

THE IMPACT OF MEDITATION ON HEALTHY AGEING — THE CURRENT STATE OF KNOWLEDGE AND A ROADMAP TO FUTURE DIRECTIONS

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Abstract

There is increasing evidence that meditation-based training promotes healthy ageing across many dimensions. This review summarizes the existing knowledge on the effects of meditation training on healthy ageing in the domains of emotions, cognition (with a special emphasis on attentional processes), and the preservation of related brain structures. Although evidence so far is promising, more rigorous randomized controlled studies with active control groups and long-term follow-up in older people are needed. We outline how these challenges can be addressed in future studies using the example of an ongoing project, Medit-Ageing (public name: Silver Santé Study), including two independent randomized controlled trials (RCT) as well as one cross-sectional study with meditation experts.

With increases in life expectancy worldwide [1], promoting healthy ageing becomes increasingly important. Healthy ageing is not only crucial for maintaining the quality of life in older individuals, but also to enable elderly people to thrive in their role in society, be it in their profession or in their private lives (e.g. as grandparents or friends). In recent years, it has been recognized that meditation-based training offers a promising strategy to promote healthy ageing [2]. Indeed, the effects of meditation training are increasingly studied in young and middle-age adults. However, there is still relatively little research on the impact of meditation training on older adults. This review summarizes evidence on how meditation can contribute to healthy ageing and optimize cognitive and emotional processes impacted by ageing. It ends by outlining future research avenues.

In order to investigate the effects of meditation training on cognition and emotion, usually two types of studies are employed: (i) cross-sectional studies comparing experienced meditators with non-meditators and (ii) longitudinal studies comparing meditation training to a control group. The most prevalent form of training employed in longitudinal studies is mindfulness meditation. Mindfulness meditation consists of cultivating a vigilant awareness of one's own thoughts, actions, emotions, and motivations. In mindfulness meditation, one learns to intentionally attend to internal or external experiences in the present moment, without making any value judgment. [3].

MEDITATION TRAINING MAY DELAY DEMENTIA AND PROMOTE HEALTHY AGEING

Dementia currently affects 50 million people worldwide [4], and is broadly defined by brain atrophy, significant decline in cognitive and/or behavioral functioning, and loss of ability to live independently [5]. In so far as meditation practice has been shown to improve cognition, wellbeing, and health in older age, it could potentially contribute to delay onset of dementia.

PRELIMINARY EVIDENCE SUGGESTS THAT MEDITATION TRAINING PRESERVES BRAIN STRUCTURE, GLUCOSE METABOLISM, AND BRAIN CONNECTIVITY IN OLDER ADULTS

Cross-sectional evidence from several studies in expert meditators suggests that meditation may preserve brain structure and glucose metabolism. First studies in this domain showed a preservation of cortical thickness and grey matter volumes in young and middle-aged meditation experts [6], as well as reduced age-related atrophy of brain grey matter volume in meditators compared to non-meditators, particularly in hippocampus, frontal and temporal brain regions [7,8]. In a recent study, grey matter brain volumes and glucose metabolism from six older-adult expert meditators were compared with 67 age-matched controls [9]. As summarized in Figure 1, meditation experts had more preserved grey matter volume and/or more glucose metabolism at rest than non-meditators in brain regions sensitive to ageing, including ventromedial prefrontal cortex, anterior cingulate cortex, bilateral temporo-parietal junction, insula and posterior cingulate cortex [9]. In another study, a machine learning algorithm trained to identify anatomical correlates of age in the brain revealed that structural brain characteristics of expert meditators appeared 7.5 years younger than those of age-matched controls [10]. Moreover, long-term expert meditators had larger fractional anisotropy than controls, indicating more numerous, dense, and fast fiber tract connections [11]. As cross-sectional studies with expert meditators can be biased by self-selection, it is important to corroborate these findings in longitudinal studies. One longitudinal study assessing the impact of eight weeks of mindfulness-based meditation on brain connectivity found that meditation versus relaxation training decreased network connectivity within default mode in older adults, which may indicate more efficient cognitive processes [12]. Overall, these preliminary neuroimaging studies suggest that meditation practice could help to preserve grey matter brain structures, brain glucose metabolism and brain connectivity in older age. However, more research is needed to test in how far such effects also extend to older novice meditators.

