from these analyses can help establish the severity of preventing problems among tortured refugees, including the relevance of pain to their symptoms of distress and

overall levels of disability. It can also help to further validate the DRI and underline the importance of assessing both pain and disability in tortured and traumatized refugees.

Method

Participants (n=197) were adult refugees whom had survived torture or other organized violence, referred to outpatient treatment at DIGNITY (previously RCT). Pre-treatment scores on DRI and HADS were collected 2006-2011. This data was compared with data from the Swedish National Register for Pain Rehabilitation (NRS) pre-treatment data for DRI (NRS, 2008) and HADS (NRS, 2013), and DRI validation study with data from multiple sclerosis (MS) patients (Salen et al., 1994). This DRI-validation study provides data on degrees of MS disability ranging from zero/very low (healthy persons) to extreme (wheelchair bound) and in-between (with ascending degrees of disability). Comparing the DRI scores with this data, provides qualitative information about comparative degree of dysfunction. Since only median scores (and standard deviations) were given in this study, no parametric comparison was possible. Instead, Chi2 tests were computed.

The second part of this study investigates a presumptive underestimation of psychiatric disability in another Danish refugee-sample (including 31% torture survivors) (Palic et al., 2014). In this study, Health of Nations Outcome Scores (HoNOS) was used to rate psychiatric disability and compared to a psychiatric inpatient group from the same region. In the Palic et al. (2014) study, patients suffering from psychosis and/or substance abuse was excluded, which led to the psychiatric disability ratings of the refugee-sample were probably lowered. The data was re-analyze including this data.

Results

The current sample had an at least equal degree of functional disability compared to the Swedish NRS pain group. The DRI-scores in comparison with the pain subgroups in the DRI-validation study are to be found in the upper end of the hierarchy, only exceeded by wheelchair bound MS-patients. Both anxiety and depression mean scores for the current sample were significantly larger compared to the Swedish NRS pain patients, with a large effect size.

The results for the re-analyses of the effect sizes of the other Danish refugee-sample and psychiatric in-patients showed that all averaged effect sizes increased when either the substance abuse or the hallucination/delusion items were excluded. The exclusion of patients with substance abuse and psychotic symptoms from the refugee sample collected in the DRI validation study by Palic et al. (2014) may have resulted in an underestimation of the extent of disability within the refugee patients, relative to the psychiatric inpatient groups.

Table 1. Median, means and standard deviations (Sd) for Disability Rating Index (DRI) scores (mean of 12 items) for the RCT-DRI sample and scores reported in the Swedish annual report 2008 of the National Register for Pain Rehabilitation (NRS).

	RCT	NRS annual report 2008			DRI evaluation study				
	(n=197)	NRS 1 (n= 1470)	NRS 2 n=186)	NRS 3 (n=818)	Neck/ shoulder (n=127)	Neck/ Sh. + LBP (n=39)	Arthritis knee (n=24)	Arthritis hip (n=23)	Multiple sclerosis (n=16)
Median	62				27	39	50	65	85
Mean	57	54	50	53					
Sd	22	21	20	18					
t =		1.92	3.35	2.48					
chi^2=					58.96	15.39	2.22	.85	33.53
p		.056	.001	.014	<.01	<.01	= .14	= .36	<.01
d =		.15	.34	.22					

NRS 1 – patients who have only been assessed
NRS 2 – patients who have participated in rehabilitation without ambition to improve working ability (t)/(d)/(chi)
NRS 3 – patients with the ambition to improve working ability
(d) Results for Student t-test comparisons and Cohen effect sizes and chi^2 results for comparisons of the proportion of RCT cases > the median of each pain-subsample from the DRI validation study.[4]

Table 2. Medians, means and standard deviations (Sd) for Hospital Anxiety and Depression Scale (HADS), sum-scores for anxiety and depression for the RCT refugee sample and pain patients reported in the annual report 2013 of the National Register for Pain Rehabilitation (NRS).

	RCT		NRS annual report 2013	
	HADS-Anxiety	HADS-Depression	HADS-Anxiety	HADS-Depression
n =	147	147	1994	1996
Median	18	16	9	8
Mean	16,48	15.50	8.9	8.3
Sd	4.29	4.15	4.86	4.46
t =			20.48	20.19
p <			.000	.000
d =			1.57	1.62

Results for Student t-test comparisons and Cohen effect sizes (d).

Table 3: Health of Nation Outcome Scales (HoNos) sum score (12 items) for refugee patients at intake for rehabilitation at the Clinic for PTSD andTranscultural Psychiatry,Aarhus University Hospital (CPTP) and psychiatric in-patients at intake at the Psychiatric Center North Zealand. Group wise mean effect sizes (d) of differences between the refugee and all other groups for all items and for the substance abuse and hallucination items and both excluded; the effect sizes are computed based on the item-wise effect sizes provided by Palic et al.

	CPTP refugees	Schizo-phrenia	Affective disorders	Anxiety disorders	Personal. disorders	Addiction	Dementia
n =	448	3175	3081	1781	1030	950	950
Sum for all items (Sd)	15.70 (5.60)	12.16 (5.87)	9.90 (5.19)	9.01 (4.96)	10.24 (5.17)	13.32 (6.54)	15.55 (7.32)
Sum without substance and hallucination item	14.95	9.43	9.34	8.14	8.93	9.86	13.83
Mean d all items		.32	.49	.62	.51	.17	.05
Mean d without substance abuse item		.40	.57	.71	.61	.44	.08
Mean d without hallucination item		.46	.52	.67	.55	.20	.11
Mean d without substance abuse and hallucination items		.56	.61	.77	.67	.50	.15

Discussion

The current sample of tortured and traumatized refugees show levels of functional disability that are comparable to psychiatric inpatients suffering from chronic pain. The degree of anxiety and depression is much higher than the levels found in the compared chronic pain samples. The refugee-population in the study of Palic et al. (2014) have a higher total disability than the psychiatric inpatients compared to in the study. The available comparative data support the experience of many clinicians that traumatized refugees in Denmark suffer from multiple disabling complaints, including pain and emotional distress, with high degrees of symptom load.

