Published in final edited form as:
Psychother Psychosom. 2014 ; 83(5): 315–317. doi:10.1159/000359956.

Tai Chi Meditation Effects on Nuclear Factor-κB Signaling in Lonely Older Adults: A Randomized Controlled Trial

David S. Black[a], **Michael R. Irwin**[b], **Richard Olmstead**[b], **Ellen Ji**[b], **Elizabeth Crabb Breen**[b], and **Sarosh J. Motivala**[b]

[a]Department of Preventive Medicine, Keck School of Medicine, University of Southern California, University of California, Los Angeles, Calif., USA

[b]Cousins Center for Psychoneuroimmunology, Semel Institute for Neuroscience and Human Behavior, University of California, Los Angeles, Calif., USA

Older adults who experience loneliness have an increased risk of all-cause mortality and morbidity [1], and among the biological mechanisms implicated, increases in inflammation might contribute. In older adults reporting high levels of loneliness and/or psychological stress, nuclear factor (NF)-κB shows increased activity [2]. NF-κB is a transcription factor that may be an important mediator for the translation of social stress into inflammation [3] as NF-κB controls the expression of genes that code for multiple inflammatory cytokines [4], and stress activation of the sympathetic nervous system stimulates NF-κB [3]. A meditation technique, Tai Chi Chih (TCC), is thought to act on stress response pathways [5] that may be sensitized in lonely individuals due to hypervigilance for social threat and feelings of vulnerability. TCC is a multidimensional behavioral therapy that integrates moderate physical activity, deep breathing and meditation to promote regulation of emotional and affective responses to stress, with downregulation of sympathetic nervous system outflow [6]. Findings show that TCC and other meditation forms also reduce markers of inflammation [6, 7] and the expression of genes bearing NF-κB response elements [8]. However, the effect of TCC on levels of the NF-κB transcription factor has not been examined.

Given evidence that chronic stress leads to a progressive rise in inflammation in older adults [9], and that both stress and increased expression of genes bearing NF-κB response elements are associated with loneliness, we hypothesized that TCC would reduce stress and slow the rate of increase in NF-κB levels in lonely older adults, as compared to those who receive a stress and health education (SHE) intervention. Twenty-six older adults (≥ 60 years), naïve to Tai Chi, who scored ≥ 40 on the UCLA Loneliness Scale, participated in this study approved by the UCLA Institutional Review Board (NCT01204021). Excluded were those with current psychotherapy, behavioral therapy and/or use of antidepressants, current DSM-IV (SCID-IV) psychiatric disorder, body mass index >33, cognitive impairment (Mini-Mental State Examination <27), tobacco use and medical condition (e.g. uncontrolled hypertension, pacemaker, cancer, autoimmune disease, steroid use).

David S. Black, PhD, MPH 2001 N. Soto Street Ste. 302D, MC 9239 Los Angeles, CA 90032 (USA) davidbla@usc.edu.

Participants were computer randomized 1:1 to a 12-week group-based program delivered weekly in 2-hour sessions. At both pre- and postintervention visits, psychological stress (14-item Perceived Stress Scale, PSS) and NF-κB were assessed. Blood was collected between 8 and 11 a.m. by an indwelling venous catheter, placed in heparinized vacutainer tubes and processed for peripheral blood mononuclear cells using Ficoll density gradient centrifugation. Nuclear extracts were prepared to quantify the amount of activated NF-κB p65 present in the nucleus using the TransAM NF-κB p65 ELISA kit (Active Motif, Carlsbad, Calif., USA) and assayed in duplicate as previously described [10]. Two assay data points (one from each condition) >3 standard deviations from the mean were dropped from analysis. One subject refused blood sampling and all NF-κB values were missing for this single case.

The TCC intervention consisted of 20 guided meditative movements under the instruction of a certified teacher as previously detailed [11]. SHE controlled for nonspecific treatment effects of time, attention, expectancy and group support, similar to prior protocols [11]. The session format was didactic, with guest presenters lecturing on health (e.g. stress, aging, exercise and nutrition).

Intention-to-treat analyses were performed in SPSS version 20 (IBM Corp., Armonk, N.Y., USA). Changes in PSS and levels of NF-κB from pre- to postintervention time points were tested using linear mixed modeling, adjusted for pre-intervention levels. Twenty-six enrollees were evenly randomized to treatment and provided pre-intervention data, 22 (85%) completed the postintervention visit (10 in TCC and 12 in SHE).

The two treatment groups showed similar demographic and clinical characteristics (table 1). Psychological stress as indexed by the PSS significantly differed between the two groups after intervention [$F(1, 23.92) = 4.49$, $p = 0.04$] covarying for pre-intervention levels. From pre- to postintervention visits, decreases in PSS were observed in the TCC group ($p < 0.01$) but not in the SHE control ($p = 0.75$; fig. 1 a). NF-κB significantly differed between the two groups after intervention [$F(1, 106.79) = 5.24$, $p = 0.02$] covarying for pre-intervention levels. From pre- to postintervention visits, increases in NF-κB levels were observed in the SHE group ($p < 0.05$), but not in the TCC group ($p = 0.34$; fig. 1 b). The pre- to postintervention changes in PSS levels were correlated with changes in NF-κB levels (Spearman's $r = 0.46$, $p = 0.05$, $n = 19$, fig. 2).

