

## Original article

# Psychological morbidity and autonomic reactivity to emotional stimulus in parental cancer: a study with adult children caregivers

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## Psychological morbidity and autonomic reactivity to emotional stimulus in parental cancer: a study with adult children caregivers

Literature suggests that parental cancer can provoke aversive emotional arousal in adult children, who may perceive caregiving as a traumatic experience. Limited research has been conducted on emotional and physiological impact of family caregiving for cancer patients undergoing chemotherapy. The aim of the present study was to examine psychological and physiological responses in parental cancer's caregivers. Two matched groups of adult children, with 78 participants each (parental cancer vs. control), completed psychological measures of distress, post-traumatic stress disorder (PTSD) symptoms, and burden. Additionally, each participant visualised standardised pictures with different emotional valences, while cardiovascular (heart rate) and electrodermal responses (skin conductance) were recorded. Between-group analysis showed significant differences on all psychological variables, and on skin conductance for all types of pictures. However, for the heart rate responses, differences were found only for pictures with unpleasant emotional arousal. In the parental cancer group, the heart rate peak response stood out as a predictor of PTSD symptoms, after controlling for distress and burden. This study highlights the important role of psychophysiological measures of family caregiving in oncology. Physiological responses may explain a higher prevalence of PTSD symptoms. Therefore, biofeedback combined with targeted psychosocial interventions for relaxation could be of great clinical value for this population.

*Keywords:* parental cancer, caregiving, adult children, emotional, psychophysiological research.

## INTRODUCTION

Caring for a family member is a psychologically demanding experience, associated with more non-psychiatric hospitalisations (Chentsova-Dutton *et al.* 2000), chronic diseases, medication use (Schulz *et al.* 1995), and even mortality (Schulz & Beach 1999), than non-caregivers. In addition to concerns regarding the family member's welfare, caregivers of cancer patients report high levels of psychological distress. However, it remains unclear

whether this distress also has an effect on the physical body. Research has reported a broad array of humoral, immune, cardiovascular and metabolic alterations in caregivers of patients with dementia (Vedhara *et al.* 1999; Vitaliano *et al.* 2002, 2003; Kiecolt-Glaser *et al.* 2003; Gallagher-Thompson *et al.* 2006; von Känel *et al.* 2006); however, it has not explored in depth, whether caregiving demands a similar toll on the bodies of those caring for a family member with cancer. In comparison with other caring contexts, caregivers in oncology present distinct characteristics: they are usually younger and provide assistance for shorter periods of time for patients that often have specific symptoms (e.g. pain, vomiting) (Chentsova-Dutton *et al.* 2002; Hauser & Kramer 2004). Some preliminary reports suggest the possibility that cancer caregiving may increase vulnerability to coronary

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disease, as well as other metabolic, autoimmune, inflammatory, and psychiatric conditions (Vanderwerker *et al.* 2005; Rohleder *et al.* 2009).

Physiological measures may help to explain the associations between caregiving and illness, much earlier than the manifestation of chronic diseases (Vitaliano *et al.* 2003). In oncology, few investigations have been performed on the interaction between the bio-behavioural responses to stress in household care providers. For Sherwood *et al.* (2008), physiological responses are considered 'adaptive' in the initial reaction to acute stress (e.g. a diagnosis of primary malignant brain tumour and initial treatment); however, for continuous stress or chronic situations (e.g. disease progression or long-term treatment), physical responses may lead to changes in the cardiovascular and immune systems (via cortisol), which will compromise the state of general physical health of the caregiver. In this context, recent studies have shown that caregivers of cancer patients manifest increased cardiac activity (sympathetically controlled) as well as an increase in systolic and diastolic blood pressure (Weitzner *et al.* 2000; Lucini *et al.* 2008; Corà *et al.* 2012), two cardiovascular measures commonly used in Psychophysiology (Orr & Roth 2000). Cardiovascular activity varies depending on psychological aspects (emotional changes) and is, therefore, important as an autonomic physiological variable (Arangüena & Dorado 2000). Many epidemiological studies on the impact of elevated heart rate (HR) on health, report an increased risk of all-cause mortality and cardiovascular events (Dimsdale 2008), particularly in hypertensive caregivers (Vitaliano *et al.* 1993; Shaw *et al.* 2003).

Another common physiological variable is electrodermal activity, an important indicator of the sympathetic nervous system's activation, especially useful to assess emotional reactivity (Orr & Kaloupek 1997; Sequeira *et al.* 2009). No studies were found with caregivers of cancer patients that included electrodermal activity as a measure. In general, research on the use of this physiological variable in studies with caregivers is very scarce, presenting results that are either inconclusive (Stamper *et al.* 1997; Thompson *et al.* 2004; Lewis *et al.* 2008) or contradictory (Moya-Albiol *et al.* 2011).

