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***THE INFLUENCE OF EARLY STRESSFUL LIFE
EVENTS ON FIBROMYALGIA AND OTHER
PSYCHIATRIC CO-MORBIDITIES: A FAMILIAR
APPROACH***

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Resumo

Introdução: a fibromialgia (FM) é um síndrome controverso caracterizado por dor musculoesquelética generalizada crónica com uma duração mínima de 3 meses. É frequentemente associada a comorbilidades psiquiátricas, nomeadamente ansiedade e depressão. Várias hipóteses tem sido geradas em relação à sua etiologia, como o papel de factores ambientais (neste caso, eventos traumáticos precoces) cuja contribuição no desenvolvimento destes distúrbios se deve a alterações na modulação do eixo Hipotálamo-Hipófise-Suprarrenal e Sistema Nervoso Autónomo.

Objectivo: O objectivo deste trabalho prende-se com a confirmação de que mulheres com fibromialgia apresentam maior história de trauma precoce quando comparadas com as irmãs sem a doença. Averiguou-se também qual o tipo de trauma mais frequente. Por fim, tentou-se aferir se a mãe corroborava o acontecimento de tais traumas ou se o seu relato se deveria a uma hipervalorização por parte da doente.

Métodos: a população consistiu em 20 famílias compostas por uma filha com fibromialgia, a sua irmã saudável e a mãe de ambas. Usou-se o Early Trauma Inventory para avaliar a história de traumas nas doentes e controlos. A mãe respondeu também a este inquérito em função de cada uma das filhas. O Hospital Anxiety and Depression Scale foi usado para medir os níveis de depressão e ansiedade em doentes e controlos.

Resultados: os resultados demonstram que as doentes com FM reportavam maior quantidade de traumas durante a infância, por oposição às irmãs saudáveis (53,4% vs 33,7%). Esta informação foi corroborada pela mãe. O tipo de trauma mais frequente foi Trauma Geral. Demonstrou-se uma correlação estatisticamente significativa positiva entre diferentes tipos de trauma no grupo das doentes. Mostrou-se ainda uma correlação

positiva entre eventos traumáticos precoces e altos níveis de ansiedade e depressão nas doentes.

Conclusão: A hipótese de que eventos traumáticos precoces estão correlacionados com o desenvolvimento de fibromialgia no futuro foi confirmada. Nesta população é claro que mais traumas ocorreram na vida das doentes quando comparados com o número de traumas na vida das suas irmãs saudáveis. Este facto foi reconhecido pela mãe e está também associado a maior prevalência de distúrbios psiquiátricos como a ansiedade.

Abstract

Background: Fibromyalgia (FM) is a controversial syndrome characterized by a history of widespread musculoskeletal pain for at least three months and is frequently associated with psychiatric co-morbidities such as anxiety and depression. Several hypothesis have been suggested for its etiology, namely the role of environmental factors (traumatic events) on the development of these disorders, mainly involving the Hypothalamus-Pituitary-Adrenal (HPA) axis and the Autonomic Nervous System (ANS).

Objective: The main goal of this study is try to understand if female patients with fibromyalgia have had a bigger history of early traumatic events compared to their healthy sisters and which dimension of trauma was more frequent. Also, we tried to ascertain if the mother corroborated the happening of those traumatic events, or if they had been hyper valorized as trauma.

Methods: the population consisted in 20 families composed by a daughter with FM, a healthy sister and their mother. We used the Early Trauma Inventory to access the history of traumatic events on the lives of both patients and controls. Also, the mother answered the same questionnaire regarding each daughter. The Hospital Anxiety and Depression Scale has been used to measure depression and anxiety levels.

Results: Results showed that the FM patients reported a higher number of traumas during childhood, opposing to their healthy sisters. This information has been corroborated by the mother. The most frequent dimension of trauma reported was “General Trauma”. There was a positive statistically significant correlation between different dimensions of trauma on the FM group. Also, a positive correlation has been established between the incidence of traumatic events and high levels of anxiety and depression on the patients.

Conclusions: The hypothesis that early traumatic events are associated with the development of FM in the future has been confirmed. In this population it's clear that more traumas occurred in the FM patients, and less on the healthy sisters. This fact is recognized by their mothers and is also related to the development of psychiatric disorders such as anxiety.

Introduction

Presenting Fibromyalgia

Fibromyalgia (FM) is a controversial syndrome characterized by a history of widespread musculoskeletal pain for at least three months, combined with pain in no less than 11 out of 18 predefined musculoskeletal points [1]. With an estimated prevalence of 3,6 % on the Portuguese population[2], it's frequently associated with other symptoms/ co morbidities, such as chronic fatigue, poor quality sleep, mood disturbances such as anxiety and depression, irritable bowel syndrome and headaches [3]. For all of this, FM determines an immeasurable suffering for the patient, conditioning a negative impact on emotional, social and professional aspects of the person's life.

