A pilot study of yogic meditation for family dementia caregivers with depressive symptoms: effects on mental health, cognition, and telomerase activity[†]

H. Lavretsky¹, E.S. Epel⁴, P. Siddarth¹, N. Nazarian¹, N. St. Cyr¹, D.S. Khalsa³, J. Lin⁵, E. Blackburn⁵ and M.R. Irwin^{1,2}

¹Department of Psychiatry and Biobehavioral Sciences and the Semel Institute for Neuroscience, University of California, Los Angeles, CA, USA ²Cousins Center for Psychoneuroimmunology, University of California, Los Angeles, CA, USA

³Alzheimer's Research and Prevention Foundation, Tucson, AZ, USA

⁴Department of Psychiatry, University of California, San Francisco (UCSF), San Francisco, CA, USA

⁵Blackburn Laboratory, University of California, San Francisco, CA, USA

Correspondence to: H. Lavretsky, MD, MS, E-mail: hlavrets@ucla.edu

[†]This article was published online on March 11, 2012. Errors were subsequently identified. This notice is included in the online and print versions to indicate that both have been corrected [March 30, 2012].

Background: This study examined the effects of brief daily yogic meditation on mental health, cognitive functioning, and immune cell telomerase activity in family dementia caregivers with mild depressive symptoms.

Methods: Thirty-nine family dementia caregivers (mean age 60.3 years old (SD = 10.2)) were randomized to practicing Kirtan Kriya or listening to relaxation music for 12 min per day for 8 weeks. The severity of depressive symptoms, mental and cognitive functioning were assessed at baseline and follow-up. Telomerase activity in peripheral blood mononuclear cells (PMBC) was examined in peripheral PBMC pre-intervention and post-intervention.

Results: The meditation group showed significantly lower levels of depressive symptoms and greater improvement in mental health and cognitive functioning compared with the relaxation group. In the meditation group, 65.2% showed 50% improvement on the Hamilton Depression Rating scale and 52% of the participants showed 50% improvement on the Mental Health Composite Summary score of the Short Form-36 scale compared with 31.2% and 19%, respectively, in the relaxation group (p < 0.05). The meditation group showed 43% improvement in telomerase activity compared with 3.7% in the relaxation group (p = 0.05).

Conclusion: This pilot study found that brief daily meditation practices by family dementia caregivers can lead to improved mental and cognitive functioning and lower levels of depressive symptoms. This improvement is accompanied by an increase in telomerase activity suggesting improvement in stress-induced cellular aging. These results need to be confirmed in a larger sample. Copyright © 2012 John Wiley & Sons, Ltd.

Key words: dementia caregiver; stress; depression; resilience; cognition; Kirtan Kriya; yoga; meditation; relaxation; telomerase; NFkB

History: Received 21 December 2011; Accepted 25 January 2012; Published online 11 March 2012 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/gps.3790

The prevalence of dementia and the number of family caregivers will increase dramatically in the next two decades adding to the cost of clinical care and burden as the US aging population increases. Currently, at least five million Americans provide care for someone with dementia (Schulz and Martire, 2004). The detrimental impact to personal, social, and health outcomes of informal dementia caregiving has been well documented in recent years (Lavretsky, 2005; Lavretsky *et al.*, 2010).

Chronic stress places caregivers at a higher risk for developing depression. On average, the incidence and prevalence of clinical depression in family dementia caregivers approaches 50% (Lavretsky, 2005). Caregivers are twice as likely to report high levels of emotional distress (Lavretsky, 2005). The trend of impaired resilience to stress with advancing age indicates an increased rate of cardiovascular disease and mortality. Although the relation between mental and physical health has been previously documented, the mechanistic links are beginning to be understood at the cellular level (Miller et al., 2009). Telomere length has recently been proposed as a useful 'psychobiomarker' linking chronic psychological stress and diseases in aging (Epel et al., 2006). A telomere is a region of repetitive DNA sequences at the end of a chromosome, which protects the end of the chromosome from deterioration. Shortened telomere length and reduced telomerase (the cellular enzyme primarily responsible for telomere length and maintenance) are associated with premature mortality and predict a host of health risks and diseases (Lin et al., 2009), which may be regulated in part by psychological stress (Epel et al., 2004; Ornish et al., 2008; Epel et al., 2009). Over the long term, high telomerase likely promotes improvement in telomere maintenance and immune cell longevity (Jacobs et al., 2011). Although the link between replicative senescence and exhaustion that control T-cell proliferative activity and function is still not clear (Akbar and Henson, 2011), the change in these parameters in the context of randomized mind-body interventions is of interest. A recent study (Jacobs et al., 2011) showed that meditation and positive psychological change was associated with higher levels of telomerase activity.