Research shows that adult children of parents with chronic illness have an increased risk of developing emotional and behavioural problems than adult children of healthy parents. The risk, however, depends on individual and family variables related to the disease itself (Korneluk & Lee 1998). Cancer is currently conceptualised as a possible precipitator of post-traumatic stress disorder (PTSD) symptoms (American Psychiatric Association 2000), both in patients and in first-degree relatives.

Research suggests that first-degree relatives of patients with cancer have significantly higher levels of intrusive cancer-related thoughts and avoidance, compared with relatives without a family history of cancer (Zakowski *et al.* 1997; Baider *et al.* 1999), 4% showed symptoms consistent with a PTSD diagnosis, 7% showed symptoms consistent with subclinical levels of potential PTSD (probably cancer-related) (Lindberg & Wellisch 2004), and 53% had considerable intrusive thoughts, comparable to those found in studies of individuals exposed to other types of trauma (Lerman *et al.* 1993). However, the unique aspects of the cancer experience associated with other types of trauma, and the overlap between normative reactions to cancer and the PTSD response, confounds the interpretation of these results.

Given the great variability in distress levels among first-degree relatives of patients with cancer (Lerman *et al.* 1993; Erblich *et al.* 2000), it is important to assess the main predictors of their responses to stress. Considering the limited research with physiological variables among cancer caregiver's samples, an experimental design was used in order to assess and compare adult children caregivers of cancer patients with a control group. Research widely supports the importance of considering physiological variables in the study of PTSD (Pole 2007). For example, enhanced physiological reactivity to trauma cues has been shown to be a robust correlate of PTSD (Elsesser *et al.* 2009). Considering the most commonly used experimental designs in this field (Orr & Roth 2000; Bryant *et al.* 2003; Elsesser *et al.* 2004, 2005, 2009; O'Donnell *et al.* 2007; Ehlers *et al.* 2010; Suendermann *et al.* 2010), the paradigm of affective picture viewing (with different valences) (Lang *et al.* 1993) was the selected method to evoke and register physiological responses.

In the present study, adult children caregivers with parental cancer and controls were compared for psychological morbidity, evoked HR, and skin conductance responses (SCR) to idiosyncratically caregiving-related (unpleasant) and control pictures (pleasant and neutral). In keeping with some previous reports, the parental cancer group was expected to exhibit a higher level of psychological morbidity and enhanced psychophysiological reactivity than controls. Finally, distress, burden and physiological reactivity were expected to be predictive of PTSD symptoms in parental cancer participants.

## METHODS

### Procedures and participants

A cross-sectional experimental study with two convenience samples was used. The research design was approved

by the Ethic Committee of a general hospital in northern Portugal. Participation was voluntary. The parental cancer group ( $n = 78$ ) consisted of adult children who, during the period of data collection, accompanied the parent diagnosed with cancer to chemotherapy. Among these eligible caregivers, only one refused to participate in the study. Seventy-seven per cent were women, with a mean age of 34.4 years ( $SD = 9.2$ ); 53% had a partner; 76% had graduated from high school. Parents' tumour sites were heterogeneous. Inclusion criteria required participants to be  $\geq 18$  years old; have a parent (or both) in chemotherapy; accompany the parent to the hospital for treatment; and not suffer from oncological, psychiatric, or neurological disease. Sixty per cent reported to provide care for less than one year, and only 39% provided care for more than a year. Only 19% of adult children perceived the parent in treatment as completely dependent on their caregiving. The control group ( $n = 78$ ) consisted of adult children without a chronically ill parent, recruited at a university. Seventy-six per cent were women, with a mean age of 32.2 years ( $SD = 9.8$ ); 56% had a partner; 86% had graduated from high school. Comparatively, groups showed no significant differences in terms of gender [ $\chi^2(1, N = 156) = 0.035, P = n.s.$ ], age [ $t(160) = -1.459, P = n.s.$ ], marital status [ $\chi^2(1, N = 156) = 0.233, P = n.s.$ ], and education level [ $\chi^2(1, N = 156) = 2.641, P = n.s.$ ].

Each participant completed self-report measures, and was subjected to an experimental task that consisted of a psychophysiological test in which autonomic responses were evoked through the presentation of pictures with different emotional valences. Participants were informed that the purpose of the task was to measure bodily responses to pictures. They were instructed to sit down in a comfortable position and try to move as little as possible during the task. They were asked to look at each picture carefully. An effort was made to control environmental conditions, such as temperature and noise. Data of three participants were discarded from statistical analysis due to the presence of artefacts in their recordings.

