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Post-traumatic stress and major depressive disorders in parent caregivers of children with a chronic disorder

C. Carmassi[a], M. Corsi[a,*], C.A. Bertelloni[a], V. Pedrinelli[a], G. Massimetti[a], D.G. Peroni[b], A. Bonuccelli[b], A. Orsini[b], L. Dell'Osso[a]

[a] Psychiatric Clinic, Department of Clinical and Experimental Medicine, University of Pisa, Via Roma 67, 56100, Pisa, Italy
[b] Pediatric Clinic, Department of Clinical and Experimental Medicine, University of Pisa, Via Roma 67, 56100, Pisa, Italy

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ABSTRACT

Post-traumatic Stress Disorder (PTSD) and Major Depressive Disorder (MDD) are the most common psychiatric consequences among caregivers of pediatric patients affected by severe chronic illnesses.

The aims of this study were to describe rates of PTSD and MDD in a sample of parents of epileptic children, and to examine the correlations between symptoms of post-traumatic stress and depression.

Parents of children with epilepsy were enrolled and screened by means of the PTSD module of the Semi-Structured Clinical Interview for DSM-5 (SCID-5) and of the Hamilton Rating Scale for depression (HAM-D). They also completed the Trauma and Loss Spectrum Self-Report (TALS-SR), an international instrument to evaluate post-traumatic stress spectrum symptoms.

Results revealed PTSD rates of 15.7% (19.5% mothers, 8,1% fathers; $p = .043$) and MDD rates of 7.5% (10.2% mothers,1.8% fathers; $p = .064$). A model of multiple linear regression indicated a significant B linear regression coefficient between being mothers ($p = .012$), witnessing tonic-clonic seizures ($p = .015$) and having higher TALS-SR total score ($p < .001$) as predictors of HAM-D total score.

Our findings highlight the relationship between PTSD and MDD, evidencing the need for further studies on pediatric caregivers aimed to develop specific intervention programs of healthcare prevention and assistance.

1. Introduction

Parents of children affected by severe chronic illnesses have recently received increasing attention for the development of a wide range of psychopathological symptoms in the aftermath of their children's diagnosis (Dolgin et al., 2007; Stoppelbein and Greening, 2007; Norberg and Boman, 2008; Virtue et al., 2014; Carmassi et al., 2018). As yet only scant data is available. Studies focus predominantly on children with cancer, diabetes mellitus type I, and polytrauma. Very few studies have been conducted so far on epilepsy, despite the fact that this illness may provide unpredictability and social stigma due to its characteristics of chronicity. This makes it a perfect model of parental stress related to severe traumatic experience that is often repeated (Carmassi et al., 2017). Seizures are, in fact, repetitive accidental events that parents experience with apprehension and powerlessness. They do not know what is happening to their loved ones or how to handle the severe medical situation (Iseri et al., 2006; Carmassi et al., 2013,**2014**; Dell'Osso et al., 2018; Reilly et al., 2018a,b).

The first study that observed the presence of psychological distress in mothers of children with epilepsy dates back to 1984 (Hoare, 1984). Subsequently, other studies highlighted associations between dysfunctional maternal adaptation to the disease and depressive symptoms (Mu et al., 2001; Shore et al., 2004; Wood et al., 2008). Others, however, established correlations only between maternal depression and children's attention and behavioural problems (Wood et al., 2008). Recent systematic reviews report that up to 58% of parents score in the clinical range for anxiety symptoms and up to 50% of mothers are at risk for depression (Puka et al., 2018).

Nevertheless, Post-Traumatic Stress Disorder (PTSD), a psychopathological condition specifically related to traumas, has been poorly investigated in parents of children with epilepsy. A Turkish group, more than ten years ago, established the same prevalence of PTSD (31.5%) and Major Depressive Episode (56%) (Iseri et al., 2006). In a sample of parents of children with epilepsy, some of us previously found rates of PTSD of 13% and 4.5% in mothers and fathers respectively (Carmassi et al., 2018).

* Corresponding author.
E-mail addresses: dott.martinacorsi@gmail.com (M. Corsi), gabriele.massimetti@med.unipi.it (G. Massimetti), diego.peroni@unipi.it (D.G. Peroni), dott.bonuccelli@alice.it (A. Bonuccelli), liliana.dellosso@med.unipi.it (L. Dell'Osso).

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Researchers agree that comorbidity in PTSD is the rule, rather than the exception. Very commonly, PTSD co-occurs with other psychiatric disorders, sharing a complex comorbidity relationship. On the one hand it seems that PTSD can play a causal role in the development of a depressive condition with anxious characteristics (Breslau et al., 1997; Ginzburg et al., 2010; Stander et al., 2014; Flory and Yehuda, 2015; Giordano et al., 2018). On the other hand, the presence of different mood disorders would determine an increased vulnerability to the development of PTSD following exposure to trauma (Brady et al., 2000; Zlotnick et al., 2006; Schindel-Allon et al., 2010; Dell'Osso et al., 2010; Dell'Osso et al., 2012; Farren et al., 2016).

