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Sleep Disturbances and Chronic Pain as Potential Indicators for Therapeutic Intervention in Subjects with Post-Traumatic Stress Disorder

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Abstract

Background: Post-traumatic stress disorder (PTSD) is a debilitating psychiatric disorder that can develop after experiencing a potentially traumatic event (PTE). PTSD often co-occurs with other physical and psychiatric disorders and the most common physical comorbidities of PTSD are sleep disturbances (SDs) (insomnia and nightmares) and pain (chronic). Most individuals do not link their physical pain and SDs with past trauma, and as a result, many will turn to medications (often self-medication(s)) and unhealthy coping mechanisms, such as tobacco and alcohol, which can precipitate addiction problems. The aim of the pilot study was to collect information on sociodemographic factors and comorbidities reported by PTSD subjects, such as SDs and chronic pain, and identify characteristics and behaviours that could be targeted for therapeutic interventional modalities.

Methods: Seventy-eight subjects (N = 78; n = 39 control participants; n = 39 clinically diagnosed PTSD participants) were included in this study. Sociodemographic and clinical history was recorded for each participant to include, age, gender, ethnicity, BMI, pulse, systolic BP, diastolic BP, behaviours (tobacco and alcohol use, substance abuse, and self-reported sleeping habits), physical comorbidities, psychological and psychiatric comorbidities, medications, pain score and type, and how pain interfered with their social activities and engagement with others.

Results: Compared to controls, almost all the PTSD participants reported SDs and chronic physical pain. PTSD participants took more medications, abused alcohol more frequently, and had high rates of suicidal ideation. PTSD participants also had higher incidences of anxiety, depression and panic disorder, when compared to control subjects. PTSD participants also indicated that their physical pain interfered with their mood, general activity, normal work, enjoyment of life, and relations with others, when compared to the control subjects. In addition, types of pain were significantly different between the control and PTSD participants; which included nagging, radiating and sharp.

Conclusion: Managing SDs and chronic pain may be an important strategy for ameliorating PTSD symptoms. Sleep disturbances and chronic pain should be potential targets for therapeutic intervention.

Keywords

PTSD, Chronic pain, Sleep disturbances, Substance abuse, Depression, Anxiety, Blood pressure, Medications

Introduction

Post-traumatic stress disorder (PTSD) is a mental health condition that is triggered by a potentially traumatic event (PTE) (e.g., violent personal assault, mugging, robbery or serious road accident) either experienced or witnessed, in which the individual experiences extreme emotions of helplessness, fear of harm, or death [1]. PTSD occurs in 5 to 12% of the population and is often twice as common in women as in men [2]. PTSD can develop immediately after the PTE, or it can occur weeks, months or even years later. PTSD affects approximately 1 in 3 people who have a PTE, but it is unclear exactly why some people develop the condition

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and others do not [3]. PTSD impacts multiple pathobiological systems including neurocirculatory and brain chemistry, cellular, immune, endocrine and metabolic pathways [4]. PTSD causes a heightened sense of threat and danger and the natural fight or flight response is altered, causing stress and fear when no actual danger exists [5]. After a PTE, it is normal to have strong feelings of anxiety, sadness, or stress. Furthermore, some individuals may experience nightmares and intrusive memories about the PTE, or problems sleeping. For most individuals, this early distress will self-resolve, however, for others it may develop into PTSD [6].

When PTSD presents, if left untreated, it is unlikely to fully self-resolve and can contribute to behavioural, physiological, psychiatric, and psychological comorbidities such as chronic pain, depression, drug, and alcohol abuse, that may lead to further functional impairment [7]. Chronic pain is common after a traumatic injury and often co-occurs with PTSD. However, patients with PTSD can demonstrate a unique paradoxical pain profile; hyperresponsiveness together with hyposensitivity to pain [8]. Some individuals recover quickly however, in other cases, the condition may become chronic [9].

Across all types of PTEs, variables such as female gender, low socio-economic status, pre-existing mental illness, previous trauma exposure, lower intelligence and childhood adversity, consistently predict higher PTSD symptom levels [10,11]. Furthermore, sleep disturbances (SDs) and substance use have also been shown to augment PTSD symptoms [12-15].