## Materials

### *Depression anxiety stress scales*

The Portuguese version of the 21-item Depression Anxiety Stress Scales (DASS-21; Lovibond & Lovibond 1995; Pais-Ribeiro *et al.* 2004) was used. It comprises a 4-point set (0–3) of three subscales (depression, anxiety, and stress). In this study, only the total score was used. Higher scores in the DASS-21 indicate greater 'distress'. The internal consistency in the parental cancer group and in the control group was 0.96 and 0.87 respectively.

### *Burden assessment scale*

The Portuguese version of the Burden Assessment Scale (BAS; Reinhard *et al.* 1994) was used. This is a 19-item measure that evaluates burden in an objective way, i.e. the amendment of caring for someone with limitations imposed on activities and resources of the caregiver. BAS uses a 4-point scale (1–4), with higher scores indicating greater levels of caregiving burden. Control participants were asked to focus on any experience of their personal life in which they had provided some type of care to a loved one. The internal consistency in the parental cancer group and in the control group was 0.84 and 0.89 respectively.

### *Impact of event scale – revised*

To assess PTSD-related symptoms, the Portuguese version of the Impact of Event Scale – Revised (IES-R; Weiss & Marmar 1997) was used. This is a 22-item self-report measure of current subjective distress related to a specific traumatic event. Respondents are asked to rate on a 5-point scale (0–4) how distressing symptoms of avoidance, hyperarousal, and intrusion have been in the past 7 days. In this study, only the total score was used. Control participants were asked to rate items with regard to their most stressful life-event. Research supports the score of 33 on the IES-R as representing the best cut-off for a probable diagnosis of PTSD (Creamer *et al.* 2003; Wang *et al.* 2011). Whereas the scores of the subscales and total IES-R are expressed as means (Weiss & Marmar 1997), for cut-off analysis purposes the sum of the results in the 22 items, was used. The internal consistency in the parental cancer group and in the control group was 0.93 and 0.94 respectively.

### *Visual stimuli*

Pictures were drawn from the International Affective Picture System (IAPS; Lang *et al.* 2008). Participants viewed 15 idiosyncratic pictures related to the oncology caregiving condition and considered as 'unpleasant'<sup>1</sup> (e.g. mastectomy, ventilator), 15 'neutral' pictures (e.g. table, lamp, mug), and 15 'pleasant' pictures (e.g. sunset, baby, tiger). The pictures were presented in a predefined order so that the same category was not presented twice in a row, to minimise habituation effects. After a 120 s baseline,

<sup>1</sup>IAPS No (unpleasant): 9432, 2141, 2205, 3220, 7521, 2490, 9596, 2590, 3261, 2900, 7520, 2700, 2800, 3230, 6000; (neutral): 7010, 6150, 7002, 7009, 7020, 7000, 7040, 7004, 7012, 7175, 7150, 7025, 7185, 7170, 7006; (pleasant): 1460, 1440, 2550, 1811, 2530, 2540, 2057, 2165, 2170, 2340, 8497, 2360, 2341, 1463, 5829.

each picture was presented for 6 s followed by an inter-stimulus interval of 12 s. Pictures were selected from a larger set in a pilot study that tested the suitability of the stimulus material with 16 healthy volunteers. Pleasant and unpleasant pictures had similar arousal levels, whereas the neutral ones presented a lower arousal level (Lang *et al.* 2008). The classification of IAPS stimuli by 'pilots' was performed with a simple table in which each picture was evaluated for valence: unpleasant, pleasant, or neutral.

### Apparatus and physiological recording

The I-330-C2 recording device and USE3 Physioblab software (both by J&J Engineering) were used, a system that digitally records physiological data online at a sample rate of 1.024 samples/s across all channels. Raw ECG data were collected with gel-free sensor MC-5D, a reusable HR sensor placed in a standard bilateral configuration on the palmar side of each wrist. The data were processed through a 1–400 Hz bandpass filter designed to maximise R-wave frequency. Skin conductance (SC) levels were obtained using a skin resistance sensor cable MC-6SY (range 0–20 microsiemens;  $\mu\text{S}$ ) connected to SE-35 electrodes (Ag-AgCl) placed on the middle phalanx of the second and third fingers of the non-dominant hand. During the presentation of pictures, the participant's HR and SC were recorded continuously.