Many of the existing psychosocial interventions for caregiver stress and depression show only modest benefits in caregiver outcomes (Lavretsky, 2005). In our recent study of dementia caregiver depression, we demonstrated greater improvement in depression and resilience with the standard antidepressant treatment using escitalopram compared with a placebo (Lavretsky et al., 2010). However, many caregivers may be opposed to the use of medication because of the associated cost and drug side-effects and prefer to use complementary and alternative medicine for stress reduction. These considerations motivated us to test a brief mind-body intervention for stress reduction. We performed a randomized pilot study of Kundalini yoga Kirtan Kriya meditation compared with passive relaxation with listening to instrumental music for 12 min per day for 8 weeks. The relaxation control group was selected to test whether relaxation response was responsible for the effect of Kirtan Kriya on distress and cognition in caregivers, in which case

both groups would have similar outcomes. Two prior studies indicated changes in the brain blood flow with Kirtan Kriya (Khalsa *et al.*, 2009; Newberg *et al.*, 2010). However, it is unclear whether there are any other mechanisms that contribute to the meditation response compared with relaxation.

We hypothesized that Kirtan Kriya practice will result in improved levels of primary (i.e., mental health and depression) and secondary outcomes (i.e., cognition) compared with passive-listening-to-music relaxation in an 8-week intervention study. We also anticipated that meditation would increase telomerase activity as compared with the relaxation based on prior findings that caregiver stress is associated with cellular senescence (Epel et al., 2009), and that a meditation intervention can increase telomerase levels (Jacobs et al., 2011). The primary outcome was identified as response with 50% improvement in the Hamilton Depression Rating Scale score (HAMD) (Hamilton, 1960) and in the Mental Health composite summary score (MCS) of the Medical Outcomes Study Short Form 36-Item Health Survey (SF-36) (Ware and Sherbourne, 1992), an instrument that measures mental and physical functioning.

Methods

Over a period of 12 months, we screened a total of 69 family caregivers and recruited 49 family caregivers (45–91 years of age, two men, 36 adult children, 13 spouses) who were taking care of their relatives with dementia. After completing a full description of study to the subjects, written informed consent was obtained in accordance with the procedures set by the UCLA Institutional Review Board.

Potential subjects were required to be adult or older caregivers of patients with dementia being evaluated by the geriatric psychiatry and memory clinics. In addition, the subjects were identified by the patient or clinical staff as the primary source of assistance and/or support and were in contact with the dementia patient at least three days per week. First, subjects were screened using the Structured Clinical Interview for the DSM-IVR (SCID) was administered by a single rater (HL) to exclude those with major depressive disorder because of the restriction on psychotropic drug use or any other treatment for depression (Spitzer et al., 1992). The Hamilton Rating Scale for Depression (HAM-D-24 item) was used to rule out major depression that would require other treatment modalities (Hamilton, 1960). Those who had scores between 5 and 17 signifying mild-to-moderate levels of depressive symptoms were invited to participate in

the trial. Lastly, a score of 26 or higher on the Folstein Mini-mental State Examination (MMSE) was required for inclusion (Folstein *et al.*, 1975). Exclusion criteria were: (i) a history of any other psychiatric illness; (ii) alcohol and/or substance abuse or dependence; (iii) severe or acute medical illness; (iv) acute suicidal or violent behavior; and (v) any other central nervous system disease or dementia.

Procedures

All subjects were randomized using a computergenerated randomization table by a masked statistician to participate in either Kirtan Kriya practice or a relaxation practice for 12 min per day for 8 weeks. The protocol for Kirtan Kriya is standard for the Kundalini Yoga practice as taught by Yogi Bhajan that was utilized in the previous studies in older adults (Newberg et al., 2010). We assessed the severity of depressive symptoms, mental and physical functioning and cognition at baseline, at the end of the 8-week study, or upon early termination. In addition to the treatment protocol, all caregivers also received psychoeducation about the course and prognosis of dementia and about caregiver health, which was intended to address identified shortcomings in the care of their care-recipients.

Intervention protocol

We provided samples of both the meditation and relaxation CDs during screening visits to assess if subjects were amenable to the interventions. Only subjects who were comfortable with either intervention and agreed to participate were recruited.

Meditation group procedures

Meditation was introduced to caregivers during their baseline visit. A brief 12-m yogic practice included an ancient chanting meditation, Kirtan Kriya, which was performed every day at the same time of the day for a total of 8 weeks, based on a utilized and previously tested protocol with recorded CD (Newberg *et al.*, 2010). The meditation involved repetitive finger movements or mudras, as well as chanting of the mantra 'Saa, Taa, Naa, Maa,' meaning 'Birth, Life, Death, and Rebirth' that are chanted first aloud, then in a whisper, and silently for the total of 11 min with 1 min allocated to 'tuning in' at the beginning and the final deep breathing relaxation accompanied by the visualization of light ('Alzheimer's research & prevention foundation: Arpf research: Kirtan kriya', 2011).

