Holocaust survivors: the pain behind the agony. Increased prevalence of fibromyalgia among Holocaust survivors

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ABSTRACT

Objectives. *To assess the frequency of fibromyalgia among a population of Holocaust survivors in Israel as well as the occurrence of post-traumatic stress disorder (PTSD) and concurrent psychiatric symptoms, including depression and anxiety among survivors.*

Method. *Eighty-three survivors of the Nazi Holocaust and 65 age-matched individuals not exposed to Nazi occupation were recruited. Physical examination and manual tender point assessment was performed for the establishment of the diagnosis of fibromyalgia and information was collected regarding quality of life (SF-36), physical function and health (FIQ), psychiatric symptoms (SCL-90) and PTSD symptoms (CAPS).*

Results. *Significantly increased rates of fibromyalgia were identified among Holocaust survivors compared with controls (23.81% vs. 10.94, $p<0.05$). Significantly increased rates of post-traumatic symptoms and measures of mental distress were also identified among survivors.*

Conclusion. *The results indicate a significantly increased prevalence of fibromyalgia among Holocaust survivors six decades after the end of the Second World War. This finding furthers our knowledge regarding the long-term effect of stress on the development of fibromyalgia.*

Introduction

Fibromyalgia syndrome (FMS) is a condition characterised by the presence of chronic widespread pain throughout the musculoskeletal system accompanied by diffuse tenderness. FMS is a common disorder with far-reaching effects on quality of life (1) and is currently conceived of as part of a spectrum of functional disorders, sharing the pathogenetic feature of central nervous system sensitisation to pain (2, 3). This spectrum includes an ever growing array of inter-related clinical entities including, among others, chronic fatigue syndrome, irritable bowel syndrome, temporomandibular joint disorder and others (3). Considerable progress has been made over the last two decades in elucidating the pathogenesis of FMS. Thus, although a familial/genetic background is presumed, external precipitating factors have been linked with the development of FMS. Physical trauma (4) and infection (5) are classical examples of such triggers. In addition, a large body of research has focused on the association between stress and the etiology of FMS. The extent of this association has been investigated in various settings, including both acute and chronic forms of stress. On the whole, in most models investigated, a positive correlation has been observed between stress and FMS (6-10).

The unique condition of holocaust survivors is characterised by prolonged exposure to the combination of intense stress, severe physical deprivation and overwhelming bereavement. Due to the period of time since the end of World War II (WWII), current holocaust survivors inevitably endured this suffering during childhood, puberty or early adulthood. Holocaust survivors also share a relatively homogeneous ethnic background, being of Jewish European origin.

Although much interest has been traditionally directed towards the issues of post-traumatic stress-disorder as well as depression (11, 12) and suicide (13, 14) among holocaust survivors, surprisingly little data is available concerning the relationship between early life exposure to the atrocities of the holocaust and the subsequent development of functional disorders. A single study has demonstrated an increased prevalence of chronic pain among survivors (15), and an increase in chronic

functional gastrointestinal symptoms has also been documented (16).

In the current study we have attempted to assess the frequency of fibromyalgia among a population of holocaust survivors in Israel. We also evaluated the occurrence of PTSD among survivors, as well as concurrent psychiatric symptoms, including depression and anxiety.

Methods

Participants

A sample of 83 survivors of the Nazi Holocaust and 65 age-matched individuals not exposed to Nazi occupation were recruited. The criteria for inclusion were knowledge of Hebrew and the absence of psychotic symptoms or significant cognitive impairment likely to interfere with study procedures or with informed consent.

Holocaust survivors were identified as having lived in any axis country or European country that was occupied by the Nazi regime in 1938–1945. Non-Holocaust survivors all lived in non-axis European countries during WWII. The response rate in both groups was 90%. The main reason for refusal was poor health. All participants gave written informed consent after receiving a detailed explanation of the purpose and design of the study. After signing an informed consent, the participants were evaluated by one observer (M.A).

Study instruments

The questionnaires were filled out in the presence of an interviewer and subjects were assisted in answering the questions, if needed. Each interviewer ensured that all subjects clearly understood the content of each item and the different aspects of the various component questions. All subjects completed the following questionnaires:

- Demographics and background

Participants were asked to answer questions regarding their personal background (*e.g.* family status, country of origin, level of education). Furthermore, the survivor group was asked whether they had been in concentration camps, labour camps, ghettos, or hiding during the Holocaust.

Table I. Demographic characteristics of the survey participants.