### Data reduction

#### HR responses

R-R intervals (time between heartbeats) were converted online into HR (in beats per minute; 'bpm'), and outputted to obtain one weighted HR estimate for each second. HR recordings were inspected for artefact control. By picture set (unpleasant, neutral, and pleasant), the following data were obtained: pre-stimulus HR baseline, HR response for each second of picture presentation, and peak HR response. For each picture, the pre-stimulus baseline HR was defined as the HR during the last second prior to picture onset (Hamm *et al.* 1997; Bradley *et al.* 2001; Elssesser *et al.* 2004). HR response was assessed as the relative change from baseline during the 6 s of stimulus presentation (Ehlers *et al.* 2010), i.e. for each second of stimulus presentation, the pre-stimulus baseline HR was subtracted from the HR during that second. Finally, the maximum of the HR responses for each second of stimulus presentation was used to index peak HR response. Some literature claims the use of an additional

cardiac indicator, namely the relative acceleration in HR (Blanchard *et al.* 1996; Elssesser *et al.* 2005; Ehlers *et al.* 2010). Therefore, considering that this acceleration is more prevalent during the presentation of aversive stimuli, this record was only calculated for the selected unpleasant pictures, i.e. in case of a mean acceleration over 1 bpm, relative to pre-stimulus baseline.

#### SC responses

Skin conductance data were outputted in quarters of a second (0.25 s), in order to produce a more accurate latency. Artefact-free SCR were scored as the largest change (peak-valley difference) above 0.01  $\mu\text{S}$  occurring in a 1–4 s time window following picture onset (Levinson & Edelberg 1985; Dawson *et al.* 2007). All responses lower than 0.01  $\mu\text{S}$  were computed as zero (SCR magnitude was the preferred outcome). To avoid positive asymmetry and leptokurtic distribution issues, a logarithmic transformation [ $\text{Log}(\text{SCR} + 1)$ ] was conducted to normalise the data (Venables & Christie 1980; Dawson *et al.* 2007). For each picture set (unpleasant, neutral, and pleasant), an average record of the normalised SCR magnitude was obtained.

### Statistical analyses

Socio-demographic group differences were analysed using *t*-tests and chi-squared. For differences between groups considering psychological variables, ANOVA was used. Differences in PTSD severity (categorical variable) were analysed using chi-squared. Although the 'classical' method for data analysis in Psychophysiology is the analysis of variance (ANOVA with Repeated Measures), in this study for group comparisons of physiological data, the multivariate approach (MANOVA) was preferred (Jennings & Gianaros 2007) as it has the advantage, compared with the classical ANOVA-RM, of not requiring the assumption of sphericity, which causes some authors to advocate its use (Field 2006; Tabachnick & Fidell 2006). Hierarchical multiple regression analysis was conducted in order to examine the main psychological and physiological predictors of PTSD symptoms. Finally, a hierarchical logistic regression analysis was performed with the same previous predictors, in order to examine the main contributors to a probable diagnosis of PTSD based on a cut-off point in the IES-R. This methodological option was preferred to discriminant analysis, due to the fact that one of the independent variables included in the model was dichotomous (HR acceleration >1 bpm).

## RESULTS

## Group differences

Participants with and without parental cancer did not differ in gender, age, marital status, or education. As expected, the parental cancer group reported more distress, burden, and PTSD symptoms, compared with the group without parental cancer (see Table 1). These differences were also significant for PTSD severity. As shown in Table 1, the selected cut-off in the IES-R permitted the determination of the prevalence of PTSD possible cases in the parental cancer group ( $n = 36$  patients, 46.2%) and in the control group ( $n = 10$  cases, 12.8%), with a sensitivity of 46% and a specificity of 87% [ $\chi^2(1, N = 156) = 20.841$ ,  $P < 0.001$ ,  $\Phi = 0.366$ , OR = 6.14].

Baseline HR (120 s) differ between participants with parental cancer ( $M = 79.90$ ,  $SD = 11.86$ ) and those without chronically ill parents ( $M = 75.11$ ,  $SD = 10.53$ ),  $P < 0.01$ . The same was found in SC baseline (120 s), since participants with parental cancer ( $M = 10.45$ ,  $SD = 7.28$ ) showed higher electrodermal reactivity at baseline compared with participants without a chronically ill parent ( $M = 6.22$ ,  $SD = 3.63$ ),  $P < 0.001$ .

After obtaining baseline HR data, significant differences between groups were found in all picture valences (unpleasant, neutral, and pleasant) but solely on pre-stimulus baseline HR (see Table 1). However, for unpleasant pictures, other cardiac indicators differ between groups, namely the mean HR of the 6 s, and the HR acceleration above 1 bpm. Considering that the mean HR is the relative difference from pre-stimulus baseline, the parental cancer group showed greater HR responses, combined with a less pronounced deceleration, to unpleasant pictures compared with controls ( $P < 0.01$ ). Regarding data of the HR acceleration exceeding 1 bpm for unpleasant stimuli, they allowed the disclosure of differences between groups, with the parental cancer group ( $n = 15$  cases, 19.2%) showing a greater acceleration, compared with controls ( $n = 6$  cases, 7.7%) [ $\chi^2(1, N = 156) = 4.457$ ,  $P < 0.05$ ,  $\Phi = 0.169$ , OR = 2.89]. The mean peak HR responses did not differ in any picture valence. However, for unpleasant pictures there was a trend ( $P = 0.085$ ) for higher scores in the parental cancer group (Table 1).