Such a substantial problem requires all consideration in a way to obtain a better comprehension at all levels, because only by doing that we will be able to deal with the disease and work on one of the most important missing aspects: treatment. Several approaches have been tried, but the pharmacological component didn't provide the answer and other strategies such as Cognitive Behavioral Therapy or exercise failed to obtain success.[4]

FM etiology remains unclear, although several theories have been proposed, namely genetic influence (familiar predisposition), abnormal functioning of neuroendocrine pathways and of the Autonomous Nervous System (dysregulation in central pain processing), environmental factors (physical and psychological trauma and stress) [5] and immunologic basis (association with auto-immune diseases) [4].

This study has been designed with the goal of better understanding the influence of environmental factors which is one of the grey areas of etiology. By exploring the various natures of trauma history during childhood of patients and controls, we will try to ascertain a possible connection between that factor and the present FM diagnosis, as well as associated disturbances such as depression and anxiety.

The association between FM and trauma history

Several studies have already described a strong association between traumatic events throughout the patients lives and FM [6, 7 , 8]. A peculiarity of this connection, which is the nuclear concept of this study, is the relation between traumatic events during childhood and developing chronic diseases, namely FM.

Stress can be defined as a threat (or the perception of a threat) to the organism homeostasis, caused by physical assault or psychosocial burden. This threat ends up activating neuronal, hormonal and behavioral genetically determined programs – *Stress response system* – aiming at the preservation and restoration of the equilibrium.

At the foundation of the stress response system are neuroendocrine pathways, namely the Hypothalamus-Pituitary-Adrenal (HPA) axis and the Autonomic Nervous System (ANS).

Early trauma can affect the HPA axis function, causing inappropriate stress response at long term. These alterations are described as hyporeactivity of these systems to mental and physical stressors, and this reduction has been frequently seen in FM.[9] After the occurrence of a physical assault or psychosocial burden, the stress response system may suffer a “neurobiological switch”, from hyperactivity to hyporeactivity, associated with functional or even structural receptor changes. [10]. This could cause disturbance on the

central pain processing mechanism, as well as immunologic and neuronal systems, leading to an extended nociceptive input from the spinal chord to the brain, even in the absence of a painful stimuli [9].

As we stand today, the cause for this “loss of resilience” of stress response system remains unclear [11]. It’s been suggested that this dysregulation may take place in different levels of the HPA axis, such as stress-induced down regulation of CRH receptors, resistance to glucocorticoids or increased sensitivity of the axis to negative feedback [12].

Some studies have proved that children are particularly vulnerable to long term negative effects of a traumatic experience, as they’re at the most active phase of brain development [13, 14, 15] and their perception of trauma is distinct from that of an adult, due to cognitive [16] and emotional [17] different level of maturity.

What do we want to know?

This project intends to analyze the frequency of early stressful life events on women with FM by comparison with a healthy sister, resorting to their mother for corroboration of the facts, through the interpretation of the results of a questionnaire that explore different types of trauma occurred during the subjects’ childhood.

By comparing the answers of the patients and sisters, we aim to assess if traumas have been more frequent, their nature and which have had a stronger impact, exploring a possible relation with the disease. Also, we will investigate if there is a particular age in which more situations of trauma are referred or have been more outstanding. As the mother was asked to answer the questionnaire in regard of each daughter, we will try to

discern if eventually the diseased daughter hyper valorizes certain events occurred during infancy , also diminishing the risk of recall bias by the sisters.

At last, we will evaluate the association of early trauma with anxiety levels and depression in adulthood.

Population and methods.

Population

In order to address the hypothesis described above we decided to study female patients with fibromyalgia paired with an unaffected sister and the mother of both .

Participants were drawn from a list of 712 patients with an established diagnosis of FM from a single site (all diagnosed and followed by Prof. J.A.P. da Silva). The following screening criteria were used for selection: Female gender, age between 18 and 55 years, absence of any other chronic pain condition, residence within a radius of 100 Km from the study centre. Selected patients were contacted by phone and invited to participate if 1. they had at least one unaffected sister, 2 if they had the same mother, still alive and capable of participating and providing reliable information, and 3. all the family members were willing to travel to the research site and participate in the study, which involved signing an informed consent, responding to questionnaires, providing a blood sample and undergoing physical examination. Participants were reimbursed for transportation costs but no other compensations were offered.

The study was approved by Ethical Committee of the Faculty of Medicine of the Universidade de Coimbra.

Data Collection.

All research proceedings were performed in the morning. After receiving and explanation of the study procedures and having an opportunity to present any questions and discuss all issues, participants signed an informed consent form. Breakfast was offered to participants before the procedures were started.

Methods

This study involved a team of 9 investigators, working together in the FM SCAN project, each exploring a specific topic through the application of distinct questionnaires to the same population.

The Early Trauma Inventory SR short form

In the particular case of this study, the topic is early life trauma and its relation with fibromyalgia. As such, all participants were asked to answer a self-report questionnaire – The Early Trauma Inventory self report short form (ETI-SR short form) [18]. This instrument was created and validated by Bremner et al for the assessment of trauma occurring before the age of 18, designed as self-report shortened version of the original 56 clinician administered ETI. It comprehends a total of 27 items, including 11 for general trauma, 5 for physical abuse, 5 for emotional abuse and 6 for sexual abuse. For each item, the subjects answered “yes” (in this case, accompanied by the age of occurrence), “no” or “I don’t want to answer”.

Within each of these 4 domains, scorings were built by summing all positive items. Higher scores in each domain indicate more traumatic experiences.