Relaxation group procedures

Participants in the relaxation group were asked to relax in a quiet place with their eyes closed while listening to the instrumental music on the relaxation CD for 12 min every day at the same time for 8 weeks. The music was provided to the subjects on a CD along with instructions to find a quiet place without distractions and close their eyes and try to relax. The choice of control was motivated by the intention to test whether relaxation response was solely responsible for the effect of meditation. Because Kirtan Kriva involved melodic chanting, we chose to control with relaxation while listening to instrumental music. Compliance and satisfaction with either intervention were monitored at each visit by direct interview and review of daily diaries documenting the length of and adherence to the practice.

Assessment instruments

Several instruments were used to assess psychological distress and coping. MCS score was assessed by using the Medical Outcomes Study SF 36-Item Health Survey (Ware and Sherbourne, 1992), an instrument that measures health-related quality-of-life, mental, physical, and social functioning. The Hamilton Rating Scale for Depression (HRSD-24 item) (Hamilton, 1960) was used to quantify mood symptoms.

The remaining instruments were used to compare groups at baseline. Cognitive performance was measured by the MMSE (Folstein *et al.*, 1975). The Cumulative Illness Rating Scale (Miller *et al.*, 1992) was used for rating global chronic medical illness burden.

Cognitive functioning

We administered a brief neuropsychological assessment battery that measured the domains likely to show impairment in geriatric depression. The battery was comprised of the following instruments: California Verbal Learning Test II (CVLT II) (Delis *et al.*, 2000), to test verbal memory, Trail Making A (Reitan, 1958) to test attention and speeded information processing, and Trail Making B to test executive function.

Blood sample collection, PBMC isolation, and telomerase extract preparation

Peripheral blood mononuclear cells (PBMC) were isolated from heparinized whole blood by density

gradient separation (Ficoll-paque PLUS), then washed three times in phosphate-buffered saline. Live cells were counted by Trypan Blue dye exclusion using a hemocytometer. Extracts corresponding to 5000 live cells/ μ L were made based on the protocol provided in the TRAPeze telomerase detection kit (Chemicon, Temecula, CA, USA). The extracts were frozen and stored at -80 °C, then shipped on dry ice to the University of California, San Francisco Blackburn Laboratory for analyses.

Telomeric repeat amplification protocol

Quantification of telomerase activity was measured from the extract using the telomeric repeat amplification protocol (TRAP) as previously described witha commercial kit according to the kit manual (TRAPeze[®]). Between 2000 and 10 000 cells were used for TRAP reactions to ensure that the assay was in linear range for each sample (Lin et al., 2009). The polymerase chain reaction program used was: 94°C for 2 min; 94 °C for 30 s, 59 °C for 30 s for 30 cycles. The products were fractionated on a 10% polyacrylamide-8 M urea sequencing gel and scanned on a STORM 860 molecular imager (GE Healthcare, Piscataway, NJ, USA). The 293 T cell line was used as a positive telomerase activity control and reference standard. Telomerase activity was quantified using the software ImageQuant 5.2 (GE Healthcare, Piscataway, NJ) as previously described (Lin et al., 2010), which reports activity per 10000 cells.

Statistical analysis

All data were entered into the database at the time of their collection. The participants in the two treatment groups were compared on all demographic and clinical measures at baseline to assess the success of the randomization procedures using chi-square tests for the categorical measures and two-sided *t*-tests for the continuous measures.

Mental health, the primary outcome, was compared using two measures—the Mental Health Scale of the SF-36 and HAM-D. Subjects who improved by 50% or more in the Mental Health Scale of the SF-36 and HAM-D were classified as responders. Fisher's exact test was used to test response in the meditation group compared with the relaxation group. Cognition, the secondary outcome measure, was analyzed using a multivariate analysis of covariance (MANCOVA; controlling for age) with the MMSE score, Trail Making A (time), Trail Making B (time) and CVLT (long delay cued recall) as the dependent variables. If the MANCOVA was significant, analyses of covariance (ANCOVAs) were performed to determine which, if any, individual measures contributed to the significant difference. As exploratory studies, changes in telomerase levels in the two groups were analyzed using a separate ANCOVA, controlling for age. We also explored the association between changes in telomerase with changes in depression and health functioning using Pearson correlation coefficients. Significance was set at $p \le 0.05$. Two-sided *p*-values are reported for all baseline comparisons; and in keeping with the directional hypotheses of the study, one-sided *p*-values are reported for all the univariate tests pertaining to change scores.