The relationship between PTSD and excessive alcohol use is well documented [16,17]. Moreover, the hypothesis of alcohol misuse as 'self-medication' to attenuate psychological suffering has gained wide popularity [18]. However, studies investigating alcohol and cigarette use in chronic PTSD have reported that weekly alcohol consumption was substantially below that of the general population [19,20].

Unfortunately, experiencing trauma is common, and almost 60% of men and 50% of women will experience at least one or two PTEs in their lifetime [21]. In a recent study of 2,647 US adults who had experienced a PTE, almost 11% met the full criteria for lifetime PTSD [22]. Furthermore, over half of the remaining non-PTSD participants experienced trauma-related disturbances to their sleep [22]. PTSD affects both civilians and active duty military personnel, although the latter are at an increased risk, especially after combat tours [23]. A better understanding of how to mitigate symptoms and disorder development may improve the quality of life for those who have been exposed to PTE's.

Over 90% of individuals diagnosed with PTSD report SDs [24,25]; the exact aetiology is unknown [26]. However, recent studies have suggested that PTSD disrupts sleep by increasing the duration of light sleep; decreasing restorative sleep, and interfering with rapid eye movement (REM) sleep [27-29]. REM sleep is important for storing memories and processing emotions [28,30]. As a result, individuals diagnosed with PTSD have reported difficulty falling asleep, waking up more often during the night, and having trouble falling back asleep, resulting in daytime agitation and fatigue [26]. Additionally, individuals with SDs before a PTE are more likely to develop PTSD [31]. Disruptions in sleep and encoding can interfere with one's ability to properly cope with PTE exposure [32].

In addition to SDs, 15 to 35% of patients with chronic pain have PTSD [33,34]. Moreover, 20-80% of individuals who have PTSD report chronic pain concerns [35]. In one study, almost 51% of patients with chronic lower back pain had PTSD symptoms [36]. For individuals with chronic pain, the pain may serve as a reminder of the PTE, which triggers re-experiencing symptoms, traumatic memories, which tend to perpetuate PTSD symptoms [37].

The aim of the pilot study was to collect information on the relationship between clinical, sociodemographic factors and comorbidities of PTSD such as SDs and pain, to identify patient characteristics and behaviours that could be targeted for therapeutic interventional modalities. Previously [38], we identified blood biomarkers that could be used in combination with the PCL-5 to potentially measure treatment efficacy; we suggested that by improving sleep quality (measured by an increase in serum EGF), working with participants in an attempt to attenuate intrusive memories (measured by a decrease in serum tPA), and sustained pain relief (measured by a decrease in serum IL-8), serum biomarkers, in combination with the PCL-5 (score), [biomarker risk score (BRS) + clinical risk score (CRS) = patient management] pre and post-treatment(s), could serve as indicators of improved well-being and treatment efficacy. Further studies investigating these relationships and potential treatment options, using both PCL-5 score and blood biomarker measurements in larger patient cohorts are warranted.

Materials and Methods

Study participants

Seventy-eight participants were recruited to an age and gender-matched case-control study (N = 78; control n = 39; PTSD n = 39). Participants were recruited in the US between January and June 2019 by PrecisionMed (California, US) and Discovery Life Sciences (California, US). A comprehensive clinical history, including clinical factors, participant behaviours, physical comorbidities, psychiatric and psychological comorbidities, medications, pain score and type of pain, were collected from all participants. Formal written informed consent was obtained from all subjects. The study conformed to all Data Use Agreements. Participant samples were deidentified and publicly available and are thus exempt from the requirement of the Institutional Review Board (IRB) approval (Exempt Category 4). General inclusion criteria: participant signed an approved written informed consent; male or female subject is ≥ 18 years of age, and subject is of any ethnic origin. General exclusion criteria: subjects < 18 years of age, evidence of neuropsychiatric disease, body weight < 45 kg, pregnancy.

Psychological and psychiatric assessment

Clinical diagnosis of PTSD was confirmed by qualified psychologists and/or psychiatrists using the CAPS-5. A PTSD

checklist (PCL-5) was completed for all control participants [39,40]. A CAPS-5 or PCL-5 score < 33 was considered negative for PTSD [41]. A detailed description of the psychological assessment has been described previously [38].