Both the patient and the sister filled in the ETI-SR short form about themselves as a self-report. The mother answered the same questions in regard of each of her two daughters. Due to difficulties related to the age and, in some cases, illiteracy, the questionnaire was presented to the mother by the clinician/investigator.

Hospital Anxiety and Depression Scale – HADS [19]

The HADS is a brief questionnaire that consists of two subscales, one measuring anxiety, with seven items, and one measuring depression, with seven items, which are

scored separately. Each item is answered on a 4-point (0-3) scale so the possible scores ranged from 0 to 21 for anxiety and 0 to 21 for depression. It takes 2-5 minutes to complete. The HADS manual indicates that a score between 0 and 7 is “normal”, between 8 and 10 “mild”, between 11 and 14 “moderate” and between 15 and 21 “severe”.

Mini Mental State Examination

The MMSE [20] is a brief 30-point questionnaire design to screen for cognitive impairment. A score matching 25 or higher is effectively normal (intact); the score can indicate mild (24-21), moderate (10-20) or low (<9) cognition.

This questionnaire was used to guarantee that all mothers had the cognition level required to consider their answers reliable: participants with a score below 25 were excluded.

Physical Examination

All subjects underwent a short physical exam, in order to eliminate the possibility of any of the sisters having undiagnosed FM criteria, in which case the whole family would have to be excluded from the study. They were asked about history of widespread pain and, in need, tender points were scanned.

Statistical analysis

The statistical study was executed through the use of the statistical software PASW (IBM edition of SPSS), version 18.0.

On a first approach, a descriptive analysis of all variables of the study was performed. Thus, the means and standard deviations of numerical variables were calculated, as well as the frequency and percentage of the categorical variables [21].

On the inferential analysis, differences were considered as statistically significant if the probability value (p) associated to the statistical test was less than 0.05. [22].

To check for statistically significant differences between an independent variable with two categories and a numerical dependent variable, the Student's t-test for independent sample was used [22]

To measure the association between two numerical variables Pearson product-correlation was calculated. [22]

To do crosstabs between two dicotomic variables the Fisher test was used (Fisher exact test). [22]

Results

The screening criteria described above, reduced the potential population to 317 individuals, which were contacted by phone. Of these, 278 were excluded for the following reasons: 121 did not have an unaffected sister, for 27 their sister lived too far away to attend, 73 were already orphans or their mother was not capable of participating and 57 were not reachable through the phone. Of the remaining 39 families, satisfying inclusion criteria, 11 refused to participate and 6 never made themselves available to attend the research centre.

Altogether, 22 families, composed of a FM patient(A), one unaffected sister(B) and the mother of both(C) were initially included in the study. At a later stage two had to be excluded because 1. one of the sisters also had FM criteria and 2. one of the mothers had a significant cognitive impairment as assessed by the MMSE (Mini Mental State Evaluation). Their demographic characteristics are presented in table I. All the participant were female.

Table I – Socio-demographic characteristics of the population in study

Subject Group	Age (years)					Years of education					Age at the beginning of symptoms				
	N	Min	Max	M	SD	N	Min	Max	M	SD	N	Min	Max	M	SD
A	20	19	56	42.16	10.19	19	5	21	12.16	4.13	18	15	49	33.50	12.85
B	20	20	53	41.84	9.75	19	4	20	11.42	4.86	-	-	-	-	-
Mother	20	47	86	69.00	10.94	19	0	11	3.89	3.54	-	-	-	-	-

The results will be displayed according to the scheme: A – patient with FM; B – healthy sister; MonA - mother regarding A; MonB - mother regarding B. Each question answered with “yes” on the questionnaire was defined as an occurrence (trauma event).

In all dimensions, the average number of occurrences reported by the mother was inferior to those identified by each of the daughters.

The FM group reported, on average, a higher number of occurrences, being the highest score correspondent to “General Trauma” dimension, with a mean of 2 occurrences (SD=1.89) and the lowest to “Sexual Events” dimension. (Table II)

Table II: Mean (M) and Standard-deviation (SD) of the number of trauma occurrences considering the patient and controls reports.

Subject Groups	General Trauma			Physical Punishment			Emotional Abuse			Sexual Events		
	N	M	SD	N	M	SD	N	M	SD	N	M	SD
A	19	2.00	1.89	17	.94	1.20	20	1.50	1.67	20	.40	.82
B	20	1.35	1.39	19	.42	.77	20	.40	.75	20	.05	.22
MonA	19	1.37	1.53	19	.37	.60	19	.32	.67	19	.05	.23
MonB	19	1.00	1.29	19	.21	.42	19	.26	.74	19	.11	.45

There results can also be seen considering the division between the que subjects who reported occurrences of trauma and didn't. As we can see on Table III there a larger number of A reporting occurrences than B. When reporting to their daughters the mothers counted for less occurrences than the girls.

Table III: Distribution of trauma occurrences regarding patient and control reports. (n=20; 100.0%).