Results

Of 49 recruited subjects, 45 were randomized and 39 (80%) completed the intervention: 23 subjects in the meditation group and 16 subjects in the relaxation group. Total of 10 subjects (20%) dropped out: four dropped out prior to randomization and post-randomization, four dropped out from the relaxation group and two from the meditation group. Dropouts in either group occurred because of lack of interest in the intervention or inability to commit to the study schedule (Figure 1), and did not differ from the participants on any characteristics. Table 1 presents the baseline demographic and clinical characteristics of the completers in the two subject groups.

The groups did not differ on any of the baseline characteristics with the exception of body-mass index (BMI). The meditation group had lower mean BMI of 23.5 (SD = 2.5) compared to the relaxation group 29.4 (6.9) (t = -3.8; p < 0.01). Because of the significant group difference in BMI, we investigated whether BMI was associated with any of the outcome measures (mental health, depression, cognition and telomerase activity) at baseline. None of the measures were correlated with BMI at baseline (all *p*-values > 0.1). Hence, given these results and the fact that the intervention was not designed to target physical activity nor BMI, we did not control for BMI in further analyses that examined change in outcomes during the treatment trial. The groups did not differ on the time spent in support or the psychoeducation activities. Age was the only demographic variable that correlated with the outcome measures (age was associated with cognitive measures at baseline, p < 0.001-0.0001; hence, age was used as a covariate in the analyses.

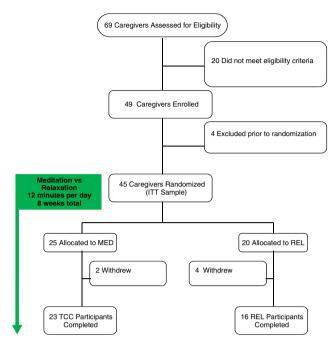


Figure 1 Participant flow and distribution of subjects in the study.

Mental health. As indexed by a response of 50% or greater improvement on the MCS score of the SF-36, 12 subjects (52.2%) responded in the meditation group, whereas three subjects (18.7%) responded in the

relaxation group (p = 0.02, one-tailed Fisher's exact test). Similarly, for HAM-D, 15 subjects (65.2%) responded in the meditation group, whereas five subjects (31.2%) responded in the relaxation group (p = 0.03, one-tailed Fisher's exact test).

Cognition. The MANCOVA showed significant group differences in change of cognition (F(4,33) = 3.82, p = 0.01). Individually, the MMSE total and Trail Making B (time) showed significant improvement in the meditation group compared with the relaxation group (Table 2).

Telomerase activity. The meditation group showed 43.3% improvement in telomerase activity compared with 3.7% improvement in the relaxation group (Figure 2). ANCOVA controlling for age revealed a significant increase in telomerase activity from baseline to post-intervention in the meditation group versus the relaxation group (F(1,33) = 2.75, p = 0.05; Table 2).

Significant correlations were found between increased telomerase activity, a decrease in levels of depression (r = -0.33; p = 0.05), and mental health score of SF-36 (r = 0.44; p = 0.01; Figure 3) in the full sample. The association of increased telomerase activity with an improved

Table 1 Comparison of the baseline demographic, clinical, and biological characteristics in the two treatment groups

	Meditation ($N = 23$) Mean (SD) or N (%)	Relaxation ($N = 16$) Mean (SD) or N (%)	t/Chi-square	<i>p</i> -value
Age in years	60.5 (28.2)	60.6 (12.5)	0.03	0.9
Male gender*	0 (0%)	2 (13%)	3.0	0.08
Education, years	16.1 (2.1)	15.1 (2.8)	1.2	0.2
Months of depression	45.1 (35.4)	39 (21.2)	0.6	0.5
Years of caregiving	4.7 (2.4)	4.2 (2.9)	0.6	0.6
Hours of care per week	47.8 (35.8)	63.3 (36.2)	-1.3	0.2
Medical burden		х <i>у</i>		
CIRS	3.0 (2.3)	4.6 (3.1)	-1.8	0.08
CVRF	5.2 (3.7)	7.4 (6.4)	-1.4	0.2
Mental Health	· · · ·	х <i>У</i>		
HAM-D	11.9 (4.1)	11.4 (4.0)	0.4	0.7
MCS of SF-36	34.4(10.2)	37.3 (11.0)	-0.8	0.4
Cognition		х <i>у</i>		
MMSE	29.45 (1.0)	29.6 (0.6)	-0.3	0.6
Trails A time	35.3 (15.4)	51.2 (41.1)	-1.7	0.1
Trails B time	76.3 (36.7)	97.8 (58.4)	-1.4	0.2
CVLT long delay	12.9 (2.7)	11.3 (2.8)	1.7	0.1
cued recall	· · · ·	х <i>У</i>		
Biological activity				
Telomerase, unit/10 000	2.7 (1.3)	3.0 (1.3)	-0.6	0.6

*Chi-square statistics (df = 1) reported for gender ratio; t-statistics (df = 37) for all other variables; two-sided *p*-values reported for all variables. SF-36 MCS, Short Form-36 Mental Health composite summary scores; MMSE, Mini-Mental State Examination Scale; HAM-D, Hamilton Depression Rating Scale; CIRS, Cumulative Illness Rating Scale; CVRF, Cerebrovascular Risk Factors Scale, Trail A, time in seconds; Trail B, time in seconds; CVLT, California Verbal Learning Test.