Our findings show that among lonely older adults who received a health education control, levels of psychological stress persisted, and these elderly showed significant increases in nuclear levels of activated NF-κB from pre- to postintervention time points. Conversely, among lonely older adults who received TCC, psychological stress decreased, while NF-κB levels remained constant. Further, change in psychological stress was correlated with change in NF-κB activation from pre- to postintervention examinations, which together suggests that treatment-induced reduction in stress may attenuate increases in NF-κB activation.

Previous work indicates that chronic stress in older adults is associated with an accelerated rate of increase in inflammatory markers such as interleukin-6 [9]. Lonely adults show elevated psychological stress scores as well as physiological indicators of stress, and they

have been conceptualized as a chronically stressed population [12]. Ours is the first study to show that TCC has the capacity to alter stress levels in lonely older adults and to attenuate the rate of increase in a key transcription factor, NF-κB, involved in the upstream inflammatory cascade. Limitations of this study include its small sample size and the predominance of women, which limit the generalizability of our results; hence, these findings require future replication. A larger sample would enable more appropriate tests of whether changes in stress mediate the changes in NF-κB. History of loneliness was not assessed, so the chronic nature of stress in the sample was unknown. Future studies should account for a previous history of loneliness. Levels of NF-κB were only measured in peripheral blood mononuclear cells, and it is possible that the changes in NF-κB reported here are due to changes in lymphocyte subset distribution. However, such changes in immune cell trafficking occur primarily in the context of acute stress manipulation, and chronic stress has not been associated with changes in immune cell numbers. The meditation intervention TCC significantly reduced psychological stress and attenuated the rise of NF-κB activation that is otherwise found in lonely older adults.

Acknowledgments

This work was supported by grants from the NIA (K23 AG027860) to S.J.M., a training grant (T32-MH19925) to D.S.B., and by R01-AG034588, R01-AG026364, R01-CA160245-01, R01-CA119159, R01-HL095799, R01-DA032922-01, P30-AG028748 to M.R.I. and E.C.B., and by UCLA CTSI UL1TR000124 and the UCLA Cousins Center for Psychoneuroimmunology.

References

1. Tilvis RS, Laitala V, Routasalo PE, Pitkälä KH. Suffering from loneliness indicates significant mortality risk of older people. J Aging Res. 2011; 2011:534781. [PubMed: 21423600]
2. Cole SW, Hawkley LC, Arevalo JM, Sung CY, Rose RM, Cacioppo JT. Social regulation of gene expression in human leukocytes. Genome Biol. 2007; 8:R189. [PubMed: 17854483]
3. Bierhaus A, Wolf J, Andrassy M, Rohleder N, Humpert PM, Petrov D, Ferstl R, Von Eynatten M, Wendt T, Rudofsky G. A mechanism converting psychosocial stress into mononuclear cell activation. Proc Natl Acad Sci USA. 2003; 100:1920–1925. [PubMed: 12578963]
4. Liang Y, Zhou Y, Shen P. NF-kappaB and its regulation on the immune system. Cell Mol Immunol. 2004; 1:343–350. [PubMed: 16285893]
5. Irwin MR, Cole SW. Reciprocal regulation of the neural and innate immune systems. Nat Rev Immunol. 2011; 11:625–632. [PubMed: 21818124]
6. Motivala SJ, Sollers J, Thayer J, Irwin MR. Tai Chi Chih acutely decreases sympathetic nervous system activity in older adults. J Gerontol A Biol Med Sci. 2006; 61:1177–1180.
7. Irwin MR, Olmstead R. Mitigating cellular inflammation in older adults: a randomized controlled trial of Tai Chi Chih. Am J Geriatr Psychiatry. 2012; 20:764–772. [PubMed: 21934474]
8. Black DS, Cole SW, Irwin MR, Breen E, St Cyr NM, Nazarian N, Khalsa DS, Lavretsky H. Yogic meditation reverses NF-κB and IRF-related transcriptome dynamics in leukocytes of family dementia caregivers in a randomized controlled trial. Psychoneuroendocrinology. 2013; 38:348–355. [PubMed: 22795617]
9. Kiecolt-Glaser JK, Preacher KJ, MacCallum RC, Atkinson C, Malarkey WB, Glaser R. Chronic stress and age-related increases in the proinflammatory cytokine IL-6. Proc Natl Acad Sci USA. 2003; 100:9090–9095. [PubMed: 12840146]
10. Irwin MR, Wang M, Ribeiro D, Cho HJ, Olmstead R, Breen EC, Martinez-Maza, Cole S. Sleep loss activates cellular inflammatory signaling. Biol Psychiatry. 2008; 64:538–540. [PubMed: 18561896]

11. Irwin MR, Olmstead R, Oxman MN. Augmenting immune responses to varicella zoster virus in older adults: a randomized, controlled trial of Tai Chi. J Am Geriatr Soc. 2007; 55:511–517. [PubMed: 17397428]