Study II - Pain and Posttraumatic Stress Disorder in refugees who survived torture: The role of pain catastrophizing and trauma-related beliefs

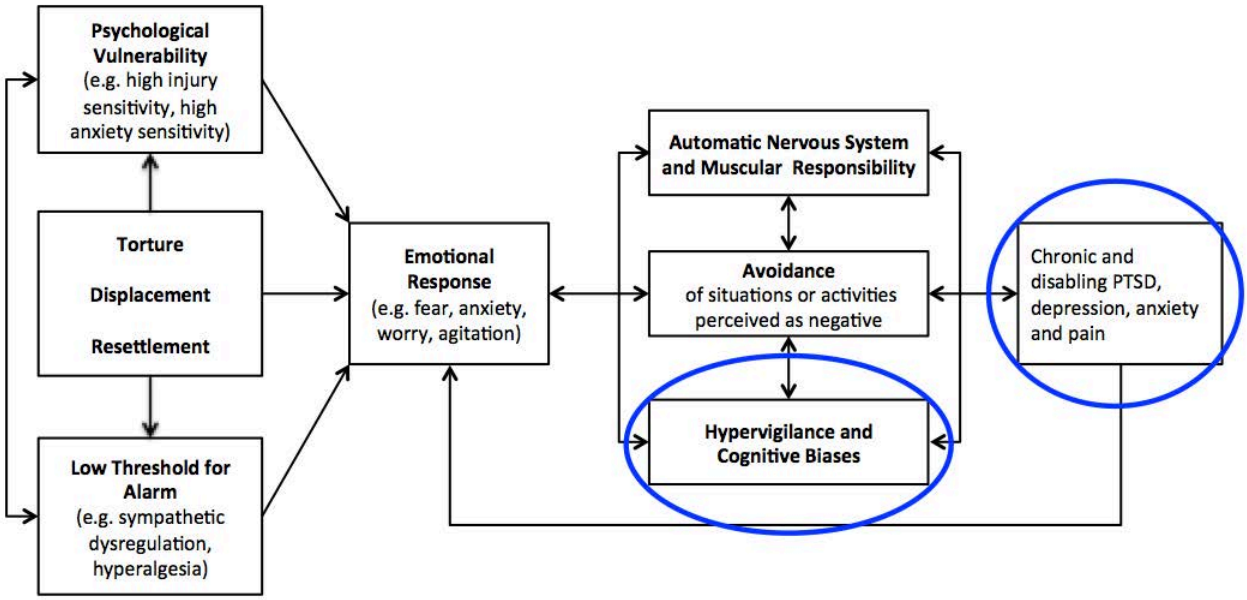

Figure 1. Shared Vulnerability Model (Asmundson & Katz, 2009)

Introduction

This study focuses on the two boxes to the right in the shared vulnerability model, circled (figure 1). It has been suggested that PTSD and pain may interact in a mutually maintaining fashion through a combination of mechanisms, identification of which may aid in the development of more effective treatments (Asmundson et al., 2002; Otis et al., 2003; Sharp & Harvey, 2001). Pain catastrophizing (PC) may increase the attention (or sensitivity) to the pain signals that are then appraised in a catastrophic manner. This cycle of biased attention to, and catastrophic misinterpretation of, pain signals might strengthen negative trauma-related beliefs (TRBs) that the individual has been permanently damaged by the trauma and more vulnerable to future harm. Depression may be another mechanism through which pain and PTSD interact, but this variable is often neglected in tests of mutual maintenance (Asmundson & Katz, 2009). This study attempts to addresses two aspects. First, we examine the contribution of pain, depression, PC, and TRBs to the severity of PTSD in a large sample of treatment-seeking traumatized refugees. Second, and in a preliminary fashion, we examine whether PC and TRBs mediate the relationship between pain and PTSD, after controlling for depression.

Method

Participants were adult refugees (n = 197; 119 men, 78 women) referred to the Danish Institute Against Torture (DIGNITY) in Copenhagen for outpatient treatment. At the time of referral and start of treatment, all patients completed a questionnaire designed to assess socio-demographic characteristics and traumatic exposure, as well as standardized measures of mental and physical health. In addition to descriptive statistics on the symptom and mediator measures, means were provided on these measures from published studies sampling other clinical populations. Thereafter, pairwise correlations and multiple regression analyses were carried out to investigate the contribution of depression, pain severity, PC, and TRBs to the severity of PTSD symptoms. We then undertook a series of mediational analyses using version 3 of the PROCESS Macro (Model 4) for SPSS (available online: http://www.processmacro.org/index.html) following the procedures outlined by Hayes (Hayes, 2013).

Results

Consistent with previous studies, patients in this study reported high levels of functional disability, PTSD, depression, anxiety, pain symptoms, interference from pain, pain catastrophizing (PC), and negative trauma-related beliefs (TRBs); levels that often exceed those found in other traumatically-exposed populations. PC and TRBs correlated in the moderate to strong range with PTSD, depression, disability, pain severity, and pain interference. A large proportion of the variance in PTSD severity (66%) was accounted for by the combined contributions of pain severity, depression, PC, and TRBs. Depression accounted for the largest portion (57%) of the variance in PTSD. Nevertheless, both PC and TRBs made significant, albeit small contributions to the variance in PTSD severity. When depression was removed from the equation, pain severity, PC and TRBs accounted for 48.3% of the variance in PTSD severity. After controlling for the effects of depression, PC and TRBs each separately mediated the relationship between pain interference and PTSD severity, and between pain severity and PTSD severity. PC only mediated the relationship between pain severity and PTSD severity.

Table 4. Means, standard deviations, proportion above clinical cut-offs, and published norms for measures of PTSD, depression, anxiety, pain, pain catastrophizing, negative trauma-related beliefs, and disability.

Measure	N	M (SD)	% Above Cut-Off	Published Norms M (SD)
PTSD (HTQ)	197	3.15 (0.47)	90.8	3.24 (0.42)[1]
Depression (HSCL-25)	195	3.03 (0.52)	99	3.18 (0.47)[1]
Anxiety (HSCL-25)	195	3.02 (0.56)	98	3.12 (0.58)[1]
Pain Severity (BPI)	190	6.29 (2.14)	NA	5.3 (2.0)[2]
Pain Interference (BPI)	190	6.95 (2.32)	NA	5.7 (2.3)[2]
Overall Functioning (WHODAS 2.0)	181	66.71 (17.31)	91	44.27 (18.51)[3]
Negative Trauma-Related Beliefs (PTCI)				
PTCI-Total	153	174.5 (31.6)	NA	
PTCI-Self	153	5.5 (1.1)	NA	4.0 (1.3)[4]
PTCI-World	153	6.0 (0.9)	NA	5.3 (1.0)[4]
PTCI-Blame	153	3.6 (1.5)	NA	12.1 (7.6)[4]
Pain Catastrophizing (CSQ-24-CAT)	152	26.1 (8.9)	NA	12.1 (7.6)[5]

Note: HTQ = Harvard Trauma Questionnaire; HSCL-25 = Hopkins Symptom Checklist-25; BPI = Brief Pain Inventory; WHODAS 2.0 = World Health Organization Disability Assessment Schedule-2.0, PTCI = Posttraumatic Cognitions Inventory; CSQ-24-CAT = Coping Strategies Questionnaire-24 Catastrophizing Subscale. [1] = (Buhman et al., 2014); [2] = (Poundja, Fikretoglu, Guay, & Brunet, 2007); [3] = Marx et al., 2015; [4] = (King et al., 2013), [5] = (Jensen, 1993).