A BENEFICIAL EFFECT OF MEDITATION TRAINING ON COGNITION AND ATTENTION

Cognitive decline is one of the greatest concerns of older adults. Cognitive domains primarily affected by ageing are memory, executive functions, and attention [13]. Decline in these domains may also indicate an increased risk of developing dementia [14]. Cross-sectional studies that have examined relationships between long-term meditation and standardized measures of cognition in older adults are scarce. However, emerging evidence suggests that long-term meditators have higher levels of attention, executive function, and fluid intelligence (reasoning and problem solving) compared with nonmeditators [15–17]. Whether long-term meditation also improves episodic memory in older adults has – to our knowledge – not been tested yet.

Pertaining to short-term training, reviews of age-related effects from short-term meditation training on cognitive abilities (only six of which were randomized control trials) also reported improvements in memory, attention, and executive function [18,19]. It is not yet resolved, however, to what degree meditation training is superior to active control groups. Whereas some studies found no differential benefit of mindfulness interventions when compared to active control groups or comparison conditions on cognition outcomes [20,21,22], other studies suggest that meditation training can be superior to other interventions. A positive effect of mindfulness-intervention by comparison to active control conditions was thus observed in two studies including participants with (i) clinical anxiety and/or depression and cognitive concerns (all indicators of increased dementia risk) [23] and (ii) people with dementia [24]. Interestingly, improvements in memory and executive function were associated with a reduction in worry in the first study and to preserved global cognitive function in the second one. Although these results suggest that meditation may be particularly effective at preserving cognition against age-related decline rather than ‘improving’ cognition per se, more rigorous randomized-control studies with long-term interventions, active control conditions and follow-ups are needed, especially in the population of older adults with cognitive impairments or at heightened risk of dementia.

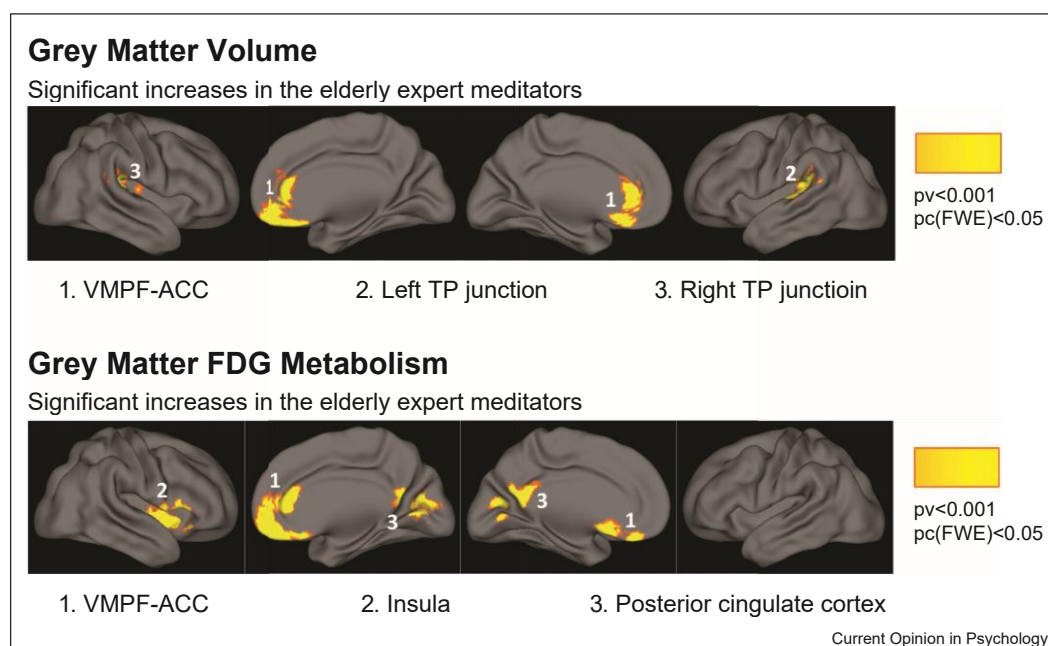
Attentional functioning seems particularly susceptible to meditation practice. Indeed, a main component of mindfulness-based meditation is the ability to regulate attention in order to maintain the focus on immediate experiences [25]. In their 2012 review on attentional functioning, Petersen and Posner stated that meditation training could be an interesting tool to develop attentional brain processes and networks [26]. Accordingly, reviews and meta-analyses show that extensive meditation practice is associated with brain structure and activity changes in a fronto-parietal network associated to attentional functioning [26,27], and increased brain efficiency in these regions during performance on attentional tasks [28].

