Mindfulness (2025) 17:1–25
https://doi.org/10.1007/s12671-025-02718-1

REVIEW

The Effects of Mindfulness-Based Interventions on Physiological Markers of Stress in Older Adults: A Systematic Review and Synthesis

Samantha Galluzzi[1] · Claudio Singh Solorzano[1] · Moira Marizzoni[2] · Elena Gatti[1] · Carlotta Gualco[3] · Mariangela Lanfredi[4] · Roberta Rossi[4] · Annamaria Cattaneo[2,5] · Giovanni B. Frisoni[6] · Cristiano Crescentini[7] · Emilio Di Maria[3,8] · Michela Pievani[1]

Accepted: 26 October 2025 / Published online: 2 December 2025

Abstract

Objectives Given the rapid increase in population ageing and considering the great impact that mental disorders have on global disability, there is a critical need for mental health promotion in older adults. Mindfulness-based interventions (MBIs) have been widely used to improve mental health. However, a comprehensive understanding of their neurobiological effects is still missing. We therefore conducted a systematic review of controlled clinical trials evaluating the effects of MBIs on the physiological markers of stress in older adults.

Method A systematic literature search was conducted in five electronic databases and the ClinicalTrials.gov registry. Controlled trials of mindfulness-based stress reduction or mindfulness-based cognitive therapy programs for older adults measuring any physiological outcome were identified. The combined *p*-value analysis, following the Synthesis Without Meta-analysis reporting guidelines, was used for data synthesis. A sensitivity analysis and subgroup analysis by the study population were also conducted.

Results Based on 22 eligible studies, the synthesis shows a positive effect of MBIs on 43 physiological outcomes grouped by five stress-related systems, i.e., brain circuits and signalling (combined p-value < 0.001), the sympathetic-adrenomedullar axis (combined p-value $= 0.004$), the hypothalamus-pituitary-adrenal axis (combined p-value $= 0.011$), the immune system (combined p-value $= 0.037$), and gene expression and epigenetic mediators (combined p-value < 0.001). The effects on brain circuits and signalling were noticeable in both clinical and community populations.

Conclusions These findings preliminarily support the influence of MBIs on pathophysiological pathways related to chronic stress at a system level. Limitations of the included studies (e.g., outcome heterogeneity, small sample size, concern for risk of bias) and future perspectives are discussed.

Preregistration A protocol of this systematic review was registered with PROSPERO (Registration No. CRD42023390236).

Keywords Mindfulness-based stress reduction · Mindfulness-based cognitive therapy · Chronic stress · Biomarkers · Physiological outcomes

Emilio Di Maria and Michela Pievani shared co-last authorship.

✉ Samantha Galluzzi
sgalluzzi@fatebenefratelli.eu

1 Laboratory Alzheimer's Neuroimaging & Epidemiology, IRCCS Istituto Centro San Giovanni Di Dio Fatebenefratelli, Brescia, Italy

2 Laboratory of Biological Psychiatry, IRCCS Istituto Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy

3 Department of Health Sciences, University of Genoa, Genoa, Italy

4 Unit of Psychiatry, IRCCS Istituto Centro San Giovanni Di Dio Fatebenefratelli, Brescia, Italy

5 Department of Pharmacological and Biomolecular Sciences, University of Milan, Milan, Italy

6 Memory Center, Geneva University and University Hospitals, Geneva, Switzerland

7 Department of Languages and Literatures, Communication, Education and Society, University of Udine, Udine, Italy

8 University Unit of Medical Genetics, Galliera Hospital, Genoa, Italy

The general population has aged considerably in recent years (World Health Organization, 2022). Although life expectancy is continuously increasing, the disability burden on older adults remains persistent (GBD 2019 Ageing Collaborators, 2022). Age-related biological processes, such as the gradual accumulation of molecular and cellular damage and accompanying physiological changes in multiple body systems (e.g., musculoskeletal, sensory, and neurological), place older adults at increased risk of chronic diseases and functional loss (Kirkwood, 2008). In addition, stressful life events (e.g., retirement, relocation, loss of loved ones, social isolation, loss of independence) and related affective disorders (e.g., depression, anxiety) are more prevalent in older adults than in younger adults (Luo et al., 2023; World Health Organization, 2023). Chronic stress has also been associated with an increased risk of mental health disorders, such as dementia and depression (Tafet & Nemeroff, 2016; Wallensten et al., 2023). Notably, the 2015 World Report on Ageing and Health recommends an improved alignment of health promotion strategies to the older population based on an integrated person-centred model of care that takes into account the unique physiological and psychological challenges encountered by older adults (Beard et al., 2016).

Mental disorders account for 10.6% of total disabilities (World Health Organization, 2023). Therefore, interventions that are able to enhance mental health are considered part of public health strategies to lower the overall disability burden (Leggett & Zarit, 2014) and promote healthy ageing (World Health Organization, 2023). Interventions that act at multiple psychological and cognitive levels may be valuable for stress reduction and promotion of mental health in older adults. Specifically, interventions aimed at cultivating mindfulness lead to a shift in the perspective of life experiences, referred to as "reperceiving" (Kriakous et al., 2021). This new skill enables practitioners to reduce the power of "habitual or automatic stress reactions", by employing more adaptive stress coping mechanisms (Brown & Ryan, 2003; Brown et al., 2012; Kriakous et al., 2021). Mindfulness-Based Stress Reduction (MBSR) is the most common and widely studied mindfulness-based intervention (MBI) (Kabat-Zinn, 2003). It consists of a standardised 8-week group program in which mindfulness is trained via both formal and informal practices. Another well-investigated MBI is Mindfulness-Based Cognitive Therapy (MBCT) (Segal et al., 2002), which was developed to prevent the relapse of major depression by integrating aspects of cognitive-behavioural therapy for depression into the MBSR programme. MBIs have shown preliminary evidence of beneficial effects on depression, anxiety, rumination, well-being, worry, cognitive function, stress perception, and sleep quality in clinical and nonclinical samples of older adults (Chiesa & Serretti,2009; Geiger et al., 2016; Tomlinson et al., 2018; Hazlett-Stevens et al., 2019; González-Martín et al., 2023). However, the size of the observed effects is typically only small or small-to-moderate.

The measurement of physiological outcomes might represent a useful addition to the overall understanding of the effects of MBIs and might shed new light on the interplay between physiological changes and clinical effectiveness. The biological pathways underlying MBIs are not well understood. However, modulation of the function of the stress system may be involved (Creswell et al., 2019; Taylor et al., 2010). The stress system controls responses to stressful stimuli by activating a complex neuroendocrine-immune response that involves the sympathetic-adrenomedullar (SAM) axis, the hypothalamus-pituitary-adrenal (HPA) axis, the immune system, and the brain regions associated with stress processing (Godoy et al., 2018). This response is adaptive to cope with physical or psychological stimuli that disrupt the body's homeostasis. However, prolonged exposure to stressors requires continual adjustment of these physiological pathways, which leads to maladaptation, allostatic overload and poor health outcomes (Juster et al., 2010). In addition, chronic stress induces long-lasting changes in stress system regulation through epigenetic mechanisms (Dion et al., 2022).

The effect of MBIs on the stress system has been suggested by systematic reviews showing a positive effect of MBIs on brain structure and function (Fox et al., 2016; Gotink et al., 2016; Lomas et al., 2015; Pernet et al., 2021; Sezer et al., 2022; Young et al., 2018), the autonomic system (Geiger et al., 2023), endocrine secretion (Rogerson et al., 2024; Sanada et al., 2016), the immune system (Black & Slavich, 2016; Dunn & Dimolareva, 2022; Sanada et al., 2020), and gene expression (Buric et al., 2017). Although these systematic reviews contributed to elucidating the neurobiological substrates of MBIs, they focused on individual biological systems taken as isolated systems. A comprehensive approach that addresses the complexity of stress response mechanisms (i.e., brain circuits and their interaction with peripheral neuroendocrine-immune mediators) in a systems and integrative perspective may be more appropriate. A few reviews have attempted to review the literature by adopting a similar approach. Three meta-analyses focused on peripheral markers of stress, revealing an effect of mindfulness meditation on physiological outcomes at the autonomic, endocrine, and immune levels (Grasmann et al., 2023; Heckenberg et al., 2018; Pascoe et al., 2017); however, they did not address brain pathways associated with stress processing. To the best of our knowledge, only one systematic review embraced a whole-system approach, showing that MBSR has an effect on 14 biological markers, which can be traced back to stress markers of allostatic load at multiple brain, immune, inflammatory, and autonomic levels (Reive, 2019).