Table 5. Pairwise correlations among the measures of PTSD, depression, anxiety, trauma-related beliefs, pain catastrophizing, and overall functioning/disability.

	Correlation (r)									
Measure	1	2	3	4	5	6	7	8	9	10
1. HTQ-PTSD	-									
2. HSCL-25 Depression	.76**	-								
3. HSCL-25 Anxiety	.64**	.64**	-							
4. BPI Pain Severity	.30**	.18*	.32**	-						
5. BPI Pain Interference	.42**	.32**	.47**	.73**	-					
6. PTCI-Total	.64**	.58**	.44**	.22**	.33**	-				
7. PTCI-Self	.67**	.64**	.45**	.25**	.39**	.96**	-			
8. PTCI-World	.45**	.36**	.30**	.17*	.28**	.75**	.64**	-		
9. PTCI-Blame	.19*	.11	.15	.04	.03	.53**	.31**	.27**	-	
10. CSQ-24-CAT	.56**	.50**	.50**	.37**	.61**	.52**	.52**	.34**	.13	-
11. WHODAS 2.0	.66**	.63**	.61**	.36**	.56**	.61**	.61**	.43**	.13	.59**

Note: HTQ = Harvard Trauma Questionnaire; HSCL-25 = Hopkins Symptom Checklist-25; BPI = Brief Pain Inventory; WHODAS 2.0 = World Health Organization Disability Assessment Schedule-2.0; PTCI = Posttraumatic Cognitions Inventory; CSQ-24-CAT = Coping Style Questionnaire-24 Catastrophizing Subscale. **p < 0.01 (2-tailed); *p < 0.05 (2-tailed).

Table 6. Results of hierarchical multiple regression showing the amount of variance in PTSD severity explained together and separately by depression, pain severity, pain catastrophizing, and negative trauma-related beliefs.

Independent Variables	*R*	R^2	*ΔR2*	*β*
Depression (HSCL-25)	.76	.57	.57***	.76***
Pain Severity (BPI)	.78	.60	.03***	.18***
Pain Catastrophizing (CSQ-24-CAT)	.80	.63	.03***	.21***
Trauma-Related Beliefs (PTCI)	.82	.66	.03***	.24***

Note: Dependent variable = HTQ-PTSD = Harvard Trauma Questionnaire - PTSD severity scale; HSCL-25 = Hopkins Symptom Checklist-25; BPI = Brief Pain Inventory Severity Rating; PTCI = Posttraumatic Cognitions Inventory Total Score; CSQ-24-CAT = Coping Strategies Questionnaire-24 Catastrophizing Subscale; ***p ≤ .001; **p < 0.01; *p < 0.05.

Table 7. Results of univariate mediation analysis testing whether the effect of pain severity and pain interference on PTSD severity are mediated by pain catastrophizing and trauma-related appraisals after controlling for depression.

	Model	Mediator (M)	Effect of IV on M a path	Effect of M on DV b path	Total Effect of IV on DV c path	Direct Effect of IV on DV c' path	Indirect effect of IV on DV c - c'	95% CI of Indirect effect (LL, UL)
(1)	*IV* = Pain Severity (BPI) *DV* = PTSD Severity (HTQ)	Pain Catastrophizing (CSQ-24-CAT)	1.50**	.027**	.075**	. 034*	.041	(.020, .066)
		Trauma Related Beliefs (PTCI)	3.01*	.009**	.068**	.042*	.027	(.008, .052)
(2)	*IV* = Pain Interference (BPI) *DV* = PTSD Severity (HTQ)	Pain Catastrophizing (CSQ-24-CAT)	2.32**	.025**	.095**	.038*	.057	(.035, .085)
		Trauma Related Beliefs (PTCI)	4.35**	.008**	.087**	.051**	.036	(.016, .061)
(1)	*IV* = Pain Severity (BPI) *DV* = PTSD Severity (HTQ) *Cov* = Depression (HSCL-25)	Pain Catastrophizing (CSQ-24-CAT)	1.09**	.011 **	.037**	.025*	.012	(.003, .023)
		Trauma Related Beliefs (PTCI)	1.33	.004**	.033**	.028*	.005	(-.001, .013)
(2)	*IV* = Pain Interference (BPI) *DV* = PTSD Severity (HTQ) *Cov* = Depression (HSCL-25)	Pain Catastrophizing (CSQ-24-CAT)	1.89**	.009**	.041**	.023	.018	(.005, .035)
		Trauma Related Beliefs (PTCI)	2.01*	.009**	.039**	.030*	.009	(.002, .017)

Note. IV = independent variable; DV = dependent variable; Cov = covariate; CI = confidence interval; LL = lower limit; UL = upper limit; HTQ = Harvard Trauma Questionnaire; HSCL-25 = Hopkins Symptom Checklist-25; BPI = Brief Pain Inventory; PTCI = Posttraumatic Cognitions Inventory; CSQ-24-CAT = Coping Strategies Questionnaire-24 Catastrophizing Subscale. Mediation is indicated where the 95% CI for the indirect effect (c – c') does not cross zero. **p < 0.01, *p < 0.05

Discussion

Taken together, these results suggest that PC and TRBs play an important role in the relationship between pain and PTSD severity. The relationship is likely complex given that these cognitions are also significantly correlated with depression, which in turn was strongly related to levels of pain and PTSD.

The findings suggest that the severity of PTSD in traumatized refugees is clearly related to their current levels of comorbidity, in this case depression and chronic pain. Dysfunctional cognitions, indexed by PC catastrophizing and negative TRB, appear to play a significant role in this comorbidity and may exacerbate the effects of both depression and pain severity on PTSD. Such a view is consistent with previous literature examining PC and TRBs separately, which find that these variables are significantly related to the severity of PTSD in patient groups with comorbid depression and chronic pain (Andersen et al., 2016). The present findings suggest that both forms of cognitions may be important targets for treatment in refugees with PTSD, depression and chronic pain.