In contrast with PTSD, a prevalence of Major Depressive Disorder (MDD) of about 50% is estimated both for women and men (Flory and Yehuda, 2015), while Italian data is more spread out among clinical and non-clinical subsamples (Favaro et al., 2000; Faravelli et al., 2004; Dell'Osso et al., 2011; Carmassi et al., 2013; Carmassi et al., 2014).

PTSD and MDD could be related also to sequential causality, in which MDD would occur secondarily to prolonged PTSD. In the NCS data, 78.4% of traumatized individuals reported the onset of a mood disorder following PTSD (Brady et al., 2000).

Although the debate in establishing most commonly occurring psychopathological disorder following a traumatic event is still ongoing (Afzali et al., 2017; Hurlocker et al., 2018), the main manifestations common to both disorders, PTSD and MDD, include sleep disorders, difficulty in concentrating, avoidance, anhedonia, isolation and detachment from others, and a sense of guilt (Schindel-Allon et al., 2010; Elhai et al., 2011; Post et al., 2011; Browne et al., 2015; Price and van Stolk-Cooke, 2015; Byllesby et al., 2017). The key differentiation for PTSD is that these symptoms are necessarily secondary to trauma. However, in the case of repeated traumas, as happens with seizures, it is difficult to determine the timing of symptom onset (Flory and Yehuda, 2015).

The present paper fits into the context of a larger study aimed at investigating post-traumatic stress symptomatology in caregivers of children affected by chronic illness. It has the specific purpose of better understanding the impact of PTSD and MDD and their relationship with each other. The main aim of this study was to describe the rates of MDD and PTSD, even in their partial forms, among a sample of parents of epileptic children. A further objective was to examine the correlation between post-traumatic stress symptomatology, variables related to children's diseases, and depressive symptoms.

2. Method

2.1. Participants and procedures

The sample comprised mothers and fathers of pediatric patients, aged between 1 and 18 years old, followed at the outpatient Neuropediatric Unit of the Pediatric Clinic of a major University Hospital in central Italy (*Azienda Ospedaliero-Universitaria Pisana, AOUP, Pisa*, Italy) for a diagnosis of idiopathic/cryptogenic or symptomatic epilepsy.

Subjects affected by a psychiatric disorder with onset before epileptic diagnosis in their child were excluded from the study in order to reduce risk of bias. All eligible subjects, after being informed of the study procedures and having had the opportunity to ask questions, provided written informed consent. Withdrawal from the study did not have any effect on the treatment received by patients who were following current intervention protocols provided by the Pediatric section of the AOUP.

The study was conducted in accordance with the Helsinki Declaration and received the approval of the Ethics Committee of *Area Vasta Nord Ovest Toscana* (April 2015).

The study sample was investigated by means of the PTSD modules of the Semi-Structured Clinical Interview for DSM-5 (SCID-5) for PTSD diagnosis according to the DSM-5 criteria. Additionally, the Hamilton Rating Scale for depression (HAM-D) was utilized for depressive symptoms. According to the literature on DSM-5 criteria, a Partial A PTSD diagnosis and a Partial B PTSD diagnosis were also considered by means of the fulfilment of 3 out of 4 or 2 out of 4 of the B-E symptomatological criteria for PTSD, respectively (Dell'Osso et al., 2011; McLaughlin et al., 2015; Carmassi et al., 2017; Carmassi et al., 2018; Dell'Osso et al., 2018). The PTSD module of SCID-5 and the HAM-D were administered in Italian, using the officially translated versions of the tools, by psychiatrists trained and certified in the use of these instruments (MC, CAB, VP).

All recruited subjects were also invited to fill in the “Trauma and Loss Spectrum - Self Report” (TALS-SR), a questionnaire which explores post-traumatic stress spectrum symptoms. The TALS-SR was developed by the authors, who are part of an international (Italian-American) collaboration research project named Spectrum Project (http://www.spectrum-project.org/). The Spectrum Project was established to develop and test assessment instruments for assessment of the spectrum of clinical features associated with the current version of the DSM psychiatric disorders. In the Italian version, test-retest / inter-rater reliability was excellent, with infraclass correlation coefficient values exceeding 0.90 for each of the domains (Dell'Osso et al., 2008; Dell'Osso et al., 2009).

2.2. Measures: Instruments and assessment

The HAM-D, originally published by Max Hamilton (Hamilton, 1960; Hamilton, 1967), is a specific questionnaire for assessing the depressive state of a subject. The original version of the scale contains 17 items designed to assess the severity of depression by probing mood, feelings of guilt, suicidal ideation, insomnia, restlessness and delay, anxiety, weight loss, and somatic symptoms. We used a modified version of the scale consisting of 21 items (Guy, 1976). The evaluation criteria are, for most of the items, the result of the integration between objective observation of the signs and the subjective exposure of the symptoms, even if the severity criterion mainly refers to the objective aspects. The HAM-D (Hamilton, 1960; Hamilton, 1967), evaluated by the researchers to estimate the degree of depression in subjects screened for PTSD, can provide objective and subjective results.

The TALS-SR is an instrument developed for assessing post-traumatic stress spectrum symptoms. It includes 116 items exploring the lifetime experience of a range of losses and/or traumatic events and lifetime symptoms, including behaviours and personal characteristics that might represent manifestations and/or risk factors for the development of a stress response syndrome. In accordance with the aims of the study, all participants were asked to report symptoms related to their child's epileptic syndrome, such as seizure episodes or the time of diagnosis. (Dell'Osso et al., 2009).