Clinical characteristics

Demographic and clinical history were recorded for each participant to include, age, gender, ethnicity, BMI, pulse, systolic blood pressure (BP), diastolic BP, behaviours (tobacco and alcohol use, substance abuse and self-reported sleeping habits), physical comorbidities, psychiatric and psychological comorbidities, medications, pain score and type of pain, and how pain interfered with their social activities and engagement with others [38].

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, New York). Continuous variables are presented as mean ± standard deviation (mean ± SD). Comparisons were made using the Mann-Whitney U test. Categorical variables are presented as percentage (%) and were compared using a chi square (χ^2) test. A $p < 0.05$ was considered significant.

Results

Sociodemographic and clinical factors

Study participants were age and gender matched (Table 1). No differences were observed for subject ethnicity, BMI, pulse, or systolic BP. However, a significant difference was noted for diastolic BP between the control group and PTSD participants.

Participant behaviours

There were more tobacco smokers in the control group (Table 2). Control subjects smoked more cigarettes per day and for longer (years). Surprisingly, alcohol consumption was not significantly different between the two groups. However, unsurprisingly, alcohol abuse was significantly different between control and PTSD participants (0/39 (0.0%) vs. 10/39 (25.6%), respectively).

Participant comorbidities

Clinical cases of arthritis, asthma, diabetes, and migraine were significantly higher in the PTSD participant group (Table 3). Interestingly, of the n = 8 cases of arthritis noted for the PTSD participants, all were female.

Psychological and psychiatric comorbidities of the participants

Psychological and psychiatric comorbidities such as anxiety, attention deficit disorder (ADD), bipolar disorder, depression, panic disorder and suicidal ideation, were all significantly higher in the PTSD participants (Table 4).

PTSD subjects presented with more than one psychological/psychiatric comorbidity e.g., anxiety, depression, ADD (and combinations thereof), and in many instances with multiple physical comorbidities e.g., arthritis, asthma etc.

Table 1: Sociodemographic and clinical factors of study participants.

Clinical Factors	Control	PTSD	p value
Age (years)	37.1 ± 7.2 (n = 39)	41.9 ± 12.1 (n = 39)	0.150
Gender (Male)	18/39 (46.2%)	17/39 (43.6%)	0.820
Ethnicity (Caucasian)	16/38 (42.1%)	23/39 (59%)	0.139
BMI	30.8 ± 8.3 (n = 38)	28.1 ± 6.6 (n = 39)	0.446
Pulse	74.4 ± 10.2 (n = 39)	75.8 ± 16.0 (n = 28)	0.990
Systolic BP	128.7 ± 17.1 (n = 39)	129.0 ± 18.3 (n = 28)	0.689
Diastolic BP	77.3 ± 11.1 (n = 39)	86.9 ± 11.9 (n = 28)	0.004

Continuous variables were expressed as mean ± SD or as % for categorical variables. The difference in continuous variables was analysed using Mann-Whitney U test, while chi square (χ^2) test was used for categorical variables. A $p < 0.05$ was considered significant. BP: Blood pressure.

Table 2: Study participant behaviours.

Behaviours	Control	PTSD	p value
Smoker	24/39 (61.5%)	13/39 (33.3%)	0.013
Cigarettes/day	8.6 ± 9.9 (n = 39)	2.8 ± 7.2 (n = 39)	0.012
Smoking years	9.2 ± 9.8 (n = 39)	3.6 ± 8.3 (n = 39)	0.003
Alcohol	23/39 (59.0%)	15/39 (38.5%)	0.070
Alcohol abuse	0/39 (0.0%)	10/39 (25.6%)	0.001

Continuous variables were expressed as mean ± SD or as % for categorical variables. The difference in continuous variables was analysed using Mann-Whitney U test, while chi square (χ^2) test was used for categorical variables. A $p < 0.05$ was considered significant.

Table 3: Study participant comorbidities.