Changes in attentional functioning are present in normal ageing [29]. To date, encouraging preliminary evidence suggests that meditation practice may increase attentional efficiency in older adults. It was thus observed that longterm meditation practice has a protective effect against the age-related decrease of attentional functioning [17,30,31] and that short (8 to 12-weeks) meditation training can improve attentional functioning in healthy ageing [32,33] and in patients at risk of or with dementia [22,34,35].

In addition to the limitations outlined above, in the domain of attention it is not yet resolved whether the beneficial effects of meditation on attention in ageing are global or affect only specific processes,

such as selective attention, or sustained attention. Further studies are needed to firmly establish the extent to which meditation can help improve attentional abilities in normal ageing and dementia, as the improvement of attentional abilities is prone to influence cognition and daily life functioning [13].

Figure 1



Cross-sectional results point to preserved grey brain volume and glucose metabolism in six older-adult meditators compared to 67 age-matched controls. VMPFC-ACC: ventromedial prefrontal and anterior cingulate cortex; TP: temporo-parietal. Image modified with permission under the creative commons license (<https://creativecommons.org/licenses/by/4.0/>) from: Ref. [9].

MEDITATION TRAINING CAN REDUCE NEGATIVE AFFECT AND INCREASE POSITIVE AFFECT

Another route through which meditation training may benefit healthy ageing is through the reduction of negative affective states, such as anxiety and depression, and through the promotion of positive affective states, such as compassion. Symptoms of anxiety, depression, and stress are recognized as risk factors for cognitive decline and dementia [36–39], and meta-analytic evidence shows that meditation training can decrease these symptoms [40–42]. This beneficial effect of meditation on anxiety, depression, and stress is confirmed by some preliminary studies in older adults [43–45]. In this context, it is interesting to note that brain structures, such as medial prefrontal cortex, anterior cingulate cortex and insula, which are affected by depression and anxiety [46], were shown to be preserved in expert meditators [9]. This may offer an insight into the brain mechanisms, through which meditation may protect against depression, anxiety, and consequently dementia.

With regard to the promotion of positive emotions, meditation practices aimed at cultivating feelings of benevolence for oneself and others (including loving kindness and compassion meditation) have been particularly promising in young and middle-age adults. These trainings were found to broaden people's personal resources (such as purpose in life, social support and illness symptoms) through an

increase in positive emotions [47], to increase helping behavior [48] and to increase positive other regarding emotions even when it comes to facing the suffering of others [49]. Furthermore, there are beneficial effects of compassion training versus a range of active control trainings in the domains of compassion, depression, anxiety, psychological distress, and wellbeing [50].

While studies on the beneficial effects of meditation training on positive emotions in elderly are still scarce, first findings are encouraging. A study that compared the effects of 12 weeks of regular meditation training to 12 weeks of regular music listening in older adults with subjective cognitive decline found that meditation training improved mood and psychological well-being more than music listening [51]. Another study compared the effects of eight weeks of meditation training to relaxation training in elderly [52]. This study found that participants in the meditation group evaluated negative pictures as more positive and positive pictures as less positive after the meditation training, while no changes in valence ratings were observed in the relaxation group [52]. This finding confirms previous findings of increased positive affect to negative stimuli after meditation training [49] and suggests an increase in equanimity, as shown by the reduction in positive feelings to negative stimuli.