Study III: Pre-treatment pain predicts outcomes in multimodal treatment for tortured and traumatized refugees: a pilot investigation

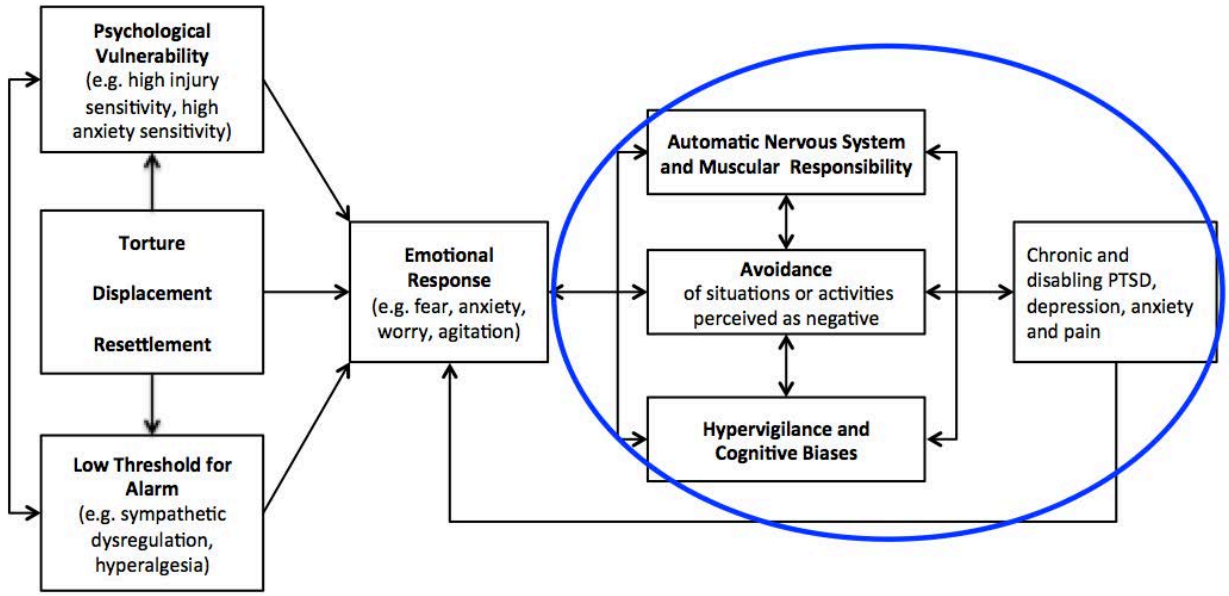

Figure 1. Shared Vulnerability Model (Asmundson & Katz, 2009)

Introduction

This study focuses on the boxes circled in the shared vulnerability model (figure 1). Evidence-based treatments, particularly for PTSD and depression, have been adapted for use with refugees; either trauma-focused mono-therapies or multimodal interventions targeting mental, physical, and social difficulties (Drozdek, 2015). The primary purpose of this study was to investigate the extent to which pre-treatment pain (severity and interference) predicts treatment outcomes in PTSD, depression, and anxiety. The effects of gender, age, and the number of treatment sessions, were also evaluated as previous studies have identified these as outcome predictors in traumatized refugees (Drozdek, 2015; Lambert & Alhassoon, 2015; Stammel et al., 2017; Stenmark et al., 2014).

Method

Participants were refugees (n = 276; 170 men, 106 women) referred to DIGNITY (Copenhagen) for outpatient treatment over a three-year period. The treatment is a multidisciplinary approach delivered by teams of four professionals (medical

doctor, clinical psychologist, physiotherapist, and social counselor), individualized according to patient needs with standard components. All patients complete standardized measures of mental and physical health at the time of referral (Time 0), just prior to treatment (Time 1), at post-treatment (Time 2), and again at a 9-month, post-treatment follow-up (Time 3). Treatment outcome was analyzed using a 2-level, mixed multi-level model design. Effect size was calculated with Cohen's d. It was also investigated whether age, gender, number of treatment sessions, pain severity and pain interference (measured at pre-treatment) predicted scores at post-treatment on the outcome measures.

Results

Table 8. Results of multi-level mixed model assessing the effects of treatment on PTSD, depression, anxiety, disability, and pain.

Parameter	B	(SE)	d
PTSD (HTQ)			
Intercept	3.16***	(.04)	-
Time Pre- to Post Treatment	-.27***	(.04)	.55
Time Pre Treatment to Follow up	-.23***	(.06)	.47
Depression (HSCL-25)			
Intercept	3.07***	(.05)	-
Time Pre- to Post Treatment	-.25***	(.05)	.43
Time Pre Treatment to Follow up	-.18**	(.06)	.32
Anxiety (HSCL-25)			
Intercept	3.06***	(.05)	-
Time Pre- to Post Treatment	-.24***	(.05)	.41
Time Pre Treatment to Follow up	-.13	(.06)	-
Disability/Participation (WHODAS-2)			
Intercept	68.67***	(1.39)	-
Time Pre- to Post Treatment	-2.7	(1.37)	-
Time Pre Treatment to Follow up	-4.18	(1.77)	-
Pain Severity (BPI)			
Intercept	6.37**'	(.15)	-
Time Pre- to Post Treatment	-.35	(.17)	-
Time Pre Treatment to Follow up	-.12	(.22)	-
Pain Interference (BPI)			
Intercept	7.13***	(.17)	-
Time Pre- to Post Treatment	-.43	(.2)	-
Time Pre Treatment to Follow up	-.08	(.26)	-
No. of Pain Locations			
Intercept	19.51***	(.78)	
Time Pre- to Post Treatment	-2.78**	(.82)	.25
Time Pre Treatment to Follow up	-.64	(1.08)	

p-value adjusted for multiple comparison with Bonferroni
* p < 0.05, ** p < 0.01, *** p < 0.001
DV=Dependent Variable

Table 9. Results of multi-level mixed model, assessing whether gender, age, number of treatment sessions, and pain predicts pre-to-post treatment changes in PTSD, depression, and anxiety.

Parameter	B	(SE)
PTSD (HTQ)		
Intercept	1.96***	(.26)
Time Pre- to Post Treatment	-.28***	(.05)
Time Pre Treatment to Follow up	-.21**	(.07)
Gender	-.05	(.08)
No. of treatment sessions	.00	(.00)
Age	.01*	(.00)
BPI Severity pre-treatment	.00	(.03)
BPI Interference pre-treatment	.12***	(.03)
Depression (HSCL-25)		
Intercept	2.12***	(.32)
Time Pre- to Post Treatment	-.2**	(.06)
Time Pre Treatment to Follow up	-.12	(.08)
Gender	-.1	(.1)
No. of treatment sessions	.00	(.00)
Age	.01	(.01)
BPI Severity pre-treatment	-.03	(.03)
BPI Interference pre-treatment	.14***	(.03)
Anxiety (HSCL-25)		
Intercept	2.11***	(.31)
Time Pre- to Post Treatment	-.23***	(.06)
Time Pre Treatment to Follow up	-.03	(.08)
Gender	-.18	(.10)
No. of treatment sessions	-.00	(.00)
Age	.01	(.01)
BPI Severity pre-treatment	.12	(.03)
BPI Interference pre-treatment	.12***	(.03)

p-value adjusted for multiple comparison with Bonferroni
* p < 0.05, ** p < 0.01, *** p < 0.001
DV=Dependent Variable

The treatment program yielded moderate effect size reductions in PTSD, depression, and anxiety, and small effects for the number of pain locations. No improvements in pain severity, pain interference, or health-related disability, except for a single domain of functioning (participation in society), were observed. Improvements were maintained at the 9-month follow-up for PTSD, depression, and participation in society, but not for anxiety or any of the pain indices. No improvements on any of the outcome measures occurred for participants while on the waitlist for treatment. Multilevel modeling suggested that participants with higher levels of pain interference at pre-treatment experienced a poorer response to

treatment in respect of PTSD, depression, and anxiety. Older participants experienced slightly poorer responses to treatment as indexed by PTSD symptoms. Otherwise, age, gender, and the number of treatment sessions were unrelated to outcome.