As a further shortcoming in the field, many of the aforementioned reviews have examined the physiological effects of a broad range of meditative approaches (e.g., mind-body therapies, open monitoring, self-transcending, mantra recitation, compassion meditation, and yoga), which increases the potential of confounders on outcome measurement (Van Dam et al., 2018). A focus on MBSR and MBCT, which are standardised interventions in terms of duration, course content and home practice, can overcome this variability. Notably, the reviews that assessed MBSR or MBCT were carried out in mixed populations of both younger and older adults. However, the ageing process can affect the adaptive stress response through changes in the endocrine, autonomic, and immune systems (Lavretsky & Newhouse, 2012). Therefore, the body's ability to respond to stressors may be reduced with increasing age, which can lead to increased biological vulnerability to even mild stressors and a limited capacity for recovery (Maragkakis et al., 2023). As a consequence, the physiological mechanisms of MBIs in older adults may differ from those in younger adults. The growing scientific evidence that links meditation to reduced ageing-related processes (Kurth et al., 2017) suggests that studying the physiological mechanisms through which MBI effects may be mediated in older individuals may be valuable.

Hence, we provided a comprehensive overview of the effects of MBIs (i.e., MBSR or MBCT) on physiological markers of stress in older adults. We applied the theory of change to describe how MBIs were expected to influence physiological markers on the basis of key pathophysiological pathways associated with chronic stress (Fig. 1). We subsequently tested whether this theory of change was empirically supported by clinical trials examining the physiological effects of MBIs in older adults.

Method

We followed the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins & Green, 2019) and PRISMA guidelines (Liberati et al., 2009). The protocol was preregistered on PROSPERO (CRD42023390236). The PICOD framework allowed us to outline the target group of participants (population), the specific intervention being studied (intervention), the control group or comparator (comparison), the types of outcomes that were of interest (outcome), and the types of study design (design).

Search Strategy and Selection Criteria

We searched the PubMed, Scopus, Web of Science (via Clarivate Analytics), CINAHL and Psycinfo (via EBSCO) databases, and the ClinicalTrials.gov registry from inception to January 23, 2023. The search strategy for each database followed an iterative process to ensure sensitivity. According to the PICOD framework, three domains ("mindfulness"; "biomarkers"; "study design") were defined by combining Medical Subject Heading terms and keywords using the Boolean operator "or"; the three domains were combined with "and"; records were filtered for language (English). Grey literature was not searched due to methodological challenges, including few repositories, no standardised methods for searching, low yield in terms of the search results, and potentially high risk of bias (Adams et al., 2016; Benzies et al., 2006). Several tests were run to ensure the best sensitivity. The full search strategies are shown in Online Resource 1. Manual searches of references from review articles and included papers complemented the electronic searches. All retrieved records were exported locally and managed by using the EndNote™ X8 software.

We included studies that met the following inclusion criteria: (i) population: older adults (aged ≥ 60 years) regardless of health status (i.e., both patients and community-dwelling persons were eligible); (ii) intervention: MBSR or MBCT programs delivered in person according to a standardised curriculum or adapted in content and/or length for specific populations; adapted protocols had to report reference to the standard curriculum and describe the specific adaptations; (iii) comparator: any type of active or inactive comparator; (iv) outcome: any type of physiological marker; and (v) design: randomised or non-randomised clinical trial, with a pre-post intervention design. The exclusion criteria were as follows: (i) studies written in non-English languages or not peer-reviewed (i.e., dissertations, theses) or published in journals without peer review, (ii) study protocols, and (iii) personal communications. With respect to the cut-off for age, no universally accepted criterion for defining older people exists: a cut-off of over 60 or 65 years is often used (Shenkin et al., 2017). As chronic stress may accelerate biological ageing (Polsky et al., 2022), we adopted a less stringent threshold of 60 years.

Title, abstract, and full-text screenings were carried out on Rayyan (Ouzzani et al., 2016). The screening team (SG, EG, CG, and CSS) conducted dual and independent screening at the title, abstract, and full-text levels. Specifically, titles and abstracts were independently screened by EG and CG. If the data reported in the title/abstract were not enough to determine eligibility, the record was moved to the next eligibility phase. Full-text manuscripts of eligible studies were screened by the entire screening team. Any disagreements were resolved by consensus discussion and by consulting an external reviewer (CC), when necessary. If multiple articles reported different physiological outcomes from the same study sample, each was considered a separate study.