Comorbidities	Control	PTSD	p value
Acid Reflux	0/39 (0.0%)	1/39 (2.6%)	0.314
Arthritis	1/39 (2.6%)	8/39 (20.5%)	0.013
Asthma	0/39 (0.0%)	4/39 (10.3%)	0.040
Diabetes	0/39 (0.0%)	4/39 (10.3%)	0.040
Heart Attack/Angina	0/39 (0.0%)	1/39 (2.6%)	0.314
Hypercholesterolemia	2/39 (5.1%)	2/39 (5.1%)	1.000
Hypertension	5/39 (12.8%)	8/39 (20.5%)	0.362
Irritable Bowel Syndrome	0/39 (0.0%)	1/39 (2.6%)	0.314
Lupus	0/39 (0.0%)	1/39 (2.6%)	0.314
Medullary Sponge Kidney	1/39 (2.6%)	0/39 (0.0%)	0.314
Migraine	0/39 (0.0%)	4/39 (10.3%)	0.040
Multiple Sclerosis	0/39 (0.0%)	1/39 (2.6%)	0.314
Musculoskeletal Injuries	2/39 (5.1%)	6/39 (15.4%)	0.135
Nerve Pain	0/39 (0.0%)	3/39 (7.7%)	0.077
Oedema	0/39 (0.0%)	2/39 (5.1%)	0.152
Skin Disorders	0/39 (0.0%)	1/39 (2.6%)	0.314
Sleep Apnoea	0/39 (0.0%)	2/39 (5.1%)	0.152
Stroke	0/39 (0.0%)	1/39 (2.6%)	0.314
Thyroid Disease	1/39 (2.6%)	1/39 (2.6%)	1.000
Ulcers	0/39 (0.0%)	1/39 (2.6%)	0.314

A chi square (χ^2) test was used for categorical variables and a $p < 0.05$ was considered significant.

Table 4: Psychological and psychiatric comorbidities of the study participants.

Psychological and Psychiatric Comorbidities	Control	PTSD	p value
Anxiety	2/39 (5.1%)	25/39 (64.1%)	< 0.001
Attention Deficit Disorder	0/39 (0.0%)	4/39 (10.3%)	0.040
Bipolar Disorder	0/39 (0.0%)	4/39 (10.3%)	0.040
Dementia, Alzheimer's Disease	0/39 (0.0%)	1/39 (2.6%)	0.314
Depression	4/39 (10.3%)	23/39 (59.0%)	< 0.001
Sleep Disturbances	9/39 (23.1%)	33/39 (84.6%)	< 0.001
Obsessive Compulsion Disorder	0/39 (0.0%)	1/39 (2.6%)	0.314
Panic Disorder	0/39 (0.0%)	11/39 (28.2%)	< 0.001
Suicide ideation	0/39 (0.0%)	8/39 (20.5%)	0.003

A chi square (χ^2) test was used for categorical variables and a $p < 0.05$ was considered significant.

Sleep disturbances

Disturbances to sleep were recorded as 0 = absent; 1 = mild/subthreshold; 2 = moderate/threshold; 3 = severe/markedly elevated, and 4 = extreme/incapacitating.

The number of subjects that experienced SDs were significantly different between control and PTSD participants (9/39 (23.1%) vs. 33/39 (84.6%), respectively) (Table 4). On average, PTSD participants self-reported a maximum of 4.8 ± 1.43 (n = 18) (range 3.5 to 9.0) hours (broken) sleep each night. Where answers were recorded, PTSD participants self-reported that they wakened every 1 or 2 hours throughout the night. In all cases, PTSD participants noted that their SDs were a direct result of the PTE that they had experienced. The average number of hours PTSD participants self-reported they thought that they should be sleeping ranged from 6.0 to

Table 5: Total medications and pain scale (score) of the study participants.

Medications and Pain	Control	PTSD	p value
Total medications[1]	0.7 ± 1.2 (n = 39)	3.2 ± 2.6 (n = 39)	< 0.001
Rating of current pain (Scale 0-10)[‡]	1.1 ± 2.3 (n = 39)	2.3 ± 2.6 (n = 19)	0.174
Rating of pain at its worst within the last 24 hours (Scale of 0-10)[‡]	1.4 ± 2.6 (n = 39)	3.4 ± 3.1 (n = 19)	0.058
Rating of pain at its least within the last 24 hours (Scale 0-10)[‡]	0.5 ± 1.3 (n = 39)	1.1 ± 1.3 (n = 19)	0.064
Rating of pain on average (Scale 0-10)[‡]	1.3 ± 2.1 (n = 39)	2.7 ± 2.5 (n = 19)	0.079
Chronic pain	16/39 (41%)	14/19 (73.7%)	0.019

[1]a detailed list of participant medications is given in Table 8; [‡] 0-10 where 0 represents no pain, 1-3 mild pain (nagging, annoying, interfering with activity of daily living (ADL)), 4-6 moderate pain (interferes significantly with ADL), 7-10 severe pain (disabling; unable to perform ADL).

