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Aging & Mental Health

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Cognitive–behavioural group therapy improves a psychophysiological marker of stress in caregivers of patients with Alzheimer's disease

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Background: Family caregivers of patients with dementia frequently experience psychological stress, depression and disturbed psychophysiological activity, with increased levels of diurnal cortisol secretion.
Objectives: To compare the effects of a cognitive–behavioural group therapy (CBT) to a psychoeducation group programme (EDUC) on cortisol secretion in caregivers of patients with moderate Alzheimer's disease (AD).
Method: Caregivers of AD outpatients were semi-randomly allocated to one of two intervention programmes (CBT or EDUC) consisting of eight weekly sessions. Twenty-six participants completed the study. Before and after intervention, salivary cortisol was collected at four different times of the day. Effects of the interventions were evaluated with self-report psychological scales and questionnaires related to functional abilities and neuropsychiatric symptoms of the AD relative.
Results: Only in the CBT group did salivary cortisol levels significantly decrease after intervention, with a large effect size and high achieved power. Both groups reported a reduction of neuropsychiatric symptoms of their AD relative after intervention.
Conclusion: Psychoeducation for caregivers may contribute to a reduction of neuropsychiatric symptoms of AD patients while CBT additionally attenuates psychophysiological responses to stressful situations in caregivers, by reducing diurnal cortisol levels. This may lead to a positive impact in the general health of the caregiver, eventually resulting in better care of the AD patient.

Keywords: Alzheimer; burden; caregiver; stress; cortisol; cognitive–behavioural therapy; psychoeducation; neuropsychiatric symptoms; dementia

Introduction

Stress and depression are highly prevalent in individuals in care for a family member with dementia, as the psychological burden may be important and even higher than in those caring for physically handicapped elders (Parks & Novielli, 2000; Pinquart & Sorensen, 2006). Family caregivers of patients with dementia often experience social isolation, decreased leisure activities, family distress and financial problems (Parks & Novielli, 2000). In addition, they are particularly prone to physical health problems, due to engagement in 'risky behaviours' (e.g. nicotine and alcohol abuse and altered sleep patterns) and to stronger psychophysiological reaction to chronic stress, leading to negative effects on the immune system (Kiecolt-Glaser & Glaser, 2001; Lovell & Wetherell, 2011).

Chronic stress is associated with dysregulation of the hypothalamic–pituitary–adrenal axis (HPA), resulting in increased secretion of diurnal cortisol by the adrenal gland and failure of the negative feedback loop to inhibit secretion of corticotrophin releasing hormone by the hypothalamus and adrenocorticotropic hormone by the pituitary gland. Cortisol levels follow a regular circadian variation and are high in the morning, decreasing progressively throughout the day. A flattened daily pattern or an increase in cortisol levels by the end of the day are markers of psychological stress and are associated with higher general health risks (Kumari, Shipley, Stafford, & Kivimaki, 2011). Several studies have demonstrated increased cortisol levels in caregivers of patients with dementia when compared to non-caregivers, at awakening (de Vugt et al., 2005; Wahbeh, Kishiyama, Zajdel, & Oken, 2008), during the day (Bauer et al., 2000) or at the end of the day, displaying a flattened curve (Gallagher-Thompson et al., 2006). Chronic excessive release of cortisol may lead to decreased immunologic activity (Vedhara et al., 1999) or other endocrine problems (Chrousos, 2009) that may contribute to the occurrence of acute or chronic illness. This may further interfere with caregivers capacity of keeping up their caregiving role. Therefore, taking care of the caregiver's psychological and physiological burden may eventually result in improved quality of care of elders suffering from dementia.