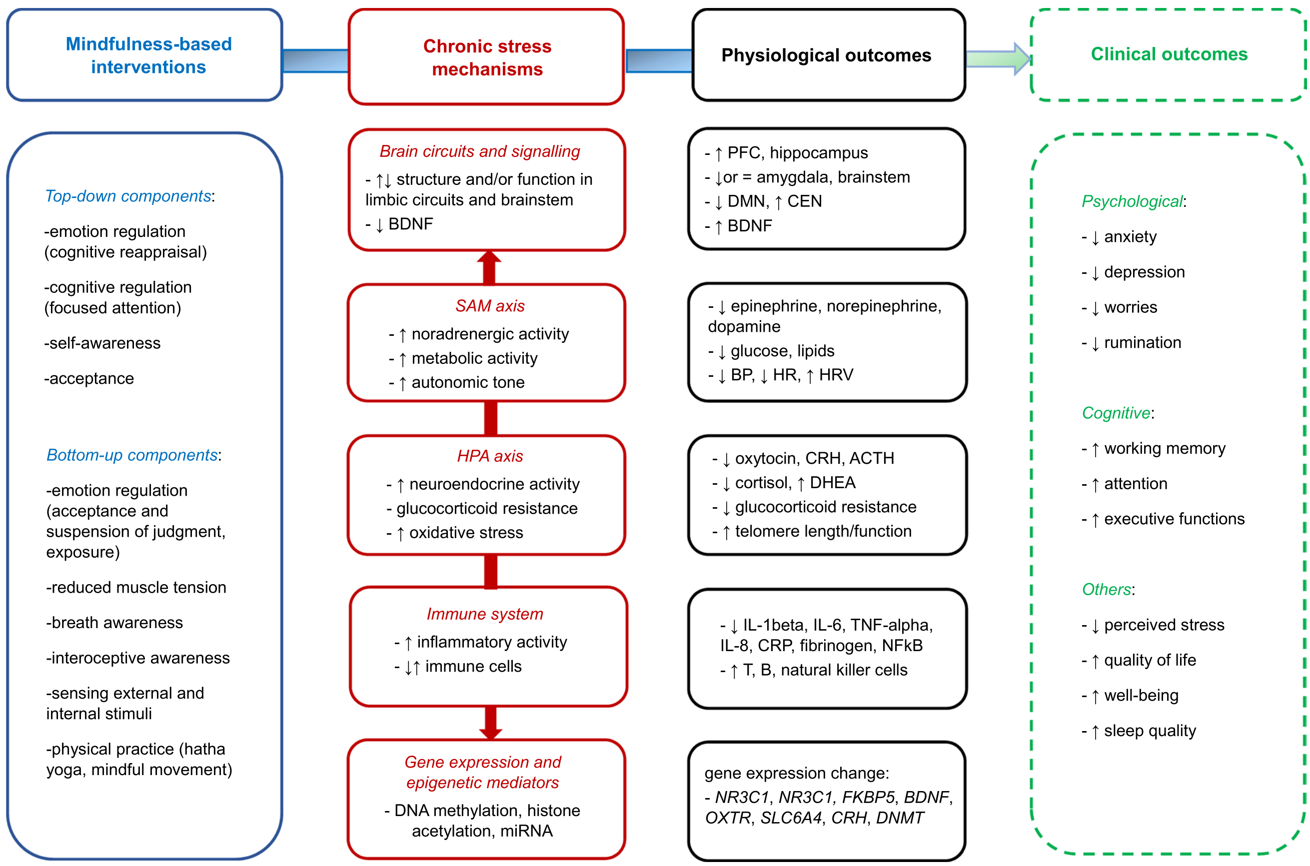

Fig. 1 Logic model illustrating the theory of change on how chronic stress can act as a mediating mechanism between mindfulness-based interventions and physiological outcomes. **Mindfulness-based interventions**: MBSR/MBCT can have an impact on the stress system by either top-down or bottom-up components (Chambers et al., 2009; Chiesa et al., 2013; Hölzel et al., 2011; Sipe & Eisendrath, 2012; Taylor et al., 2010). Top-down components are those initiated via mental processing, with an impact at the brain circuits and signalling level. Bottom-up components are those initiated via sensory or visceral processes, with an impact at the periphery level. Top-down and bottom-up components are closely interconnected and MBSR/MBCT involve a combination of both mechanisms. **Chronic stress mechanisms**: chronic stress mechanisms were defined a priori by the authors following the identification of pathophysiological pathways considered key mechanisms in the literature (Juster et al., 2010; Dragos & Tănăsescu, 2010; Tang et al., 2015; Godoy et al., 2018; Schneider & Schwerdtfeger, 2020; Bainomugisa & Mehta, 2022; Lenart-Bugla et al., 2022; Dee et al., 2023; Tong et al., 2023; Cardoner et al., 2024). Five stress systems were identified (i.e., brain circuits and signalling, SAM axis, HPA axis, immune system, and gene expression and epigenetic mediators). While they are depicted as separate boxes for illustrative purpose, they reciprocally interact in a bidirectional communication (see arrow). **Stress physiological markers**: the definition of chronic stress mechanisms allowed the identification of stress markers that can be regarded as the physiological outcomes of MBSR/MBCT interventions. Thin arrows within each box indicated the plausible effect direction of intervention, which is hypothesized to counteract chronic stress mechanisms. **Clinical outcomes**: physiological changes can be associated with clinical outcomes; this relationship was not examined in this review (dotted box). ACTH, adrenocorticotropic hormone; BDNF, brain-derived neurotrophic factor; BP, blood pressure; CEN, central executive network; CRH, corticotropin-releasing hormone; CRP, C-reactive protein; DHEA, dehydroepiandrosterone sulfate; DMN, default mode network; *DNMT*, DNA methyltransferase gene; DNA, deoxyribonucleic acid; HPA, hypothalamus-pituitary-adrenal; *FKBP5*, glucocorticoid receptor regulator gene; HR, heart rate; HRV, heart rate variability; IL, interleukin; MBSR, mindfulness-based stress reduction; MBCT, mindfulness-based cognitive therapy; miRNA, micro-ribonucleic acid; NFkB, nuclear factor kappa-light-chain-enhancer of activated B cells; *NR3C1*, glucocorticoid receptor gene; *NR3C2*, mineralocorticoid receptor gene; *OXTR*, oxytocin receptor gene; PFC, prefrontal cortex; SAM, sympathetic-adrenomedullar; *SLC6A4*, serotonin transporter gene; TNF, tumor necrosis factor

Data Extraction

Data were extracted independently by SG and CSS into a piloted spreadsheet in duplicate. Any disagreements were resolved by discussion and consensus. We extracted the following data: (i) characteristics of the study participants, including age, education, sex, diagnosis, inclusion and exclusion criteria, and sample size. The study population was coded as "clinical" if the study included participants who had a clinical diagnosis according to standardised criteria, or "community" otherwise; (ii) type of intervention (i.e., MBSR, MBCT, or adapted MBSR/MBCT), including the number and frequency of training sessions; (iii) type of control (i.e., inactive, if studies utilised waitlist or treatment as usual, or active); (iv) type of physiological outcome measure, including the instrumental exam or biological matrix used for measurement, the type or method of measurement, the number of participants in the intervention group for whom the physiological outcome was measured, measurement timepoints, physiological findings as reported in the study, *p*-values of statistical models used to assess the effect of the intervention, and effect direction, as reported in the study. If multiple physiological outcomes were reported in the same study, data were extracted separately for each outcome.

Quality Assessment

Study quality was assessed independently by EG and CG using the Revised Cochrane Risk of Bias (RoB 2) tool (Sterne et al., 2019), separately for parallel and cross-over design studies. Any disagreements were resolved by consensus discussion. A third reviewer (SG) was consulted when necessary. The tool implements signalling questions for five domains: the randomisation process, deviations from the intended interventions (e.g., "intention-to-treat" effect), missing outcome data, outcome measurement, and selection of the reported results. An overall rating of low/high/medium concern for risk of bias was assigned.

Data Synthesis

Considering the heterogeneity of outcomes and the different statistical models tested, meta-analysis of effect estimates was not possible. We then used an alternative synthesis method following the Synthesis Without Meta-analysis reporting guidelines (Campbell et al., 2020).

First, we accounted for outcome heterogeneity by outcome grouping. Physiological outcomes were grouped according to the five biological systems that were recognised in the literature as the key pathophysiological pathways associated with chronic stress: brain circuits and signalling, the SAM axis, the HPA axis, the immune system, gene expression and epigenetic mediators. The outline is shown in the logic model (Fig. 1). Within the brain circuits and signalling system, we sub-grouped physiological outcomes by brain structure or function. Within the SAM axis, we sub-grouped physiological outcomes by autonomic or metabolic functional domains. The physiological outcomes that were not outlined in the logic model were included in the system most relevant to its physiological significance.

Second, we quantified the effects of the intervention by combined *p*-value analysis (Becker, 1994; McKenzie & Brennan, 2023). The method allowed us to synthetise the intervention effects of studies that reported at least *p*-values and directions of effects. To increase the methodological robustness of our quantitative synthesis, we included only the outcomes for which the exact *p*-value of the time × intervention interaction at pre-post MBIs was available. This analysis allowed us to answer the following main question: "Is there evidence of a positive effect of MBIs compared with the control in at least one physiological outcome involved in the stress system?" Two-sided *p*-values were transformed into one-sided *p*-values according to the effect direction. A positive effect indicated a significant effect of MBI vs. the control on the physiological outcome. Conversely, a negative effect indicated a significant effect of the control vs. the MBI. Fisher's method was used to compute the combined *p*-values by the stress system via the "*metap*" R package, v 1.9 (Cinar & Viechtbauer, 2022). A minimum of three outcomes was needed to derive a combined *p*-value (McKenzie & Brennan, 2023).

To assess the robustness of the results obtained via Fisher's method, we conducted a sensitivity analysis using Stouffer's weighted Z-method (Whitlock, 2005). Stouffer's method allows weighting by the study size, thereby accounting for the relative contribution of each study to the overall signal. Specifically, we assigned weights on the basis of the square root of the sample size for each included study and computed a combined Z score, which was then converted to a *p*-value. This approach is particularly useful when the precision of *p*-values varies across studies, as it can reduce the influence of small studies with extreme results.

A subgroup analysis was used to examine whether the study population (i.e., clinical vs. community) moderated the results of the combined *p*-value analysis by the stress-related system. Thus, we divided the physiological outcomes by study population and stress-related system and computed the combined *p*-values, if the minimum requirement of three outcomes per subgroup was satisfied.

An albatross plot (Harrison et al., 2017) was used to visualise the *p*-value and effect direction (on the *x*-axis) against sample size (on the *y*-axis) for a given outcome by the stress-related system. Contour lines were drawn on the plot, representing an approximation of the standardised effect size (i.e., standardised mean difference) for a given *p*-value and sample size. Values of 0.20, 0.50, and 0.80 were indicative of small, medium, and large effect sizes, respectively (Cohen, 1988). The outcomes indicative of positive effects (i.e., in favour of MBIs) appear at the right of the plot, with null effects towards the middle and negative effects (i.e., in favour of controls) at the left of the plot. The "null" effect area (p-value = 1) is included between the contour lines representing the ± 0.20 values. All analyses were performed using R Statistical Software, v4.3.2 (R Core Team, 2023).

Results

Study Selection

A total of 7773 records were initially identified from databases, and 2001 were identified from clinicaltrials.gov. After duplicate exclusion (2827 records), 6947 records were identified from the title and abstract screening. Five hundred thirty-eight full texts were assessed, of which 20 met the inclusion criteria. Two additional records that met the inclusion criteria were identified from citation searches, resulting in a total of 22 papers (Fig. 2).

Study Characteristics

Information from the individual studies is shown in Table 1. The sample size of each study ranged from 20 to 585 participants (median 60). The mean age of the included participants ranged from 67 to 79 years. The mean proportion of female participants was 70%. Twelve studies (55%) (# 1; 3; 5–8; 10; 14; 18; 20–22) enrolled participants from the general community. Ten studies (45%) (# 2; 4; 9; 11–13; 15–17; 19) enrolled participants from clinical populations. The majority ($n=9$) included outpatients with a diagnosis of psychiatric ($n=4$) (# 2; 4; 17; 19) or cognitive ($n=5$) (# 9; 11; 13; 15–16) disorders. One study included inpatients with type 2 diabetes (# 12).