Continuous variables were expressed as mean ± SD or as % for categorical variables. The difference in continuous variables was analysed using Mann-Whitney U test, while the chi square (χ^2) test was used for ordinal and categorical variables. A $p < 0.05$ was considered significant.

Table 6: Type of pain described by the study participants.

Type of Pain	Control	PTSD	p value
Aching	13/39 (33.3%)	7/19 (36.8%)	0.792
Burning	1/39 (2.6%)	1/19 (5.3%)	0.597
Cramping	3/39 (7.7%)	3/19 (15.8%)	0.342
Dull	2/39 (5.1%)	2/19 (10.5%)	0.446
Exhausting	0/39 (0.0%)	2/19 (10.5%)	0.103
Gnawing	0/39 (0.0%)	1/19 (5.3%)	0.148
Miserable	2/29 (5.1%)	1/19 (5.3%)	0.983
Nagging	4/39 (10.3%)	6/19 (31.6%)	0.044
Numb	1/39 (2.6%)	0/19 (0.0%)	0.481
Penetrating	2/39 (5.1%)	3/19 (15.8%)	0.175
Radiating	2/39 (5.1%)	5/19 (26.3%)	0.020
Sharp	3/39 (7.7%)	6/19 (31.6%)	0.018
Shooting	5/39 (12.8%)	1/19 (5.3%)	0.375
Squeezing	1/39 (2.6%)	0/19 (0.0%)	0.481
Stabbing	2/39 (5.1%)	3/19 (15.8%)	0.175
Tender	0/39 (0.0%)	2/19 (10.5%)	0.103
Throbbing	4/39 (10.3%)	0/19 (0.0%)	0.148
Tiring	0/39 (0.0%)	2/19 (10.5%)	0.103
Unbearable	3/39 (7.7%)	0/19 (0.0%)	0.214

A chi square (χ^2) test was used for categorical variables and a $p < 0.05$ was considered significant.

9.0 (7.68 ± 0.61 (n = 14)) hours per night. This information was not recorded for the control group.

Participant total medications and pain score

PTSD participants were prescribed significantly more medications (Table 5). Almost 75% of PTSD subjects reported chronic pain (i.e., pain of duration ≥ 1 month): lower back pain (7/19 (36.8%) vs. 2/39 (5.1%)); neck pain (4/19 (21.1%) vs. 1/39 (2.6%)); knee pain (5/19 (26.3%) vs. 6/39 (15.4%)); shoulder pain (1/19 (5.3%) vs. 1/39 (2.6%)); finger and toe pain (1/19 (5.3%) vs. 0/39 (0.0%)); arm pain (1/19 (5.3%) vs. 0/39 (0.0%)); feet and ankle pain (1/19 (5.3%) vs. 2/39 (5.1%)); head pain (1/19 (5.3%) vs. 1/39 (2.6%)); hip pain (0/19 (0.0%) vs. 1/39 (2.6%)) and tongue pain (1/19 (5.3%) vs. 0/19 (0.0%)), PTSD vs. control, respectively. However, when participants were asked to rate their pain for the past 24 hours; pain at its worst and least (scale 0-10 where 0 represents no pain, 1-3 mild pain (nagging, annoying, interfering with activity of daily living (ADL)), 4-6 moderate pain (interferes significantly with ADL), 7-10 severe pain (disabling; unable to perform ADL), no significant differences were observed between the PTSD participants and the control subjects. Albeit there was a trend in the PTSD participants to report higher ADL levels of pain. Furthermore, when participants were asked to rate their current pain and their pain on average (0 = no pain; 10 = extreme pain), there was also no significant differences between the PTSD participants and the control subjects.

Type of pain described by study participants

The type of pain(s) described by the study participants are noted in Table 6. Nagging, radiating, and sharp pain were significantly different between the control and the PTSD participants.