2.3. Data analysis

For the gender comparison on categorical demographic and clinical variables, the Chi-square test (or Fisher when appropriate) was used. For the quantitative comparisons the Student's unpaired T-test was used if the distribution was normal. Otherwise, the non-parametric Mann-Whitney test was used (as in the case of the TALS-SR and HAM-D scores). A multiple linear regression was used to study the relationship between gender, clinical features of the child, total TALS-SR score, and total HAM-D score.

3. Results

A total of 199 pediatric parent caregivers (134 mothers with a mean age of 42.3 ± 6.9 and 65 fathers with a mean age of 45.9 ± 7.3 years) provided initial written informed consent.

Socio-demographic characteristics and clinical features of the children for the overall sample are divided by gender and shown in Table 1.

Table. 1
Sociodemographic and clinical characteristics of children of total sample (N = 199) and divided by gender, Mothers (n = 134) and Fathers (n = 65).

	Total mean ± SD, range	Mothers mean ± SD, range	Fathers mean ± SD, range	*P
Age (years)	43,4 ± 7,2;27–60	42,3 ± 6,9;27–60	45,9 ± 7,3;29–60	.000
	N;%	N;%	N;%	
Education				
• Primary or secondary school	56; 28.1%	34; 25.4%	22; 33.8%	n.s.
• High school	112; 56.3%	78; 58.2%	34; 52.3%	n.s.
• Degree	31; 15.6%	22; 16.4%	9; 13.8%	n.s.
Occupation				
• Employed	155; 77.9%	94; 70.1%	61; 93.8%	.000
• Unemployed	15; 7.5%	13; 9.7%	2; 3.1%	n.s.
• Homemaker	29; 14.6%	27; 20.1%	2; 3.1%	.001
Number of children				
• 1	63; 31.8%	42; 31.6%	21; 32.3%	n.s.
• ≥2 (1 affected by chronic diseases)	95; 48%	62; 46.6%	33; 50.8%	n.s.
• ≥2 (>1 affected by chronic diseases such as epilepsy, diabetes etc.)	40; 20.2%	29; 21.8%	11; 16.9%	n.s.
Parents' psychiatric family history				
• No	147; 73.9%	98; 73.1%	53; 81.5%	n.s.
• Yes	31; 15.6%	23; 17.2%	12; 18.5%	
Type of epilepsy				
• Tonic-clonic	65;32.7%	45;33.6%	13;20%	n.s,
• Others	134;67.3%	89;66.4%	52;80%	
Number of seizures in children				
• 1–2	89; 44.7%	56; 41.8%	33; 50.8%	n.s.
• 3–5	44; 22.1%	34; 25.4%	10; 15.4%	n.s.
• >5	63; 31.7%	41; 30.6%	22; 33.8%	n.s.
Therapy				
• No	73; 36.7%	44; 32.8%	29; 44.6%	n.s.
• Yes	125; 62.8%	89; 66.4%	36; 55.4%	
Response to therapy				
• No	46; 23.1%	31; 23.1%	15; 23.1%	n.s.
• Partial	29; 14.6%	17; 12.7%	12; 18.5%	n.s.
• Complete	83; 41.7%	58; 43.3%	25; 38.5%	

* $p < .05$.

In particular, within the total sample, 28.1% of subjects had a primary school qualification, 56.3% had a high school diploma, and 15.6% had a college degree. Further, most of them were employed (77.9%). 31.8% of parents had only one child. About half had 2 or more children, of whom one suffering from chronic illness. 20.2% had two or more children of whom two or more suffering from chronic diseases such as diabetes or epilepsy. Most of the subjects declared no family history of psychiatric illnesses, while only 15.6% declared that they did. About half of the caregivers (44.7%) had children who had experienced between one and two acute events. 22.1% of the caregivers' children experienced between 3 and 5, and 31.7% experienced more than 5. As a whole, 62.8% of parents had children taking anti-epileptic drugs. Of these, 41.7% had a complete response.

3.1. PTSD and MDD

Within the total sample, 185 participants (93%) completed the PTSD modules of the SCID-5 interview. A diagnosis of PTSD was detected in 29 of them (15.7%): 5 fathers (8.1%) and 24 mothers (19.5%, p = .043). Furthermore, 34 subjects (18.4%), 6 fathers (9.7%) and 28 mothers (22.8%, p = .030) presented a diagnosis of partial PTSD, as they only satisfied 3 out of the 4 qualifying symptom per the DSM-5 (McLaughlin et al., 2015).

Also within the whole sample, 174 participants (87.4%), 118 mothers(88.1%) and 56 fathers (86%), had the HAM-D interview. 13 parents (7.5%) reported a total score of at least 14 corresponding to moderate depression. This breaks down as being present in 1 father (1.8%) and 12 mothers (10.2%).