Subject Groups	Occurrences	General Trauma		Physical Punishment		Emotional Abuse		Sexual Occurrences	
		N	%	N	%	N	%	N	%
A	Absent	5	25.0	9	45.0	8	40.0	15	75.0
	Present	15	75.0	11	55.0	12	60.0	5	25.0
B	Absent	7	35.0	13	65.0	14	70.0	19	95.0
	Present	13	65.0	7	35.0	6	30.0	1	5.0
Mon A	Absent	8	40.0	13	65.0	15	75.0	18	96.7
	Present	12	60.0	7	35.0	5	25.0	1	5.3
MonB	Absent	10	50.0	15	75.0	16	80.0	18	96.7
	Present	10	50.0	5	25.0	4	20.0	1	5.3

When it comes to age at the time of the occurrence, both daughters systematically reported higher values than their mothers and the “General Trauma” and “Emotional Abuse” presented the higher age mean. (Table IV)

Table IV: Mean (M) and standard-deviation (SD) of the age of trauma occurrence considering the patient and control reports

Subject Groups	General Trauma			Physical Punishment			Emotional Abuse			Sexual Events		
	N	M	SD	N	M	SD	N	M	SD	N	M	SD
A	15	12.17	3.33	10	10.58	3.30	13	12.78	2.82	3	14.67	3.21
B	12	12.52	3.97	6	10.86	3.79	5	11.40	3.21	1	8	-
MonA	11	8.88	4.23	6	9.67	5.05	4	11.00	5.35	1	11	-
MonB	9	7.76	3.21	4	7.25	5.19	3	12.11	2.59	1	10	-

Confirmation of trauma by mothers – The FM daughter

When matching the FM group answers with their mother’s report through inferential statistics, concordance between the subjects was found and statistically significant differences weren’t present in the answers given in “General Trauma”, “Physical Punishment” and “Sexual Events” dimensions. (Table V)

However, when it comes to the “Emotional Abuse” dimension, the mother’s reports showed statistically inferior means of occurrence (MonA group: $M=.32$, $SD=.67$ < A group: $M=1.50$, $SD=1.67$) meaning that the FM group reported a higher number of emotional abuse events than those pointed out by their mother. (Tables II and V).

Table V: T-test (t) comparing group A and MonA answers reporting the number of trauma events, considering the patient and mother reports.

Subject Groups	General Trauma			Physical Punishment			Emotional Abuse			Sexual Events		
	ΔM	t	p	ΔM	t	P	ΔM	t	p	ΔM	t	p
A												
MonA	.63	1.143	.261	.57	1.784	.088	1.18	2.932	.007	.35	1.819	.082

ΔM = Mean differences between groups

No statistically significant differences were found between the answers of the mother and daughter regarding the age of trauma occurrence in the “Physical Punishment” and “Emotional abuse” dimensions. (Table V). Still, when it comes to the “General Trauma” dimension, the mother reported a significantly lower age means than the daughter (A group: $M=12.17$, $SD=3.33$ > MonA group: $M=8.88$, $SD=4.23$) (Table III and VI).

Regarding the age mean for the “Sexual Events” dimension, the sample wasn’t large enough ($n=4$) to apply the statistical test.

Table VI: T-test (t) comparing group A and MonA answers regarding the age at the time of trauma events, considering the patient and mother reports..

Subject Groups	General Trauma			Physical Punishment			Emotional Abuse		
	Δ M	T	p	Δ M	T	p	Δ M	t	p
A MonA	3.29	2.218	.036	.92	.443	.665	1.78	.640	.561

Δ M= Mean difference between groups

Confirmation of trauma by mothers – The healthy daughter

When comparing B group answers to their mother’s reports, no statistically significant differences were found concerning the number of occurrences of any dimension and no significant trends were identified. (Table VII).

Table VII: T-test (t) comparing group B and MonB answers reporting the number of trauma events, considering the control and mother reports.

Subject Groups	General Trauma			Physical Punishment			Emotional Abuse			Sexual Events		
	Δ M	t	p	Δ M	t	p	Δ M	t	p	Δ M	t	p
B MonB	.35	.815	.421	.21	1.048	.301	.14	.574	.569	.06	.482	.633

Δ M= Mean differences between groups

However, when matching the ages, the “General Trauma” dimension results showed that the mother reported significantly lower age means than those pointed out by their daughters. (B group: M=12.52, SD=3.97 > MonB : M=7.76, SD=3.21) (Tables III and VIII).

Student T-test was not calculated for the rest of the age differences as a result of the reduced number of effectives on the three variables (table III). Also, there was a lower

number of elements in the group B reporting occurrences and less pointed out occurrences.

Table VIII: Student T-test comparing group B and MonB answers regarding the age at the time of trauma events, considering the control and mother reports.

Subject Groups	General Trauma		
	ΔM	t	p
B MonB	4.75	2.938	.008

ΔM = Mean difference between groups

In the relation between variables of trauma/abuse we could verify distinct correlation patterns within the dimensions at study. For instance, A group presents statistically significant positive correlation between “General Trauma” and other dimensions, being the strongest with “Physical Punishment” ($r=.63$). Also, a strong, statistically significant association can be established between “Physical Punishment” and “Emotional Abuse” dimensions ($r=.67$) (Table IX).