Participant pain noted during the previous 24 hours that interfered with both social activities and engagement with others

Study participants were asked to describe, during the past 24 hours, how pain had interfered with their social activities and engagement with others (0 = does not interfere; 10 = completely interferes) (Table 7). Over 50% of the PTSD participants noted that pain interfered with their general activity, mood, normal work, engagement with others, and their enjoyment of life.

Prescribed and over the counter medication classes

The main categories of medications that were prescribed for the study participants included antidepressants/ antipsychotics, antianxiety and pain relief medication(s). A detailed list of medication (type) prescribed for each participant is described in Table 8 and Supplementary 1. Many of the prescription medications were also used to ameliorate SDs, and there was significant overlap in their diagnostic use.

Table 7: Pain noted during the previous 24 hours that interfered with study participants' social activities and their engagement with others.

Pain Interference	Control	PTSD	p value
General Activity	10/39 (25.6%)	11/19 (57.9%)	0.016
Mood	10/39 (25.6%)	12/19 (63.2%)	0.006
Walking ability	10/39 (25.6%)	9/19 (47.4%)	0.098
Normal work	9/39 (23.1%)	11/19 (57.9%)	0.009
Relations with other people	7/39 (17.9%)	10/19 (52.6%)	0.006
Enjoyment of life	10/39 (25.6%)	12/19 (63.2%)	0.006

A chi square (χ^2) test was used for categorical variables and a $p < 0.05$ was considered significant.

Table 8: Prescribed and over the counter medication(s) classes for study participants.

Medications	Control	PTSD	p value
Alcohol withdrawal/substance abuse	0/39 (0.0%)	1/39 (2.6%)	0.314
Antibiotics	0/39 (0.0%)	3/39 (7.7%)	0.077
Anticoagulant	0/39 (0.0%)	1/39 (2.6%)	0.314
Antihistamine	0/39 (0.0%)	4/39 (10.3%)	0.040
Antihypertensive	4/38 (10.5%)	10/39 (25.6%)	0.086
Anxiety	0/39 (0.0%)	6/39 (15.4%)	0.011
Asthma	0/39 (0.0%)	2/39 (5.1%)	0.152
Autoimmune	0/39 (0.0%)	2/39 (5.1%)	0.152
Bipolar disorder/schizophrenia	0/39 (0.0%)	7/39 (17.9%)	0.006
Depression	0/39 (0.0%)	7/39 (17.9%)	0.006
Diabetes	0/39 (0.0%)	4/39 (10.3%)	0.040
Diuretic	0/39 (0.0%)	1/39 (2.6%)	0.314
Hormone	3/39 (7.7%)	0/39 (0.0%)	0.077
Migraine	0/39 (0.0%)	2/39 (5.1%)	0.152
Muscle relaxant	1/39 (2.6%)	4/39 (11.4%)	0.165
Nicotine substitute	0/39 (0.0%)	1/39 (2.6%)	0.314
Pain relief	6/39 (15.4%)	17/39 (43.6%)	0.006
PPI	1/39 (2.6%)	1/39 (2.6%)	1.000
Sedative	0/39 (0.0%)	7/39 (17.9%)	0.006
SSRI	4/39 (11.4%)	23/39 (59.0%)	< 0.001
Statin	1/39 (2.6%)	3/39 (7.7%)	0.305
Steroid	1/39 (2.6%)	0/39 (0.0%)	0.314
Thyroid	0/39 (0.0%)	1/39 (2.6%)	0.314
Vitamins and supplements	4/39 (11.4%)	1/39 (2.6%)	0.165

SSRI: Selective serotonin reuptake inhibitor; PPI: Proton pump inhibitor.

A chi square (χ^2) test was used for categorical variables and a $p < 0.05$ was considered significant

Exposure type (trauma)

PTSD participants were asked to complete a Life Events Checklist and describe what happened and trauma type (whether experienced, witnessed, learned about, or exposed to aversive details). In addition, the participants were also asked to indicate if their experience was a threat to life, serious injury or sexual violence, or combination(s) thereof. Almost all PTSD participants (38/39 (97.4%)) indicated that they had directly experienced the trauma; 12/39 (30.8%) also witnessed the event; 32/38 (84.2%) indicated a threat to their life; 31/37 (83.8%) suffered serious injury, and 16/37 (43.2%) were subjected to sexual violence.