Variable	Holocaust survivors n=83	Control Group n= 65	ANOVA
Age, years	77.5 ± 6.3	77.4 ± 6.4 NS	
Range, years	62–97	66–90	
Sex: % Males	43.37%	43.0%	NS
Education, years	11.6 ± 3.7	12.8 ± 3.4	F(1,246)=4.2, $p<0.05$
Range, years	0–19	5–20	
Dwelling place/Domicile: (%)			
Home	76.4%	48.9%	Pearson $\chi^2=11.5$, df=2, $p<0.0035$
Elderly citizens' home	8.3 %	8.9%	
Protected accommodation	15.3%	42.2%	
Physical diseases: (%)			
Metabolic diseases	86.2%	80%	NS
Lung diseases	6.9%	4.44%	
Cancer diseases	6.9%	13.3%	
Psychiatric diseases:	n=32 – 38.55%	n=15 – 23.0%	$\chi^2=4.03$, $p<0.05$
Depression	79.3%	70%	NS
Post-traumatic Stress Disorder	17.2%	10%	
Psychosis	0%	0%	
Neurosis	3.5%	20%	
Duration of years since diagnosis	26.7 ± 18.8	18.6 ± 10.8	
Range, years	1–58	6–34	NS
Duration of treatment	13.7 ± 16.3	6.2 ± 2.75	
Range, years	1–57	3–12	NS
Psychiatric medications: (%)			
Antidepressants	51.7%	10%	
Anxiolytic drugs	31.0%	10%	NS
Sleep medications	17.3%	80%	
Combination:	48.3%	69%	
Psychology/psychotherapy support	30.55%	6.7%	Pearson $\chi^2=7.05$, df=1, $p<0.008$
Suicide attempt in the past (%)	9.7%	0%	Pearson $\chi^2=4.65$, df=1, $p<0.0035$
Suicide attempt in the closed family (%)	9.7%	11.1%	NS
Divorce	12.5%	1%	Pearson $\chi^2=6.0$, df=1, $p<0.015$
Divorce in the closed family	31.9%	33.3%	NS

Results are expressed as mean and SD or percentage. One-way ANOVA: between groups (Holocaust survivors *vs.* control group) or Chi squared test.
NS: not significant.

- Physical function assessment

Physical function and health status were assessed using the Fibromyalgia Impact Questionnaire (FIQ)(17).

The first part of the FIQ focuses on the patient's ability to perform daily tasks (*i.e.* driving, cleaning, walking, gardening, *etc.*) and contains 10 items with responses ranked 0 to 3, where 0 ="always able", and 3 ="never able". The item scores were normalised to range from 0 to 10 for uniformity, with 10 representing worst physical function. The mean of the items yields a single physical function score. The FIQ was translated and validated by us (18).

- Quality of life assessment

Quality of life (QoL) was assessed by SF-36 (19, 20). This is a health-related profile of QoL that contains 36 items and measures health status across three domains: functional status, wellbeing and overall evaluation of health. The Hebrew translation of the SF-36 was validated in an adult general population (21), and our group have used it on patients with widespread pain, with and without FMS (22). The SF-36 contains eight scales: physical functioning, social functioning, and role limitations attributable to physical and emotional problems, mental health, vitality, bod-

ily pain, and general health. Each scale generates a score from 0 to 100, with a high score indicating better health and less body pain.

- The Psychiatric Symptom Check List comprising 90 items measuring 9 psychiatric clinical subscales

The SCL-90 was developed as a measure of general psychiatric symptom severity as a descriptive measure of psychopathology (23). The clinical subscales are: somatisation (12 items), obsession-compulsion (10 items), interpersonal sensitivity (9 items), depression (13 items), anxiety (10 items), hostility (6 items), phobic anxiety (7 items), paranoid ideation (6 items) and psychoticism (10 items). The SCL-90 has been extensively used and validated in Hebrew (24).

Subjects are required to rate specific complaints on a 5-point Likert scale running from 0 = "never" to 4 = "frequently". Higher scores indicate greater distress. Cronbach's alpha values for the scales of somatisation, depression, anxiety and hostility in this study were 0.89, 0.90, 0.92, and 0.91, respectively.

- Clinician administered Post-Traumatic Stress Disorder Scale (CAPS)

PTSD symptoms were assessed using the Hebrew version of the CAPS (25). This is a structured interview for assessing PTSD according to DSM-IV criteria. The Hebrew version of the scale has been extensively used and validated (26). The questionnaire quantifies symptom frequency and intensity for each of the criteria, yielding both a continuous measure of symptom severity and a dichotomous classification into PTSD status. A severity score for each symptom is calculated by summing the frequency and intensity scores. Thus, the total range of the instrument is 0–136. If no event was present, CAPS was not applied, and individual items were automatically scored as zero (0), as a default option.