As for the B group, no significant association was noticed between the dimensions of trauma, as none of them presents statistically significant results. (Table IX)

The Matrix constructed for the mother regarding the A group daughters revealed positive statistically significant associations between “general trauma” and “physical punishment” ($r=.57$) and “general trauma” and “sexual events” ($r=.73$). When concerning the B group, there was a very higher correlation value ($r=.93$), which in this case means that mothers recognize the non existence of this type of occurrences regarding the daughters. Still considering mother’s regarding B group daughters, a

statistically significant correlation is present between “Sexual events” and “physical punishment” dimensions. (table IX).

Table IX: Correlation matrix (Pearson product-moment coefficient) between trauma occurrence variables, separating the subject groups

Trauma dimensions	A			B			MonA			MonB		
	1	2	3	1	2	3	1	2	3	1	2	3
General Trauma (1)	1			1			1			1		
Physical Punishment (2)	.63**	1		.05	1		.57*	1		.21	1	
Emotional Abuse (3)	.59**	.67**	1	.13	.38	1	-.12	.11	1	.24	.35	1
Sexual Events (4)	.51*	.35	.37	-.05	-.14	-.12	.73**	.26	-.11	.19	.46*	.91*

**p<.01; *p<.05

As for the association between reported trauma occurrences and anxiety and depression levels, we can see a clear positive statistically significant correlation between anxiety and “Physical Punishment” ($r=.61$) and “Emotional Abuse” ($r=.44$) in the FM group. Also in this group, there is a important correlation between depression and “Physical Punishment” ($r=.52$). When it comes to the B group, only depression could be associated to the trauma dimensions, namely a positive statistically significant correlation with “Physical Punishment” ($r=.46$), “Emotional Abuse” ($r=.64$) and “Sexual Events” ($r=.60$) (Table X).

Table X: Pearson product-moment coefficient between trauma occurrences and Anxiety (A) and Depression (D) variables regarding patient and control.

	A		B	
	A	D	A	D
General Trauma	.40	.32	-.05	-.11
Physical Punishment	.61**	.52*	-.07	.46*
Emotional Abuse	.44*	.37	.37	.64**
Sexual Events	.30	.29	-.15	.60**

**p<.01; *p<.05

Discussion

The present study was aimed at establishing a correlation between early trauma and the development of FM in female patients. Also, we wanted to assess if these trauma reports were confirmed by others than the patient. Our results confirmed those hypothesis.

Our conclusions are consistent with prior studies that have proven an association between early trauma and long term pain syndromes, such as FM [10][23][24][25]. Some have even stated that about 40-60% of FM patients reported a childhood abuse history [26].

The present study showed that, although the reporting of traumatic occurrences was relatively low, the events reported were systematically (at descriptive level) enough to conclude that the subjects who reported higher number of trauma were the FM patients (53,4%). Accordingly, their sisters, who haven't developed the disease, reported less trauma events (33,7%).

It's convenient to refer that in FM, as in most illnesses with a genetic component, environmental factors play an important role on triggering the development of the disease [27]. Taking in consideration that the patients and controls are sisters, they share a similar genetic background. The fact that only one of them developed the disease, might be due to the impact of environmental factors, like traumatic experiences, as we tried to prove in our study.

This being said, results show that, in our population, the most frequently described trauma fits in the "General Trauma" dimension, which comprehends "a range of traumatic events that can be mostly secondary to chance events" [18], followed by the

“Emotional abuse” dimension, . This might suggest that the traumatic experiences included in these dimensions could possibly cause more long term consequences to the patient, having more impact in the development of the disease.

The less referred trauma dimension was “Sexual Events”. This may be due to either to the fact that sexuality is still perceived with shame in our society, keeping people from assuming that problems in that area have ever happened or that it did, in fact, occurred less frequently.

Among the daughters with FM, a positive correlation between different trauma dimensions has been identified. This means that different types of trauma tend to occur, or at least perceived as having occurred, in the lives of FM patients. More specifically, our data showed that when patients report higher number of “General Trauma” events, they also report an elevated number of “Physical Punishment” occurrences ($r=.63$). They also tend to associate “Physical Punishment” events with the occurrence of “Emotional Abuse” ($r=.67$). This doesn't seem to happen among the healthy sisters, which might be due to a more punctual occurrence of each trauma, when they did occur.

Results demonstrated that mothers significantly corroborate the description of trauma occurrence stated by their ill daughters, confirming that the traumatic events took place. This was visible in three out of four trauma dimensions. This result defies the hypothesis previously raised that fibromyalgic patients could hyper valorize determined events as being traumatic, and consequently over reporting them. An interesting finding, however, is that this conclusion only fits the “General Trauma”, “Physical punishment” and “Sexual events” dimensions. The “Emotional abuse” dimension didn't reveal agreement between the mother and the ill daughter answers, as mothers systematically reported less number of events. This might be attributed to the fact that emotional abuse

could be defined as “verbal communication with the intention of humiliating or degrading the victim”[18]; as such, considering that at the time frame contemplated in this study the patients referred the mother as their maternal figure, mothers would be the principal perpetrators of the emotional abuse. If this thought is correct, it’s predictable that the mothers would have difficulty assuming their responsibility in inducing trauma to their child, explaining why the reports differ.

