



Cognitive Vitality Reports[®] are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-indevelopment, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Meditation

Evidence Summary

Meditation is likely to have some beneficial impact on several chronic diseases; however, there are a lack of high-quality studies.

Neuroprotective Benefit: Meditation may have beneficial effects on some aspects of cognition, though there is conflicting data and studies may be too short in duration to know the long-term impacts of meditation.

Aging and related health concerns: There is some evidence that meditation may have a beneficial impact on telomere biology, blood pressure reduction, insomnia, and reduction of chronic pain.

Safety: Although there are no studies specifically looking at safety outcomes from long-term clinical trials, evidence to date suggest there are no negative effects of meditation.

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What is it?

Meditation is the act of training the mind to increase attention, awareness, or achieving emotional calm.

Dahl et al (2015) classifies three styles of meditation: attentional, constructive, and deconstructive.

Attentional: a group of meditation practices that trains the regulation of attention. These practices involve building the capacity to initiate, direct, and sustain attention while becoming aware of thinking, feeling, and perceiving (i.e. 'meta-awareness' – being aware of conscious processes). In addition to increasing the capacity for attention, these practices may reduce the fusion of experiences with emotion and reduce mind-wandering. Practices include breath counting, body awareness, mindfulness-based stress reduction (MBSR), and mindfulness-based cognitive therapy (MBCT).

Constructive: a group of meditation practices that foster a sense of well-being by targeting maladaptive psychological processes and replacing them with more adaptive patterns. Two processes are central to these types of meditations: cognitive reappraisal (i.e. changing how you think about a certain situation and changing your response) and perspective taking (i.e. considering how you or another would feel in a certain situation). Examples include loving-kindness meditation, CCARE compassion cultivation training, and cognitively-based compassion training.

Deconstructive: a group of meditation practices that attempt to undo maladaptive cognitive patterns through 'self-inquiry'. Self-inquiry is the analysis and examination of conscious experiences. Deconstructive meditations are practiced to elicit and sustain insight and improve problem solving. Examples include analytical meditation and Koan practice (in Zen meditation).

The three most studied meditation practices are MBSR, transcendental meditation, and Kirtan Kriya.

MBSR is a standardized program amenable to research. Developed in the 1970s by Jon Kabat-Zinn, MBSR is an 8-week program consisting of weekly group meetings (~2.5 hours), instructions for daily meditation practice at home (~45 minutes), and one day-long retreat. Meditation techniques taught include mindfulness meditation, body scanning, and simple yoga poses.

Transcendental meditation is a practice developed by the Maharishi Mahesh Yogi and is run by the <u>Transcendental Meditation Foundation</u>. It involves two 20-minute sessions per day with a focus on a personalized mantra given during a one-on-one session.

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Kirtran Kriya meditation is a 12-minute meditation that involves sitting and repeating a series of sounds (saa, taa, naa, maa) along with a specific finger tapping and visualization protocol (Khalsa, 2015).

Although there is an abundance of clinical research on meditation, several issues persist in interpreting the literature. First, control groups are necessarily imperfect, as there is no "placebo" pill or sham procedure. Some studies use wait-list controls, individuals who expect to get the treatment, or they may employ a different relaxation technique, such as progressive muscle relaxation or music listening. Second, many studies are relatively short (6-12 weeks) compared to cross-sectional studies that examine individuals who might have meditated for years. Third, study design varies greatly (in procedure, type of meditation, etc.), and different types of meditation may impact cognition in different ways. For instance, focused attention (e.g. breath counting) meditation may impact attentional and executive function networks while open monitoring meditation may engage emotional non-reactivity (Vago et al, 2019).

A review of the evidence suggests meditation is likely associated with multiple minor beneficial effects on cognition and healthy aging. However, the field is crowded with many studies that are small, short, and at a high risk of bias.

Interestingly, meditation may have an impact on telomere biology and immune function. It is thought that meditation may improve allostatic states in response to acute stress and could reduce chronic stress which is associated with dysregulated allostatic states. In addition, perseverative thinking, such as worry and rumination, may serve as internal stressors and could be deleterious to telomere biology. By impacting the body's response to stress and perseverative thinking, meditation may have an impact beyond focused attention (Conklin et al, 2019).

Neuroprotective Benefit for: Meditation may have beneficial effects on some aspects of cognition, though there is conflicting data and studies may be too short in duration to know the long-term impacts of meditation.