Change scores	Meditation (N = 23) Mean (SD)	Relaxation (<i>N</i> = 16) Mean (SD)	<i>F</i> (1,36)*	p-value*	Effect size Cohen's d
Mental health					
HAM-D	-7.4 (3.7)	-5.3 (4.5)	2.43	0.06	0.51
MCS of SF-36	12.8 (9.7)	6.3 (10.6)	3.87	0.03	0.64
Role emotional scale	33.3 (30.2)	-0.01 (47.2)	7.08	0.005	0.84
Energy scale	19.6 (20.6)	5.0 (16.7)	5.68	0.01	0.78
Cognition					
MMSE	0.2 (0.7)	-0.9(1.2)	13.79	0.0003	1.12
Trails A time	-3.6 (10.4)	-1.3 (18.7)	0.32	0.29	0.15
Trails B time	-11.2 (19.7)	9.9 (30.5)	7.46	0.005	0.82
CVLT long delay cued recall	-0.6 (2.4)	-0.8 (2.5)	0.10	0.38	0.08
Biological activity	· · ·	. ,			
Telomerase, units/10,000	0.9 (2.5)	-0.2 (1.2)	2.75	0.05	0.56

Table 2 Comparison of the change scores in clinical outcomes and biological measures in the two treatment groups

**F*-statistics (df = 1,33 for telomerase only) and one-sided *p*-values are reported for all variables.

SF-36 MCS, Short Form-36 Mental Health composite summary scores; MMSE, Mini-Mental State Examination Scale; HAM-D, Hamilton Depression Rating Scale; Trail A, time in seconds; Trail B, time in seconds; CVLT, California Verbal Learning Test.

mental health score was significant only in the meditation group (r = 0.59; p = 0.01); this finding was not significant in the relaxation group.

Discussion

Our study is the first to investigate the efficacy of daily practice of Kirtan Kriya to improve: (i) depressive symptoms; (ii) mental health; (iii) cognition; and (iv) telomerase activity in family dementia caregivers with mild depressive symptoms in a randomized controlled study [Correction made here after initial online publication.]. One prior pilot study used yogic meditation and mindfulness to improve coping, but in comparison with our study, no biological or cognitive correlates of stress reduction were reported. (Oken *et al.*, 2010). Despite the fact that caregivers in our study had higher levels of distress and mild depressive symptoms compared with other studies of caregiver stress (Teri *et al.*, 1992; Roth *et al.*, 2003), we found an improvement across measures of mental health and cognitive functioning, psychological distress, and telomerase activity in caregivers performing daily Kirtan Kriya compared with the relaxation group.

Multiple psychosocial intervention studies aimed at decreasing the burden of caregiving have shown that they can enhance mental health. The effects of psychosocial interventions vary greatly (Sorensen *et al.*, 2002) and rarely include biological measures of stress-response (Wisniewski *et al.*, 2003). In the recent meta-analysis, Pinquart and Sorensen (2006) integrated the results of 127 intervention studies with dementia caregivers published or presented between 1982 and 2005 (Pinquart and Sorensen, 2006) and demonstrated small effects on caregiver burden, depression, and subjective well-being.

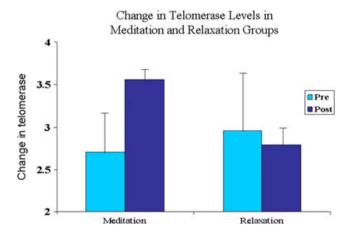


Figure 2 Change in telomerase levels in meditation and relaxation groups.

Given the magnitude of the caregiver burden, it is surprising that very few interventions translated into clinical practice. The financial burden of complex psychosocial interventions in the community is one of many explanations for the lack of translation into community practice. Our study suggests a low-cost behavioral intervention that can enhance coping and quality of life of the caregivers.