Discussion

The present study adds to a small but growing body of literature suggesting that traumatized refugees with PTSD and comorbid pain are more symptomatic overall and function less well on a day-to-basis (Rometsch-Ogioun El Sount et al., 2019). It is possible that dysfunctional responses to pain that have built up over months or years (e.g., behavioral restriction, avoidance, self-medication, rumination, catastrophizing) may make it harder for the person to engage in interventions that require confrontations with traumatic reminders, behavioral activation to improve mood, and modification of negative, trauma-related beliefs. If true, adding interventions that are specific to dysfunctional pain responses, or that target trans-diagnostic processes like experiential avoidance, to current multimodal interventions for refugees may improve outcomes for PTSD, depression, pain, and overall functioning.

Study IV: Cognitive Impairment in Tortured and Traumatized Refugees with Traumatic Brain Injury

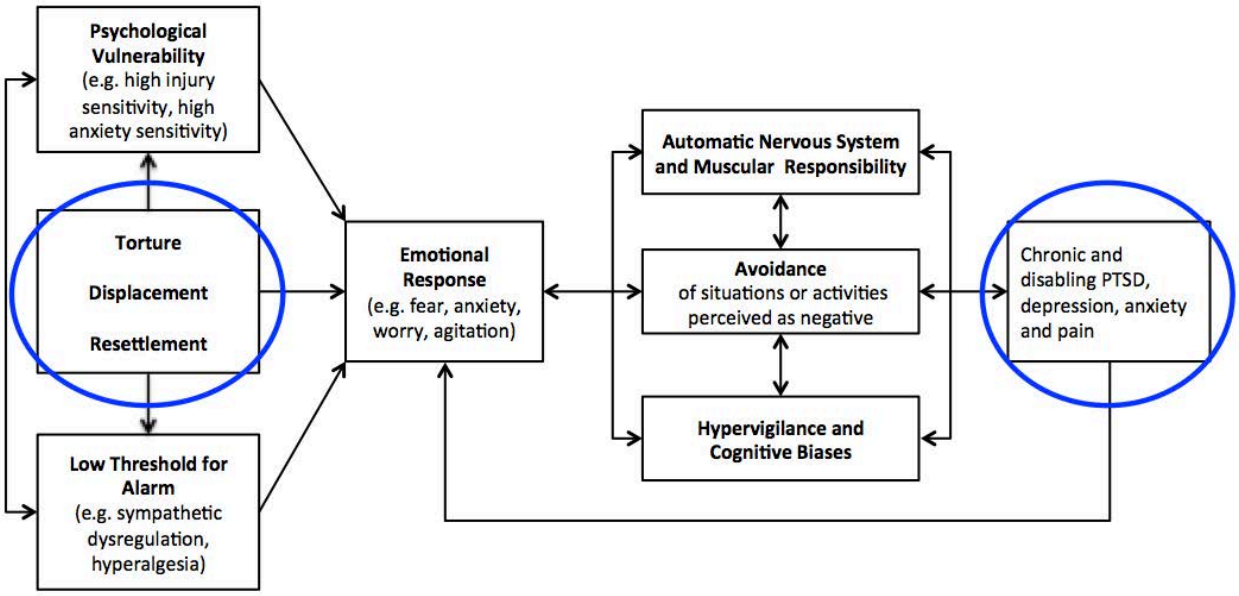

Figure 1. Shared Vulnerability Model (Asmundson & Katz, 2009)

Introduction

This study focuses on the two boxes circled in the shared vulnerability model (figure 1). The present study examines the relationship between TBIs, cognitive impairments, and PTSD, depression, pain, and psychosocial functioning in tortured refugees seeking treatment for these conditions. It was anticipated that the severity of cognitive impairments (measured by SDMT) (A. Smith, 1982), would be significantly correlated with the severity of PTSD, depression, anxiety, pain and health-related disability. It was also predicted that refugees with a history of TBIs would self-report more severe cognitive impairments, PTSD, depression, anxiety, pain, and health-related disability than those with a history of head injury and no loss of consciousness.

Method

Participants were 141 adult refugees (38% women) referred to DIGNITY who were screened with the SDMT pre-treatment. The study was observational and cross-sectional. Approximately half of the participants were also screened for possible head traumas, at pre-treatment. For all participants, the proportion scoring in the clinical

range for cognitive impairments on the SDMT was calculated, as were the pairwise correlations between scores on the SDMT and the measures of PTSD, depression, anxiety, pain, and health-related disability. Subgroup analyses were then undertaken wherein participants who reported a head trauma injury with or without a loss of consciousness were compared on the measures of cognitive impairment (SDMT), PTSD (HTQ-4), anxiety and depression (HSCL-25), pain (BPI), and health-related disability (WHODAS 2.0) via one-way analysis of variance (ANOVA).

Results

A high proportion (88%) of the participants in this study provided evidence of significant cognitive impairment. Participants scored, on average, 1.5 to 3.1 standard deviations published norms (Laura K. Sheridan et al., 2006), putting the present sample between the 0.1 and 7th percentiles for cognitive functioning when compared to the general population. Participants in this study with lower scores on the SDMT had significantly higher levels of interference in day-to-day functioning from pain and overall health-related disability. Also, and consistent with expectation, those with more severe symptoms of PTSD, depression, anxiety, and pain performed least well on the SDMT.

A high proportion of the participants who were screened for head traumas reported one or more TBIs. Nevertheless, when compared to refugees who reported a head trauma but no loss of consciousness, those with TBIs (all of whom were above threshold for PTSD) had significantly higher levels of cognitive impairment and health-related disability. Contrary to expectation, participants with TBIs did not differ from those with a history of head traumas but no loss of consciousness in relation to the severity of their symptoms of PTSD, depression, anxiety or pain.