Types of evidence:

- Several systematic reviews and meta-analyses in healthy individuals
- A systematic review of individuals with age-related cognitive decline
- Several systematic reviews and meta-analyses of cross-sectional studies examining brain structure in expert meditators and healthy controls
- Three pilot studies in patients with MCI

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Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function?

In a systematic review of 6 studies, 8-week MBSR or MBCT in healthy older adults improved some aspects of memory, executive function, and processing speed. However, most of the studies were small, many were not randomized with a control group, and most had a high risk of bias (<u>Berk et al, 2017</u>). In the largest study included in the review, 97 healthy older adults (avg age 69) were randomized to either MBSR or reading and relaxation. There were no significant differences in any cognitive measure, although quality of life improved in the meditation group (<u>Mallya and Fiocco, 2015</u>).

There are several explanations for the lack of cognitive benefit in the <u>Mallya and Fiocco (2015)</u> study. There could be a ceiling effect on cognitive measures in healthy elderly adults. Alternatively, the control group, which consisted of reading and progressive muscle relaxation, could be beneficial itself. In addition, an 8-week meditation program may not be long enough to see any cognitive benefits.

Another systematic review of 12 (largely non-overlapping) studies in subjects with age-related cognitive decline reported some preliminary evidence of positive effects for attention, memory, executive function, processing speed, and general cognition. However, the results were mixed, and many of the results were no longer significant after accounting for multiple outcomes (<u>Gard et al, 2014</u>).

Sixty patients with subjective cognitive decline (SCD) were randomized to either 3 months of Kirtan Kriya meditation or classical music listening for 12 minutes per day. After 3 months participants were told they could continue the intervention if they wished. At 3 and 6 months, both groups performed better compared to baseline on measures of memory, executive function, and psychomotor speed, with mid to high effect sizes in the meditation group (i.e. 0.5-1.0) (Innes et al, 2017). Both groups also improved on measures of stress, mood, well-being, and sleep quality compared to baseline (Innes et al, 2016).

A systematic review of 23 studies (15 controlled or RCTs, 8 cross-sectional) of different types of mindfulness-based meditation programs in different populations (i.e. healthy, traumatic brain injury, depression) reported improvement in sustained attention in 2/7 RCTs and 3/3 cross-sectional studies. The study reported similar findings with other aspects of cognition (i.e. other types of attention, working memory, memory specificity, executive function) where results from intervention studies tended to be mixed where cross-sectional studies with expert meditators showed improvements (<u>Chiesa et al, 2011</u>).

Another systematic-review of 18 studies in mostly middle age individuals examining the effects of MBSR and MBCT reported trends toward benefits for attention and executive function with potential benefits

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for working memory, autobiographical memory, cognitive flexibility, and meta-awareness (<u>Lao et al</u>, <u>2016</u>).

A meta-analysis of 10 studies comparing expert meditators (2-25 years of experience) to control subjects found that meditators had increased functional activation in wide networks of brain regions. Additionally, meditation was associated with increased gray matter volume in regions of the frontal lobe, precuneus, and fusiform gyrus (Boccia et al, 2015). Another review of cross-sectional studies reported that expert meditators had increased whole-brain gray matter and increases in multiple brain regions including the hippocampus and multiple cortical and subcortical regions (Luders and Kurth, 2019). However, these studies are cross-sectional and do not consider whether meditators have larger brains from birth that predispose them the meditation, other lifestyle factors that could influence brain volume, or how much meditation it would take to have an effect on brain volume.

Human research to suggest benefits to patients with dementia

In an open-label study, 12 patients with mild cognitive impairment (MCI) participated in 8 weekly 1.5 hour group sessions and were instructed on formal (e.g. body scan, breath, or loving-kindness) and informal (awareness to everyday activities) meditation techniques. They were not instructed on how much to meditate each week (though they received a meditation audio recording). Cognition improved after 7 weeks (1.83 points on MoCA) as did their reported mindfulness. However, there were no changes in depression, anxiety, stress, or activities of daily living. Also, the study did not correct for multiple comparisons. One year after the intervention, there were no significant benefits on any outcome measure, though there was a positive correlation between the amount of weekly meditation and cognitive function (Pearson's r = 0.59) and activities of daily living (Pearson's r = 0.59), suggesting that more meditation led to more benefits (<u>Wong et al, 2017</u>).