A statistically significant difference between mothers and fathers emerged in the HAM-D total score (p = .000) as well as in two domains: somatic anxiety (p = .000) and cognitive symptoms (p = .016). (See Table 2)

A total of 151 subjects also filled in the TALS-SR where a statistically significant difference in the total mean score between mother and fathers emerged. Mothers had a mean score of 85.8 (25.4 ± 14.7) and fathers had a mean score of 60.3 (17 ± 11.8, p = .000).

A multiple linear regression model, which considered the HAM-D score as the independent variable and the TALS-SR total score, gender, and elements of the epileptic disease (therapy, response to therapy, number of seizures, type of seizures) as dependent variables, showed significant regression coefficients for the female gender, generalized seizures, and the total score at the TALS-SR (See Table 3).

The statistical analyses were carried out using SPSS (version 23.0).

4. Discussion

To the best of our knowledge this is the first study aimed at exploring both post-traumatic stress and depressive symptoms in a large sample of parents of epileptic children. We believe that a recruitment of more than 60 fathers should be considered relevant considering the scarcity of paternal samples in studies on pediatric caregivers (Mu et al., 2001; Iseri et al., 2006; Wood et al., 2008; Carmassi et al., 2018).

The results revealed a percentage of full PTSD of more than 15%. The percentage rises 20% both in the sub-sample of mothers and in partial clinical pictures (2 out of 3 main PTSD criteria) (McLaughlin et al., 2015). On the other hand, the number of subjects who satisfied MDD criteria at the HAM-D is around 7%. It further increases to 10% in the sub-sample of mothers.

We managed to increase the number of fathers involved thanks to phone calls and awareness campaigns on the importance of the topic. This made the comparison possible between the two genders.

PTSD percentages demonstrate a higher significance than those of MDD and are in line with results from previous studies on parents of severely ill children who had been admitted to pediatric intensive care

Table. 2
Comparisons between mothers' (n = 118) and fathers' (n = 56) on domains and total scores.

	Mothers n; Mean ± SD; Mean rank	Fathers *n*; Mean ± SD; Mean rank	*z*	**p*
I)Anxiety/Somatization	96.7; 0,4 ± 0.4;96.7	68.1; 0.2 ± 0.3;68.1	-3.625	**.000**
II) Weight	88.7; 0.1 ± 0.3;88.7	85.0; 0.01 ± 0.13;85.0	-1.230	.219
III) Cognitive disturbance	93.5; 0.2 ± 0.2;93.5	74.9; 0.1 ± 0.1;75.0	-2.419	**.016**
IV) Diurnal variation	88.7; 0.1 ± 0.3;88.7	85.0; 0.0 ± 0.0;85.0	-1.558	.119
V) Retardation	90.8; 0.3 ± 0.4;90.8	80.6; 0.2 ± 0.2;80.6	-1.395	.163
VI) Sleep disturbance	91.4; 0.3 ± 0.5;91.4	79.3; 0.2 ± 0.4;83.3	-1.701	.089
Total	97.1; 5.9 ± 5.2;97.1	67.3; 3.0 ± 3.3;67.3	-3.662	**.000**

* $p < .05$.

Table. 3
Multiple linear regression: explanatory variables of HAM-D total score.

	B (ES)	CI 95.0%	*t*	*p*
Gender	2.0 (1.5)	0.5–3.9	2.560	**.012**
Therapy	-0.6 (1.1)	-2.9 to 1.6	-0.578	.564
Number of seizures	0.6 (0.5)	-0.5 to 1.7	1.117	.266
Response to therapy	-0.3 (0.6)	-1.5 to 0.8	-0.607	.545
Type of seizure	-2.2 (0.9)	-4.0 to -0.5	-2.479	**.015**
Total TALS-SR	0.2 (0.0)	0.1 to 0.2	5.214	**.000**

r^2: 0.345; adjusted r^2: 0.307.

units. These parents sometimes underwent major surgical procedures or suffered from other severe chronic diseases such as cancer and diabetes (Landolt et al., 2003, 2005; Cabizuca et al., al.,2009; Dell'Osso et al., 2018; Carmassi et al., 2018). This data suggests that PTSD seems to be the main psychopathological consequence following this particular type of trauma. Nevertheless, the development of a possible MDD is still noteworthy, especially with respect to mothers suffering from post-traumatic stress symptoms.

The linear regression for the analysis of possible predictive factors in the development of a depressive framework seems to corroborate our hypothesis. It demonstrates a significant predictability to have higher HAM-D scores not only for the female gender and for characteristics of the seizures (generalized seizures rather than absences), but also higher scores on the self-assessment tool for post-traumatic stress spectrum symptoms (the TALS-SR). In our previous studies on post-traumatic stress symptomatology, no statistically significant differences emerged stratifying the sample on clinical characteristics of the children's disease (Carmassi et al., 2017, 2018). By contrast, it now seems that a mother who witnesses generalized seizures in her child and who experiences higher rates of post-traumatic stress spectrum symptoms is more prone to develop a depressive symptomatology (MDD) (Breslau et al., 1997; Iseri et al., 2006; Tolin and Foa, 2006; Dell'Osso et al., 2011; Carmassi et al., 2014).

