t (202) = 11.246, p = 0.000. The clinical diagnosis also explained a significant proportion of the variance among the participants, R^2 = 0.385, $F(1,202) = 126.477$, $p = 0.000$. Analysis of covariance to look at the clinical diagnosis adjusted for age, sex, years in education, and social class showed a significant association with the ACE-R, $F(6,163) = 12.180$, $p = 0.000$; and with the radiological findings, $F(5,163) = 8.728$, $p = 0.000$. When considering the diagnosis as "yes" or "no," the clinical diagnosis was significantly associated with the ACE-R, X^2 (6, N = 205) = 203.534, $p = 0.000$; and with the radiological findings, X^2 (5, $N = 205$) = 203.367, $p = 0.000$.

With a cut-off score for diagnosing dementia of 82, the overall accuracy of the ACE-R was 61%, sensitivity of 80%, specificity of 71%, PPV of 56%, and NPV of 51%. These results differ from the original work of Mathuranath *et al.* (2000). The authors reported that at a cut-off score of 83, they had an optimal sensitivity (82%) and specificity (96%), and maintained a reasonably high PPV and NPV at different prevalence rates of dementia. However, the original paper was administered to a smaller, younger group of patients whereas this study reflects clinical practice in that there was no selection of patients by disease category, no application of exclusion criteria, and the fact that all patients had at least a complaint of impaired cognition (usually of memory) hence their referral. Larner (2005) similarly found that the ACE-R is an easy-to-use and acceptable test for patients, which also has excellent sensitivity. There is scope for further research to evaluate the ACE-R diagnostic accuracy in mixed dementia or DLB.

The authors confirm that the ACE-R is a useful test to use in a community memory clinic as it is practical and simple to use. We believe that there is good evidence for using the ACE-R – and currently ACE-III – with regards to early diagnosis. It is the authors' opinion that clinical history, carer interview, neurocognitive assessment, blood investigations, brain scanning, and whenever applicable, biomarkers testing, should be the basic practice in every memory clinic. Clinical judgment is important but when incorporated with all the above it will increase the overall diagnostic accuracy.

Conflict of interest

None.

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Induction of salivary nerve growth factor by Yogic breathing: a randomized controlled trial

Nerve growth factor (NGF), a trophic factor involved in the development, maintenance, and

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survival of the peripheral nervous system and the cholinergic neurons of the central nervous system, is significantly reduced in Alzheimer's Disease (AD) patients (Aloe *et al.*, 2012). Particularly basal forebrain complex (BFC) neurons are highly affected in AD patients. NGF protects BFC neurons in experimental trauma models and in age-associated cholinergic decline. Therefore, administration of NGF is investigated as a therapeutic option for AD patients (Aloe *et al.*, 2012). NGF therapy is limited by hyperalgesia, limited bioavailability, and use of invasive methods including intracranial injection of adeno-associated virus-based gene delivery vector, which constitutively expresses human NGF. In this context, non-pharmacological modes of treatment such as meditation and Yoga have been considered as alternative approaches to treat neurological disorders. Yogic breathing (YB, also called *Pranayama*) is a collection of techniques to regulate breathing voluntarily. YB induces a strong relaxation response via vagal and parasympathetic stimulation (Jerath *et al.*, 2006). Such responses are causally linked to rapid changes in gene expression, particularly to those genes controlling stress, inflammation, and metabolism. Saliva is a known source of NGF, and incidentally, Yoga and relaxation stimulate salivation. Saliva (0.75–1.5 L/day in humans) contains numerous biologically active molecules to be potentially useful as diagnostic markers and as therapeutic clues. Salivary secretion regulates the digestive, nervous, immune, and respiratory systems. We conducted a pilot study to investigate whether YB could potentially stimulate salivary expression of NGF in cognitively normal healthy volunteers. This could serve as a model for future studies in AD patients.