A few relatively small pilot studies evaluated the effects of meditation on caregiver stress with reported improvement in coping. In a study similar to ours, Oken et al. (2010) reported the results of a pilot randomized trial of a Mindfulness-Based Cognitive Therapy program in the two active comparison groups and a respite-only group serving as a pragmatic control (Oken et al., 2010). The investigators reported a significant effect on levels of distress, with both active interventions showing improvement compared with the respite-only group. Franco et al. (2010) reported the effects of a mindfulness development meditation program on psychological discomfort and burden in 36 family dementia caregivers (Franco et al., 2010). Oman et al. (2008) reported positive effects in self-efficacy assessment by professional caregivers after spiritual wisdom-based mindfulness training (Oman et al., 2008). Finally, Waelde et al. (2004) reported the effects of a six-session manualized yoga-meditation program in 12 older female dementia family caregivers (Waelde et al., 2004) with significant reductions in depression and anxiety and improvements in perceived self-efficacy. To summarize, all of the recent pilot studies were more limited in assessing multifaceted outcomes of mindbody interventions on caregiver stress and did not report the biological and cognitive correlates of stress reduction in dementia caregivers compared with our study.

Very few studies evaluated cognitive impairment among caregivers and converged to suggest that chronic stress of caregiving can have a negative effect on cognition. Stress and sleep deprivation can impair cognitive abilities, ranging from attention to implicit and procedural learning and episodic memory (Lupien et al., 2005) that may reduce the caregivers' ability to monitor their performance (Mackenzie et al., 2007). Our study found beneficial effects of meditation on the global measure (MMSE) and on measures of attention and executive function (Trails B) compared with the effects of relaxation. In support of cognitive changes with meditation, there is an increasing literature of structural and functional neuroimaging identifying regional changes with meditation (Lazar et al., 2000; Lazar et al., 2005; Luders et al., 2009; Lutz et al., 2009; Slagter et al., 2009; Davidson, 2011; Holzel et al., 2011a; Holzel et al., 2011b; Kerr et al., 2011; Luders et al., 2011).

Cellular mechanisms of mind-body interventions are only beginning to be understood (Miller et al., 2009). The relationship between telomere-dependent senescence, telomerase and stress remains a subject of debate (13). It has been observed that psychological stress can boost inflammation and oxidative stress (Epel et al., 2004), as well as accelerate telomere attrition. Chronic stress has been linked to telomere length and telomerase activity (Epel et al., 2004). Shortened telomere length and reduced telomerase predict a host of health risks and diseases (Lin et al., 2009), and new findings suggest they may be regulated in part by psychological stress, stress appraisals, and well-being (Epel et al., 2004; Epel et al., 2009). Jacobs et al. (2011) reported increased telomerase activity in 30 meditation retreat participants with a 6-h daily meditation practice for 3 months compared with 30 wait-list control participants matched by age, sex, and prior meditation experience (Jacobs et al., 2011). Our study is the first to indicate changes in telomerase levels in distressed caregivers with Kirtan Kriva meditation. In our study, BMI was not related to telomerase activity at baseline and BMI did not change during the short period of the intervention. Nevertheless, we explored any potential role of baseline BMI. Higher BMI at baseline related to a decrease in telomerase in the control (relaxation) group, but did not contribute to changes in telomerase found in the meditation group. With this small sample, it is difficult to infer whether obesity indeed affects telomerase dynamics over time, but this is an important question for future studies.

In comparison to previous reports, our pilot results are striking given a brief daily Kirtan Kriya practice can lead to improvement in mental health, cognition, and telomerase activity over the course of 8 weeks. Observed close relationships between changes in telomerase levels, levels of depression, and anxiety and distress are novel and deserve further examination. Controlling for relaxation by the virtue of having the relaxation control group, gave us an opportunity to separate the effects of relaxation on outcomes from other meditation-specific effects. Some of the observed effects could be due to the relaxation response in both groups (e.g., improved depression), whereas the effects on cognitive and mental functioning and telomerase activity (Epel et al., 2004) were specific to the Kirtan Kriya. Because Kirtan Kriya had several elements of using chanting, mudras, and visualization, there was a 'brain fitness' effect in addition to stress-reduction that contributed to the overall effect of the meditation. We will confirm this potential mechanism in the follow-up neuroimaging study of Kirtan Kriya.

One might consider the characteristics of our samples as the limitations of the study that includes a mixed and relatively small sample size of adult children and spousal caregivers. On the other hand, this sample is representative of community caregivers. Other limitations of our study include the relatively large number of assessment instruments given the relatively small pilot sample that may introduce the possibility of finding a significant difference by chance alone, especially with respect to telomerase levels. Although not statistically significant, the relaxation group had higher medical burden compared with the meditation group that may have contributed to the group differences in outcomes. Nevertheless, we are encouraged by the overall pattern of improvement in distress, cognition, and inflammatory biomarkers, as well as an observed close relationship between changes in these variables. Our approach, may offer valuable and cost-effective prevention strategy of treating depressive symptoms in a highrisk population for major depression. Cultural acceptability of a particular mind-body technique to an individual is a limitation among older participants and has to be carried out with cultural sensitivity. Our results will need to be replicated in a larger sample to document the effects of mind-body approaches on stress reduction and depression prevention in this difficult-to-manage population.