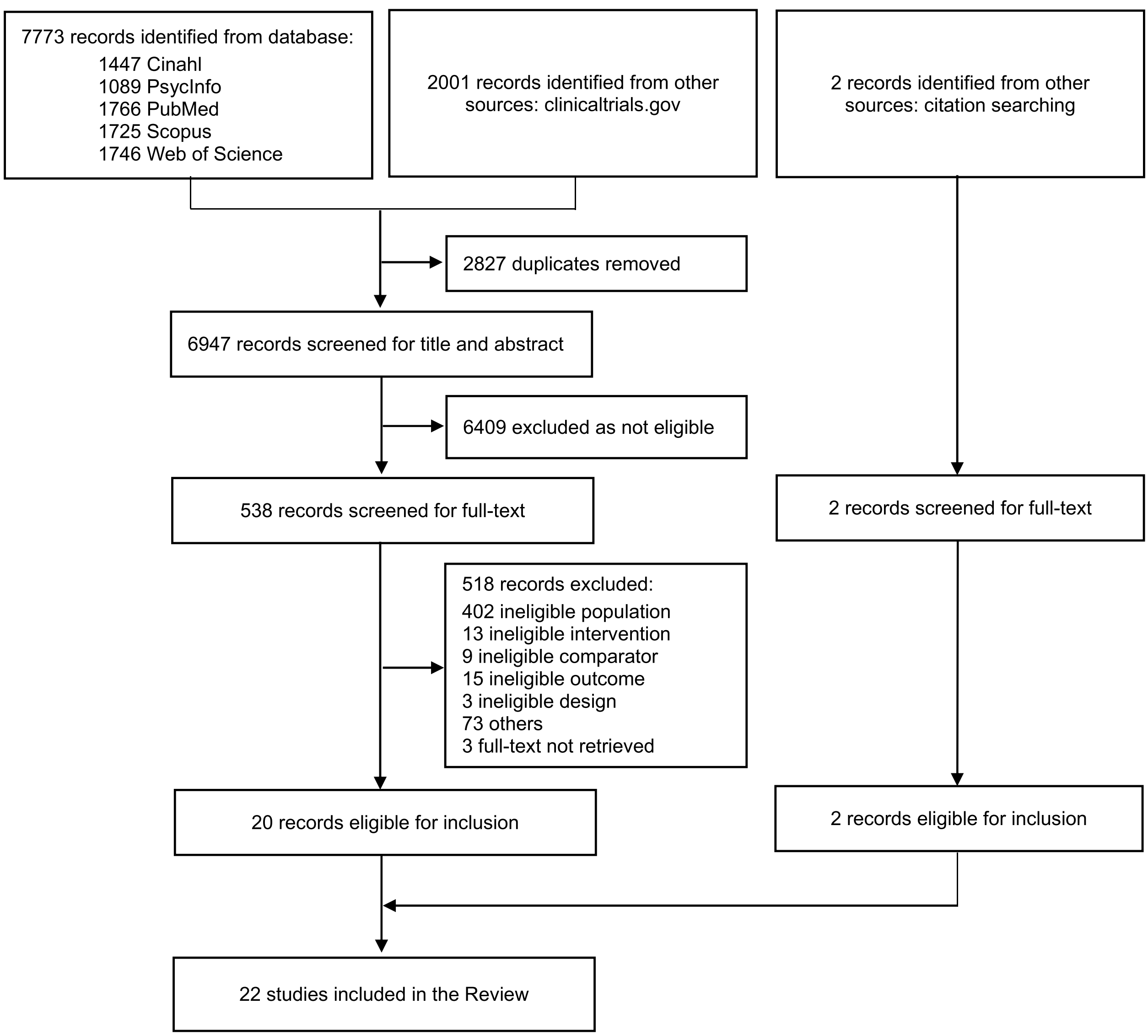

Fig. 2 PRISMA flow diagram

Table 1. Overview of the studies examining the physiological effects of mindfulness-based interventions (MBIs) in older adults

Study number	Author/year	Study population°	Main inclusion/exclusion criteria	Country	MBI/control	Number/frequency of sessions	Sample size*	Age *M* (*SD*) [*SE*]	Education *M* (*SD*)	Gender (% F)	Clinical outcome	Physiological outcome
# 1	Lenze et al., 2022	*community*:[a] older adults with subjective cognitive concerns	self-reported cognitive concern; no dementia (Short Blessed Test < 10); MCI allowed	USA	MBSR + exercise/active	8/weekly + 16/monthly	585	71.5 (4.8)	16.2 (2.2)	73	memory and executive functions, functional cognitive capacity, memory concerns	hippocampal volume; dorsolateral prefrontal cortex: surface area and cortical thickness
# 2	Li et al., 2022	*clinical*:[b] outpatients with late-life depression	diagnosis based on DSM-IV; no dementia diagnosis; MMSE > 26	China	adapted MBCT/inactive	8/weekly	60	67.4[¤]	13.1[¤]	77	depression, anxiety	whole brain functional connectivity; middle frontal gyrus-amygdala tract: fractional anisotropy
# 3	Lindsay et al., 2022	*community*:[c] older adults with subjective loneliness	Short Form Loneliness scale > 8, Telephone Interview for Cognitive Status > 30, Beck Depression Inventory < 29	USA	MBSR/active	8/weekly	190	69.8 [0.3]	NR	78	loneliness	Interleukin-6
# 4	Liu et al., 2022	*clinical*:[b] outpatients with late-life depression	diagnosis based on DSM-IV; no dementia diagnosis; MMSE > 26	China	MBCT/inactive	8/weekly	60	67.4[¤]	13.1[¤]	77	positive and negative affect	whole brain activation to negative emotions
# 5	Snyder et al., 2022	*community*:[a] older adults with subjective cognitive concerns	self-reported cognitive concern; no dementia (Short Blessed Test < 10); MCI allowed	USA	MBSR + exercise/active	8/weekly + 16/monthly	585	71.5 (4.8)	16.2 (2.2)	73	memory and executive functions, functional cognitive capacity, memory concerns	whole brain functional connectivity

Table 1. (continued)

Study number	Author/year	Study population°	Main inclusion/exclusion criteria	Country	MBI/control	Number/frequency of sessions	Sample size*	Age *M* (*SD*) [*SE*]	Education *M* (*SD*)	Gender (% F)	Clinical outcome	Physiological outcome
# 6	Belliveau et al., 2021	*community*: older adults with depressive and/or anxiety symptoms	score > 10 on Patient Health Questionnaire and/or General Anxiety Disorder-7, no acute psychotic symptoms	Canada	adapted MBCT/inactive	8/weekly	61	68.0 (6.2)	NR	65	depression, anxiety	*CRP*, *MCP1*, *IL-1beta*, *NR3C2* gene expression
# 7	Hashizume et al., 2021	*community*: older adults	no severe hypertension, heart disease, psychiatric disorders, and upper and lower limb motor difficulties	Japan	adapted MBCT/inactive	12/three times a week	46	78.1[¤]	11.1[¤]	76	global cognition	microRNA expression
# 8	Lindsay et al., 2021	*community*:[c] older adults with subjective loneliness	Short Form Loneliness Scale > 8, Telephone Interview for Cognitive Status > 30, Beck Depression Inventory < 29	USA	MBSR/active	8/weekly	190	69.8 [0.3]	NR	78	loneliness	functional glucocorticoid resistance
# 9	Ng et al., 2021	*clinical*:[d] outpatients with mild cognitive impairment	diagnosis based on DSM-V, no dementia, no major psychiatric condition	Singapore	adapted MBSR/active	12/weekly + 6/monthly	55	71.3 (6.0)	4.4[¤]	74	NR	amyloid beta-42
# 10	Sevinc et al., 2021	*community*: older adults	no psychiatric diagnosis, no use of cholinesterase inhibitors and memantine	USA	adapted MBSR/active	8/weekly	146	70.6[¤]	16.7[¤]	54	global cognition	hippocampus and posteromedial cortex: volume and functional connectivity

Table 1. (continued)