In another study, 14 patients with MCI participated in an 8-week MBSR program. Control patients underwent usual care. Patients in the meditation group had significantly increased functional connectivity between the posterior cingulate cortex (PCC) and bilateral medial prefrontal cortex (MPFC) and between the PCC and the left hippocampus. There was also a trend toward less hippocampal atrophy in the meditation group. There were no significant changes in cognition (measured with ADAS-cog) (Wells et al, 2013).

Another pilot study enrolled 15 subjects with memory impairment, MCI, or moderate Alzheimer's disease and were randomized to either an 8-week Kirtan Kriya meditation program or music listening. In

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the meditation group there were alterations in cerebral blood flow in several brain regions and in several measures of cognition (<u>Newberg et al, 2010</u>).

APOE4 interactions: None Reported

Aging and related health concerns: There is some evidence that meditation may have a beneficial impact on telomere biology, blood pressure reduction, insomnia, and reduction of chronic pain.

Types of evidence:

• Systematic reviews or meta-analyses for several age-related indications (telomere biology, insomnia, immune function, chronic pain).

Lifespan: MIXED/POTENTIAL BENEFIT

<u>Conklin et al (2018)</u> recently reviewed 19 studies examining the relationship between telomere biology and meditation. Two cross-sectional studies found longer telomeres in meditators versus meditationnaïve individuals. 11 studies measured telomerase activity after various types of meditation (with different types of or without controls), and nine reported increased telomerase activity. Of nine studies looking at telomere length, only two reported an increase in telomere length.

They conclude that evidence suggests meditation may improve telomere maintenance. However, it is not clear what kind of meditation program is the best, how long it would take telomere length to increase, or how long the effect would last. Additionally, they suggest that future studies should look at telomere length in a more stable cell population (e.g. buccal cells). Most studies examined telomere length in blood samples; however, meditation may shift the population of immune cells in the blood which may itself change the reported telomere length.

In one study, telomere length in PBMCs increased (equivalent to 104.2 bp) in participants after 3 weeks at an Insight meditation retreat both compared to the beginning of the retreat and a control group of regular meditators who did not go on the retreat. There was no change in telomerase activity. The increase was greatest in individuals with low agreeableness, high neuroticism, and high openness, suggesting meditation may have different effects in different populations (<u>Conklin et al, 2018</u>).

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In a more recent study comparing loving-kindness meditation, mindfulness meditation, and a wait-list control group over 6 weeks in 124 middle age adults found that loving-kindness meditation, but not mindfulness meditation, prevented a reduction in telomere length compared to the control group (Nguyen et al, 2019).

On the other hand, a study comparing the effects of three meditation training modules (attention, compassion, or perspective taking) in 332 individuals over 9 months found no change in leukocyte telomere length compared to a passive control (Puhlmann et al, 2019).

Insomnia: POTENTIAL BENEFIT

In a meta-analysis of 6 RCTs ranging from 6-8 weeks in length, mindfulness meditation was associated with significantly improved total wake time (SMD = -0.44, p=0.03) and sleep quality (SMD = 0.68, p=0.003) but not other measures including sleep onset latency, total sleep time, wake after sleep onset, sleep efficiency, insomnia severity index, Pittsburgh Sleep Quality Index (PSQI), or the Dysfunctional Beliefs and Attitudes about Sleep Scale. In two of the studies, the control arm was pharmacotherapy or cognitive behavioral therapy, so a subgroup analysis was conducted with the other four studies. There were significant improvements in sleep onset latency (SMD = -.053, p=0.02), sleep efficiency (SMD = 0.68, p=0.003), and PSQI (SMD = -1.09, p<0.001), but not total sleep time (Gong et al, 2016).

Another meta-analysis with 18 RCTs (largely non-overlapping from the previous meta-analysis) reported that mindfulness meditation (most studies were MBSR) did not improve sleep quality compared to a specific active comparator (e.g. progressive muscle relaxation, exercise, pharmaceuticals). However, it did improve sleep quality compared to a non-specific active comparator (e.g. sleep hygiene education, health education, stress management education) (Hedges' g = 0.33; 95%CI 0.17, 0.48). There were mixed results whether there was a dose-response effect (Rusch et al, 2019).

Cardiovascular Risk Reduction: POTENTIAL BENEFIT

A consensus statement from the American Heart Association suggest a possible, though not definitive, benefit of meditation on cardiovascular risk reduction. Although there is an abundance of clinical research on meditation, limitations of the current research include a lack of long-term RCTs, a lack of blinding of the studies, inadequate power for study outcomes, a potential risk of publication bias, and most research is conducted by investigators who might have financial or intellectual bias in study outcomes. Some studies have reported benefits for psychological health and some studies have shown improvements in blood pressure reductions (Levine et al, 2017).