Key points

- This study examined the effects of brief daily yogic meditation, Kirtan Kriya, on mental health, cognitive functioning, and immune cell telomerase activity in 39 family dementia caregivers with mild depressive symptoms [Correction made here after initial online publication.].
- This pilot study found that brief daily meditation practices by family dementia caregivers can lead to improved mental and cognitive functioning and lower levels of depressive symptoms. This improvement was accompanied by an increase in telomerase activity suggesting improvement in stress-induced cellular aging.

Acknowledgements

This work was supported by the Alzheimer's Research and Prevention Foundation grant, and the NIH grants MH077650, MH086481 and AT003480 to Dr Lavretsky, and NIH grants T32-MH19925, HL 079955, AG 026364, CA 10014152, CA116778, RR00827, P30-AG028748, the UCLA Cousins Center at the Semel Institute for Neurosciences, and the UCLA Older Americans Independence Center Inflammatory Biology Core to Dr. Irwin, the Bernard and Barbro Fund to Dr. Blackburn.

Conflict of interest

Dr.'s Epel, Lin, and Blackburn are co-founders in Telome Health, Inc, a telomere measurement company [Correction made here after initial online publication.].

References

- Akbar AN, Henson SM. 2011. Are senescence and exhaustion intertwined or unrelated processes that compromise immunity? Nat Rev Immunol 11(4): 289–295.
- Alzheimer's research & prevention foundation: Arpf research: Kirtan kriya. Kirtan Kriya 2011. http://www.alzheimersprevention.org/kirtan_kriya.htm.
- Davidson RJ. 2011. Empirical explorations of mindfulness: Conceptual and methodological conundrums. *Emotion* 10(1): 8–11.
- Delis DC, Kramer JH, Kaplan E, Ober BA. 2000. Cvlt-ii: California verbal learning test, adult version, manual. The Psychological Corporation: San Antonio, TX.
- Epel ES, Blackburn EH, Lin J, et al. 2004. Accelerated telomere shortening in response to life stress. Proc Natl Acad Sci USA 101(49): 17312–17315.
- Epel E, Daubenmier J, Moskowitz JT, Folkman S, Blackburn E. 2009. Can meditation slow rate of cellular aging? Cognitive stress, mindfulness, and telomeres. Ann N Y Acad Sci 1172: 34–53.
- Epel ES, Lin J, Wilhelm FH, et al. 2006. Cell aging in relation to stress arousal and cardiovascular disease risk factors. Psychoneuroendocrinology 31(3): 277–287.
- Folstein MF, Folstein SE, McHugh PR. 1975. "mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 12(3): 189–198.
- Franco C, Sola Mdel M, Justo E. 2010. [reducing psychological discomfort and overload in alzheimer's family caregivers through a mindfulness meditation program]. *Rev Esp Geriatr Gerontol* 45(5): 252–258.
- Hamilton M. 1960. A rating scale for depression. J Neurol Neurosurg Psychiatry 23: 56–62.
- Holzel BK, Carmody J, Evans KC et al. 2011a. Stress reduction correlates with structural changes in the amygdala. Soc Cogn Affect Neurosci 5(1): 11–17.
- Holzel BK, Carmody J, Vangel M, et al. 2011b. Mindfulness practice leads to increases in regional brain gray matter density. *Psychiatry Res* 191(1): 36–43.
- Jacobs TL, Epel ES, Lin J, et al. 2011. Intensive meditation training, immune cell telomerase activity, and psychological mediators. *Psychoneuroendocrinology* 36(5): 664–681.
- Kerr CE, Jones SR, Wan Q, et al. 2011. Effects of mindfulness meditation training on anticipatory alpha modulation in primary somatosensory cortex. Brain Res Bull 85(3-4): 96–103.
- Khalsa DS, Amen D, Hanks C, Money N, Newberg A. 2009. Cerebral blood flow changes during chanting meditation. Nucl Med Commun 30(12): 956–961.
- Lavretsky H. 2005. Stress and depression in informal dementia caregivers. *Health and Aging* 1(1): 117–133.
- Lavretsky H, Siddarth P, Irwin MR. 2010. Improving depression and enhancing resilience in family dementia caregivers: A pilot randomized placebo-controlled trial of escitalopram. Am J Geriatr Psychiatry 18(2): 154–162.
- Lazar SW, Bush G, Gollub RL, et al. 2000. Functional brain mapping of the relaxation response and meditation. Neuroreport 11(7): 1581–1585.
- Lazar SW, Kerr CE, Wasserman RH, et al. 2005. Meditation experience is associated with increased cortical thickness. *Neuroreport* **16**(17): 1893–1897.
- Lin J, Epel ES, Blackburn EH. 2009. Telomeres, telomerase stress and aging. In Handbook of neuroscience for the behavioral sciences (Vol. chapter **65**), Bernston GG, Cacioppo JT (eds.). Wiley: New Jersey.
- Lin J, Epel E, Cheon J, et al. 2010. Analyses and comparisons of telomerase activity and telomere length in human t and b cells: Insights for epidemiology of telomere maintenance. J Immunol Methods 352(1–2): 71–80.
- Luders E, Clark K, Narr KL, Toga AW. 2011. Enhanced brain connectivity in longterm meditation practitioners. *Neuroimage* 57(4): 1308–1316.