In the future, it would also be interesting to test in how far different forms of meditation training elicit specific effects. Affective meditation trainings, for instance, have been shown to be more efficient than mindfulness meditation trainings when it comes to decreasing cortisol levels, a physiological marker of stress, in response to a laboratory stress test [53]. In addition to cortisol, a wide range of biomarkers related to chronic stress and inflammation were reduced by meditation practices in various clinical populations [54]. The allostatic load [55], a cumulative measure of these biomarkers, appears to be a promising candidate to capture the effects of meditation training on stress-related physiological dysregulations across multiple systems.

FUTURE DIRECTIONS

Although meditation may be a promising intervention when it comes to promoting healthy ageing, randomized controlled studies with sufficiently large sample sizes, active control groups, and a long-term follow-up are scarce in this domain. The inclusion of active control groups is particularly important, as older adults are particularly responsive to the effects of social activity [56], and mindfulness-based interventions are often not superior to active control groups when it comes to psychological health and well-being [41,57]. Furthermore, it will be important for future studies to reduce risks in biases that may for instance stem from not blinding experimenters to the condition of the participants, to include biological measures in addition to self-reports, and to test the impact of meditation-based trainings in elderly and in populations at risk for dementia in the domains of brain structure, function and emotions.

The Medit-Ageing project received funding from the European Commission to investigate the impact of meditation training on mental health and well-being in the ageing population. The study uses a multi-method approach combining self-reports and a range of behavioral and biological measures (including measures of cognition, emotion, brain function, brain volume, and blood-based biomarkers) to explore how individual characteristics modulate the impact of meditation on specific measures (e.g. if there is a link between baseline attentional abilities and the meditation effect on emotion regulation) and to identify common versus distinct mechanisms underlying the effects of meditation on different

domains (e.g. is grey matter volume in the anterior cingulate cortex influencing the effect of meditation on both, attention and emotions). More specifically, the Medit-Ageing project is composed of three studies with older adults: (i) the AgeWell observational study, a cross-sectional study comparing expert meditators to non meditators [58], (ii) the Age-Well clinical trial, a longitudinal study in which an 18-month meditation intervention is compared to an active control group (English training) and a passive control group [59], and (iii) the SCD-Well clinical trial [60], a longitudinal study in which participants with subjective cognitive decline, a known risk factor for dementia [61], are assigned to a two-month meditation intervention (with four-month follow-up) or a health education intervention [23,62]. To reduce the risk of bias, the longitudinal studies are clinical, randomized controlled trials, in which experimenters are blinded to the condition of the participants, and in which data analyses of the primary endpoints are analyzed externally. Importantly, both the 18-month and the two-month interventions combine elements of mindfulness especially tailored for elderly adults [63] and loving kindness and compassion meditations.

An important question that remains to be investigated in more depth in the future is in how far the effects of meditation interventions differ from other interventions, for instance those focusing on health, music, physical activity, or cognitive training and in how far mindfulness and compassion meditations have specific effects on ageing.

ACKNOWLEDGEMENTS

The Medit-Ageing project is funded through the European Union in Horizon 2020 program related to the call PHC22 'Promoting mental wellbeing in the ageing population. Inserm, Région Normandie, and the Fondation d'entreprise MMA des Entrepreneurs du Futur also contribute to fund parts of this project that were not included in the initial grant (not covered by the European Union funding). Funding sources are not involved in the studies design, data acquisition, data analysis, or manuscript writing. The authors would like to thank all the contributors of the Medit-Ageing project, Tim Whitfield in particular.