Several reviews and meta-analyses noted the effects of interventions in caregiver's psychological well-being (Pinquart & Sorensen, 2006; Selwood, Johnston, Katona, Lyketsos, & Livingston, 2007; Thompson et al., 2007; Van Mierlo, Meiland, Van der Roest, & Droes, 2012). Among the different types of interventions, those providing

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psychoeducation coupled with an active participation of caregivers within a cognitive–behavioural therapy (CBT) framework are considered to be the most effective in reducing burden and increasing general well-being (Losada Baltar, Izal Fernandez de Troconiz, Montorio Cerrato, Marquez Gonzalez, & Perez Rojo, 2004; Pinquart & Sorensen, 2006; Selwood et al., 2007; Thompson et al., 2007). CBT for caregivers of dementia patients usually focuses on modifying beliefs related to the disease and to their role as caregivers, involving other family members in the care, and encouraging them to engage in pleasant activities (Fialho, Koenig, Santos, Barbosa, & Caramelli, 2012; Roth, Mittelman, Clay, Madan, & Haley, 2005; Vernooij-Dassen, Draskovic, McCleery, & Downs, 2011).

An improvement of psychophysiological parameters of stress, with decreased secretion of cortisol after CBT was reported in studies with different clinical populations such as women presenting hypothalamic amenorrhea (Michopoulos, Mancini, Loucks, & Berga, 2013), patients with chronic medical conditions (Matousek, Pruessner, & Dobkin, 2011), hypertension (Sung, Woo, Kim, Lim, & Chung, 2012), specific phobia (Brand, Annen, Holsboer-Trachsler, & Blaser, 2011) and depression (Sharpley, 2010). Only two studies assessed changes in cortisol release in caregivers of dementia patients after a psychological intervention (Vedhara et al., 2003; Williams et al., 2010). Vedhara et al. (2003) did not observe any changes in salivary cortisol despite improved immunologic response in participants assigned to the intervention group. Williams et al. (2010) proposed an individual video-based coping skill programme with telephone coaching but failed to find significant differences in cortisol pattern or levels after the intervention. Thus, so far no evidence has been found for a positive effect of psychotherapy on psychophysiological markers of stress in caregivers of dementia patients.

In the present study, we aimed to compare the effects of a group CBT to those of an isolated psychoeducation programme (EDUC) on circadian levels of cortisol. Our hypothesis was that CBT would be effective in reducing cortisol levels, and more so than EDUC as it offers stress management and coping strategies besides providing general information about Alzheimer's disease (AD). Further, we investigated intervention effects on psychosocial well-being of caregivers as well as on the independence and neurobehavioural symptoms of cared-for patients.

Methods

Ethical approval

The Ethical Committees on Human Experimentation from Universidade de São Paulo (USP) and Universidade Federal de São Paulo approved this study and written informed consent was obtained from each participant.

Participants

Inclusion criteria

(1) Informal caregivers (family members only) of patients with clinical diagnosis of possible or probable AD in the moderate or severe stage. Diagnosis and staging were defined by clinical consensus,[1] based on the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV), the Functional Assessment Staging – FAST (Reisberg, 1988) and the Portuguese version of the Mini Mental State Examination – MMSE (Bertolucci, Brucki, Campacci, & Juliano, 1994) (scores between 5 and 20); (2) being a primary caregiver; (3) being a caregiver for at least six months; (4) providing care for at least three hours per day.

Exclusion criteria

(1) Pre-existent neuroendocrine disease; (2) use of steroidal anti-inflammatory medication, immunosuppressant therapy, neuroleptic or anti-convulsant treatment; (3) sporadic use of anxiolytics (those regularly taking anxiolytics at least for the past three months were allowed to enrol in the study); (4) regular use of alcohol or illicit psychoactive substance.

Recruitment and procedures

The recruitment was carried out at the Cognitive Disorders Reference Center – CEREDIC of the Medical School of Universidade de São Paulo – Clinical Hospital (HC-FMUSP). Eligibility criteria were determined by analysing the medical file of outpatients diagnosed five years prior to the study. Basic information on the caregiver, such as familial relationship and contact, was indicated in the file. Participants were contacted by phone and those who accepted to participate were invited for a first visit, where further information on the study was given and they gave written informed consent. During this visit, participants also answered the pre-intervention assessment questionnaires. A second appointment before the beginning of the intervention was scheduled for the returning of saliva samples and blood sample collections by a certified nurse. Figure 1 shows the participant flow chart. Reasons mentioned by participants for discontinuing interventions included lack of availability, lack of interest in the programme and not feeling concerned by the topic.