Yogic meditation for stress reduction in dementia caregivers

- Luders E, Toga AW, Lepore N, Gaser C. 2009. The underlying anatomical correlates of long-term meditation: Larger hippocampal and frontal volumes of gray matter. *Neuroimage* 45(3): 672–678.
- Lupien SJ, Fiocco A, Wan N, et al. 2005. Stress hormones and human memory function across the lifespan. Psychoneuroendocrinology 30(3): 225–242.
- Lutz A, Greischar LL, Perlman DM, Davidson RJ. 2009. Bold signal in insula is differentially related to cardiac function during compassion meditation in experts vs. Novices. *Neuroimage* 47(3): 1038–1046.
- Mackenzie CS, Smith MC, Hasher I, Leach I, Behl P. 2007. Cognitive functioning under stress: Evidence from informal caregivers of palliative patients. J Palliat Med 10(3): 749–758.
- Miller G, Chen E, Cole SW. 2009. Health psychology: Developing biologically plausible models linking the social world and physical health. Annu Rev Psychol 60: 501–524.
- Miller MD, Paradis CF, Houck PR, *et al.* 1992. Rating chronic medical illness burden in geropsychiatric practice and research: Application of the cumulative illness rating scale. *Psychiatry Res* **41**(3): 237–248.
- Newberg AB, Wintering N, Khalsa DS, Roggenkamp H, Waldman MR. 2010. Meditation effects on cognitive function and cerebral blood flow in subjects with memory loss: A preliminary study. J Alzheimers Dis 20(2): 517–526.
- Oken BS, Fonareva I, Haas M, *et al.* 2010. Pilot controlled trial of mindfulness meditation and education for dementia caregivers. *J Altern Complement Med* **16**(10): 1031–1038.
- Oman D, Richards TA, Hedberg J, Thoresen CE. 2008. Passage meditation improves caregiving self-efficacy among health professionals: A randomized trial and qualitative assessment. J Health Psychol 13(8): 1119–1135.
- Ornish D, Lin J, Daubenmier J, et al. 2008. Increased telomerase activity and comprehensive lifestyle changes: A pilot study. Lancet Oncol 9(11): 1048–1057.

- Pinquart M, Sorensen S. 2006. Helping caregivers of persons with dementia: Which interventions work and how large are their effects? Int Psychogeriatr 18(4): 577–595.
- Reitan RM. 1958. Validity of the trail making test as an indicator of organic brain damage. *Percept Mot Skills* 8: 271–276.
- Roth DL, Burgio LD, Gitlin LN, et al. 2003. Psychometric analysis of the revised memory and behavior problems checklist: Factor structure of occurrence and reaction ratings. Psychol Aging 18(4): 906–915.
- Schulz R, Martire LM. 2004. Family caregiving of persons with dementia: Prevalence, health effects, and support strategies. Am J Geriatr Psychiatry 12(3): 240–249.
- Slagter HA, Lutz A, Greischar LL, Nieuwenhuis S, Davidson RJ. 2009. Theta phase synchrony and conscious target perception: Impact of intensive mental training. J Cogn Neurosci 21(8): 1536–1549.
- Sorensen S, Pinquart M, Duberstein P. 2002. How effective are interventions with caregivers? An updated meta-analysis. *Gerontologist* 42(3): 356–372.
- Spitzer RL, Williams JB, Gibbon M, First MB. 1992. The structured clinical interview for dsm-iii-r (scid). I: History, rationale, and description. *Arch Gen Psychiatry* 49(8): 624–629.
- Teri L, Truax P, Logsdon R, et al. 1992. Assessment of behavioral problems in dementia: The revised memory and behavior problems checklist. Psychol Aging 7(4): 622–631.
- Waelde LC, Thompson L, Gallagher-Thompson D. 2004. A pilot study of a yoga and meditation intervention for dementia caregiver stress. J Clin Psychol 60(6): 677–687.
- Ware JE Jr., Sherbourne CD. 1992. The mos 36-item short-form health survey (sf-36). I. Conceptual framework and item selection. *Med Care* 30(6): 473–483.
- Wisniewski SR, Belle SH, Coon frefere, et al. 2003. The resources for enhancing alzheimer's caregiver health (reach): Project design and baseline characteristics. *Psychol Aging* 18(3): 375–384.