When the CAPS-5 scores (indicative of PTSD symptom severity) were compared, there was no significant difference where the subject indicated that their experience and/or witnessed trauma was a threat to life (45.5 ± 10.8 (n = 32) vs. 41.7 ± 1.5 (n = 6)), serious injury (42.0 ± 4.3 (n = 31) vs. 45.7 ± 10.7 (n = 6)), or sexual violence (45.9 ± 11.8 (n = 16) vs.

44.0 ± 7.5 (n = 21)). Furthermore, there was no difference in the CAPS-5 score by gender (46.3 ± 12.0 (n=17) vs. 43.6 ± 7.9 (n = 22), male vs. female, respectively); we have previously reported similar results [11].

Discussion

PTSD is a debilitating psychiatric condition which can follow a potentially traumatising event (PTE) and it is estimated that approximately one third of those exposed to a PTE will develop PTSD; with the majority remaining psychologically well [6]. However, the pathophysiology of the condition and heterogeneous nature of the pathology make diagnosis and treatment challenging for the attending physician. Unfortunately, there is no 'one size' fits all for PTSD subjects.

The aim of this pilot study was to investigate the relationship between clinical, sociodemographic factors and comorbidities of PTSD, such as SDs and chronic pain, to identify characteristics and behaviours that could be targeted for therapeutic interventional modalities. It is common to see higher rates of physical comorbidities with individuals who have PTSD. Therefore, it was unsurprising that in this study, PTSD participants presented with more cases of arthritis, diabetes, asthma, and migraine.

An intriguing finding from the study was that the resting diastolic BP was higher for individuals with PTSD, indicating that the pressure when the heart rests between beats was higher than in control subjects. This could suggest that individuals with PTSD do not have the same relaxation system and ability to rest/decompress. Moreover, these individuals may stay at a heightened level of activation (some individuals with PTSD have difficulty controlling their anger and regulating their mood). This heightened level of activation may have longer term negative implications for their health, taxing their system, and impacting their ability to relax enough to sleep. For example, research has shown that it is difficult to initiate sleep when a potential threat is present (or perceived), and this may be an indicator of the heightened hyperarousal experienced by individuals with PTSD [26,42,43]. Furthermore, it has also been suggested that improving sleep quality could counteract the elevated diastolic BP and act as a potential intervention for subjects with PTSD [43]. Elevated diastolic BP can also impact the PTSD subject's sensation/perception of pain, given that the system is already exhausted [44] and therefore could be more sensitive to impact pain thresholds; in other words, just as we may be more irritable when hungry or tired, imagine how pain could be perceived on an already "exhausted/taxed" nervous system?

Stress and tension migraines are common in individuals with PTSD [45,46], in alignment with increased tension, and hyperarousal within the body. As a result, many individuals with PTSD are prescribed β-blockers (such as atenolol or propranolol) to lower BP to ameliorate migraines. This may be one of the reasons why there were more anti-hypertensive medications prescribed for the PTSD participants.

Interestingly, in this study there were also significantly more asthmatics in the PTSD participant cohort. Previous studies have reported a link between asthma and PTSD [47]. Moreover, recent research by Allgire, et al. [48] also found that 'peripheral immune-brain pathways may translate asthma inflammation to PTSD.'

Alcohol consumption was not significantly different between groups. However, alcohol abuse was significantly different between the control and PTSD subjects. Individuals with PTSD are known to abuse alcohol, using it as a self-medication strategy to relax/cope with anxiety, and to initiate sleep [26]. Additionally, alcohol can serve as a REM suppressant, which can contribute to a reduction in nightmares temporarily, but also reduces the ability for the brain to engage in the useful parts of REM sleep for memory consolidation and other cognitive functions which can perpetuate PTSD and impair response to treatment, such as prolonged exposure (PE) and cognitive processing therapy [27,28]. Consequently, improving sleep quality and reducing pain, and perceptions of pain in PTSD subjects, may influence alcohol usage and improve treatment adherence and potential outcomes.