Study design and intervention programmes

An intervention phase was preceded by an assessment phase (T1) and followed by a second assessment phase (T2) in which most of the measures taken at T1 were repeated.

Participants were semi-randomly assigned to the EDUC or CBT groups. The assignment to each group was done during the first contact by phone, in alternating order. Both interventions (Figure 2) were led by the same therapist (Tatiana Aboulafia Brakha) and included psychoeducation about AD, but in one of them participants additionally benefited from group CBT.

(1) EDUC group: in this group, caregivers participated in eight 60-minute group sessions held once a week, with up to 17 participants together. They received information on AD. The programme was

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                    ┌─────────────────────────────────┐
                    │  Assessed for eligibility (n=85)  │
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Excluded (n=50)
- ◆ Not meeting inclusion criteria (n=31)
  - 26 MMSE>20,
  - 3 MMSE <5,
  - 2 MMSE score unavailable
- ◆ Declined to participate (n=11)
- ◆ Other reasons (n=8)
  - 3 deceased,
  - 1 institutionalized,
  - 4 unreachable

Enrollment

Accepted and allocated (n=35)

Allocation

Allocated to CBT intervention (n=17)
- ◆ Completed base line (T1) (n=15)
  Did not show up at T1 (n=1)

Allocated to EDUC intervention (n=18)
- ◆ Completed baseline (T1) (n=17).
  Did not show up at T1 (n=1)

Post-intervention (T

Completed intervention (n=12)
Discontinued intervention (n=3)

Completed intervention (n=15)
Discontinued intervention (n=2)

Analysis

- ◆ Salivary cortisol data analysed (n=12)
- ◆ Psychometric data analysed (n=11)
  Excluded from analysis (partial literacy) (n=1)

- ◆ Salivary cortisol data analysed (n=14)
  Excluded from analysis (salivary samples a T2 poorly stored) (n=1)
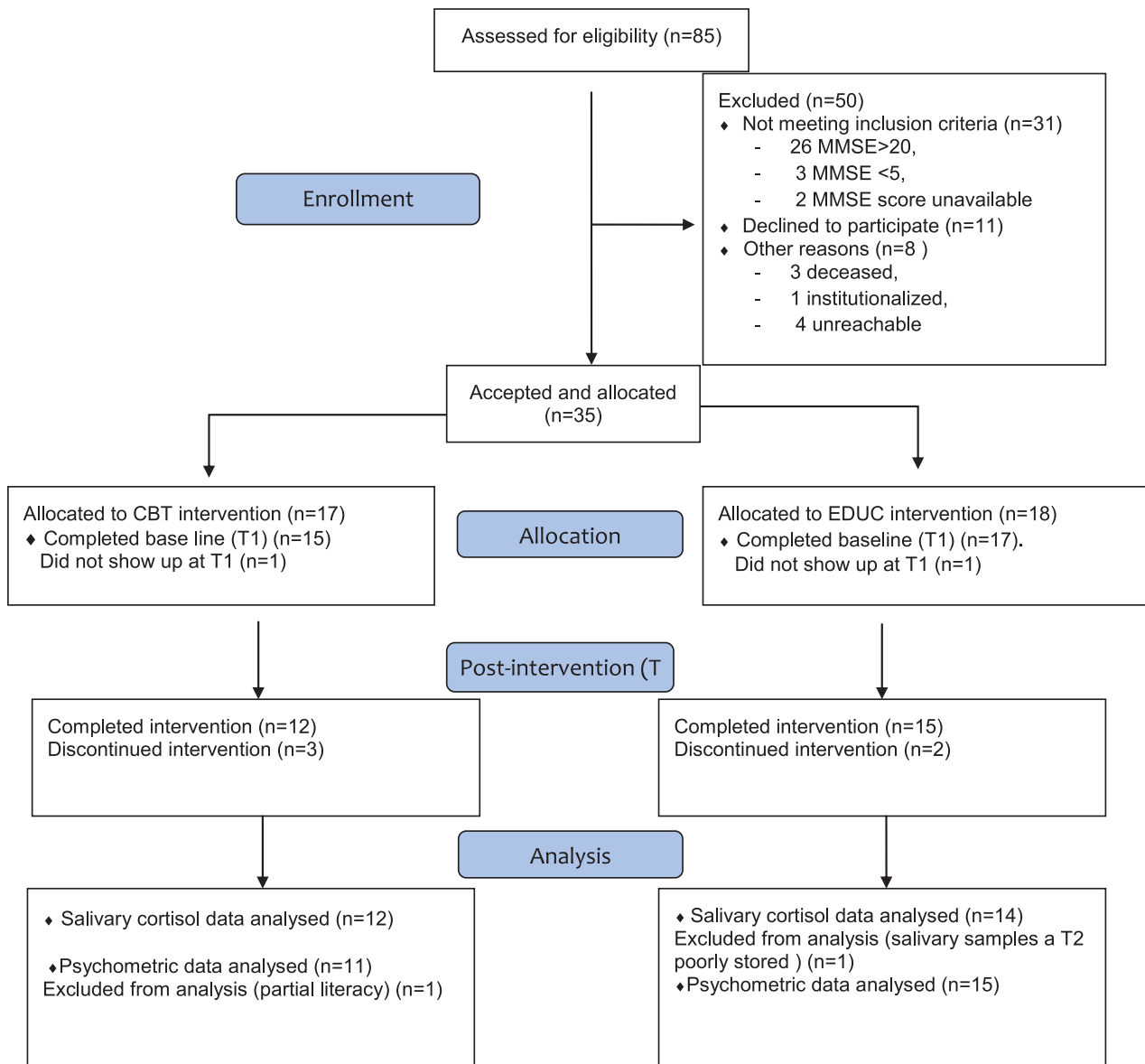- ◆ Psychometric data analysed (n=15)