Study number	Author/year	Study population°	Main inclusion/exclusion criteria	Country	MBI/control	Number/frequency of sessions	Sample size*	Age *M* (*SD*) [*SE*]	Education *M* (*SD*)	Gender (% F)	Clinical outcome	Physiological outcome
# 11	Yu et al., 2021	*clinical*:[d] outpatients with mild cognitive impairment	Petersen criteria: < 1.5 *SD* in six cognitive domains; diagnosis made by consensus panel	Singapore	adapted MBSR/active	12/weekly + 6/monthly	54	71.4[¤]	4.3[¤]	74	working memory, verbal memory, divided attention, verbal fluency, visuospatial processing	cortical thickness
# 12	Chen et al., 2020	*clinical*: inpatients with type 2 diabetes	no obvious delirium, confusion or current psychiatric illness	Taiwan	adapted MBSR/inactive	9/weekly	128	78.9 (7.3)	NR	65	depression, relocation stress	glycated haemoglobin
# 13	Fam et al., 2020	*clinical*:[d] outpatients with mild cognitive impairment	Petersen criteria: < 1.5 *SD* in six cognitive domains; diagnosis made by consensus panel	Singapore	adapted MBSR/active	12/weekly	47	71.7[¤]	4.1[¤]	74	general cognition, memory	temporal network efficiency
# 14	Monin et al., 2020	*community*: older couples with and with no metabolic syndrome	at least one partner with three out of abdominal obesity, hypertension, hypertriglyceridemia, low HDL, fasting glucose	USA	MBSR/inactive	8/weekly	22	67.7[¤]	NR	NR	perceived stress, self-reported health, mindfulness, relationship satisfaction	LDL, HDL, fasting glucose, triglycerides; systolic and diastolic blood pressure
# 15	Ng et al., 2020	*clinical*:[d] outpatients with mild cognitive impairment	diagnosis based on DSM-V, no dementia, no major psychiatric condition	Singapore	adapted MBSR/active	12/weekly + 6/monthly	55	71.3 (6.0)	NR	74	NR	BDNF, DHEA-S, hs-CRP, IL-1beta, IL-6, cortisol

Table 1. (continued)

Study number	Author/year	Study population°	Main inclusion/exclusion criteria	Country	MBI/control	Number/frequency of sessions	Sample size*	Age *M* (*SD*) [*SE*]	Education *M* (*SD*)	Gender (% F)	Clinical outcome	Physiological outcome
# 16	Lim et al., 2018	*clinical*: outpatients with mild cognitive impairment	*z*-score < 1.5 on one NPS test, independent function, no dementia	Singapore	adapted MBSR/active	12 weekly	60	NR	NR	NR	NR	multiple genes
# 17	Ashton et al., 2017	*clinical*: outpatients with depressive and/or anxiety symptoms	current diagnosis of a depressive and/or anxiety disorder, cognitive concerns, no dementia (Short Blessed Test)	USA	adapted MBSR/active	8/weekly	103	72.1 (5.7)	15.8 (2.8)	72	memory, executive functions, subjective cognitive concerns, anxiety and depression, chronic worry	REST, BDNF, RANTES, PAI-1
# 18	Smart et al 2017	*community*:[e] older adults with and with no subjective cognitive decline	self-reported cognitive concern; no dementia (Dementia Rating Scale < 136, MMSE < 25); MCI not allowed	Canada	adapted MBSR/active	8/weekly	38	69.8[¤]	16.8[¤]	53	anxiety, mood regulation, mindfulness	error-related negativity, error positivity
# 19	Wetherell et al., 2017	*clinical*: outpatients with depression or anxiety and cognitive concerns	diagnosis based on DSM-IV, cognitive concerns, no dementia diagnosis and Short Blessed Test < 10	USA	adapted MBSR/active	8/weekly	103	71.9 (5.4)	15.6 (2.6)	73	memory, cognitive control, worry, depression, anxiety, global improvement	cortisol

Table 1. (continued)

Study number	Author/year	Study population°	Main inclusion/exclusion criteria	Country	MBI/control	Number/frequency of sessions	Sample size*	Age *M* (*SD*) [*SE*]	Education *M* (*SD*)	Gender (% F)	Clinical outcome	Physiological outcome
# 20	Smart et al., 2016	*community*:[e] older adults with and without SCD	self-reported cognitive concern; no dementia (Dementia Rating Scale < 136, MMSE < 25); MCI not allowed	Canada	adapted MBSR/active	8/weekly	38	69.8[¤]	16.8[¤]	53	cognitive complaints, depression, memory self-efficacy, mindfulness	whole brain volume; P3 amplitude
# 21	Moynihan et al., 2013	*community*: older adults	no cognitive deficit (MMSE < 24); no psychiatric disorders (screening interview)	USA	MBSR/inactive	8/weekly	228	73.4[¤]	16.4[¤]	62[¤]	executive functions, depression, perceived stress, mindfulness	frontal alpha asymmetry
# 22	Palta et al., 2012	*community*: older adults	African-Americans living in low-income senior housing facility	USA	adapted MBSR/active	8/weekly	20	72.9[¤]	11.6[¤]	NR	NR	systolic and diastolic blood pressure

The studies are ordered by year and first author. °Same letter indicates same study sample. The articles were considered as separate studies because they examined different physiological outcomes. *Total number of randomized participants. [¤]Data estimated based on weighted mean in MBI and control groups. *NR*, not reported

BDNF, brain-derived neurotrophic factor; *CRP*, C-reactive protein; *DHEA-S*, dehydroepiandrosterone sulfate; *DSM*, Diagnostic and Statistical Manual; *ES*, error standard; *HDL*, high-density lipoprotein; *hs-CRP*, high-sensitivity C-reactive protein; *IgG*, immunoglobulin G; *IL*, interleukin; *LDL*, low-density lipoprotein; *MBCT*, mindfulness-based cognitive therapy; *MBSR*, mindfulness-based stress reduction; *MCI*, mild cognitive impairment; *MCP*, monocyte chemoattractant protein; *MMSE*, Mini Mental State Examination; *NR*, nuclear receptor (mineralocorticoid receptor); *PAI*, plasminogen activator inhibitor; *RANTES*, regulated on activation, normal T cell expressed and secreted; *REST*, repressor element 1-silencing transcription; *SCD*, subjective cognitive decline; *SD*, standard deviation

Seven studies (32%) used the standard curriculum of MBSR ($n = 6$) (# 1; 3; 5; 8; 14; 21) or MBCT ($n = 1$) (# 4), whereas 15 studies (68%) used adapted MBSR ($n = 12$) (# 9–13; 15–20; 22) or adapted MBCT ($n = 3$) (# 2; 6–7) programs. In adapted MBSR/MBCT, typical adaptations include shortening the duration of sessions, reducing the number of sessions or omitting the retreat day, adapting the psychoeducational content on the basis of the target population, or adapting the mindful movement for participants with reduced mobility. The most active comparators ($n = 14$, 64%) were health education programs that consisted of health talks encompassing general topics (e.g., diet, sleep, exercise) and/or topics pertinent to common medical conditions (hypertension, diabetes, depression, dementia). One study used a cognitive fitness training program based on puzzle solving. All the active comparators were designed to match the time frame and attention received by the intervention group. The inactive comparator was treatment as usual ($n = 4$) or waiting list ($n = 3$).

Quality Assessment

A summary of the risk of bias assessment and details for individual studies is provided in Online Resource 2. The overall rating was indicative of medium concern for risk of bias in 14 studies (64%) (# 2; 4–6; 10–13; 16–18; 20–22), high risk in one study (# 7), and low risk in the remaining seven studies (# 1; 3; 8–9; 14–15; 19).

Synthesis of Results

An overview of the physiological outcomes grouped by the stress-related system is provided in Table 2. The physiological outcomes that contributed to the quantitative synthesis. They are numbered to be identified in the albatross plots. It follows the list of outcomes that did not contribute to data synthesis, with the reason for exclusion. A brief description of the physiological findings is provided for all the outcomes (see Table 2 for details).

Figure 3 shows the albatross plots for the stress-related system. Overall, more than half (24 out of 43) of the data points were rightward distributed, indicating that the physiological outcomes conveyed a positive effect of MBIs on the stress system. A third of the physiological outcomes (14 out of 43) were related to brain circuits and signalling, indicating that this stress-related system was a key target for examining the physiological effects of MBIs in older adults. The data points were scattered across the *y*-axis, indicating great heterogeneity in terms of sample size, ranging from 14 (# 20) to 542 (# 1) participants. The *p*-value analysis revealed a significant positive effect of MBIs on brain circuits and signalling (combined p-value < 0.001, $n = 14$ physiological outcomes, $n = 10$ studies), and the estimated effect size ranged from low to medium.

Concerning the number of outcomes, the HPA axis and the immune system were the least studied—only four physiological outcomes for each one. The sample size ranged from 55 (# 15) to 182 (# 3; 8). Quantitative data synthesis revealed a significant positive effect of MBIs on both stress-related systems: the combined *p*-values were $p = 0.011$ for the HPA axis ($n = 4$ physiological outcomes, $n = 3$ studies) and $p = 0.037$ for the immune system ($n = 4$ physiological outcomes, $n = 2$ studies). The physiological outcomes fell between the standardised mean difference contours of 0.20 and 0.50, indicating a small effect size.