For each second of picture presentation, differences between groups were found for unpleasant pictures, while

**Table 1.** Differences between groups ( $n$  and percentages, or mean and standard deviation)

Variables	Parental cancer group ( $n = 78$ )	Control group ( $n = 78$ )	Statistics for group differences	Effect size	$P$
Distress*	34.84 (26.63)	19.71 (12.63)	$F(1,154) = 20.537$	$d = 0.92$	0.000
Burden†	37.51 (9.43)	29.52 (9.38)	$F(1,154) = 28.093$	$d = 0.85$	0.000
PTSD symptoms‡	4.20 (2.06)	2.61 (1.76)	$F(1,154) = 26.651$	$d = 0.83$	0.000
PTSD severity§					
Without probable PTSD	42 (54%)	68 (87%)	$\chi^2(1, N = 156) = 20.841$	$\Phi = 0.366$	0.000
With probable PTSD	36 (46%)	10 (13%)			
Unpleasant pictures¶					
HR pre-stimulus baseline	79.07 (10.73)	75.01 (10.44)	$F(1,154) = 5.735$	$d = 0.38$	0.018
HR peak value	3.61 (2.05)	3.09 (1.67)	$F(1,154) = 3.001$		0.085
HR mean for 6 s	0.19 (1.14)	-0.42 (1.09)	$F(1,154) = 11.825$	$d = 0.55$	0.001
HR acceleration >1 bpm	0.19 (0.39)	0.08 (0.26)	$\chi^2(1, N = 156) = 4.457$	$\Phi = 0.169$	0.035
SC response**	0.06 (0.05)	0.03 (0.04)	$F(1,154) = 12.703$	$d = 0.66$	0.000
Neutral pictures¶					
HR pre-stimulus baseline	79.25 (10.69)	75.01 (10.20)	$F(1,154) = 6.416$	$d = 0.41$	0.012
HR peak value	3.35 (1.96)	3.14 (1.83)	$F(1,154) = 0.453$		0.502
HR mean for 6 s	0.04 (1.09)	-0.27 (1.13)	$F(1,154) = 3.157$		0.078
SC response**	0.04 (0.04)	0.01 (0.03)	$F(1,154) = 14.184$	$d = 0.85$	0.000
Pleasant pictures¶					
HR pre-stimulus baseline	79.47 (10.83)	74.72 (10.17)	$F(1,154) = 7.958$	$d = 0.45$	0.005
HR peak value	3.50 (2.19)	3.52 (1.84)	$F(1,154) = 0.005$		0.946
HR mean for 6 s	0.10 (1.32)	0.13 (1.12)	$F(1,154) = 0.021$		0.884
SC response**	0.04 (0.04)	0.02 (0.03)	$F(1,154) = 17.031$	$d = 0.57$	0.000

Note. For each significant comparison, Cohen's  $d$  and Cramér's  $\Phi$  were calculated as indexes of effect size.

\*Depression Anxiety Stress Scales.

†Burden Assessment Scale.

‡Impact of Event Scale-Revised.

§Using the cut-off of 33 in the IES-R.

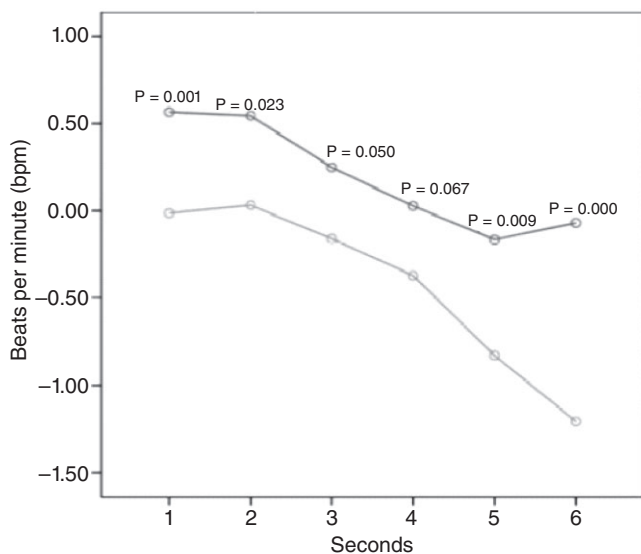
¶IAPS pictures emotional valence.

\*\*Log (SCR + 1).

PTSD, post-traumatic stress disorder; HR, heart rate; SC, skin conductance.

this was not the case for neutral or pleasant ones. These differences were significant at all seconds, except for the fourth second (only a trend was found,  $P = 0.067$ ). Figure 1 shows the mean HR responses to the unpleasant pictures during the 6 s of stimulus presentation for both groups.