Figure 1.   Participant flow diagram.

based on the work of Zarit, Anthony, and Boutselis (1987) and Parks and Novielli (2000), and covered the diagnosis process, cognitive symptoms, different stages of the disease and available treatment methods. Advices concerning interaction with the patient, how to deal with neuropsychiatric symptoms such as disinhibition, aggressiveness and delusions, as well as security issues were also given. Information was transmitted in a structured format with the aid of presentation software. At the end of the sessions, participants were allowed to ask questions, but little opportunity was given for discussion of personal issues and interactions between participants.

(2) CBT group: caregivers allocated to this group were divided in small groups of six to eight participants. They benefited from eight 90-minute group sessions held once a week, with pre-established discussion themes. These included life activities before and after caring for their AD relative, the family dynamic around the affected member and the caregiver relationship with his/her relative. Using cognitive–behavioural techniques, such as cognitive restructuring and behaviour modifications, participants were encouraged to resume some of the activities they had abandoned after becoming a caregiver and to favour the inclusion of other family members in caregiving activities. For example, in one of the sessions, participants chose one activity they wanted to carry out during the next week and that was feasible if someone else took care of their proxy. Cognitions and emotions related to this attitude were discussed prior to exposure, and participants could also benefit from encouragement of the other group fellows. The following week, they were invited to share their experience in the group, where alternative ways of thinking and feeling about the situation were identified. Further,

Session	Topics
1	**Introducing participants, group rules and identifying individual expectations.**[a] Alzheimer's disease mechanisms and diagnosis.
2	**Life before assuming caregiver's role; identifying changes brought by the relative's disease.** Disease manifestations (cognitive impairment and behavioural symptoms) and progression.
3	**Implicating other relatives in caregiving; engaging in leisure activities.** Treatment options and healthcare facilities.
4	Understanding and dealing with cognitive symptoms.
5	Understanding and dealing with behavioural manifestations.
6	**Identifying aspects of previous relationship with the cared-for person; re-establishing affective bonds.** Security issues and leisure activities for the patient.
7	**Anticipatory grief and disease progression.** Identifying signs of stress and burden in caregivers; advice for better coping.
8	**Recall of session topics, participant's feed-back and closure.**

Figure 2. Intervention topics.
a. In bold, material covered only in CBT; in plain font, material covered in CBT and EDUC

psychoeducation facts transmitted to the EDUC group (including management of AD's neuropsychiatric symptoms) were also covered in the CBT group, but in an interactive manner, which explains the need for slightly longer sessions. Discussions between group members and role-plays were regularly encouraged in order to strengthen the understanding of the different topics. In order to test and apply the skills learned during the sessions, homework tasks were recommended, such as practicing *in vivo* what was rehearsed in role-plays.