The questionnaires were filled out by an interviewer, and subjects were assisted in answering the questions, if needed. The interviewer made sure that all subjects clearly understood the content of each item and the different aspects of various components.

Table II. WWII Experience.

Variable	Holocaust survivors n=83
Pubertal stage at Holocaust period:	
Child:	n=70, 84.3%
Adult (mature):	n=13, 15.7%
Lived in a ghetto under Nazi occupation:	
n, %	n=33, 39.74%
Duration (months):	17.3 ± 14.7
Lived in concentration camps under Nazi occupation:	
n, %	n=27, 32.5%
Duration (months):	15.8 ± 10.3
Lived in labour camps under Nazi occupation:	
n, %	n=33, 39.74%
Duration (months):	30.1 ± 26.5
Were in hiding places under Nazi occupation:	
n, %	n=7, 8.4%
Duration (months):	23.0 ± 18.3
Torture	n=16, 19.3%
Medical "experiences"	n=4, 4.8%
Family or relative killed	n=67, 80.7%
Spouse killed	n=46, 55.4%

Results are expressed as mean and SD or percentage.

FMS diagnosis

In all subjects, a count of 18 tender points at 9 symmetrical sites was performed by thumb palpation. Definite tenderness at any point was considered present if some involuntary verbal or facial expression of pain occurred or withdrawal was observed. The diagnosis of FMS was made based on the 1990 American College of Rheumatology classification criteria for the diagnosis of FMS (27).

Data analysis

Means, standard deviations, and frequencies were computed to summarise the distribution of values for each variable. Age, years of education, family status, number of years of marriage, immigrant/veteran status in Israel (a country with high rates of immigrations) and number of years in Israel were analysed as continuous data and compared by one-way analysis of variance (ANOVA). The Bonferroni post hoc test was used to examine pair-wise differences between the groups. Chi-square tests were used for categorical data.

Results

Table I presents demographic data regarding Holocaust survivors and controls. As noted from the table, groups were similar regarding age and gender. The table also presents data regarding the presence of physical disease, as well as the presence of psychiatric disorders including depression, PTSD and neurosis. Use of psychiatric medications is documented, along with utilisation of psychological support. Finally, data regarding suicidal behaviour by the individual or within his / her close family is documented.

As noted in the table, the combination of depression, PTSD and neurosis was significantly more frequent among Holocaust survivors compared with controls. Utilisation of psychotherapy was also significantly higher among survivors, although use of psychiatric medications was not. A history of suicidal attempt was significantly higher among Holocaust survivors.

Table II presents data regarding the type of experience endured by the survivors during WWII. As noted, the vast majority of survivors had been children during the Holocaust; 19.3% had undergone torture and 4.8% had been subjected to medical experiments by the Nazis. An overwhelming majority (80.7%) had suffered bereavement of close family members.

The frequency of FMS among Holocaust survivors and controls is presented in Table III.

As noted in the table, FMS was sig-

nificantly more frequent among Holocaust survivors (23.8%) compared with controls (11.1%). (Chi square -χ^2-3.87, p=0.0491).

Assessment of mental distress among Holocaust survivors compared with controls

Figure 1 presents the results of the SCL90 scores measured among Holocaust survivors and controls. As noted in the figure, and as expected, survivors rated significantly higher on a range of distress-related symptoms including somatisation, obsessive-compulsive symptoms, interpersonal sensitivity, depression, anxiety and hostility.

Chronic post-traumatic stress-related symptoms

The overall prevalence of PTSD was significantly different for the two groups. The ANOVA yielded a significant difference in post-traumatic symptoms, $F(3,208)=9.95$, $p<0.001$. A ANOVA showed a significant group difference in the intensity of symptoms, $F(1,205)=7.06$; $p<0.01$. Holocaust survivors endorsed significantly more symptoms (M=7.03; SD=4.40) than non-survivors (M=5.26; SD=3.88), as well as significantly more intrusion (M=2.74; SD=1.64 *vs*. M=1.58; SD=1.52) and avoidance (M=2.10; SD=1.76 *vs*. M=1.40; SD=1.61) symptoms. Table III presents the observed prevalence of PTSD related symptoms among Holocaust survivors and controls.

Table III. FMS symptoms and chronic (post-traumatic) stress-related symptoms.