REFERENCES AND RECOMMENDED READING

1. United Nations DoEaSA, Population Division: World Population Prospects: The 2017 Revision. New York: United Nations; 2017.
2. Chételat G, Lutz A, Arenaza-Urquijo E, Collette F, Klimecki O, Marchant N: Why could meditation practice help promote mental health and well-being in aging? *Alzheimers Res Ther* 2018, 10:57.
This paper briefly outlines the rationale and theoretical model of the Silver Sante' Study.
3. Kabat-Zinn J: Mindfulness-based interventions in context: past, present, and future. *Clin Psychol—Sci Pract* 2003, 10:144-156.
4. Patterson C: World Alzheimer Report. London: Alzheimer's Disease International; 2018.
5. McKhann GM, Knopman DS, Chertkow H, Hyman BT, Jack CR, Kawas CH, Klunk WE, Koroshetz WJ, Manly JJ, Mayeux R et al.: The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement* 2011, 7:263-269.
6. Luders E: Exploring age-related brain degeneration in meditation practitioners. *Ann N Y Acad Sci* 2014, 1307:82-88.
7. Kurth F, Cherbuin N, Luders E: Reduced age-related degeneration of the hippocampal subiculum in long-term meditators. *Psychiatry Res: Neuroimaging* 2015, 232:214-218.

8. Luders E, Cherbuin N, Kurth F: Forever young(er): potential age defying effects of long-term meditation on gray matter atrophy. *Front Psychol* 2015, 5.
9. Chételat G, Mézenge F, Tomadesso C, Landeau B, Arenaza- Urquijo E, Rauchs G, André C, de Flores R, Egret S, Gonneaud J et al.: Reduced age-associated brain changes in expert meditators: a multimodal neuroimaging pilot study. *Sci Rep* 2017, 7:10160.

This study reveals preserved brain structure and glucose metabolism in old expert meditators compared to age-matched controls.

10. Luders E, Cherbuin N, Gaser C: Estimating brain age using high resolution pattern recognition: younger brains in long-term meditation practitioners. *Neuroimage* 2016, 134:508-513.
11. Luders E, Clark K, Narr KL, Toga AW: Enhanced brain connectivity in long-term meditation practitioners. *Neuroimage* 2011, 57:1308-1316.
12. Cotier FA, Zhang R, Lee TMC: A longitudinal study of the effect of short-term meditation training on functional network organization of the aging brain. *Sci Rep* 2017, 7:598.
13. Craik FI, Salthouse TA: *The Handbook of Aging and Cognition*. New York, NY: Psychology Press; 2008.
14. Tabert MH, Manly JJ, Liu X, Pelton GH, Rosenblum S, Jacobs M, Zamora D, Goodkind M, Bell K, Stern Y: Neuropsychological prediction of conversion to Alzheimer disease in patients with mild cognitive impairment. *Arch Gen Psychiatry* 2006, 63:916-924.
15. Gard T, Taquet M, Dixit R, Hözel BK, de Montjoye Y-A, Brach N, Salat DH, Dickerson BC, Gray JR, Lazar SW: Fluid intelligence and brain functional organization in aging yoga and meditation practitioners. *Front Aging Neurosci* 2014, 6:76.
16. Prakash R, Dubey I, Abhishek P, Gupta SK, Rastogi P, Siddiqui SV: Long-term Vihangam Yoga meditation and scores on tests of attention. *Percept Mot Skills* 2010, 110:1139-1148.
17. Prakash R, Rastogi P, Dubey I, Abhishek P, Chaudhury S, Small BJ: Long-term concentrative meditation and cognitive performance among older adults. *Aging Neuropsychol Cogn* 2012, 19:479-494.
18. Gard T, Hözel BK, Lazar SW: The potential effects of meditation on age-related cognitive decline: a systematic review. *Ann N Y Acad Sci* 2014, 1307:89-103.

This review summarizes a series of studies investigating the effect of various meditation practice on age-related cognitive decline.

19. Marciniak R, Sheardova K, Cermáková P, Hudec D, U R, Hort J: Effect of meditation on cognitive functions in context of aging and neurodegenerative diseases. *Front Behav Neurosci* 2014, 8:17.
20. Mallya S, Fiocco AJ: Effects of mindfulness training on cognition and well-being in healthy older adults. *Mindfulness* 2016, 7:453-465.
21. Jansen P, Dahmen-Zimmer K, Kudielka BM, Schulz A: Effects of karate training versus mindfulness training on emotional wellbeing and cognitive performance in later life. *Res Aging* 2017, 39:1118-1144.
22. Innes KE, Selfe TK, Khalsa DS, Kandati S: Meditation and music improve memory and cognitive function in adults with subjective cognitive decline: a pilot randomized controlled trial. *J Alzheimers Dis* 2017, 56:899-916.