Table 10. Means, standard deviations, percentage below clinical cut-offs, and published norms for comparative purposes for the Symbol Digit Modalities Test by age-groups for all participants (N=141)

Age	N	M (SD)	N (%) Below Cut-Off	Published Norms[1] M (SD)
<30	7	41 (12.06)	6 (86%)	58.2 (9.1)
30-55	109	25.89 (12.99)	99 (91%)	53.2 (8.9)
>55	25	21.24 (12.4)	19 (76%)	35.8 (9.6)

Note: [1] (L. K. Sheridan et al., 2006). % below cut-off is calculated as ≥ 2 standard deviations below the mean reported in the last column.

Table 11. Means, standard deviations, and results of one-way ANOVA for refugees with a history of head trauma, with and without a loss of consciousness

Measure	Head Trauma + Loss of Consciousness M (SD)	Head Trauma + No Loss of Consciousness M (SD)	*F (DF)*	*Cohen's d*
Cognitive Impairments (SDMT)	26.34 (12.95)	34.5 (15.32)	4.26 (1,76)*	.61
PTSD (HTQ)	3.1 3(.47)	2.91 (0.51)	2.37 (1,76)	
Depression (HSCL-25)	2.99 (0.55)	2.87 (0.53)	0.52 (1,76)	
Anxiety (HSCL-25)	3.01 (0.54)	2.79 (0.60)	1.87 (1,76)	
Pain Severity (BPI)	5.96 (2.29)	5.60 (1.95)	0.28 (1,74)	
Pain Interference (BPI)	6.71 (2.24)	5.97 (2.40)	1.15 (1,73)	
Health Related Dissability (WHODAS 2.0)	65.81 (18.37)	54.97 (14.61)	4.11 (1,71)*	.61

Note: SDMT=Symbol Digit Modality Test; HTQ4 = Harvard Trauma Questionnaire; HSCL-25 = Hopkins Symptom Checklist-25; BPI = Brief Pain Inventory; WHODAS 2.0 = World Health Organization Disability Assessment Schedule-2.0. Results based on 1000 bootstrap samples.

Discussion

The present study provides important information on the level of cognitive functioning in tortured refugees with a history of TBIs, and the relationship of such functioning to PTSD, depression, anxiety, pain and health-related disability. The results provide preliminary support for the clinical utility of the SDMT as a brief, culture-free screen for cognitive impairment in traumatized refugees. Since no previous study has provided SDMT data on traumatized refugees, the present findings can serve as an important resource for comparison purposes in future studies. When comparing refugees who reported a head trauma but no loss of consciousness with those who reported head trauma and loss of consciousness (TBI), those with TBI had significantly higher levels of cognitive impairment and health-related disability.

Discussion

General Discussion

There has been a large increase in the number of refugees over the past 10 years, a large proportion of whom have been exposed to multiple traumas, including torture, and the stressors associated with displacement and resettlement. Not surprisingly, refugees experience very high rates of mental health problems, with significant levels of psychiatric and psychosocial comorbidities. These difficulties are significant obstacles to adapt to life in a new country, and represents significant challenges to healthcare providers. Specialist clinics have emerged to meet the needs of tortured and traumatized refugees, most often providing multidisciplinary, multimodal treatments programs aimed at PTSD, depression, anxiety, somatic complaints, and social integration. There is evidence, albeit limited, that these treatments yield small to moderate effects for PTSD, depression, and anxiety, but negligible effects for pain. Improvements in the efficacy of these treatment programs may follow a deeper understanding of the way that pain symptoms interact with PTSD and other forms of comorbidity to affect the overall severity of these conditions and the functioning of the refugee. Another possible influence on outcome in these treatment programs is the presence of cognitive impairments that arise from traumatic brain injuries (TBIs) often tied to events during torture or other forms of trauma. This thesis aimed to fill important information gaps in the literature in respect of the relationships between pain, cognitive impairments, TBI and posttraumatic responses in tortured and traumatized refugees.

Consistent with previous studies, these studies reported high levels of functional disability, PTSD, depression, anxiety, pain symptoms, interference from pain, pain catastrophizing (PC), and negative trauma-related beliefs (TRBs); levels that often exceed those found in other trauma exposed populations. Also consistent with previous studies of tortured refugees (Mollica et al., 2014), study IV showed high proportion of the participants who were screened for head traumas reported one or

more possible traumatic brain injuries (TBIs). TBI was defined as being subjected to a possible head trauma and loosing consciousness during the ordeal. Based on results from the Symbol Digit Modality Test (SDMT), a brief measure of information processing speed that is widely used to screen individuals with suspected cognitive impairment and brain disease/injury (Lezak, 2012), a high proportion (88%) of the participants in this study provided evidence of significant cognitive impairment. Indeed, participants scored, on average, 1.5 to 3.1 standard deviations published norms (Laura K. Sheridan et al., 2006), putting the present sample between the 0.1 and 7th percentiles for cognitive functioning when compared to the general population. Lower scores on the SDMT have previously been found to be associated with increased difficulties maintaining employment (Honan, Brown, & Batchelor, 2015) and carrying out everyday life-skills such as money management and conventional use of a computer (Goverover, Chiaravalloti, & DeLuca, 2016; Goverover, Haas, & DeLuca, 2016). It is therefore important to screen tortured and traumatized refugee populations for possible TBIs and cognitive impairment.

Several trauma models suggest that the overwhelming nature of traumatic experiences prevents the person from processing the experience (Brewin et al., 1996; Ehlers & Clark, 2000). The fear avoidance model that describes the development of PTSD is derived from Ehlers and Clark's (2000) model. The model describes the development of PTSD due to a current threat with two causes: (1) the actual trauma memory, and (2) the cognitive appraisal of this trauma and/or the reactions to it afterwards. Dysfunctional cognitions on pain and trauma, indexed by pain catastrophizing (PC) and negative trauma-beliefs (TRBs), was analyzed and appeared to play a significant role in this comorbidity and may worsen the effects of both depression and pain severity on PTSD. Study II showed that PC and TRBs correlated in the moderate to strong range with PTSD, depression, health related disability, pain severity, and pain interference at pre-treatment. A large proportion of the variance in PTSD severity (66%) was accounted for by the combined contributions of pain severity, depression, PC, and TRBs.