Our data corroborates those clinical and epidemiological studies that support the thesis that the presence of a PTSD or of important post-traumatic stress symptomatology could be a risk factor for the onset of MDD (Breslau et al., 1997; Ginzburg et al., 2010; Flory and Yehuda, 2015; Stander et al., 2014). A study conducted by Oquendo and collaborators in 2005 on 230 subjects with a history of MDD similarly showed that the presence of a current or past PTSD was significantly associated with higher scores on the HAM-D and higher risk for suicidal behaviour (Oquendo et al., 2005).

We can also argue that the symptomatological clusters of the HAM-D, significantly more represented in women with somatic anxiety and cognitive symptoms, are also main core symptoms of post-traumatic stress reactions. Therefore the thesis of the overlapping symptomatology and the consequent difficulty in identifying a linear relationship between the two disorders should also be taken into account (Flory and Yehuda, 2015; Afzali et al., 2017; Hurlocker et al., 2018).

These concepts acquire even more importance in a family context with filial chronic illness since mothers are instead demonstrated to be the most exposed to seizures. Mothers are culturally and practically more involved in the management of the child's illness, undertaking the main role as parent caregiver (Lee et al., 2002; Shore et al., 2004; Wood et al., 2008; Ferro and Speechley, 2009; Carmassi et al., 2017).

The interpretation of our results should bear in mind some important limitations of the study. The most important is the lack of a control group and of homogeneity of the sample, considering the number of subsamples. In terms of both gender and completion of questionnaires, preference was given to clinical interviews rather than self-assessment questionnaires. This was done in order to minimize possible drop-outs, since parents were not always willing to give up their time and to fill out questionnaires independently. Another limitation is that the study is an observational, cross-sectional study. Therefore, the time from the onset of the symptoms in relation to the diagnosis of illness or to the first seizure varied markedly. Hence, it was not possible to evaluate the impact of time from the onset of depressive or post-traumatic stress symptoms. An additional factor not taken into account but which could interfere with the results is the presence of more than one ill child in the same family. All these issues could affect the methodological strength of our study and consequently the generalizability of our results. Further studies with a longitudinal design are desirable in future in order to more deeply characterize the relationship between MDD and PTSD in parents of children with a chronic disease.

Nevertheless, our data corroborates the thesis which contemplates chronic diseases as not limited to the child but broadened to the whole family. In particular, mothers are demonstrated to have a higher burden of post-traumatic and depressive symptoms that could cause a potentially disruptive vicious circle in the caregiving process. This means that children may potentially experience less than optimal outcomes as a result of the consequences of having primary caregivers affected by post-traumatic and depressive symptomatology.

It would be worthwhile to further analyze possible risk and resilience factors. The aim of such an undertaking would be to develop effective intervention programs for healthcare prevention and assistance for parents of chronically ill children.

Disclosures

The authors do not have an affiliation with or financial interest in any organization that might pose a conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2019.02.062.

References

Afzali, M.H., Sunderland, M., Teesson, M., Carragher, N., Mills, K., Slade, T., 2017. A network approach to the comorbidity between posttraumatic stress disorder and major depressive disorder: the role of overlapping symptoms. J. Affect. Disord. 15 (208), 490–496. https://doi.org/10.1016/j.jad.2016.10.037.

Brady, K.T., Killeen, T.K., Brewerton, T., Lucerini, S., 2000. Comorbidity of psychiatric disorders and posttraumatic stress disorder. J. Clin. Psychiatry. 61 (Suppl 7), 22–32. Retrieved from. https://www.psychiatrist.com/jcp/pages/home.aspx.

Breslau, N., Davis, G.C., Peterson, E.L., Schultz, L., 1997. Psychiatric sequelae of post-traumatic stress disorder in women. Arc. Gen. Psychiatry. 54 (1), 81–87. https://doi.org/10.1001/archpsyc.1997.01830130087016.

Browne, K.C., Trim, R.S., Myers, U.S., Norman, S.B., 2015. Trauma-related guilt: conceptual development and relationship with posttraumatic stress and depressive symptoms. J. Trauma Stress 28 (2), 134–141. https://doi.org/10.1002/jts.21999.

Byllesby, B.M., Elhai, J.D., Tamburrino, M., Cohen, G., Sampson, L., Shirley, E., Chan, P.K., Liberzon, I., Galea, S., Calabrese, J.R., 2017. General distress is more important than PTSD's cognition and mood alterations factor in accounting for PTSD and depression's comorbidity. J. Affect. Disord. 211, 118–123. https://doi.org/10.1016/j.jad.2017.01.014.

Cabizuca, M., Marques-Portella, C., Mendlowicz, M.V., Coutinho, E.S., Figueira, I., 2009. Posttraumatic stress disorder in parents of children with chronic illnesses: a meta-analysis. Health Psychol. 28 (3), 379–388. https://doi.org/10.1037/a0014512.

Carmassi, C., Shear, M.K., Socci, C., Corsi, M., Dell'osso, L., First, M.B., 2013. Complicated grief and manic comorbidity in the aftermath of the loss of a son. J. Psychiatr. Pract. 19 (5), 419–428. https://doi.org/10.1097/01.pra.0000435042.13921.73.