It is a study on patients with subjective cognitive decline showing that random assessment to meditation or music listening improved cognitive performance and subjective memory function.

23. Wetherell JL, Hershey T, Hickman S, Tate SR, Dixon D, Bower ES, Lenze EJ: Mindfulness-based stress reduction for older adults with stress disorders and neurocognitive difficulties: a randomized controlled trial. *J Clin Psychiatry* 2017, 78:e734-e743.

This is a randomized controlled study showing that mindfulness intervention as compared to health education improved worry, depression, and memory performance in older participants with subjective neurocognitive decline and anxiety or depression.

24. Quintana-Hernández DJ, Miró-Barrachina MT, Ibáñez-

Fernández IJ, Pino AS, Quintana-Montesdeoca MP, Rodriguez-de Vera B, Morales-Casanova D, Pe´ rez-Vieitez MDC, Rodriguez Garcíá J, Bravo-Caraduje N: Mindfulness in the maintenance of The impact of meditation on healthy ageing Klimecki et al. 227 cognitive capacities in Alzheimer’s disease: a randomized clinical trial. *J Alzheimers Dis* 2016, 50:217-232.

This is a randomized clinical controlled trial with patients who have Alzheimer’s disease showing that mindfulness training over two years can slow cognitive decline.

25. Tang Y-Y, Ho¨ lzel BK, Posner MI: The neuroscience of mindfulness meditation. *Nat Rev Neurosci* 2015, 16:213-225.

It is one comprehensive and critical review of the brain mechanisms associated to mindfulness meditation and of the effect of mindfulness practice on cognition and emotion.

26. Petersen SE, Posner MI: The attention system of the human brain: 20 years after. *Ann Rev Neurosci* 2012, 35:73-89.
27. Fox KC, Dixon ML, Nijeboer S, Girn M, Floman JL, Lifshitz M, Ellamil M, Sedlmeier P, Christoff K: Functional neuroanatomy of meditation: a review and meta-analysis of 78 functional neuroimaging investigations. *Neurosci Biobehav Rev* 2016, 65:208-228.
28. Kozasa EH, Balardin JB, Sato JR, Chaim KT, Lacerda SS, Radvany J, Mello LEA, Amaro E Jr: Effects of a 7-day meditation retreat on the brain function of meditators and non-meditators during an attention task. *Front Hum Neurosci* 2018, 12:222.
29. Van der Linden M, Collette F: Attention and normal ageing. In Applied Neuropsychology of Attention. Edited by Leclercq ce, Zimmermann tr. Psychology Press; 2002:205-229.

The review summarizes evidence toward the co-existence of preserved and impaired attentional processes in ageing, and the influence of general factors on attentional efficiency.