A total of 20 volunteers (male and female), aged 18 years and above, were recruited from Charleston Metro area following written informed consent. They were randomized (1:1) into YB and Attentional Control (AC) groups. (Exclusion criteria: breathing problems (inability to breath through nostrils, chronic bronchitis, emphysema, and asthma), speech problems that would prevent chanting, inability to listen and follow exercise instructions, sinus congestion, Sjogren's syndrome, chronic dry mouth due to medication or other conditions, and use of drugs that cause dry mouth.) The study protocol was approved by the Institutional Review Board of the Medical University of South Carolina, Charleston, South Carolina, USA. In a single, 20-minute one-on-one session with the Yoga instructor, the AC group quietly read a scientific text of their choice for 20 minutes whereas the YB group performed 10 minutes of Om chanting followed by 10 minutes of Thirumoolar Pranayamam (TP; Verse 568; Rajasekaran and Narayana, 2006; Thirumoolar, Himalayan Academy Publications, Hawaii, USA) as explained in the supplementary material attached to the electronic version of this paper at www.journals.cambridge.org/jid_IPG. Whole saliva samples were collected at 0 and 20 minutes from all participants and were used to measure NGF in duplicate by ELISA (enzyme-linked immunosorbent assay). The average pre-NGF values (0 minute) were compared to the average post-NGF values (20 minutes) between groups (AC and YB). In the AC group, the average difference between pre and post measures increased by a mean (SD) of 0.67 (1.40) points. In the YB group, the average difference between pre and post measures increased by a mean (SD) of 6.34 (11.02) points. A mixed model with repeated measures was used to estimate the between-group differences over time. Both duplicate post measures were used (as the repeated measures), and the model was adjusted for the baseline (average of the two duplicate pre-NGF values). We also allowed for the variances within the AC and YB groups to be different. This modeling process suggested that the control group had NGF post values 7.7 points lower than the YB group (95% CI = −18.0, 2.7). A scatter plot of NGF from these two groups is presented in Figure S1 (see Figure S1, available as supplementary material attached to the electronic version of this paper at www.journals.cambridge.org/jid_IPG). The results were further evaluated by Western blotting which showed that 60% of the samples showed a marked increase in NGF level only in the YB group but not in the AC group (see Figure S2, available as supplementary material attached to the electronic version of this paper at www.journals.cambridge.org/jid_IPG). These results indicate that NGF could be stimulated in saliva by acute YB practice, and that further study may be warranted.

Chanting Om (*Pranava Pranayamam*) is an ancient cultural practice and believed by some to be associated with physical and emotional well-being (Kumar *et al.*, 2010). In ancient Tamil texts and in present day among several populations worldwide, the symbol Om assumes a great significance. It has been suggested that chanting Om increases the cutaneous peripheral vascular resistance, auricular branch vagal nerve stimulation (VNS), and improves mid-latency auditory evoked potential (Jerath *et al.*, 2006), which is lacking in about 40% of Alzheimer's patients. VNS was beneficial in AD patients as it enhanced cognitive functions. Electrical pulsing for VNS showed deactivation of limbic brain regions. Chanting Om also caused a similar deactivation of the limbic brain regions, amygdala, hippocampus, parahippocampal

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gyrus, insula, orbitofrontal, and anterior cingulate cortices and thalamus. TP is from one of the ancient Tamil texts referring to the benefits of breathing exercise, Thirumanthiram (Rajasekaran and Narayana, 2006; Thirumoolar, Himalayan Academy Publications, Hawaii, USA). Yogic breathing increases vagal tone, increases parasympathetic dominance, decreases sympathetic discharges, and produces theta waves in brain (Jerath *et al.*, 2006). This is the first time the molecular expression of a neurotrophic factor NGF is reported in response to chanting Om and TP. How could the salivary NGF be transported to the CNS? We hypothesize that, the NGF produced by the salivary glands is taken up by (1) the innervating sensory and motor neurons of the oral organs for retrograde axonal transport to the cell body and transcytosis to reach the central neurons, and (2) the sublingual absorption route into the bloodstream to reach other distal target organs. These mechanisms are well within the theoretical framework of production and transport mechanisms established for neuromodulators. It is to be emphasized here that this pilot study is the first ever attempt to stimulate endogenous NGF expression by non-invasive methods. Our findings could lead to future studies on using salivary neuromodulators and biomarkers as outcome measures of Yoga interventions.

Conflict of interest

None.

Supplementary material

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Successfully aging predicts successful aging in successful agers: further definitional issues

I read with great interest Cheng's guest editorial “Defining successful aging: the need to distinguish pathways from outcomes.” The landscape of successful aging literature is littered with pathway – and outcome-oriented conceptualizations, making this differentiation an important issue to address. Further to the notion highlighted by Cheng is the usage (and confounding) of items surrounding successful aging. A recent review of the operational definitions of successful aging highlights the continued heterogeneity of successful aging operationalizations, identifying over 100 unique definitions of successful aging (Cosco *et al.*, 2014). Perhaps as a by-product of this pervasive definitional heterogeneity, there is an equally pervasive conceptual overlap of the constituent components of successful aging. Depending on the definition of successful aging used (and possibly the availability of variables in a dataset and theoretical background of the researcher), the same item may be used as a predictor, component, or outcome of successful aging. While Cheng (rightfully) advocates for the inclusion of psychosocial components into definitions of successful aging, these items are particularly prone to this conceptual

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