Nonetheless, we noticed that in the “Physical Punishment” and “Sexual Events” dimensions, the differences were almost statically significant ($p=0.72$ and $p=0.86$ respectively). Maybe in a similar posterior study, with a larger sample, these results may draw different conclusions.

Although in the hypothesis that were stated initially we aimed to conclude about the most frequent age of trauma occurrences, the dimension of the sample wasn’t enough to allow a valid analysis, so we decided not to take that into consideration. Once again, maybe in a posterior study with a larger sample, this component could be better ascertained.

Several studies have proved the association between FM and psychiatric co morbidities, namely depression and anxiety [27][28]. Some authors also noted that anxious/stressfull states and depression often precede or accompany the onset of FM [29][30][31]. We decided to take it a little further and verify if the occurrence of trauma in early ages could be related do psychiatric co morbidities also associated with FM. Our results show that, in this population, there is a correlation between childhood traumatic events, levels of anxiety and development of fibromyalgia, since the same conclusion couldn’t be assured when it comes to depression as the control group also revealed high levels of this disturb. These findings are consistent with other studies that claimed that

psychiatric syndromes are deeply linked to the development and maintenance of FM. [29][30][32]

Summing, this study contributed to reinforce the theory transmitted on the introduction that early trauma could play an important role on the pathophysiology of the disease.

Limitations

One of the challenges inherent to this type of study is that, as it's retrospective, recall bias may occur. Additionally, people with/without chronic pain tend to recollect past events with different accuracy, which may lead to spurious estimations of the risk associated with these events [33].

The best method to avoid this difficulty would be to design a prospective study. However, with the present data, we tried to minimize the impact by adding another source of information: the mother of both the patient and healthy control. By doing this, we tried to understand if there's a (mis)match in the events described by the subjects and the perspective of the mother.

Nevertheless, a recent review of the reliability of retrospective report of childhood maltreatment found that despite the possibility of some bias, retrospective assessment is worthwhile in research [34].

Although the ETI SF has been validated, showing good internal consistency (Cronbach coefficient $\alpha > 0.7$) [18], it has not been validated to the Portuguese population. Although this may represent a weakness, we consider that it's unlikely that such an effect would completely invalidate our findings. Careful reviewing of the literature led to the choice of the ETI SR over other questionnaires designed to assess childhood trauma for a number of reasons. Among those reasons are its psychometric properties,

the fact that it measures the impact of the trauma on the individual at the age of onset, the high number of different events it contemplates, the short amount of time it requires to be fulfilled and the simplicity of scoring method. [18]

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Appendix

Appendix 1 – Early Trauma Inventory Self Report Short Version (original)

Early Trauma Inventory Self Report-Short Form (ETISR-SF)		
J. Douglas Bremner, Emory University School of Medicine, Atlanta GA		
Participant Name or ID: _____ DOB: _____ Age: _____ Assessment Date: _____		
Part 1. General Traumas. <u>Before the age of 18</u>		
1. Were you ever exposed to a life-threatening natural disaster?.....	YES	NO
2. Were you involved in a serious accident?	YES	NO
3. Did you ever suffer a serious personal injury or illness?	YES	NO
4. Did you ever experience the death or serious illness of a parent or a primary caretaker?	YES	NO
5. Did you experience the divorce or separation of your parents?	YES	NO
6. Did you experience the death or serious injury of a sibling?	YES	NO
7. Did you ever experience the death or serious injury of a friend?	YES	NO
8. Did you ever witness violence towards others, including family members?	YES	NO
9. Did anyone in your family ever suffer from mental or psychiatric illness or have a "breakdown"?	YES	NO
10. Did your parents or primary caretaker have a problem with alcoholism or drug abuse?	YES	NO
11. Did you ever see someone murdered?	YES	NO
Part 2. Physical Punishment. <u>Before the age of 18</u>		
1. Were you ever slapped in the face with an open hand?	YES	NO
2. Were you ever burned with hot water, a cigarette or something else?	YES	NO
3. Were you ever punched or kicked?	YES	NO
4. Were you ever hit with an object that was thrown at you?	YES	NO
5. Were you ever pushed or shoved?	YES	NO
Part 3. Emotional Abuse. <u>Before the age of 18</u>		
1. Were you often put down or ridiculed?	YES	NO
2. Were you often ignored or made to feel that you didn't count?	YES	NO
3. Were you often told you were no good?	YES	NO
4. Most of the time were you treated in a cold, uncaring way or made to feel like you were not loved?	YES	NO
5. Did your parents or caretakers often fail to understand you or your needs?.....	YES	NO
Part 4. Sexual Events. <u>Before the age of 18</u>		
1. Were you ever touched in an intimate or private part of your body (e.g. breast, thighs, genitals) in a way that surprised you or made you feel uncomfortable?	YES	NO
2. Did you ever experience someone rubbing their genitals against you?.....	YES	NO
3. Were you ever forced or coerced to touch another person in an intimate or private part of their body?	YES	NO
4. Did anyone ever have genital sex with you against your will?	YES	NO
5. Were you ever forced or coerced to perform oral sex on someone against your will?	YES	NO
6. Were you ever forced or coerced to kiss someone in a sexual rather than an affectionate way?	YES	NO
<i>If you responded "YES" for any of the above events, answer the following for the one that has had the greatest impact on your life. In answering consider how you felt <u>at the time of the event</u>.</i>		
1. Did you experience emotions of intense fear, horror or helplessness?.....	YES	NO
2. Did you feel out-of-your-body or as if you were in a dream?	YES	NO
<i>Revised on 3/09</i>		