Carmassi, C., Dell'Osso, L., Manni, C., Candini, V., Dagani, J., Iozzino, L., Koenen, K.C., de Girolamo, G., 2014. Frequency of trauma exposure and Post-Traumatic Stress Disorder in Italy: analysis from the World Mental Health Survey Initiative. J. Psychiatr. Res. 59, 77–84. https://doi.org/10.1016/j.jpsychires.2014.09.006.

Carmassi, C., Corsi, M., Gesi, C., Bertelloni, C.A., Faggioni, F., Calderani, E., Massimetti, G., Saggese, G., Bonuccelli, A., Orsini, A., Dell'Osso, L., 2017. DSM-5 criteria for PTSD in parents of pediatric patients with epilepsy: what are the changes with respect to DSM-IV-TR? Epilepsy Behav. 70 (Pt A), 97–103. https://doi.org/10.1016/j.yebeh.2017.02.025.

Carmassi, C., Corsi, M., Bertelloni, C.A., Carpita, B., Gesi, C., Pedrinelli, V., Massimetti, G., Peroni, D.G., Bonuccelli, A., Orsini, A., Dell'Osso, L., 2018. Mothers and fathers of children with epilepsy: gender differences in post-traumatic stress symptoms and correlations with mood spectrum symptoms. Neuropsychiatr. Dis. Treat. 25 (14), 1371–1379. https://doi.org/10.2147/NDT.S158249.

Dell'Osso, L., Shear, M.K., Carmassi, C., Rucci, P., Maser, J.D., Frank, E., Endicott, J., Lorettu, L., Altamura, C.A., Carpiniello, B., Perris, F., Conversano, C., Ciapparelli, A., Carlini, M., Sarno, N., Cassano, G.B., 2008. Validity and reliability of the Structured Clinical Interview for the Trauma and Loss Spectrum (SCI-TALS). Clin. Pract. Epidemiol. Ment. Health. 28 (4), 2. https://doi.org/10.1186/1745-0179-4-2.

Dell'Osso, L., Carmassi, C., Rucci, P., Conversano, C., Shear, M.K., Calugi, S., Maser, J.D., Endicott, J., Fagiolini, A., Cassano, G.B., 2009. A multidimensional spectrum approach to post-traumatic stress disorder: comparison between the Structured Clinical Interview for Trauma and Loss Spectrum (SCI-TALS) and the Self-Report instrument (TALS-SR). Compr. Psychiatry 50 (5), 485–490. https://doi.org/10.1016/j.comppsych.2008.11.006.

Dell'Osso, L., Da Pozzo, E, Carmassi, C, Trincavelli, M.L., Ciapparelli, A., Martini, C., 2010. Lifetime manic-hypomanic symptoms in post-traumatic stress disorder: relationship with the 18kDa mitochondrial translocator protein density. J. Psychiatr Res. 177 (1–2), 139–143. https://doi:10.1016/j.psychres.2008.07.019.

Dell'Osso, L., Carmassi, C., Massimetti, G., Daneluzzo, E., Di Tommaso, S., Rossi, A., 2011. Full and partial PTSD among young adult survivors 10 months after the L'Aquila 2009 earthquake: gender differences. J. Affect. Disord. 131 (1–3), 79–83. https://doi.org/10.1016/j.jad.2010.11.023.

Dell'Osso, L., Carmassi, C., Musetti, L., Socci, C., Shear, M.K., Conversano, C., Maremmani, I., Perugi, G., 2012. Lifetime mood symptoms and adult separation anxiety in patients with complicated grief and/or post-traumatic stress disorder: a preliminary report. J. Psychiatr. Res. 198 (3), 436–440. https://doi.org/10.1016/j.psychres.2011.12.020.

Dell'Osso, L., Corsi, M., Gesi, C., Bertelloni, C.A., Massimetti, G., Peroni, D., Bonuccelli, A., Orsini, A., Carmassi, C., 2018. Adult Autism Subthreshold Spectrum (AdAS Spectrum) in parents of pediatric patients with epilepsy: correlations with post-traumatic stress symptoms. Compr. Psychiatry 83, 25–30. https://doi.org/10.1016/j.comppsych.2018.02.004.

Dolgin, M.J., Phipps, S., Fairclough, D.L., Sahler, O.J., Askins, M., Noll, R.B., Butler, R.W., Varni, J.W., Katz, E.R., 2007. Trajectories of adjustment in mothers of children with newly diagnosed cancer: a natural history investigation. J. Pediatr. Psychol. 32 (7), 771–782. https://doi.org/10.1093/jpepsy/jsm013.

Elhai, J.D., de Francisco Carvalho, L., Miguel, F.K., Palmieri, P.A., Primi, R., Cristopher Frue, B., 2011. Testing whether posttraumatic stress disorder and major depressive disorder are similar or unique constructs. J. Anxiety Disord. 25 (3), 404–410. https://doi.org/10.1016/j.janxdis.2010.11.003.

Faravelli, C, Abrardi, L., Bartolozzi, D., Cecchi, C., Cosci, F., D'Adamo, D., Lo Iacono, B., Ravaldi, C., Scarpato, M.A., Truglia, E., Rosi, S., 2004. The Sesto Fiorentino study: background, methods and preliminary results. Lifetime prevalence of psychiatric disorders in an Italian community sample using clinical interviewers. Psychother. Psychosom. 73 (4), 216–225. https://doi.org/10.1159/000077740.