	Holocaust survivors n=83	Control Group n= 65	Statistical analysis
FMS	23.8%	11.1%	χ^2= 3.87, p=0.0491
PTSD prevalence	n=55 66.3%	n=4 6.15%	χ^2=54.94, p<0.00001
Symptoms:			
Intrusive symptoms	16.25 ± 6.1	7.5 ± 9.8	F(1,146)=170.9, p<0.00001
Avoidance	17.9 ± 6.8	11.25 ± 8.0	F(1,146)=183.7, p<0.00001
Hyperarousal	17.2 ± 6.0	9.75 ± 7.7	F(1,146)=206.2, p<0.00001
Total scale	51.4 ± 13.9	28.75 ± 20.6	F(1,146)=242.7, p<0.00001

Results are expressed as mean ± SD.
One-way ANOVA: between groups (Holocaust survivors *vs*. control group).
NS: not significant.

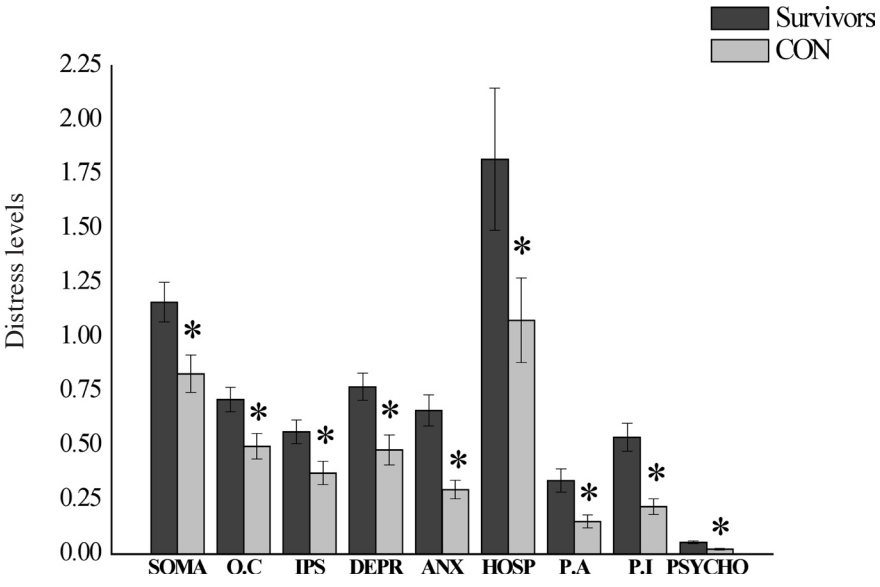

Fig. 1. Mental distress among holocaust survivors *vs*. control group according to SCL90 scores. Results are expressed as mean ± SEM.
*$p<0.05$
SOMA: somatisation; OC: Obsessive-Compulsive; IPS: Interpersonal Sensitivity; DEPR: Depression; ANX: Anxiety; HOSP: Hostility; P.A: Phobic anxiety; P.I: Paranoid ideation; PSYCHO: Psychoticism.

Discussion

In the current study we have demonstrated an increased prevalence of FMS among elderly Holocaust survivors in Israel, compared with a control group of individuals not exposed to the Holocaust. An increased prevalence of Post-Traumatic Stress Disorder (PTSD) was also demonstrated.

A complex relationship exists between stress and FMS. Epidemiological studies have shown that high baseline levels of psychological distress predict the development of chronic regional or widespread pain (OR 1.5–2) (28-31). The hypothalamic-pituitary-adrenal system, responsible for the human stress response, is an important link between stress and pain, and baseline function of the HPA stress response is a predictor of chronic widespread pain, independent of distress and other psychological factors (32). Physical trauma in general and cervical trauma in particular (4, 33), are important triggers in the development of chronic pain and FMS (4, 34-36).

While many studies have previously focused on the link between stress and chronic pain, including FMS (37), little is known about the time course of this association and about the ability of stress to induce chronic pain and FMS decades after the exposure. Most studies analysing this association have focused either on the effect of acute, highly stressful events such as terrorist attacks (38) on the appearance or exacerbation of pain symptoms, while others have looked at the capacity of stress to anticipate and predict the subsequent development of widespread pain within a framework of several years. In our study, however, conducted more than six decades after the end of WWII, we were able to detect an extremely long-term effect of stress and trauma experienced during childhood and young adulthood.