Outcome measures

Primary outcome measures

- Salivary cortisol: samples were collected in salivettes. Participants received the kit the day before collection and were instructed to chew the cotton for two minutes, to store it in the tube provided, keep the samples in the refrigerator and bring them on the following day. Samples were collected at four different times of the day: (1) immediately after waking up (when still in bed), (2) 30 minutes after waking up, (3) eight hours after the first sample and (4) immediately before going to sleep.

Once the participants returned the salivettes, these were centrifuged at 2300 rpm during 10 minutes at room temperature. Concentrations were determined by enzyme-linked immunosorbent assay (ELISA) by a commercial kit from the Diagnostic Systems Laboratories (Texas, USA).

Secondary outcome measures

- Perceived Stress Scale (PSS) (Cohen, Kamarck, & Mermelstein, 1983): assesses life situations which

are perceived as threatening and difficult to manage. Participants were asked to rate the frequency of their stress perception within the last month.
- Zarit Burden Interview, Portuguese version (Scazufca, Menezes, & Almeida, 2002): assesses different aspects of caregiving burden, including physical, emotional and financial domains.
- Beck Depression Inventory (BDI), Portuguese version (Gorenstein & Andrade, 1998): consists of a list of common depression symptoms such as sadness, irritability, pessimism and suicidal thoughts. Symptom severity is self-rated between 0 and 3, with higher scores indicating more severe depressive symptoms.
- State–Trait Anxiety Inventory (STAI-S, STAI-T), Portuguese version (Biaggio & Natalicio, 1979): is composed of two distinct self-report questionnaires (assessing respectively anxiety traits (STAI-T) and state (STAI-S). While traits are considered a stable feature and usual predisposition to act towards a perceived threat, state refers to a momentary condition that may fluctuate across time.

In addition, we asked each caregiver to rate the functional abilities and neuropsychiatric symptoms of the AD patient they cared for, with the help of the following instruments:

- Portable Functional Assessment Questionnaire (Pfeffer scale) (Pfeffer, Kurosaki, Harrah, Chance, & Filos, 1982): quantifies functional abilities such as preparing meals, shopping and handling money.
- Behave-AD (Reisberg et al., 1987): checks for the presence of neuropsychiatric symptoms such as anxiety, agitation, aggressiveness, hallucinations and delusions.

Statistical analysis

At T1: Pearson's correlation coefficients between variables were calculated considering the whole sample (both groups assembled). Between-group comparisons regarding demographic variables were performed using chi-square test for frequency data and Student's *t*-tests for continuous data. *Intervention outcomes*: For cortisol data we used a $4 \times 2 \times 2$ repeated measures analysis of covariance (ANCOVA) with measure (four daily samples), group (CBT, EDUC) and time (T1, T2) as factors. In order to decompose the main effect, the first analysis was followed up for each group with a 4×2 repeated-measures analysis of variance (ANOVA) (measure $\times$ time). Longitudinal comparisons for scores in the questionnaires were performed using 2×2 repeated-measures ANCOVA with group (CBT, EDUC) and time (T1, T2) as factors. For all ANCOVAs, gender and working status were inserted as covariates. For all cases, significance levels were established at $p < 0.05$. Effect sizes and achieved power were calculated with the aid of GPOWER*3 for longitudinal analyses only and when significance levels were reached.

Table 1. Demographic variables at T1.