12. Hawkley LC, Thisted RA, Masi CM, Cacioppo JT. Loneliness predicts increased blood pressure: five-year cross-lagged analyses in middle-aged and older adults. Psychol Aging. 2010; 25:132–141. [PubMed: 20230134]

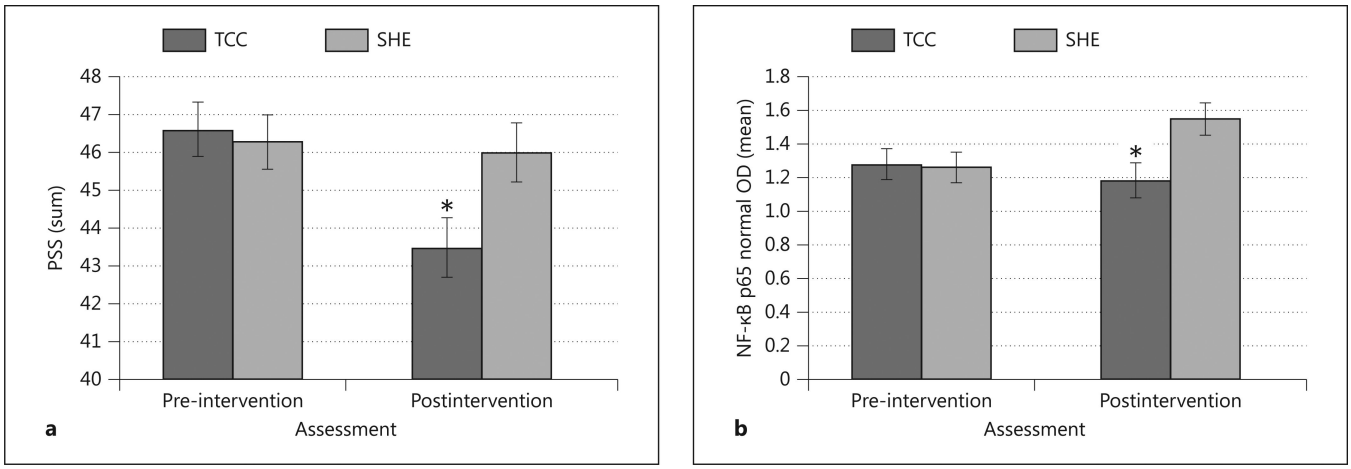

Fig. 1.

a Estimated PSS levels (±SE), covarying for pre-intervention PSS score. **b** Estimated NF-κB activation (±SE), covarying for pre-intervention NF-κB; * $p < 0.05$ for difference between groups.

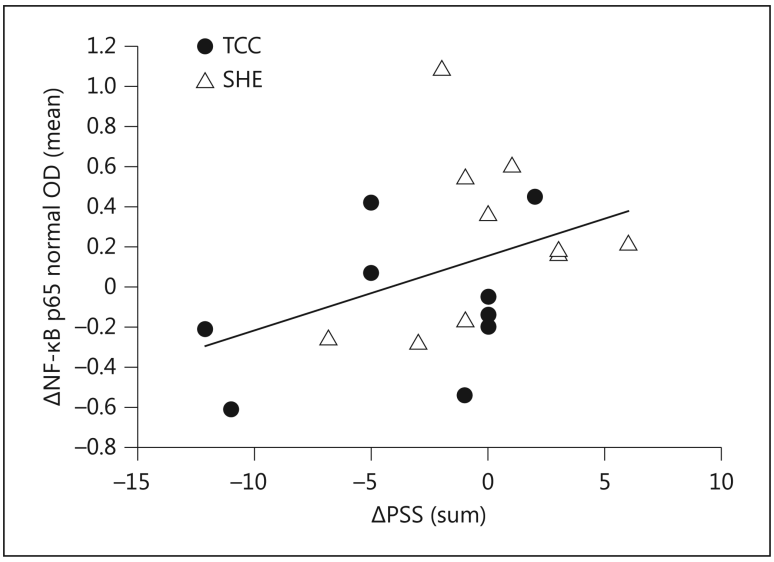

Fig. 2.

Correlation between changes from pre- to postintervention visits in PSS and NF-κB activation for the participants in the TCC and SHE control groups, Spearman's r = 0.46, p = 0.05, n = 19.

Table 1

Pre-intervention characteristics of the lonely older adult sample

Variable	Total sample (n = 26)	TCC (n = 13)	SHE (n = 13)	p
Age, years	67.1 ± 7.2	67.7 ± 7.1	66.5 ± 7.5	0.67
Education, years	16.9 ± 2.9	17.5 ± 3.2	16.3 ± 2.5	0.34
Body mass index	24.4 ± 4.4	24.0 ± 3.3	24.8 ± 5.5	0.67
Annual household income	13.8 ± 4.0	14.5 ± 3.5	13.1 ± 4.5	0.41
Females, %	80.8	69.2	92.3	0.32
Caucasian, %	65.0	61.5	69.2	0.36
Employed, %	45.8	58.3	33.3	0.41

Values are given as means ± SD unless indicated otherwise. p values were assessed by between-group comparisons from χ^2 or t test.