Appendix 2 – Early Trauma Inventory Self Report Short Version – Portuguese translation

Parte 1: Traumas gerais. ANTES DOS 18 ANOS

1. Alguma vez esteve exposta a desastres naturais que pusessem em risco a sua vida?	Sim	Não
2. Esteve envolvida em algum acidente grave?	Sim	Não
3. Sofreu alguma lesão ou doença grave?	Sim	Não
4. Passou por uma situação de lesão ou doença grave de um dos seus pais ou alguém próximo responsável por si?	Sim	Não
5. Passou pelo divórcio ou separação dos seus pais?	Sim	Não
6. Passou pela morte ou lesão grave de um parente?	Sim	Não
7. Passou pela morte ou lesão grave de um amigo?	Sim	Não
8. Testemunhou actos de violência praticados contra outras pessoas, incluindo familiares?	Sim	Não
9. Alguém na sua família sofreu de doença mental ou teve um “esgotamento”?	Sim	Não
10. Algum dos seus pais ou alguém responsável por si teve um problema de alcoolismo ou abuso de drogas?	Sim	Não
11. Alguma vez presenciou um assassinato?	Sim	Não

Parte 2: Punição física. ANTES DOS 18 ANOS.

12	Alguma vez foi “esbofeteada” na cara?	Sim	Não
13	Alguma vez foi queimada com água a ferver, um cigarro, ou qualquer outra coisa?	Sim	Não
14	Alguma vez foi alvo de socos ou pontapés?	Sim	Não
15	Alguma vez foi atingida por um objecto que tenha sido atirado contra si?	Sim	Não
16	Alguma vez foi empurrada de forma agressiva?	Sim	Não

Parte 3: Abuso emocional. ANTES DOS 18 ANOS.

17	Foi frequentemente ridicularizada ou rebaixada?	Sim	Não
18	Foi frequentemente ignorada ou sentiu que não contava para nada?	Sim	Não
19	Foi-lhe dito frequentemente que você não prestava?	Sim	Não
20	Você foi quase sempre tratada de forma fria ou fizeram-lhe sentir que não era querida ou amada?	Sim	Não
21	Frequentemente sentiu que os seus pais (ou responsáveis por si) não o entendiam, ou às suas necessidades?	Sim	Não

Parte 4: Ocorrências sexuais. ANTES DOS 18 ANOS.

22	Alguma vez lhe tocaram nas partes íntimas (por exemplo: no seio, coxas ou genitais) de uma maneira que não estava a espera ou a deixou desconfortável?	Sim	Não
23	Alguma vez notou que alguém encostava deliberadamente os genitais contra si?	Sim	Não
24	Alguma vez foi forçada ou coagida a tocar nas partes íntimas de outra pessoa?	Sim	Não

25	Alguma vez alguém a obrigou a ter relações sexuais contra a sua vontade?	Sim	Não
26	Alguma vez foi forçada ou coagida a fazer sexo oral a outra pessoa, contra a sua vontade?	Sim	Não
27	Alguma vez foi forçada ou coagida a beijar outra pessoa num sentido sexual, e não afectivo?	Sim	Não

Se respondeu SIM a alguma das questões anteriores, por favor responda às seguintes questões. Se respondeu que SIM a mais do que uma das anteriores, deverá responder às seguintes tendo em conta aquela que mais impacto teve na sua vida.

Nota: ao responder, tenha em conta o que sentiu **na altura do acontecimento**

28	Sentiu emoções de medo intenso, de horror ou de total incapacidade de reacção?	Sim	Não
29	Sentiu como se “estivesse fora do seu corpo” ou como se estivesse num sonho?	Sim	Não

Appendix 3 – Hospital Anxiety and Depression Scale – HADS

Este questionário foi concebido para ajudar a saber como se sente. Pedimos-lhe que leia cada uma das perguntas e faça uma cruz (X) no espaço anterior à resposta que melhor descreve a forma como se tem sentido na última semana.

Não demore muito tempo a pensar nas respostas. A sua reacção imediata a cada questão será provavelmente mais correcta do que uma resposta muito ponderada.

Por favor, faça apenas uma cruz em cada pergunta.