Depression is one of the most commonly occurring diagnoses in people with PTSD and they interrelate in several ways. The symptoms of PTSD can be so distressing and hindering that it can cause depression to develop. Some people with PTSD may feel detached or disconnected from friends and family. They don't find pleasure in activities they once enjoyed. Finally, they may even have difficulty experiencing positive emotions like joy and happiness. It's easy to see how experiencing these

symptoms of PTSD may make someone feel very sad, lonely, and depressed (Flory & Yehuda, 2015). Therefore it is important to both screen for depression and to control for depression when looking at mediation. The importance of controlling for depression when evaluating potential mediators of the relationship between pain and PTSD was supported by the present findings. Depression accounted for the largest portion (57%) of the variance in PTSD. Nevertheless, both PC and TRBs made significant, albeit small contributions to the variance in PTSD severity, after controlling for both depression and pain severity. When depression was removed from the equation, pain severity, PC and TRBs accounted for 48.3% of the variance in PTSD severity. After controlling for the effects of depression, PC and TRBs each separately mediated the relationship between pain interference and PTSD severity. PC only mediated the relationship between pain severity and PTSD severity. Taken together, these results suggest that PC and TRBs play an important role in the relationship between pain and PTSD severity. The relationship is likely complex given that these cognitions are also significantly correlated with depression, which in turn was strongly related to levels of pain and PTSD. Since there was no randomized control group and missing data at nine-month follow-up, PC and TRB could not be further evaluated as possible mediators for the treatment outcome results. This would be interesting to investigate further.

This population showed a high comorbidity of different complaints (PTSD, depression, disability, pain, TBIs) and was referred to a multi-modal and multi-disciplinary treatment program. The rehabilitation program was designed to incorporate all parts of these difficulties. The treatment program led to symptom reduction with moderate effect size in PTSD, depression, and anxiety, and small effects for the number of pain locations (study III). No improvements were observed for pain or health-related disability, except for a single domain of functioning (participation in society). Improvements were maintained at the 9-month follow-up for PTSD, depression, and participation in society, but not for anxiety or number of pain locations. No improvements on any of the outcome measures occurred for participants while on the waitlist for treatment.

Since the treatment program was tailored to fit the needs of the individual with only some parts being standard (trauma focused psychotherapy with exposure, behavior activation) it is not possible to investigates what parts of the treatment led to these results, but predictors of these outcomes where assessed. Multilevel modeling suggested that participants with higher levels of pain interference at pre-treatment experienced a poorer response to treatment in respect of PTSD, depression, and anxiety. Older participants experienced slightly poorer responses

to treatment as indexed by PTSD symptoms. Otherwise, pain severity, age, gender, and the number of treatment sessions did not predict outcome. Studies that previously has looked at predictors of treatment in outcomes to similar populations, are limited and have shown mixed (including null) results, and where positive findings exist, the relationship to outcomes is weak (Lambert & Alhassoon, 2015; Stammel et al., 2017; Stenmark et al., 2014). This is also the case for socio-demographic factors and outcomes from trauma-focused monotherapies for PTSD in non-refugee populations (Haagen, Smid, Knipscheer, & Kleber, 2015). In contrast to the findings from a recent meta-analysis of trauma-focused therapies for refugees (Lambert et al., 2015), Hagen et al (2015) found that the number of trauma-focused sessions, and not the total number of psychotherapy sessions, predicted treatment outcome. Only data on the total number of sessions across all treatment modalities (trauma-focused psychotherapy, physiotherapy, medical consultations, and social interventions) was available for this study. Further studies are needed that assess the relationship between outcome and the length and content/focus of the various components delivered in multimodal treatments for refugees.

There has only been one prior study that assess whether pain influences outcomes in multimodal treatments targeting PTSD, depression, anxiety, and somatic difficulties in traumatized refugees. The earlier study by Sonne et al. (2016), also of a multimodal treatment for tortured refugees resettled in Denmark, found pain severity predicted outcomes as indexed by depression but not PTSD or anxiety. In the present study, it was interference from pain and not pain severity that predicted a poorer treatment response, and in relation to PTSD and anxiety as well as depression. The different findings for pain severity may be a function of the way this variable was assessed; via a medical doctor using a single-item scale in Sonne et al. (2016) and with a four-item, patient-report scale in this study.

Study III adds to a small but growing body of literature suggesting that traumatized refugees with PTSD and comorbid pain are more symptomatic overall and function less well on a day-to-basis (Rometsch-Ogioun El Sount et al., 2019). It is possible that pain is just another marker for overall symptom load or illness burden, and thus it is not surprising that pain predicts outcomes in treatments targeting PTSD and depression in refugees. Alternatively, it is possible that dysfunctional responses to pain that have built up over months or years (e.g., behavioral restriction, avoidance, self-medication, rumination, catastrophizing) may make it harder for the person to engage in interventions that require confrontations with traumatic reminders, behavioral activation to improve mood,

and modification of negative, trauma-related beliefs. If true, adding interventions that are specific to dysfunctional pain responses, or that target transdiagnostic processes like experiential avoidance, to current multimodal interventions for refugees may improve outcomes for PTSD, depression, pain, and overall functioning. Further, studies are needed to better understand how pain relates to the traumatic response in refugees.

Study IV examines the relationship between cognitive impairment, TBI, and posttraumatic distress. TBI is one of the most common and disabling injuries sustained by this population that often results in abnormal brain function. It is a multifaceted dysfunction that presents with varying degrees of severity commonly resulting in long-term physical and mental consequences. This already complex condition can have particularly profound implications on refugees, and their families due to factors related to mental health, differences in cultural acceptance, and difficulties navigating the healthcare systems (McPherson, 2019). Participants in this study with lower scores on the SDMT had significantly higher levels of interference in day-to-day functioning from pain and overall health-related disability. Also, and consistent with expectation, those with more severe symptoms of PTSD, depression, anxiety, and pain performed least well on the SDMT. High levels of distress and disability observed in tortured and traumatized refugees with PTSD and depression may therefore also be partly owing to cognitive impairments, a dimension that is often understudied in this sample.

Previous research has shown that combat veterans with a history of both TBIs and PTSD have greater cognitive and psychosocial impairments than PTSD or TBIs alone. No such comparisons were possible in this study because nearly all of the participants scored above cut-off for a current diagnosis of PTSD. Nevertheless, when compared to refugees who reported a head trauma but no loss of consciousness, those with TBIs (all of whom were above threshold for PTSD) had significantly higher levels of cognitive impairment and health-related disability. Thus, the present findings are largely consistent with studies of combat veterans where information processing speed has been shown to differentiate PTSD patients with and without a history of TBI (Combs et al., 2015), and individuals with a history of TBIs from controls (Draper & Ponsford, 2008; Dymowski, Owens, Ponsford, & Willmott, 2015).