Farren, J., Jalmbrant, M., Ameye, L., Joash, K., Mitchell-Jones, N., Tapp, S., Timmerman, D., Bourne, T., 2016. Post-traumatic stress, anxiety and depression following miscarriage or ectopic pregnancy: a prospective cohort study. BMJ Open 6 (11), e011864. https://doi.org/10.1136/bmjopen-2016-011864.

Favaro, A., Degortes, D., Colombo, G., Santonostaso, P., 2000. The effects of trauma among kidnap victims in Sardinia, Italy. Psychol. Med. 30 (4), 975–980. Retrieved from. https://www.cambridge.org/core/journals/psychological-medicine.

Ferro, M.A., Speechley, K.N., 2009. Depressive symptoms among mothers of children with epilepsy: a review of prevalence, associated factors, and impact on children. Epilepsia 50 (11), 2344–2354. https://doi.org/10.1111/j.1528-1167.2009.02276.x.

Flory, J.D., Yehuda, R., 2015. Comorbidity between post-traumatic stress disorder and major depressive disorder: alternative explanations and treatment considerations. Dialogues Clin. Neurosci. 17 (2), 141–150. Retrieved from. https://www.dialogues-cns.org.

Ginzburg, K., Ein-Dor, T., Solomon, Z., 2010. Comorbidity of posttraumatic stress disorder, anxiety and depression: a 20-year longitudinal study of war veterans. J. Affect. Disord. 123 (1–3), 249–257. https://doi.org/10.1016/j.jad.2009.08.006.

Giordano, N.A., Bader, C., Richmond, T.S., Polomano, R.C., 2018. Complexity of the relationships of pain, posttraumatic stress, and depression in combat-injured populations: an integrative review to inform evidence-based practice. Worldviews Evid. Based Nurs. 15 (2), 113–126. https://doi.org/10.1111/wvn.12274.

Guy, W., 1976. ECDEU Assessment Manual for Psychopharmacology. Department of Health, Education and Welfare, Washington, D.C., pp. 76–338 Revised, 1976. DHEW Publication No. (ADM).

Hamilton, M., 1960. A rating scale for depression. J. Neurol. Neurosurg. Psychiatry. 23, 56–62. https://doi.org/10.1136/jnnp.23.1.56.

Hamilton, M., 1967. Development of a rating scale for primary depressive illness. Br. J. Soc. Clin. Psychol. 6 (4), 278–296. https://doi.org/10.1111/j.2044-8260.1967.tb00530.x.

Hoare, P., 1984. Psychiatric disturbance in the families of epileptic children. Dev. Med. Child Neurol. 26 (1), 14–19. https://doi.org/10.1111/j.1469-8749.1984.tb04400.x.

Hurlocker, M.C., Vidaurri, D.N., Cuccurullo, L.J., Maieritsch, K., Franklin, C.L., 2018. Examining the latent structure mechanisms for comorbid posttraumatic stress disorder and major depressive disorder. J. Affect. Disord. 15 (229), 477–482. https://doi.org/10.1016/j.jad.2017.12.076.

Iseri, P.K., Ozten, E, Aker, A.T., 2006. Posttraumatic stress disorder and major depressive disorder is common in parents of children with epilepsy. Epilepsy Behav. 8 (1), 250–255. https://doi.org/10.1016/j.yebeh.2005.10.003.

Landolt, M.A., Vollrath, M., Ribi, K., Gnehm, H.E., Sennhauser, F.H., 2003. Incidence and associations of parental and child posttraumatic stress symptoms in pediatric patients. J. Child Psychol. Psychiatry 44 (8), 1199–1207. https://doi.org/10.1111/1469-7610.00201.

Landolt, M.A., Vollrath, M., Laimbacher, J., Gnehm, H.E., Sennhauser, F.H., 2005. Prospective study of posttraumatic stress disorder in parents of children with newly diagnosed type 1 diabetes. J. Am. Acad. Child Adol. Psychiatry 44 (7), 682–689. https://doi.org/10.1097/01.chi.0000161645.98022.35.

Lee, M.M., Lee, T.M., Ng, P.K., Hung, A.T., Au, A.M., Wong, V.C., 2002. Psychosocial well-being of carers of people with epilepsy in Hong Kong. Epilepsy Behav. 3 (2), 147–157. https://doi.org/10.1006/ebeh.2002.0321.

McLaughlin, K.A., Koenen, K.C., Friedman, M.J., Ruscio, A.M, Karam, E.G., Shahly, V., Stein, D.J., Hill, E.D., Petukhova, M., Alonso, J., Andrade, L.H., Angermeyer, M.C., Borges, G., de Girolamo, G., de Graaf, R., Demyttenaere, K., Florescu, S.E., Mladenova, M., Posada-Villa, J., Scott, K.M., Takeshima, T., Kessler, R.C., 2015. Subthreshold posttraumatic stress disorder in the world health organization world mental health surveys. Biol. Psychiatry 77 (4), 375–384. https://doi.org/10.1016/j.biopsych.2014.03.028.