Concerning SCR's magnitude, data showed differences between groups in all picture valences (see Table 1).



**Figure 1.** Mean HR responses to unpleasant pictures for the two groups during the 6 s of stimulus presentation, relative do pre-stimulus baseline. —, parental cancer group; - - -, control group.

### Predictors of PTSD symptoms and severity in the parental cancer group

A hierarchical multiple regression analysis was used to test how accurately PTSD symptoms can be predicted based on psychological variables (previously identified) and HR responses, considering prior reports (Blanchard *et al.* 1996; Elsesser *et al.* 2005; Ehlers *et al.* 2010). Distress and caregiver burden were entered in Step 1; peak HR responses (to unpleasant, neutral, and pleasant pictures) and the HR acceleration exceeding 1 bpm were entered in Step 2. The regression model explained 48% of the observed variance [ $F(6,71) = 10.922$ ,  $P < 0.001$ ]. Table 2 shows distress and burden to be significant predictors of higher correlates of PTSD symptoms. Furthermore, peak HR responses, to unpleasant pictures, significantly increased the accuracy of prediction. Peak responses to pleasant and neutral pictures did not contribute to the model, as well as HR acceleration  $>1$  bpm to unpleasant pictures.

Statistical procedures were also performed to find whether the same psychological and physiological variables allowed a distinction of parental cancer participants based on a cut-off for a probable PTSD diagnosis. In this content, a hierarchical logistic regression analysis was conducted. Distress and burden were entered in Step 1, significantly predicting PTSD above the cut-off point with an overall diagnostic efficacy of 78.2% [ $\chi^2(2) = 35.30$ ,  $P < 0.001$ , Nagelkerke  $R^2 = 0.486$ ]. Peak HR responses and acceleration  $>1$  bpm were entered in Step 2, but did not increase the prediction efficacy of the model [ $\chi^2(4) = 3.95$ ,

**Table 2.** Hierarchical multiple regression results for psychological and physiological predictors of PTSD symptoms in the parental cancer group

Variables	PTSD symptoms <sup>‡</sup>		
	B Model 1	Model 2 B	95% CI
Constant	0.623	0.025	(-1.647, 1.697)
Distress*	0.036***	0.038***	(0.023, 0.053)
Burden <sup>†</sup>	0.062**	0.063**	(0.019, 0.106)
Peak HR to unpleasant pictures		0.487**	(0.142, 0.832)
Peak HR to pleasant pictures		-0.170	(-0.422, 0.082)
Peak HR to neutral pictures		-0.139	(-0.431, 0.152)
HR accl. $>1$ bpm to unpleasant pictures		-1.026	(-2.230, 0.178)
$R^2$	0.419	0.480	
F	27.021***	10.922***	
$\Delta R^2$		0.061	
$\Delta F$		2.088	

Note.  $n = 78$ .

\*Depression Anxiety Stress Scales.

†Burden Assessment Scale.

‡Impact of Event Scale-Revised.

\*\* $P < 0.01$ , \*\*\* $P < 0.001$ .

PTSD, post-traumatic stress disorder; CI, confidence interval; HR, heart rate.

**Table 3.** Hierarchical logistic regression results for psychological and physiological predictors of PTSD severity in the parental cancer group

Variables	PTSD severity§					
	Model 1			Model 2		
	B (SE)	OR	CI 95%	B (SE)	OR	CI 95%
<i>Constant</i>	-5.414*** (1.512)			-6.551*** (1.794)		
Distress†	0.062** (0.019)	1.064	(1.024, 1.105)	0.066** (0.020)	1.068	(1.028, 1.111)
Burden‡	0.088* (0.038)	1.092	(1.013, 1.177)	0.089* (0.040)	1.093	(1.010, 1.183)
Peak HR to unpleasant pictures				0.555 (0.334)	1.742	(0.905, 3.353)
Peak HR to pleasant pictures				-0.049 (0.206)	0.952	(0.635, 1.427)
Peak HR to neutral pictures				-0.188 (0.277)	0.828	(0.481, 1.425)
HR accel. >1 bpm to unpleasant pictures				-1.226 (1.050)	0.293	(0.037, 2.296)
R <sup>2</sup> Nagelkerke	0.486			0.528		
-2 log	72.361			68.406		

Note.  $n = 78$ .

†Depression Anxiety Stress Scales.

‡Burden Assessment Scale.

§Considering cut-off point on the Impact of Event Scale-Revised.

\* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .

CI, confidence interval; OR, odds ratio; HR, heart rate.

$P = 0.412$ , Nagelkerke  $R^2 = 0.528$ ], since it decreased to 76.9% (Table 3).