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Blood Pressure: POTENTIAL BENEFIT

In a meta-analysis of 19 RCTs ranging in length from 8-52 weeks and enrolling hypertensive and nonhypertensive individuals, transcendental meditation was associated with reduced non-ambulatory blood pressure monitored (ABPM) systolic blood pressure (SBP) of -5.57mmHg (95%CI: -7.41, -3.73) and reduced non-ABPM diastolic blood pressures (DBP) of -2.86mmHg (95%CI: -4.27, -1.44). Nontranscendental meditation was associated with reduced non-ABPM SBP of -5.09mmHg (95%CI: -6.34, -3.85) and reduced non-ABPM DBP of -2.57mmHg (95%CI: -3.36, -1.79). Results from ambulatory blood pressure monitoring were similar but smaller improvements were observed. Non-transcendental meditations included breath awareness meditation, MBSR, etc (<u>Shi et al, 2017</u>).

Inflammation/markers of stress: MIXED/POTENTIAL BENEFIT

In a systematic review of 20 RCTs ranging in length from 6-8 weeks in a variety of patient populations (e.g. cancer patients, rheumatoid arthritis patients, healthy volunteers, etc.), mindfulness meditation showed mixed results on inflammatory biomarkers. Some studies showed reductions in TNF α or CRP, though most were null results. A few studies also showed reductions in NFkB levels in PBMCs (Black and Slavich, 2016). Another meta-analysis of 34 studies found that mind-body therapies (meditation, Yoga, Tai Chi, Qi Gong) reduced levels of CRP (Cohen's *d* = 0.58; 95%CI 0.04-1.12) but not in healthy individuals. There was a small, non-significant reduction in IL-6 with no change in TNF α (Morgan et al, 2014).

In a meta-analysis of 45 RCTs comparing different types of meditation to an active control group found that meditation is associated with a reduction in cortisol, a trend for a reduction in CRP, trends for reductions in other inflammatory cytokines, no change in heart rate variability, a reduction in blood pressure, and a reduction in triglycerides(<u>Pascoe et al, 2017</u>).

Chronic pain: POTENTIAL BENEFIT

A meta-analysis of 30 RCTs ranging in length from 4-60 weeks reported that mindfulness meditation significantly reduces chronic pain symptoms (SMD 0.32; 95%CI 0.09, 0.54). These results were still significant when excluding poor quality studies and were significant in studies over 12 weeks but not for studies 12 weeks or less. The results were considered of low quality due to inconsistency, heterogeneity, and possibly publication bias (<u>Hilton et al, 2017</u>). Another systematic review reported that mindfulness meditation improved cancer-related pain symptoms in 4 out of 6 studies (<u>Ngamkham et al, 2018</u>).

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Safety: Although there are no studies specifically looking at safety outcomes from long-term clinical trials, evidence to date suggest there are no negative effects of meditation.

Types of evidence:

• Several meta-analyses in age-related conditions.

There is no indication or a biological rationale that meditation will have a negative impact. However, most studies are relatively short in duration. There is no indication that long-term meditation has any negative impact.

Drug interactions:

None

Sources and dosing:

Most studies have examined the effects of MBSR, Transcendental Meditation, or Kirtan Kriya meditation. <u>Multiple mobile apps</u> (such as Headspace or Calm) have been developed to assist in meditation practice.

Research underway:

One clinical study (<u>NCT03503669</u>) is comparing the effect of Kundalinia yoga and Kirtan Kriya meditation to memory enhancement training in women with MCI at a high risk of Alzheimer's disease. Two other <u>ongoing studies</u> are testing the effects of meditation for Alzheimer's care givers. Overall, there are <u>326</u> <u>ongoing</u> meditation clinical trials.

Search terms:

- meditation + alzheimer, lifespan
- meditation
 [meta-analysis]

Websites:

- Clinicaltrials.gov
- Pubmed

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If you have suggestions for drugs, drugs-in-development, supplements, nutraceuticals, or food/drink with neuroprotective properties that warrant in-depth reviews by ADDF's Aging and Alzheimer's Prevention Program, please contact <u>INFO@alzdiscovery.org</u>. To view our official ratings, visit <u>Cognitive Vitality's Rating page</u>.

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