The number of physiological outcomes included in the SAM axis and gene expression and epigenetic mediators was quite large ($n = 8$ and $n = 13$, respectively); however, the outcomes came from a relatively low number of studies ($n = 3$ and $n = 2$, respectively). For these stress-related systems, the combined *p*-value analysis was significant as well ($p = 0.004$ for the SAM axis and $p < 0.001$ for gene expression and epigenetic mediators). The estimated effect size was medium to high, but the sample size was very small ($n < 40$). Furthermore, it should be noted that the quality assessment was indicative of a high risk of bias for one of the two studies that examined gene expression and epigenetic mediators due to a non-randomised design.

Sensitivity analysis revealed that the effect of MBIs on stress-related systems remained significant when Stouffer's method was used (see Online Resource 3). The minimum number of outcomes needed for the subgroup analysis was available only for brain circuits and signalling. The results revealed a significant positive effect of MBIs in both the clinical (combined p-value < 0.001, $n = 7$ physiological outcomes, $n = 6$ studies) and community (combined p-value $= 0.002$, $n = 7$ physiological outcomes, $n = 4$ studies) populations (see the albatross plots in Online Resource 3).

Discussion

In this review, we examined the effects of MBIs on physiological markers related to the stress system in older adults. Quantitative data synthesis revealed that MBIs have a physiological influence on brain circuits and signalling, the SAM axis, the HPA axis, the immune system, gene expression and epigenetic mediators. The effects on brain circuits and signalling were noticeable in both clinical and community populations.

We acknowledge that the findings from this systematic review should be considered preliminary. The large heterogeneity of physiological outcomes may have caused confounding effects of MBIs. We accounted for this heterogeneity by grouping physiological outcomes by stress-related

Table 2. Effects of mindfulness-based interventions on physiological outcomes grouped by the systems involved in the stress response

Stress-related system		***Physiological outcome characteristics***			***Intervention (n)***		***Physiological findings***	***Quantitative synthesis***		***Refs***
	Measure	***Exam/sample***	***Type of measurement***	***Timepoint***	***MBI***	***Control***		***Reason for exclusion***	***ID n***	
Brain circuits and signalling										
Brain structure	whole brain	sMRI	volume	pre-post MBI	8	6	whole brain volume: increased	-	1	Smart et al., 2016
	middle frontal gyrus-amygdala tract	DWI	fractional anisotropy	pre-post MBI	29	24	middle frontal gyrus-amygdala tract FA: increased	-	2	Li et al., 2022
	whole brain	sMRI	cortical thickness	pre-post MBI 9 months	20	18	whole brain cortical thickness: no change	-	3	Yu et al., 2021
	hippocampus	sMRI	volume	pre-post MBI 18 months	274	268	hippocampal volume: no change	-	4	Lenze et al., 2022
	dorsolateral prefrontal cortex	sMRI	cortical thickness, surface area	pre-post MBI 18 months	274	268	dorsolateral prefrontal cortical thickness and area: no change	-	5, 6	Lenze et al., 2022
	left inferior temporal gyrus	sMRI	cortical thickness	pre-MBI	20	18	left inferior temporal gyrus cortical thickness: increased	no exact *p*-value time × intervention	-	Yu et al., 2021
	anterior cingulate, frontal pole	sMRI	cortical thickness	pre-MBI 9 months	20	18	left anterior cingulate decreased, right frontal pole increased (not significant after multiple correction)	no pre-post *p*-value time × intervention	-	Yu et al., 2021
	insula orbitofrontal	sMRI	cortical thickness	pre-MBI 9 months	20	18	insula and orbitofrontal cortical thickness: no change	no pre-post *p*-value time × intervention	-	Yu et al., 2021
	hippocampus posteromedial cortex	sMRI	volume	pre-post MBI	48	49	hippocampal and posteromedial cortex volume: no change	no exact *p*-value time × intervention	-	Sevinc et al., 2021
Brain function	frontal alpha asymmetry	EEG	right-left alpha power activity at mid-frontal	pre-post MBI 3 months	N/R	N/R	leftward alpha asymmetry: increased	-	7	Moynihan et al., 2013

Table 2. (continued)

Stress-related system	Measure	Physiological outcome characteristics: Exam/sample	Type of measurement	Timepoint	Intervention (n): MBI	Control	Physiological findings	Quantitative synthesis: Reason for exclusion	ID n	Refs
	temporal networks efficiency	rs-fMRI	dynamic FC	pre-post MBI	19	17	temporal global efficiency: increased temporal local efficiency: no change		8 9	Fam et al., 2020
	hippocampus- posteromedial cortex FC	rs-fMRI	seed-based correlation	pre-post MBI	48	49	left hippocampus-right angular gyrus FC: no change right hippocampus-right precuneus FC: no change	-	10 11	Sevinc et al., 2021
	P3 amplitude	EEG	ERPs: response to inhibitor control task	pre-post MBI	17	17	P3 amplitude: increased	no *p*-value time × intervention	-	Smart et al., 2016
	error-related negativity and error positivity	EEG	ERPs: response to inhibitor control task	pre-post MBI	N/R	N/R	error-related negativity: increased error positivity: no change in MBI, increased in controls	no *p*-value time × intervention	-	Smart et al., 2017
	whole brain FC	rs-fMRI	ROI-to-ROI correlation	pre-post MBI	30	25	right middle frontal gyrus-right amygdala FC: increased	no *p*-value time × intervention	–	Li et al., 2022
	whole brain activity	task-fMRI	activation to negative emotions	pre-post MBI	20	13	left superior temporal gyrus: brain activation reduced	no exact *p*-value time × intervention	-	Liu et al., 2022
	whole brain FC	rs-fMRI	correlation and covariance	pre-MBI 6 months 18 months	105	84	whole brain FC: no change	no exact *p*-value time × intervention	-	Snyder et al., 2022
Neural signalling	REST	plasma	levels	pre-post MBI	17	20	REST: increased	-	12	Ashton et al., 2017
	BDNF	plasma	levels	pre-post MBI 9 months	28	27	BDNF: no change	-	13	Ng et al., 2020
	amyloid beta-42	saliva	levels	pre-post MBI 9 months	28	27	amyloid beta-42: no change	-	14	Ng et al., 2021
	BDNF	plasma	levels	pre-post MBI	17	20	BDNF: no change	no *p*-value	-	Ashton et al., 2017
Sympathetic-adreno-medullar axis										

Table 2. (continued)

Stress-related system		*Physiological outcome characteristics*			*Intervention (n)*		*Physiological findings*	*Quantitative synthesis*		*Refs*
	Measure	*Exam/sample*	*Type of measurement*	*Timepoint*	*MBI*	*Control*		*Reason for exclusion*	*ID n*	
Autonomic	blood pressure	automated sphygmomanometer	diastolic and systolic levels	pre-post MBI	12	8	diastolic blood pressure: decreased systolic blood pressure: decreased	-	1 2	Palta et al., 2012
	blood pressure	automated sphygmomanometer	diastolic and systolic levels	pre-post MBI 3 months	12	10	diastolic blood pressure: no change diastolic blood pressure: no change	-	3 4	Monin et al., 2020
Metabolic	LDL, HDL, glucose, tryglicerides	blood	levels	pre-post MBI 3 months	12	10	LDL, HDL, glucose, triglycerides levels: no change		5–8	Monin et al., 2020
	glycated haemoglobin	medical records	levels	pre-post MBI	60	60	glycated haemoglobin decreased (in subgroup with high baseline levels)	no *p*-value time × intervention	-	Chen et al., 2020
Hypothalamus-pituitary-adrenal axis										
	functional glucocorticoid resistance	whole blood	IL-6 levels in response to dexamethasone	pre-post MBI 3 months	89	93	functional glucocorticoid resistance increase: buffered	-	1	Lindsay et al., 2021
	cortisol	saliva	daily peak	pre-post MBI	45	53	cortisol peak: decreased (in subgroup with high baseline levels)	-	2	Wetherell et al., 2017
	cortisol	saliva	levels	pre-post MBI 9 months	28	27	cortisol levels: no change	-	3	Ng et al., 2020
	DHEA-s	plasma	levels	pre-post MBI 9 months	28	27	DHEA-s levels: no change	-	4	Ng et al., 2020
Immune system										
	IL-6	whole blood	lipopolysaccharide-stimulated levels	pre-post MBI 3 months	89	93	IL-6 levels: increased	-	1	Lindsay et al., 2022

Table 2. (continued)