Contrary to expectation, participants with TBIs did not differ from those with a history of head traumas but no loss of consciousness in relation to the severity of their symptoms of PTSD, depression, anxiety or pain. This is noteworthy, as lower

scores on the SDMT were correlated with greater severity in these symptom domains in the sample overall. Research on non-refugee, trauma-exposed groups suggests that a history of mild TBIs, involving no or very brief loss of consciousness, is associated with greater PTSD severity (Dolan et al., 2012), but the relationship is less clear in moderate to severe TBIs (Mayou, Black, & Bryant, 2000). The present findings suggest a complex interaction between TBIs, cognitive functioning, and posttraumatic distress in tortured and traumatized refugees seeking treatment for PTSD. Further investigations involving larger samples, comparison groups, and a more fine-grained assessment of the possible TBIs and cognitive impairments are necessary to delineate these relationships.

Practice Implications

The results of the studies described here, when viewed within the context of the study limitation, and findings from the broader literature, raise certain issues in relations to clinical practice with trauma-exposed refugees, particularly those who have experienced torture or similar forms of organized violence. First and foremost, clinicians working with trauma-exposed refugees, even those who have been resettled for many years in a new (safe) country should view comorbidity and complexity in the clinical presentation as the norm - not the exception. While there is evidence that traumatized refugees experience clinically meaningful reductions in symptoms of posttraumatic stress with proper social supports, and irrespective of treatment (Rizkalla & Segal, 2018; Sleijpen, Haagen, Mooren, & Kleber, 2016), high rates of psychiatric disorder related to trauma have been found in refugees more than 20 years after being resettled in a new country (Marshall, Schell, Elliott, Berthold, & Chun, 2005). Other issues related to clinical practice raised by the four studies in this thesis:

Comorbid symptoms of pain are common in refugees and represent a significant contributor to overall levels of distress and disability. Clinicians working with refugees should routinely screen for symptoms of chronic pain.

Multi-modal treatments yield small to moderate effects for symptoms of posttraumatic stress but very small to negligible effects for pain. Outcomes may be improved in current treatments with modifications to better target pain or the processes that help to maintain pain, PTSD, and depression (e.g., catastrophizing, avoidance)

Before adding components to current treatments, it would be appropriate to investigate which treatment components are associated with the greatest level of improvements for symptoms/functioning overall, and for which refugees.

Furthermore, it is important to investigate other variables that might mediate the relationship between pain and PTSD, and to better understand why interference from pain is relevant and not the number of pain locations or pain severity.

Nevertheless, to date, there have been very few studies evaluating interventions that specifically address chronic pain in traumatized refugees and more studies of pain-focused interventions are needed.

Cognitive impairments, whether owing to TBIs, or as a complication of PTSD and depression, are common in trauma-exposed refugees but remains an understudied and poorly understood phenomena. Further studies are needed to investigate how the severity of cognitive impairments relate to the severity of pain and PTSD, and their comorbidity in trauma-exposed refugees.

The present findings suggest that evaluations of the effects of cognitive impairments on outcomes in trauma-focused and multi-modal treatments (and vice versa) in traumatized refugees is warranted.

Both health professionals and social agencies responsible for refugees should be aware of the high frequency of TBIs and the associated risk of cognitive impairments in refugees, when planning and implementing programs to integrate refugees into society.

Healthcare workers involved in the care of refugees and asylum seekers should be sensitive to the potential history of TBI among these populations and be able to integrate special considerations into their management and interventions. These special considerations may include direct questions related to head injuries and torture as well as observations for any apparent signs of torture during physical examinations. TBI is often poorly understood by those affected. Perception of TBI and its symptoms among refugees may lead to inadequate participation in care and unnecessary suffering. Even when individuals with TBI try to access care they may be faced with hardships related to their knowledge of the medical system and general availability of appropriate services. Due to all of these issues, refugees and asylum seekers may suffer worse long-term outcomes than others who experience TBIs.

The public's expectations (and those of many politicians) in Europe today is that refugees must move quickly (or be "forced" or "coerced") to integrate, including achieving fluency in a new language and entering the workforce. Efforts need to

be made to raise public awareness about the significant challenges traumatized refugees face in integrating as a function of their experiences and ongoing health and mental health difficulties, including TBIs, cognitive impairments, chronic pain, and posttraumatic stress reactions. Proper screening after arrival (rather than waiting for the individual to ask for help), combined with individualized and evidence-informed/based social supports and treatment, are more likely to achieve integration than scolding and shaming.

TBIs, pain, and posttraumatic stress reactions all add to the cumulative burden of stress for the refugee and likely place them at risk for the development of a range of physical diseases (asthma, diabetes, cancer, cardio-vascular diseases). Proper mental health treatments may reduce these risks and overall health costs but are not a substitute for proper screening and treatment of such conditions in this at-risk population.

Strengths and Limitations

The present study benefits from a large sample size, a long pre-treatment baseline, repeated assessments using standardized measures of symptoms and functioning, and a moderately long follow-up period. This thesis is based on a clinical population, with data collected for this specific reason, that enhances ecological and external validity and gives it a high societal relevance. Nevertheless, the study did not include a randomized control or comparison group. While the treatment program included standard interventions for PTSD, depression, anxiety, and to a lesser extent pain, the program was individualized and we do not know which components were associated with which outcomes. The participants were tortured and traumatized refugees resettled in Denmark, and the present findings may not generalize to refugees in other countries, or to other trauma groups. The population also had a high symptom burden with chronic, and highly comorbid characteristics. With mainly cross sectional, and pre to post-treatment data, it is more difficult to tell in a more conceptual approach the very nature of the comorbidity. Other methods, such as network analysis, single case study designs, path analyses with repeated measurements across time to ascertain direction of effects and mechanisms, and comparative studies on other populations would be beneficial to ensure the findings.

Not all of the language-versions of the self-report measures used in this study have been fully validated. Mediation was evaluated in a cross-sectional manner, without the benefit of a comparison group. We chose to examine the effects of pain upon PTSD through two cognitive mediators and not the effect of PTSD on pain through these mediators. This was done for pragmatic reasons; participants in this study were recruited from a clinic that only accepts refugees who have PTSD or trauma-induced depression as a primary complaint, and some form of somatic complaints – not necessarily chronic pain. Had we examined the effects of PTSD upon pain through pain catastrophizing and negative trauma-related beliefs, our analyses might have produced a different pattern of results. Finally, there are likely to be other unmeasured variables that contribute to the relationship between pain and PTSD in this sample. Further studies are needed involving longitudinal designs and comparison groups, multi-method assessments, and carried out in more diverse populations and cultures, including bot clinically-referred and non-referred groups.

The SDMT has been validated as a measure of cognitive impairment in numerous patient groups and across countries, but further validation studies with refugee populations are needed. While the SDMT was administered to all patients referred to the clinic during the study period, Part 3 of the HTQ (assessing the head trauma/TBI) was administered to slightly more than half of the participants.

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