Mu, P.F., Wong, T.T., Chang, K.P., Kwan, S.Y., 2001. Predictors of maternal depression for families having a child with epilepsy. J. Nurs. Res. 9 (4), 116–126. Retrieved from. https://journals.lww.com/jnr-twna/pages/default.aspx.

Norberg, A.L., Boman, K.K., 2008. Parent distress in childohood cancer: a comparative evaluation of posttraumatic stress symptoms, depression and anxiety. Acta Oncol. 47 (2), 267–274. https://doi.org/10.1080/02841860701558773.

Oquendo, M., Brent, D.A., Birmaher, B., Greenhill, L., Kolko, D., Stanley, B., Zelazny, J., Burke, A.K., Firinciogullari, S., Ellis, S.P., Mann, J.J., 2005. Posttraumatic stress disorder comorbid with major depression: factors mediating the association with suicidal behavior. Am. J. Psychiatry 162 (3), 560–566. https://doi.org/10.1176/appi.ajp.162.3.560.

Post, L.M, Zoellner, L.A., Youngstrom, E., Feeny, N.C., 2011. Understanding the relationship between co-occurring PTSD and MDD: symptom severity and affect. J. Anxiety Disord. 25 (8), 1123–1130. https://doi.org/10.1016/j.janxdis.2011.08.003.

Price, M., van Stolk-Cooke, K., 2015. Examination of the interrelations between the factors of PTSD, major depression, and generalized anxiety disorder in a heterogeneous trauma-exposed sample using DSM 5 criteria. J. Affect. Disord. 186, 149–155. https://doi.org/10.1016/j.jad.2015.06.012.

Puka, K., Tavares, T.P., Amderson, K.K., Ferro, M.A., Speechley, K.N., 2018. A systematic review of quality of life in parents of children with epilepsy. Epilepsy Behav. 163, 38–45. https://doi.org/10.1016/j.yebeh.2018.03.008.

Reilly, C., Atkinson, P., Memon, A., Jones, C., Dabydeen, L., Das, K.B., Cross, J.H., Neville, G.B.R., Gillberg, C., Scott, R.C., 2018a. Parenting stress and perceived stigma in mothers of young children with epilepsy: a case-control study. Epilepsy Behav. 6 (89), 112–117. https://doi.org/10.1016/j.yebeh.2018.10.016.

Reilly, C., Atkinson, P., Memon, A., Jones, C., Dabydeen, L., Das, K.B., Cross, J.H., Neville, B.G.R., Gillberg, C., Scott, R.C., 2018b. Symptoms of depression, anxiety, and stress in parents of young children with epilepsy: a case controlled population-based study. Epilepsy Behav. 80, 177–183. https://doi.org/10.1016/j.yebeh.2017.12.020.

Schindel-Allon, I., Aderka, I.M., Shahar, G., Stein, M., Gilboa-Schechtman, E., 2010. Longitudinal associations between post-traumatic distress and depressive symptoms following a traumatic event: a test of three models. Psychol. Med. 40 (10), 1669–1678. https://doi.org/10.1017/S0033291709992248.

Shore, C.P., Austin, J.K., Dunn, D.W., 2004. Maternal adaptation to a child's epilepsy. Epilepsy Behav. 5 (4), 557–568. https://doi.org/10.1016/j.yebeh.2004.04.015.

Stander, V.A., Thomsen, C.J., Highfill-McRoy, R.M., 2014. Etiology of depression comorbidity in combat-related PTSD: a review of the literature. Clin. Psychol. Rev. 34 (2), 87–98. https://doi.org/10.1016/j.cpr.2013.12.002.

Stoppelbein, L., Greening, L., 2007. Brief report: the risk of posttraumatic stress disorder in mothers of children diagnosed with pediatric cancer and type I diabetes. J. Pediatr. Psychol. 32 (2), 223–229. https://doi.org/10.1093/jpepsy/jsj120.

Tolin, D.F., Foa, E.B., 2006. Sex differences in trauma and posttraumatic stress disorder: a quantitative review of 25 years of research. Psychol. Bull. 132 (6), 959–992. https://doi.org/10.1037/0033-2909.132.6.959.

Virtue, S.M, Manne, S.L, Mee, L., Bartell, A., Sands, S., Gajda, T.M., Darabos, K., 2014. Psychological distress and psychiatric diagnoses among primary caregivers of children undergoing hematopoietic stem cell transplant: an examination of prevalence, correlates, and racial/ethnic differences. Gen. Hosp. Psichiatry 36 (6), 620–626. https://doi.org/10.1016/j.genhosppsych.2014.08.010.

Wood, L.J., Sherman, E.M., Hamiwka, L.D., Blackman, M.A., Wirrel, E.C., 2008. Maternal depression: the cost of caring for a child with intractable epilepsy. Pediatr. Neurol. 39 (6), 418–422. https://doi.org/10.1016/j.pediatrneurol.2008.08.007.

Zlotnick, C., Johnson, J., Kohn, R., Vicente, B., Rioseco, P., Saldivia, S., 2006. Epidemiology of trauma, post-traumatic stress disorder (PTSD) and co-morbid disorders in Chile. Psychol. Med. 36 (11), 1523–1533. https://doi.org/10.1017/S0033291706008282.