Stress-related system		*Physiological outcome characteristics*			*Intervention (n)*		*Physiological findings*	*Quantitative synthesis*		*Refs*
	Measure	*Exam/sample*	*Type of measurement*	*Timepoint*	*MBI*	*Control*		*Reason for exclusion*	*ID n*	
	IL-1beta	saliva	levels	pre-post MBI 9 months	28	27	IL-1beta levels: no change (decreased in male subgroup)	-	2	Ng et al., 2020
	IL-6	saliva	levels	pre-post MBI 9 months	28	27	IL-6 levels: no change (decreased in male subgroup)	-	3	Ng et al., 2020
	hs-CRP	plasma	levels	pre-post MBI 9 months	28	27	hs-CRP levels: no change	-	4	Ng et al., 2020
	RANTES, PAI-1	plasma	levels	pre-post MBI	17	20	RANTES, PAI-1 levels: no change	no *p*-value	-	Ashton et al., 2017
Gene expression and epigenetic mediators										
	multiple microRNA	neuron-derived extracellular vesicles	microRNA expression	pre-post MBI	19	10	miR-29 expression: increased miR-9, miR124, miR-181a, miR-146a expression: no change	-	1 2–5	Hashizume et al., 2021
	multiple genes	neuron-derived extracellular vesicles	gene expression	pre-post MBI	19	10	*DNMT3A, DNMT3B, BACE1* expression: down-regulated *STAT3*: no change	-	6–8 9	Hashizume et al., 2021
	CRP, *MCP1*, *IL-1beta*, *NR3C2*	peripheral blood mononuclear cells	gene expression	pre-post MBI	17	20	*NR3C2, CRP, IL-1beta, MCP1* expression: no change	-	10–13	Belliveau et al., 2021
	multiple genes	blood	gene expression	pre-post MBI	26	27	no change	no *p*-value	-	Lim et al., 2018

The physiological outcomes were included in the combined *p*-value analysis. The ID number refers to the corresponding physiological outcome in the albatross plots

BACE1, beta-site amyloid precursor protein cleaving enzyme 1; *BDNF*, brain-derived neurotrophic factor; *CRP*, C-reactive protein; *DHEA-s*, dehydroepiandrosterone sulfate; *DNMT3A*, DNA methyltransferase 3 alpha; *DNMT3B*, DNA methyltransferase 3 beta; *DWI*, diffusion-weighted imaging; *FC*, functional connectivity; *HDL*, high-density lipoprotein; *hs-CRP*, high-sensitivity C-reactive protein; *IgG*, immunoglobulin G; *IL*, interleukin; *MBI*, mindfulness-based intervention; *NR*, nuclear receptor (mineralocorticoid receptor); *LDL*, low-density lipoprotein; *MCP*, monocyte chemoattractant protein; *miR-29c*, microRNA-29c; *PAI*, plasminogen activator inhibitor; *RANTES*, regulated on activation, normal T cell expressed and secreted; *REST*, repressor element 1-silencing transcription; *rs-fMRI*, resting-state functional magnetic resonance imaging; *sMRI*, structural magnetic resonance imaging; *NA*, not applicable; *NR*, not reported

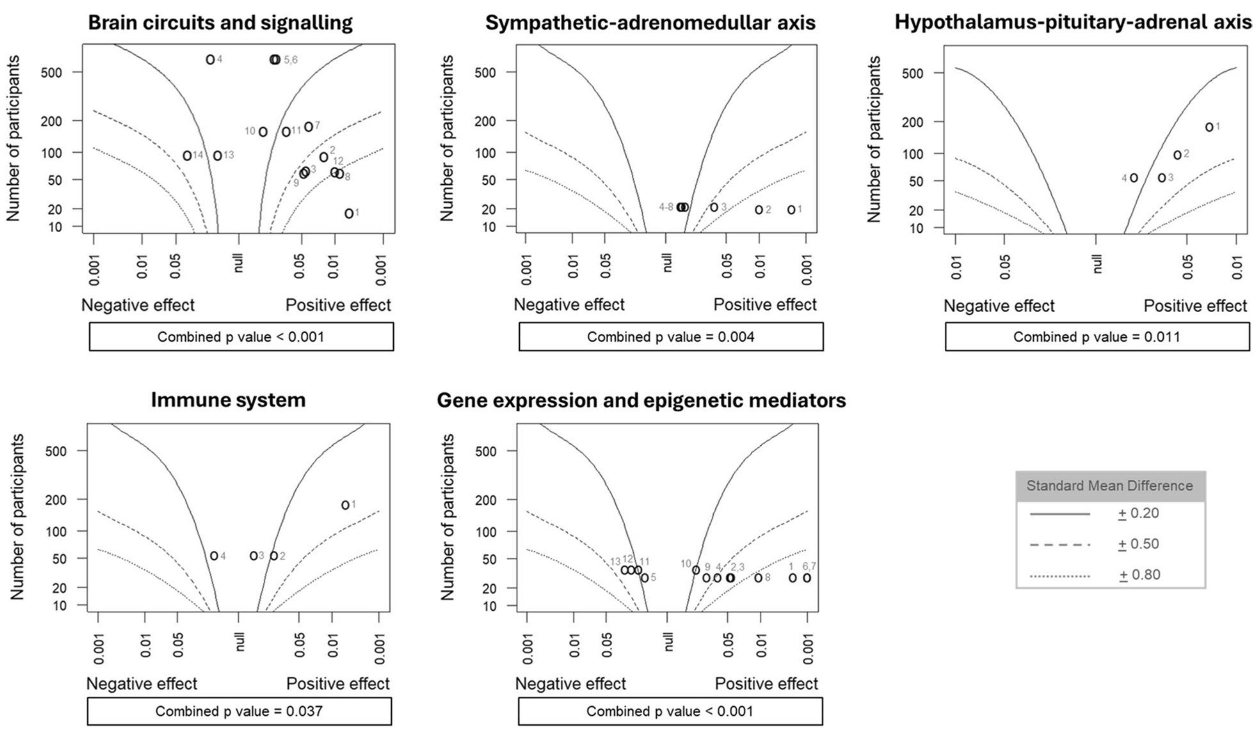

Fig. 3 Albatross plots for the physiological effects of mindfulness-based interventions compared to controls by stress-related biological system. Each circle represents a physiological outcome. For each outcome, the *p*-value and effect direction (on the *x*-axis) against the sample size (on the *y*-axis) are plotted. The light grey numbers identify the physiological outcomes in Table 2

systems; however, the variety of outcomes was apparent within each system. This was an inevitable shortcoming inherent to the scope of this review. With respect to the use of the combining the *p*-value method to our data, the exclusion from the analysis of some outcomes for which an appropriate *p*-value was not available may have been a further confounding factor, particularly when the outcome indicated no intervention effect. However, this method did not account for missing data. A further intrinsic limitation was that the analysis did not distinguish between evidence from large studies with small effects and small studies with large effects. For example, the finding of positive effects of MBIs on the SAM axis should be considered exploratory because it came from only two studies with small sample sizes. Methodological shortcomings may also be derived from the weaknesses of the included studies. In the case of gene expression and epigenetic mediators, the significance of quantitative analysis relied on a single study for which a high risk of bias (i.e., a non-randomised trial) emerged.

The effects of MBIs on brain circuits in older adults are in line with systematic reviews in younger adults that demonstrated the ability of MBIs to modulate brain function, i.e., resting-state (Gotink et al., 2016; Pernet et al., 2021; Sezer et al., 2022; Young et al., 2018) and task-related (Gotink et al., 2016; Young et al., 2018) functional connectivity, and brain structure (Gotink et al., 2016; Pernet et al., 2021). However, a major caveat that emerged from this review and the literature was the heterogeneity of outcomes and results. MBI modulation effects were observed in a wide variety of brain regions (prefrontal cortex, cingulate cortex, hippocampus, insula, amygdala, caudate nucleus, and precuneus were the most commonly studied), and subregions (e.g., ventrolateral, dorsolateral, or dorsomedial prefrontal cortex). In addition, the findings often conflicted. For example, increased or decreased activation or connectivity was found in the same brain region or network (Young et al., 2018). Methodological factors can explain this heterogeneity. First, imaging methods and analyses were quite different (e.g., resting-state vs. task-fMRI, region of interest vs. whole brain analysis, and different image preprocessing steps and algorithms). Second, the rationale for choosing outcomes differed: some studies focused on brain areas drawn from traditional meditation studies, whereas others focused on brain regions related to the clinical conditions of the target population. Starting from our conceptualisation of chronic stress as a possible mediator of MBIs, we suggest that future neuroimaging studies should examine brain areas associated with stressor processing. This can represent a valuable way to increase the consistency of findings in future studies.