## DISCUSSION

This preliminary investigation studied the presence of enhanced psychological morbidity and physiological reactivity to emotional stimuli in adult children caregivers with parental cancer, compared with matched controls (without chronically ill parents). Additionally, this study investigated if the HR responses contributed to the prediction of PTSD symptoms, and probable diagnosis, in the parental cancer group, given the scarce controlled studies relating emotional distress and cardiovascular reactivity among cancer caregivers (Chentsova-Dutton *et al.* 2002; Lucini *et al.* 2008; Corà *et al.* 2012). As expected, adult children caregivers showed higher symptoms of distress, burden, and PTSD compared with controls. These differences were also significant for PTSD severity, since the cut-off determined a six times higher likelihood of a PTSD diagnosis (36 vs. 10 cases) in the parental cancer group. However, although the cut-off did not have sufficient sensitivity (46%), it exceeded the minimum of 75% for specificity (87%), being therefore useful for diagnostic purposes. The moderate sensitivity indicates that there may be several pathways to PTSD severity in parental cancer caregivers, being physiological vulnerability an important cue to be further explored. These results support previous findings on affective disorders in caregivers and suggest a similarity between psychological consequences of caregiving in dementia (Vitaliano *et al.* 2003) and in cancer settings (Corà *et al.* 2012).

With respect to the physiological variables, results showed that adult children caregivers seem to be in greater risk for stress-related disorders. In the present study, although HR had a moderately wide normal range between participants, several studies specify that it can be considered a significant precursor of cardiovascular risk (Palatini & Julius 1997; Fox *et al.* 2007; Palatini 2009; Cooney *et al.* 2010). In general, HR levels were not clinically elevated, when compared with controls. Nevertheless, cancer caregivers tended to show higher HR parameters, with significant differences in some measurements (baseline and mean pre-stimulus baseline) for all picture types. Moreover, for unpleasant stimulus presentation, the differences were more noticeable. In the present study, adult children with parental cancer showed greater HR mean responses to unpleasant pictures than controls, as indicated by a higher HR, associated a lower mean deceleration and a trend for greater mean peak responses. The fact that the control group showed an HR deceleration to the unpleasant pictures can be interpreted as an orienting response, resembled to healthy volunteers' responses to unpleasant pictures reported in previous investigations (Lang *et al.* 1993; Bradley *et al.* 2001). There was a significant higher proportion of participants from the parental cancer group showing HR acceleration above 1 bpm, what could be interpreted as a heightened activation of the defensive system (Bradley *et al.* 1996). Supporting these results was the finding that for each second (except for the fourth one, on which only a trend was found) of unpleasant pictures presentation, the parental cancer group revealed a heightened HR response. This result can be interpreted as a learned fear response

to stimuli (Brunetti *et al.* 2010; Suendermann *et al.* 2010). Indeed, higher HR responses have been associated with higher frequency of reported autonomic symptoms, thus suggesting a possible psychophysiological pathway to stress-related cardiovascular dysfunctions, as indicated by previous findings (Lucini *et al.* 2008). Actually, elevated HR during stressful situations has been previously observed in long-lasting caregiving for dementia patients (Vitaliano *et al.* 1993). In fact, elevated HR may also compromise life expectancy, not only in patients with hypertension or diabetes but also in subjects free of disease (Jouven *et al.* 2009). Together, these results indicate that the risk associated with the acceleration of HR is not only statistically significant but also clinically relevant, and should be considered when evaluating caregivers or even patients (Perret-Guillaume *et al.* 2009). These results can drive health professionals to pay attention to caregivers' cardiac activity, and to recommend lifestyle changes or pharmacological treatment, in order to reduce cardiovascular risk.

For electrodermal reactivity, significant group differences were also found. The parental cancer group showed a higher SC tonic activity at baseline, but also a heightened SC magnitude of the response to unpleasant, neutral, and pleasant pictures. The number of published studies using SC as a measure of autonomic activity to stressors in family care providers in oncology is, to our knowledge, non-existent. In fact, researchers who study the impact of parental cancer are beginning to draw attention to the gap of biophysical methods in this area (Su & Ryan-Wenger 2007). However, it is important to note that some studies show SC increase in care-related activities. For example, maritally satisfied spouses show higher SC activation (considered a physiological 'forerunner' of empathy) compared with dissatisfied spouses, when listening to their partners describing the impact of pain on their daily lives (Stampler *et al.* 1997). In studies with caregivers of Alzheimer patients, although no significant differences were found in SC response by gender, men reported 'feeling' more relaxed than women (Thompson *et al.* 2004), whereas male Caucasian caregivers (compared with Mexican-Americans) showed lower electrodermal reactivity towards cognitive stimulation (Lewis *et al.* 2008). Although the present study did not intend to study gender or cultural/race differences, these results may motivate future research regarding physiological reactivity in men and women caregivers with different cultural backgrounds.