Measure	CBT ($n = 12$)	EDUC ($n = 15$)	Statistical test
Women	100%	67%	$X^2 = 4.91, p = 0.05$
Age (years)	59.42 (6.67)	55.07 (10.68)	$t(25) = 1.2$, ns
Time of caregiving (years)	2.92 (1.08)	3.60 (2.50)	$t(25) = 0.88$, ns
Care provided per day (hours)	6.00 (2.09)	5.40 (2.35)	$t(25) = -0.69$, ns
Familial relationship			$X^2 = 0.09$, ns
Spouse	75% (9)	80% (12)	
Parent	16.70%	13.30%	
Cohabitation	58.30%	66.70%	$X^2 = 0.19$, ns
Paid employment	8.30%	53.30%	$X^2 = 6.07, p = 0.02$

Results

Demographic characteristics

As shown in Table 1, there were no significant differences at baseline between CBT and EDUC groups regarding age, the time since participants had been providing care, the time of caregiving per day and status of cohabitation (whether living or not with the AD patient). Groups significantly differed with regard to gender ratio and working status. In the EDUC group there were more male participants and more employed participants.

Correlations at T1

In order to determine whether cortisol level is a significant predictor of subjective stress, burden, anxiety or depression in our sample, we calculated correlations between salivary cortisol and psychometric scales. Significant correlations were observed between the waking salivary cortisol (first measure of the day) and PSS ($r = 0.61, p < 0.001$), BDI ($r = 0.473, p < 0.05$) and STAI-T ($r = 0.535, p < 0.01$). No other significant correlations were observed between psychometric outcomes and salivary cortisol time-points.

Intervention outcomes

Table 2 shows the results of the ANCOVAs with group (CBT, EDUC) and time (T1, T2) as factors for psychometric measures. There were no significant effects.

The results of the $4 \times 2 \times 2$ repeated-measures ANCOVA for cortisol secretion throughout the day (Figure 3) showed a significant interaction between group and time, $F(1, 22) = 10.32, p < 0.01, \eta\rho^2 = 0.32$, with 92% achieved power. There were no significant main effects of time ($F(1, 22) < 1$, ns) or group ($F(1, 22) = 2.46$, ns). Since intervention groups had different gender composition, we also performed the analysis on cortisol data without male participants ($n = 22$), with very similar results. In order to understand the interaction better we performed separate post hoc ANOVAs on the data of each group. The CBT group showed a significant decrease of daily secretion of salivary cortisol at T2 compared to T1 ($F(1, 11) = 21.97, p = 0.001, \eta\rho^2 = 0.67$) with 98% power, while no significant changes were observed in the EDUC group ($F(1, 13) = 0.19$, ns). In addition, a trend analysis based on Figure 2 shows a reversion of the daily cortisol release pattern in the CBT group at T2 when compared to T1, with a decrease of cortisol levels in the last daily measure, while the pattern in the EDUC group at T2 remained comparable to the one observed at T1.

In order to evaluate the impact of interventions on clinical manifestations of dementia in cared-for AD patients, we compared the scores on the Pfeffer scale and the Behave-AD questionnaire at T1 and T2. A repeated-measures ANOVA with group and time on the Pfeffer scores (CBT: mean: 23.18 ± 6.55 at T1 and 24.7 ± 4.8 at T2; EDUC: mean: 20.13 ± 6.40 at T1 and 19.9 ± 8.1 at

Table 2. Intervention outcomes for psychometric measures.

Measure	Mean (sd) T1	Mean (sd) T2	Repeated-measure ANCOVA[a]
Beck			Time: $F(1, 21) = 1.5$, ns Time
CBT	12.4 (7.5)	9.4 (5.7)	X group: $F(1, 21) = 1.49$, ns
EDUC	7.3 (5.0)	7.9 (4.8)	
STAI-S			Time: $F(1, 21) = 0.61$, ns Time
CBT	41.1 (10.9)	45.0 (8.6)	X group: $F(1, 21) = 0.16$, ns
EDUC	37.1 (9.0)	39.0 (9.5)	
STAI-T			Time: $F(1, 20) = 1.37$, ns Time
CBT	47.0 (11.0)	47.4 (10.9)	X group: $F(1, 20) = 0.21$, ns
EDUC	37.9 (7.0)	39.6 (8.0)	
PSS			Time: $F(1, 20) = 0.36$, ns Time
CBT	19.9 (6.6)	19.5 (5.3)	X group: $F(1, 20) = 1.35$, ns
EDUC	15.2 (3.9)	16.8 (7.1)	
Zarit			Time: $F(1, 21) = 0.83$, ns Time
CBT	35.0 (13.5)	38.1 (12.9)	X group: $F(1, 21) = 0.01$, ns
EDUC	31.3 (11.9)	34.2 (16.3)	