30. Sperduti M, Makowski D, Piolino P: The protective role of longterm meditation on the decline of the executive component of attention in aging: a preliminary cross-sectional study. *Aging Neuropsychol Cogn* 2016, 23:691-702.
31. van Leeuwen S, Mu¨ ller NG, Melloni L: Age effects on attentional blink performance in meditation. *Conscious Cogn* 2009, 18:593-599.
32. Malinowski P, Moore AW, Mead BR, Gruber T: Mindful aging: the effects of regular brief mindfulness practice on electrophysiological markers of cognitive and affective processing in older adults. *Mindfulness* 2017, 8:78-94.
33. Moynihan JA, Chapman BP, Klorman R, Krasner MS, Duberstein PR, Brown KW, Talbot NL: Mindfulness-based stress reduction for older adults: effects on executive function, frontal alpha asymmetry and immune function. *Neuropsychobiology* 2013, 68:34-43.
34. Newberg AB, Wintering N, Khalsa DS, Roggenkamp H, Waldman MR: Meditation effects on cognitive function and cerebral blood flow in subjects with memory loss: a preliminary study. *J Alzheimers Dis* 2010, 20:517-526.
35. Smart CM, Segalowitz SJ, Mulligan BP, Koudys J, Gawryluk JR: Mindfulness training for older adults with subjective cognitive decline: results from a pilot randomized controlled trial. *J Alzheimers Dis* 2016, 52:757-774.
36. Diniz BS, Butters MA, Albert SM, Dew MA, Reynolds CF: Late-life depression and risk of vascular dementia and Alzheimer’s disease: systematic review and meta-analysis of communitybased cohort studies. *Br J Psychiatry* 2013, 202:329-335.
37. Gulpers B, Ramakers I, Hamel R, Ko¨ hler S, Voshaar RO, Verhey F: Anxiety as a predictor for cognitive decline and dementia: a systematic review and meta-analysis. *Am J Geriatr Psychiatry* 2016, 24:823-842.
38. Wilson RS, Begeny CT, Boyle PA, Schneider JA, Bennett DA: Vulnerability to stress, anxiety, and development of dementia in old age. *Am J Geriatr Psychiatry* 2011, 19:327-334.
39. Marchant NL, Howard RJ: Cognitive debt and Alzheimer’s disease. *J Alzheimers Dis* 2015, 44:755-770.

40. Chen KW, Berger CC, Manheimer E, Forde D, Magidson J, Dachman L, Lejuez C: Meditative therapies for reducing anxiety: a systematic review and meta-analysis of randomized controlled trials. *Depress Anxiety* 2012, 29:545-562.
41. Goyal M, Singh S, Sibinga EM, Gould NF, Rowland-Seymour A, Sharma R, Berger Z, Sleicher D, Maron DD, Shihab HM: Meditation programs for psychological stress and well-being: a systematic review and meta-analysis. *JAMA Intern Med* 2014, 174:357-368.
42. Khoury B, Sharma M, Rush SE, Fournier C: Mindfulness-based stress reduction for healthy individuals: a meta-analysis. *J Psychosom Res* 2015, 78:519-528.
43. Prakhinkit S, Suppakitporn S, Tanaka H, Suksom D: Effects of Buddhism walking meditation on depression, functional fitness, and endothelium-dependent vasodilation in depressed elderly. *J Altern Complement Med* 2014, 20:411-416.
44. Sullivan MJ, Wood L, Terry J, Brantley J, Charles A, McGee V, Johnson D, Krucoff MW, Rosenberg B, Bosworth HB et al.: The Support, Education, and Research in Chronic Heart Failure Study (SEARCH): a mindfulness-based psychoeducational intervention improves depression and clinical symptoms in patients with chronic heart failure. *Am Heart J* 2009, 157:84-90.
45. Perez-Blasco J, Sales A, Meléndez JC, Mayordomo T: The effects of mindfulness and self-compassion on improving the capacity to adapt to stress situations in elderly people living in the community. *Clin Gerontol* 2016, 39:90-103.
46. Via E, Gómez A, Serra-Blasco M, Wise T, Carulla-Roig M, SorianoMas C, Palao D, Arnone D, Mataix-Cols D, Raduà J et al.: Structural brain alterations in major depression and anxiety disorders: overlapping and distinct affected networks evidenced by voxel-based meta-analysis. *Eur Neuropsychopharmacol* 2016, 26:S320-S321.
47. Fredrickson BL, Cohn MA, Coffey KA, Pek J, Finkel SM: Open hearts build lives: positive emotions, induced through lovingkindness meditation, build consequential personal resources. *J Pers Soc Psychol* 2008, 95:1045-1062.
48. Leiberg S, Klimecki O, Singer T: Short-term compassion training increases prosocial behavior in a newly developed prosocial game. *PLoS One* 2011, 6:e17798.
49. Klimecki O: The plasticity of social emotions. *Soc Neurosci* 2015, 10:466-473.
50. Kirby JN, Tellegen CL, Steindl SR: A meta-analysis of compassion-based interventions: current state of knowledge and future directions. *Behav Ther* 2017, 48:778-792.