The last aim of the present study was to examine whether the magnitude of autonomic indices was directly related to PTSD symptoms and severity in participants

with parental cancer. It would be expected that distress and burden would predict higher PTSD symptoms, not only because they were significantly correlated, but also given the extensive literature on this topic (Vanderwerker *et al.* 2005; Thomas *et al.* 2012). An increasing number of studies showed that heightened physiological reactivity to trauma-related cues is indicative of a PTSD diagnosis (Orr & Roth 2000; Kibler & Lyons 2004; Ehlers *et al.* 2010). In particular, heightened HR response to standardised sets of trauma cues appeared to be an effective indicator of vulnerability to PTSD (Lindauer *et al.* 2006), reflecting an elevated sensitivity to unconditioned aversive stimuli (Orr & Roth 2000; O'Donnell *et al.* 2007). Previous reports showed that peak HR responses were an effective indicator of PTSD (Blanchard *et al.* 1996; Elsesser *et al.* 2005), as the cardiac acceleration above 1 bpm (Ehlers *et al.* 2010). In the present study, the HR peak response to unpleasant pictures increased significantly the predictive accuracy for higher PTSD symptoms, controlling for distress and burden. Even though HR peak responses to neutral and pleasant pictures, and the acceleration >1 bpm to unpleasant pictures, did not contribute to the explained variance, the hypothesis was confirmed. Contrary to Ehlers *et al.* (2010), the logistic regression with HR response to unpleasant pictures (peak response or acceleration >1 bpm) did not differentiate parental cancer participants with and without probable PTSD. However, the results are clinically relevant, suggesting that psychophysiological responses (specially HR responses) may be useful in identifying and treating cancer caregivers at risk for PTSD.

Some limitations and strengths of the present study must be acknowledged. This is the first known research study with a psychophysiological design comprising a sample of adult children caregivers in a parental cancer condition, compared with a matched control group. Important implications can be derived from present data, since it seems quite evident that parental cancer prompts psychological consequences that are 'visible' through assessment tools of peripheral autonomic responses. Another strength of the present study is the large sample size. There is not ample evidence that validates the effects of cancer patients' caregiving over time (Nijboer *et al.* 1998). Even though participants have been selected without any evidence of cardiovascular disease and properly matched, the cross-sectional design limits causal relationships between physiological correlates and PTSD symptoms. However, the obtained results are in accordance with previous longitudinal designs, reporting an elevated HR responsiveness in trauma victims that developed PTSD (Shalev *et al.* 1998; Bryant *et al.* 2003). For



example, prolonged assessments extending from the early phases of caregiving, for different stages of oncological disease, and in different contexts (e.g. home care, outpatient, chemotherapy, palliative care), should be taken in consideration, as well, in future research. It is always a sensitive issue the selected way to minimise the presence of a measurement bias in physiological research designs, due to its large variability. Thus, an additional limitation is the non-inclusion of the respiratory sinus arrhythmia (RSA) record, a well-known marker of vagal HR control (Watkins *et al.* 1998). Finally, although the selected IAPS pictures were classified by volunteers in the pilot study, a further limitation is the non-inclusion of an additional assessment task of pictures in the parental cancer group (e.g. using the Self-Assessment Manikin; Lang 1980). It would be interesting to verify if there was a correspondence between these self-assessments (in terms of arousal and valence) and physiological correlates. In fact, the IAPS is a pictorial tool with limitations when applied to people in distress, mainly because it was designed to evaluate emotions in laboratory, i.e. it remains doubtful whether, in a real life context, the results would remain the same. Moreover, it is not quite clear whether the emotional and physiological reactions revealed, by adult children caregivers, are related to the caregiving situation or if responses are generalised to any individual in the presence of the same aversive stimuli.

In conclusion, the results of the present study confirm that caregiving for a parent with cancer is a stressful condition with potentially negative physiological and psychological consequences (Pedersen & Revenson 2005), highlighting the importance of screening caregivers for both outcome reactions. The inclusion of cardiovascular variables in routine assessment can provide a more comprehensive picture of the psychophysiological risk associated with parental caregiving, thus decreasing its negative impact on physical and psychological health. With these results, a contribution is made to the advancement of knowledge of the physiological mechanisms involved in psychological morbidity in caregivers of cancer patients, with the ultimate aim of improving the diagnosis and prognosis of symptoms associated with this population. Finally, present findings allow an improvement in intervention and treatment of these individuals. These results suggest the need to carry out preventive strategies in this population, in order to improve the autonomic profile of caregivers in oncology.

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