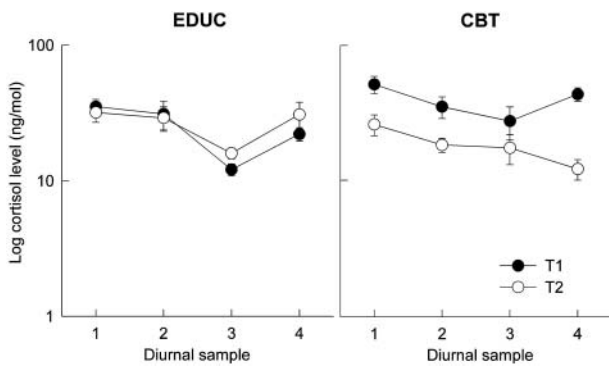[a]Gender and working status were inserted as covariates.

Figure 3. Salivary cortisol mean diurnal curves in T1 and T2 for both groups (Bars indicate standard errors from the mean).

T2) showed no significant main effects or interactions (time: $F(1, 24) = 0.84$, ns; time X group: $F(1, 24) = 1.42$, ns). In contrast, a comparable ANOVA on the data from the Behave-AD questionnaire (CBT: mean: 14.27 ± 9.60 at T1 and 9.54 ± 1.75 at T1; EDUC: mean: 11.46 ± 6.12 at T1 and 8.31 ± 1.6 at T2) revealed a significant effect of time ($F(1, 22) = 14.09$, $p = 0.001$, $\eta\rho^2 = 0.36$) with 95% achieved power, but no interaction ($F(1, 22) = 0.56$, ns), reflecting a decrease of neuropsychiatric symptoms in both patient groups after the intervention.

Discussion

We compared the effects of group CBT to a group psycho-education programme on cortisol diurnal secretion in caregivers of patients with AD. While both groups received information on cognitive and behavioural symptoms of the disease as well as advices on how to deal with them, in the CBT group participants had the opportunity to exchange personal experiences, discuss their beliefs related to the disease and their role as caregivers, and acquire new coping strategies. Prior to the intervention salivary cortisol levels at wake-up correlated significantly with scores on scales of perceived stress, trait anxiety and depression. In both groups reported neuropsychiatric symptoms of the AD relative decreased following intervention. However, only in the group of caregivers assigned to the CBT programme did we observe an overall decrease of cortisol secretion, with a large effect size and high achieved power, as well as a modification of the diurnal cortisol pattern.

The significant reduction of cortisol levels in the CBT group is in agreement with several studies reporting the effects of CBT in cortisol levels in different populations (Matousek et al., 2011; Sharpley, 2010; Sung et al., 2012). However, our findings differ from those reported by Williams et al. (2010) and Vedhara et al. (2003), who did not find significant differences in cortisol levels after a CBT intervention for caregivers of patients with dementia. This could be attributed to differences in CBT protocols used in previous studies. For example, Williams and colleagues (Williams et al., 2010) used a video-based individual programme, while in the present study sessions were held in groups where participants interacted actively among each other and with the therapist, an approach that

has been demonstrated to be particularly beneficial (Pinquart & Sorensen, 2006). The programme proposed by Vedhara and colleagues (Vedhara et al., 2003) shares many similarities with our CBT intervention, including intervention modality and therapy content. The lack of effect on cortisol levels in their study might be explained by the absence of measures of cortisol at wake-up (which is particularly high in stressed individuals) or to the shorter interval between the end of the programme and cortisol sampling. Vedhara et al. (2003) collected saliva samples within a week after the last session, whereas we waited between 7 and 10 days for the post-intervention assessment. Negative emotions such as sadness and anxiety may arise at the end of the therapy and lead to increased cortisol levels, whereas benefits may be observed later. Indeed, Vedhara and co-workers observed an increase in immune parameters in the CBT group two to four weeks after the end of the programme, suggesting a delayed reduction of HPA-axis activity.