<p>1. Sinto-me tenso/a ou nervoso/a:</p> <p><input type="checkbox"/> Quase sempre</p> <p><input type="checkbox"/> Muitas vezes</p> <p><input type="checkbox"/> Por vezes</p> <p><input type="checkbox"/> Nunca</p>	<p>8. Sinto-me mais lento/a, como se fizesse as coisas mais devagar:</p> <p><input type="checkbox"/> Quase sempre</p> <p><input type="checkbox"/> Muitas vezes</p> <p><input type="checkbox"/> Por vezes</p> <p><input type="checkbox"/> Nunca</p>
<p>2. Ainda sinto prazer nas coisas de que costumava gostar:</p> <p><input type="checkbox"/> Tanto como antes</p> <p><input type="checkbox"/> Não tanto agora</p> <p><input type="checkbox"/> Só um pouco</p> <p><input type="checkbox"/> Quase nada</p>	<p>9. Fico de tal forma apreensivo/a (com medo), que até sinto um aperto no estômago:</p> <p><input type="checkbox"/> Nunca</p> <p><input type="checkbox"/> Por vezes</p> <p><input type="checkbox"/> Muitas vezes</p> <p><input type="checkbox"/> Quase sempre</p>
<p>3. Tenho uma sensação de medo, como se algo terrível estivesse para acontecer:</p> <p><input type="checkbox"/> Sim e muito forte</p> <p><input type="checkbox"/> Sim, mas não muito forte</p> <p><input type="checkbox"/> Um pouco, mas não me aflige</p> <p><input type="checkbox"/> De modo algum</p>	<p>10. Perdi o interesse em cuidar do meu aspecto físico</p> <p><input type="checkbox"/> Completamente</p> <p><input type="checkbox"/> Não tenho o cuidado que devia</p> <p><input type="checkbox"/> Talvez cuide menos do que antes</p> <p><input type="checkbox"/> Tenho o mesmo interesse de sempre</p>
<p>4. Sou capaz de rir e de ver o lado divertido das coisas:</p> <p><input type="checkbox"/> Tanto como antes</p> <p><input type="checkbox"/> Não tanto como antes</p> <p><input type="checkbox"/> Muitos menos agora</p> <p><input type="checkbox"/> Nunca</p>	<p>11. Sinto-me de tal forma inquieto/a que não consigo estar parado/a</p> <p><input type="checkbox"/> Muito</p> <p><input type="checkbox"/> Bastante</p> <p><input type="checkbox"/> Não muito</p> <p><input type="checkbox"/> Nada</p>
<p>5. Tenho a cabeça cheia de preocupações</p> <p><input type="checkbox"/> A maior parte do tempo</p> <p><input type="checkbox"/> Muitas vezes</p> <p><input type="checkbox"/> Por vezes</p> <p><input type="checkbox"/> Quase nunca</p>	<p>12. Penso com prazer nas coisas que podem acontecer no futuro:</p> <p><input type="checkbox"/> Tanto como antes</p> <p><input type="checkbox"/> Não tanto como antes</p> <p><input type="checkbox"/> Bastante menos agora</p> <p><input type="checkbox"/> Quase nunca</p>
<p>6. Sinto-me animado/a</p> <p><input type="checkbox"/> Nunca</p> <p><input type="checkbox"/> Poucas vezes</p> <p><input type="checkbox"/> De vez em quando</p> <p><input type="checkbox"/> Quase sempre</p>	<p>13. De repente tenho sensações de pânico</p> <p><input type="checkbox"/> Muitas vezes</p> <p><input type="checkbox"/> Bastantes vezes</p> <p><input type="checkbox"/> Por vezes</p> <p><input type="checkbox"/> Nunca</p>
<p>7. Sou capaz de estar descontraidamente sentado/a e sentir-me relaxado/a:</p> <p><input type="checkbox"/> Quase sempre</p> <p><input type="checkbox"/> Muitas vezes</p> <p><input type="checkbox"/> Por vezes</p> <p><input type="checkbox"/> Nunca</p>	<p>14. Sou capaz de apreciar um bom livro ou um bom programa de rádio ou televisão:</p> <p><input type="checkbox"/> Muitas vezes</p> <p><input type="checkbox"/> De vez em quando</p> <p><input type="checkbox"/> Poucas vezes</p> <p><input type="checkbox"/> Quase nunca</p>

Appendix 4 – The Mini Mental State Examination

ORIENTAÇÃO

- Dia da semana (1 ponto)()
- Dia do mês (1 ponto)()
- Mês (1 ponto)()
- Ano (1 ponto)()
- Hora aproximada (1 ponto)()
- Local específico (apartamento ou setor) (1 ponto)()
- Instituição (residência, hospital, clínica) (1 ponto)()
- Bairro ou rua próxima (1 ponto)()
- Cidade (1 ponto)()
- Estado (1 ponto)()

MEMÓRIA IMEDIATA

- Fale 3 palavras não relacionadas. Posteriormente pergunte ao paciente pelas 3 palavras. Dê 1 ponto para cada resposta correta()
Depois repita as palavras e certifique-se de que o paciente as aprendeu, pois mais adiante você irá perguntá-las novamente.

ATENÇÃO E CÁLCULO

- (100 - 7) sucessivos, 5 vezes sucessivamente (1 ponto para cada cálculo correto)()
(alternativamente, soletrar MUNDO de trás para frente)

EVOCAÇÃO

- Pergunte pelas 3 palavras ditas anteriormente (1 ponto por palavra)()

LINGUAGEM

- Nomear um relógio e uma caneta (2 pontos)()
- Repetir "nem aqui, nem ali, nem lá" (1 ponto)()
- Comando: "pegue este papel com a mão direita dobre ao meio e coloque no chão" (3 pts)()
- Ler e obedecer: "feche os olhos" (1 ponto)()
- Escrever uma frase (1 ponto)()
- Copiar um desenho (1 ponto)()

ESCORE: (___/30)