This one is a meta-analysis on randomized controlled trials testing the effects of compassion training on self-reports of compassion, mindfulness, depression, anxiety, distress and well-being.

51. Innes KE, Selfe TK, Khalsa DS, Kandati S: Effects of meditation versus music listening on perceived stress, mood, sleep, and quality of life in adults with early memory loss: a pilot randomized controlled trial. *J Alzheimers Dis* 2016, 52:1277-1298.
52. Shao R, Keuper K, Geng X, Lee TM: Pons to posterior cingulate functional projections predict affective processing changes in the elderly following eight weeks of meditation training. *EBioMedicine* 2016, 10:236-248.
53. Engert V, Kok BE, Papassotiropoulos I, Chrousos GP, Singer T: Specific reduction in cortisol stress reactivity after social but not attention-based mental training. *Sci Adv* 2017, 3:e1700495.
54. Bottaccioli AG, Bottaccioli F, Minelli A: Stress and the psyche— brain—immune network in psychiatric diseases based on psychoneuroendocrineimmunology: a concise review. *Ann N Y Acad Sci* 2018, 1437:31-42.
55. Crimmins EM, Johnston M, Hayward M, Seeman T: Age differences in allostatic load: an index of physiological dysregulation. *Exp Gerontol* 2003, 38:731-734.
56. Bath PA, Deeg D: Social engagement and health outcomes among older people: introduction to a special section. *Eur J Ageing* 2005, 2:24-30.

57. Keng S-L, Smoski MJ, Robins CJ: Effects of mindfulness on psychological health: a review of empirical studies. *Clin Psychol Rev* 2011, 31:1041-1056.
58. Lutz A, Klimecki OM, Collette F, Poisnel G, Arenaza-Urquijo E, Marchant NL, De La Sayette V, Rauchs G, Salmon EG, Vuilleumier P et al.: The Age-Well observational study on expert meditators in the Medit-Ageing European project. *Alzheimers Dement: Transl Res Clin Interv* 2018, 4:756-764.

This paper describes the rationale and protocol for the expert study of Medit-Ageing.

59. Poisnel G, Arenaza-Urquijo E, Collette F, Klimecki OM, Marchant NL, Wirth M, de La Sayette V, Rauchs G, Salmon E, Vuilleumier P et al.: The Age-Well randomized controlled trial of the Medit-Ageing European project: effect of meditation or foreign language training on brain and mental health in older adults. *Alzheimers Dement: Transl Res Clin Interv* 2018, 4:714-723.
60. Marchant N, Barnhofer T, Klimecki O, Poisnel G, Lutz A, Arenaza-Urquijo E, Collette F, Wirth M, Schild A, Coll-Padro's N et al.: The SCD-Well randomized controlled trial: effects of a mindfulness-based intervention versus health education on mental health in patients with subjective cognitive decline (SCD). *Alzheimers Dement: Transl Res Clin Interv* 2018, 4:737-745.

This paper describes the rationale and protocol for the SCD-WELL study of Medit-Ageing.

61. Jessen F, Amariglio RE, Van Boxtel M, Breteler M, Ceccaldi M, Chételat G, Dubois B, Dufouil C, Ellis KA, Van Der Flier WM: A conceptual framework for research on subjective cognitive decline in preclinical Alzheimer's disease. *Alzheimers Dement* 2014, 10:844-852.
62. Lorig K, Holman H, Sobel D, Laurent D, González V, Minor M: *Living a Healthy Life with Chronic Conditions: Self-Management of Heart Disease, Arthritis, Diabetes, Depression, Asthma, Bronchitis, Emphysema and Other Physical and Mental Health Conditions*. edn 4. Boulder, CO: Bull Publishing Company; 2012.
63. Zellner Keller B, Singh NN, Winton ASW: Mindfulness-Based Cognitive Approach for Seniors (MBCAS): program development and implementation. *Mindfulness* 2014, 5:453-459.