Before the intervention, both EDUC and CBT groups showed a particular diurnal pattern of salivary cortisol secretion, with higher levels in the evening sample compared to the afternoon sample. This is an indication of increased levels of stress since cortisol levels are usually expected to decrease in the evening (Gallagher-Thompson et al., 2006). In our study, the abnormal pattern of cortisol secretion was maintained after the EDUC intervention but was reversed after CBT, with lower cortisol concentrations in the last sample of the day. The cortisol pattern observed in both groups at T1 may be attributed to the stressing routine AD caregivers face at the end of the day due to mealtime, showering and putting patients to bed. Furthermore, the frequency and intensity of neuropsychiatric symptoms such as aggressiveness, hallucinations and delusions tend to increase at sunset (an effect termed the 'sundown syndrome') and are often correlated with caregiver's burden (Allegri et al., 2006; Khachiyants, Trinkle, Son, & Kim, 2011). CBT reduces anger and aggressiveness in patients with brain injury (Aboulafia-Brakha, Greber Buschbeck, Rochat, & Annoni, 2013), and the frequency of these symptoms also decreases in AD patients following psychosocial interventions for their caregivers (Stella et al., 2011). In line with this finding, in the current study caregivers reported a significant reduction of neuropsychiatric symptoms of their AD relatives, with a large effect size and high statistical power. As this was observed for both groups, it is likely that this finding is related to the psychoeducation component. Indeed, both programmes included information and suggestions on how to deal with neuropsychiatric symptoms, such as making an effort to interact with their relative with more empathy, patience and kindness. However, since the reduction of neuropsychiatric symptoms was observed in both groups, it does not explain the modified cortisol pattern in caregivers attributed to the CBT group. The latter finding may better be explained by a change in abilities to cope with stressful situations, either by changing the way caregivers think about the situation or by delegating tasks to other family members; strategies encouraged and trained during this group's meetings.

The significant correlations observed between salivary cortisol levels and perceived stress, anxiety and depression are in line with previous findings (Morris, Rao, & Garber, 2012) and reinforce the knowledge of the association between psychological and psychophysiological activities. However, while we observed significant changes in cortisol release following CBT, there were no corresponding changes in psychometric scores. One possible explanation is that with both interventions participants became more aware of their feelings and attitudes and tended to emphasize psychological symptoms that were underestimated at T1. Another possibility is that the questionnaires used were not sufficiently precise to capture the subtleties of changes in coping with caregiving activity, which might better be quantified with specific coping scales.

Our study has some methodological limitations. Thus, there were significant differences between groups at T1 regarding gender and working status. We controlled possible effects of these variables by including them as covariates in our analysis. Our results show that intervention effects were independent of these confounding variables. Another limitation is the relatively small sample size in each intervention group. However, as large effects sizes and high achieved power were observed the intervention effects can be considered statistically safe despite a limited sample size. Despite some drawbacks our study makes an important contribution to the understanding of intervention effects on caregiver health. The inclusion of a physiological marker of stress as primary outcome variable is particularly important, as it may capture effects of the intervention that cannot be measured with self-report questionnaires.

In conclusion, psychoeducation for caregivers may result in a reduction of neuropsychiatric symptoms of AD patients while CBT may additionally attenuate psychophysiological responses to stress in caregivers. Thus, from a clinical perspective, our CBT programme, which consisted of psychoeducation, analysis of changes in family dynamics provoked by the disease, encouragement of participants to include other relatives in care giving, to regain activities of their former lives and to re-establish affective bonds with the cared-for person, may improve caregiver's health. As a consequence it may eventually lead to a better care of the AD patient. Therefore CBT interventions should be recommended for caregivers of patients with moderate to severe dementia in order to decrease their psychological and psychophysiological burden.

For future studies in this area, it would be of interest to investigate psychological mechanisms underlying psychophysiological changes by assessing caregiver's specific coping strategies and emotion regulation skills. In addition, psychophysiological effects of CBT interventions could also be studied in caregivers of patients with acquired brain injury, such as stroke or traumatic brain injury.

Funding

Note

1. Diagnosis established by a consensus by the CEREDIC medical staff composed of neurologists, psychiatrists and geriatrics as well as neuropsychologists, all experienced in the diagnosis and treatment of dementia.

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