Contrary to previous studies, there were more tobacco smokers in the control group and control subjects smoked more cigarettes per day and for longer (years). In a meta-analysis of 29 studies, subjects with PTSD were almost 22% more likely to smoke [49].

As expected, this research confirmed previous findings that individuals with PTSD have significant rates of comorbidity with other psychological/psychiatric conditions. For many, there are questions as to which onset first and which contributed to the development of the other. What is important to note is that emerging research is finding that when treating SDs, symptoms of depression, anxiety, and PTSD (as well as other conditions), mental health providers can also significantly reduce other risk factors. Such considerations will be important for treatment intervention planning.

While individuals with PTSD may have equal levels of pain to controls, their perception of pain is not significantly higher. However, almost 21% of PTSD participants reported arthritis as comorbidity. This may be related to the type of pain described by the PTSD participants i.e., nagging, radiating and sharp. Furthermore, this may also explain how their perception of pain interferes with their social activities and activity engagement with others.

Given the amount of inflammation and stress that PTSD participants nervous systems are under, research shows that the perception of pain is higher when the body is under higher levels of stress. For example, research by Defrin, et al. [50] found that individuals with PTSD had a hypersensitivity to pain. This aligns with current theories that individuals with PTSD are hypervigilant, constantly examining their environment, as well as their personal experiences to detect potential threats; consequently, they are hyper-attuned to their bodies and will perceive any changes (including negative pain) at lower thresholds. This has significant treatment implications as it can contribute to broader sensory perception implications that can impact *in vivo* exposures common for PE treatment as well as memories perpetuating PTSD and serving as triggers.

While there were no differences in CAPS-5 scores for trauma type, symptom presentation and comorbidities did exist. Better understanding of differences in symptom presentation is especially relevant when determining which type of therapeutic intervention to utilize [24]. For example, finding that individuals who directly experience a PTE are more likely to have nightmares, could lend itself to a provider selecting imagery rehearsal therapy as the treatment of choice versus learning that individuals who witness PTE's are more prone to insomnia symptoms, hence lending to utilization of CBT strategies. Furthermore, recognizing that individuals with chronic pain may experience relief from progressive muscle relaxation (PMR) strategies to relieve tension, which can also lead to greater relaxation and higher likelihood to fall asleep, a provider can then teach these strategies and recommend a patient/client use them as part of their night-time routine [51]. PMR can also be a relevant grounding strategy to clear the mind and increase mindfulness focusing on the physical body to quiet the mind [51].

In conclusion, the results from this study would support the idea that managing SDs, and chronic pain are important strategies for ameliorating PTSD symptoms and, as such, SDs and chronic pain should be potential targets for therapeutic intervention. Providing treatment to target lowering of BP through medication or relaxation techniques may also be important in dealing with the perception of pain and pain hypersensitivity in individuals with PTSD. Increasing our understanding of how an individual's experience, and their diagnosis of PTSD is unique to them will help the clinician/therapist to provide more targeted and personalised treatment.

Limitations of the Current Work

The main limitation of the study includes (a) The small sample size of participants; (b) Potential recall bias (previous exposure to trauma and the participants ability to recall may be unreliable and/or exaggerated; (c) Cause and effect (an association between PTSD and possible trauma does not necessarily mean one factor caused the other; (d) Sampling bias (the cases and controls recruited for the study may not truly be representative).

Data Availability Statement

The raw data supporting the conclusions of this article will be made available by the authors without undue reservation.

Ethics Statement

Formal written informed consent was obtained from all study participants. The study conformed to all Data Use Agreements. Participant samples were deidentified and publicly available and are thus exempt from the requirement of the Institutional Review Board (IRB) approval (Exempt Category 4).

Author Contributions

The authors confirm contribution to the paper as follows; study conception and design: MWR, CNR, PF, and JVL; data collection: MWR, JW, and MJK; analysis and interpretation of results: MWR, JW, and MM; and draft preparation: MWR, JW, MJK, MM, and PF. All authors contributed to the article and approved the submitted version.

Supplementary Material

The supplementary material for this article can be found online at:

Disclosures

None declared.

Conflict of Interest

MWR, JW, MJK, CR and JVL are paid employees of Randox Laboratories Ltd but hold no shares in the Company. PF is the Managing Director and owner of Randox Laboratories Ltd, a privately-owned company.

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