Notably, our group of Holocaust-survivors and controls differed significantly in regard to the percentage of individuals who were living at home at the time of the study, compared with the percentage that required protected accom-

modations. While any significant difference between the groups compared may pose a limitation, the fact that the group of Holocaust survivors were on the whole more independent, tends to strengthen our results, as it implies that this group of individuals did not suffer from more serious medical and /or psychiatric disorders, which may have had an effect on the occurrence of chronic pain. However, as noted, chronic pain was significantly more common among these individuals.

Another point to note is the higher frequency of neurosis among controls in comparison with Holocaust survivors (20% *vs*. 3.5% respectively). While various speculations may be raised in the explanation of this finding (which did not reach statistical significance), it is likely that a large proportion of psychiatric morbidity that came under the titles of depression and PTSD among Holocaust survivors overshadowed less serious neurotic symptoms. Similarly, while a larger proportion of controls declared using sleep medications (again, not reaching a statistical significance), this finding may reflect the larger proportion of Holocaust survivors using anti-depressants and anti-anxiety agents, many of which may also have a sleep inducing effect. Surprisingly, low levels of suicide attempts and divorce were recorded among our controls. We have no clear explanation for this apparently random finding in a group of elderly individuals.

These results come in the context of increasing knowledge regarding the biological underpinnings of both chronic pain and PTSD. It is well established that a significant clinical and pathogenetic overlap exists between these two seemingly dissimilar entities (39). Recently, it has been shown that elderly Holocaust survivors demonstrate alterations in specific pathways of glucocorticoid metabolism, possibly partly as a result of severe developmental adversity, including nutritional deprivation, during childhood (40). Low urinary cortisol levels have been demonstrated in Holocaust survivors suffering from PTSD (41), and after ten years of follow-up were a strong predictor of the clinical outcome (42). In animal models, early life stress is capable of inducing a cascade of neurobiological events, including changes in neural plasticity, thus influencing susceptibility to PTSD. Various neurotransmitters and mediators have been implicated as playing a role in this chain, including Brain-Derived Nerve–Growth Factor (BDNF) and cortisol (43).

"Torture syndrome" is a term which has been previously used to describe the complex psychological and physical symptoms which often arise as a late sequel of torture (44) . While a considerable number of our Holocaust survivors reported actual torture, it seems likely to assume that the ongoing deprivation, violence, humiliation, forced labour and similar hardships suffered by all the survivors over extended periods of time might in fact be as enduringly harmful as torture. The endurance of pain-related symptoms, more than 6 decades after the events, is intriguing. Neural plasticity at a young age may contribute to this phenomenon. Recent evidence indicates that chronic pain is determined by learning processes that are associated with plastic changes taking place on multiple levels of the central nervous system (45-48). This recognition directs attention towards the possibility of utilising extinction training ("unlearning") as a therapeutic modality (49), as well as implementing pharmacological agents capable of preventing or reversing neuronal plasticity (50). While remembering the atrocities of the Holocaust, as well as other acts of genocide, is an overwhelming moral imperative, this type of "explicit" and collective memory must be differentiated from what is termed "implicit" (or nondeclerative) memory. This later kind of behavioural change, which develops as the result of experience, involves non-associative learning processes such as habituation and sensitisation. "Unlearning" of these lessons may be a major challenge in the management of chronic pain (51).

In the current study we did not attempt to specifically rule out alternative conditions causing chronic pain such as osteoarthritis or inflammatory joint disease. Thus, we do not attempt to determine whether symptoms of FMS were "primary" or secondary among the individuals in whom they were surveyed. The rationale behind this approach is that we believe chronic pain is inevitably the sum result of central nervous system interpretation of peripheral nociceptive input. Thus, in every FMS patient, (and surely in octogenarians), one will find peripheral generators of pain such as degenerative joint disease of some degree. The way the CNS copes with this input is what will determine whether an individual will suffer chronic widespread pain (in other words, present clinically as suffering from FMS). Notably, it is hard to determine in retrospect for how long symptoms of chronic pain have accompanied the lives of these individuals. While our population represents a rather elderly sample as far as FMS is concerned, it is possible that many individuals have in fact suffered from some degree of pain, gradually developing into full-blown FMS, for decades.

Conclusion

In conclusion, in the current study, we have demonstrated an increased prevalence of fibromyalgia among Holocaust survivors six decades after the end of WWII. This finding expands our knowledge on the relationship between severe stress and FMS, and highlights the prolonged nature of the neuronal changes induced by such stress on the central nervous system. Further research may focus of the important issue of trans-generational effects of catastrophic events such as the Holocaust on subsequent generations. Last, but not least, these results point attention to the necessity of allocating resources for the treatment and alleviation of pain symptoms among the remaining elderly Holocaust survivors.

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