The heterogeneity of outcomes and results also characterised the immune system. Our finding indicating a positive effect of MBIs in older adults was based on IL-6, C-reactive protein, and IL-1β. These results were in line with those of a recent meta-analysis of 48 studies showing an effect of MBIs on reducing C-reactive protein and IL-6 levels and increasing the number of CD4+ cells (Dunn & Dimolareva,2022). Nevertheless, previous systematic reviews and meta-analyses reported mixed results, depending on which biomarkers they focused on (e.g., circulating cytokines and chemokines, immune cell count, antibody response) (Black & Slavich, 2016; Sanada et al., 2020). The recommendations suggested by the authors of the first systematic review on this topic are still valuable—to provide a clear rationale for studying one or more immune biomarkers and to calibrate tests for changes in immune parameters a priori to avoid false-negative results (Black & Slavich, 2016).

Methodologic issues characterised the measurement of a well-recognised chronic stress marker belonging to the HPA axis—cortisol. Previous systematic reviews and meta-analyses have shown beneficial effects of MBIs on cortisol, with effect sizes ranging from moderately low (Sanada et al., 2016) to medium (Rogerson et al., 2024) and moderate heterogeneity in terms of sample and measurement methods (Sanada et al., 2016). This heterogeneity was well exemplified by the studies included in this review: salivary cortisol was measured either as a peak (i.e., the higher of two out of three values taken at different times during wakening) (# 19) or as a level (i.e., the value taken at a fixed time frame in the morning) (# 15). The use of recommendations for cortisol measurement (Segerstrom et al., 2014) can provide more reliable and generalizable results. DHEA-s has been less studied than cortisol as a physiological outcome of MBIs (Jørgensen et al., 2021). As the secretion of DHEA-s decreases with age (Corona et al., 2013), measurement issues (i.e., concentrations lower than the limit of detection) could limit its use as an outcome of MBIs in older adults. Functional glucocorticoid resistance has also rarely been examined, likely because of technical requirements (i.e., in vitro assays). These findings warrant further consideration in larger, well-designed studies.

Metabolic outcomes, such as glucose and lipid control measures, were commonly examined in patients with type 2 diabetes. Two recent systematic reviews and meta-analyses evaluated the effect of MBIs in reducing glycated haemoglobin levels in diabetic patients, with contrasting results (Fisher et al., 2023; Heo et al., 2023). A study included in this review, which showed a positive effect only in patients with high glycated haemoglobin levels at baseline (# 12), did not contribute to data synthesis for methodological reasons; the role of glycated haemoglobin as a physiological outcome of MBIs in older adults requires further evaluation. Instead, blood pressure was included in our data synthesis and contributed to a positive effect of MBIs on the SAM axis. This finding is in line with a recent systematic review and meta-analysis showing a positive effect of MBSR in reducing systolic and diastolic blood pressure among individuals with prehypertension or hypertension (Geiger et al., 2023). Considering the high prevalence of hypertension in older adults, further studies are warranted to confirm the beneficial effect of MBIs on blood pressure levels.

Exploration of the impact of MBIs on the molecular mechanisms of gene expression and epigenetics is still in its infancy. This review revealed a positive effect of MBIs on gene expression based on two studies: one examined the expression of targeted genes involved in chronic stress (i.e., *NR3C*) and inflammation (*CRP*, *MCP1*, and *IL-1beta*) responses (# 6), while the other evaluated the expression of miRNAs (# 7). To our knowledge, only one systematic review has examined this topic (Buric et al., 2017). The authors included any type of mind-body intervention (mindfulness, yoga, tai chi, qigong, etc.), research design (cross-sectional and longitudinal, controlled and uncontrolled), or sample (clinical and nonclinical). They retrieved 18 gene expression studies, from which a general pattern of downregulation of proinflammatory genes and pathways emerged (Buric et al., 2017). Two more recent narrative reviews (Kaliman, 2019; Venditti et al., 2020) reported the findings of two studies showing the effects of MBSR on the mechanisms of methylation of stress-related genes or histone acetylation levels. The methodological challenge of selecting appropriate methods for data analysis in a rapidly evolving technology scenario has been highlighted (Kaliman, 2019).

Notably, our finding of a physiological influence of MBIs on the stress system is in line with a recent conceptual model illustrating the mediating mechanisms of mindfulness meditation in ageing. Starting from mindfulness-related changes in psychological processes (e.g., emotion and attention regulation), a cascading effect of downregulating detrimental factors, such as chronic stress, and upregulating beneficial factors, such as cognitive and brain reserves, can result in a positive influence on ageing-related processes according to the reported conceptual model (Lutz et al., 2021). The mechanisms may include activation of brain central-executive networks; enhanced peripheral-central integration of information; related changes in autonomic balance and immune function; and modulation of epigenetic regulators (Lutz et al., 2015; Taylor et al., 2010). This model is well aligned with the logic model (Fig. 1) proposed in this review.

Limitations and Future Directions

The findings of this review must be interpreted in the context of its limitations. First, the albatross plot is a visual display method, which allowed only an approximate examination of effect size (Harrison et al., 2017), preventing the drawing of definitive conclusions about the magnitude of intervention effects on single physiological outcomes. Second, the small number of studies included in this systematic review may have limited our ability to accurately represent the complex physiology of the chronic stress response, making it difficult to draw firm conclusions about the effects of MBIs at the whole-system level. In addition, the heterogeneity of the studies limited our ability to examine the moderator effect of the MBI or comparator characteristics in subgroup analyses. Stratifications by gender and geographical origin are worthy of further investigation. Finally, the list of chronic stress mechanisms and stress markers outlined in the logic model may not be exhaustive, since it stemmed from a literature search that was not conducted using systematic procedures.

Several chronic stress markers that we outlined in the logic model as potential physiological outcomes of MBI studies have not been evaluated in older adults. A short overview of these candidate physiological markers, with some hints about the potential and limitations of their measurement, was provided below. At the brain circuit and signalling level, the default mode network, salience network, and central executive network (i.e., the large-scale brain networks supporting core mental and behavioural processes) (Menon, 2011) have not been investigated as physiological outcomes of MBIs in older adults, even if they are associated with stress-related disorders (Kunimatsu et al., 2020; Szeszko & Yehuda, 2019). Unbiased data-driven analysis techniques, such as independent component analysis, should be preferred in future studies. The hypothalamus and brainstem nuclei (i.e., the locus coeruleus and nucleus of the solitary tract) should also be examined, as they activate the SAM and HPA axes, thus representing potentially sensitive physiological outcomes for MBIs. While the measurement of these regions has generally been difficult because of their small size and lack of automated tools, recent advances in imaging techniques and processing, such as automated algorithms for nuclei segmentation (Billot et al., 2020) and sensitive MRI sequences (Priovoulos et al., 2018), might facilitate the investigation of these areas in future MBI studies. At the SAM axis level, heart rate variability is decreased in chronic stress because of the prevalent influence of the sympathetic nervous system over the vagal system on heart rate. The recent use of devices (i.e., mobile apps or smartwatches) can make the measurement more feasible in older adults than traditional 24-h Holter monitoring without affecting the accuracy of the procedure (Arantes et al., 2022). At the HPA axis level, telomere length and activity can be reduced as a result of chronic activation of the HPA axis and consequent oxidative stress (Epel et al., 2004). Since they also play a role as biological determinants of cellular senescence and longevity (Rossiello et al., 2022), telomeres can represent a compelling measure of the MBI effect in older adults. Another marker linked to both the chronic stress response and biological ageing is nuclear factor kappa B. This inducible transcription factor plays a key role in regulating immune responses, cellular homeostasis, and cellular senescence (Thoms & Stark, 2021). The measurement can be taken in peripheral blood mononuclear cells. How stress affects gene expression through epigenetic modifications and how MBIs can modulate gene expression are a growing matter of interest. Studying the expression of genes involved in the regulation of both chronic stress and mechanisms of ageing, such as inflammation and oxidative stress, could be valuable in older adults. Notably, the epigenetic ageing rate (i.e., the level of deviation between the DNA methylation age and the chronological age) in meditators significantly decreases with the number of years of formal practice, suggesting protective effects and health benefits in the long term (Kaliman, 2019). Further studies on this topic are warranted.

We envisage that future research on the neurobiological effects of MBIs will increasingly focus on multiple biomarker measurements. In the research field of stress-related diseases, an allostatic load index incorporating multiple stress markers better predicted poor health outcomes than individual markers did in longitudinal studies of older adults (Seeman et al., 2001), as well as in clinical and nonclinical adult populations (Guidi et al., 2021). Interestingly, a recent study developed an allostatic index from a sample of 111 healthy older adults who underwent meditation training (Palix et al., 2025). The allostatic index was negatively associated with structural brain integrity in ageing- and stress-sensitive regions (Palix et al., 2025), suggesting its potential as a marker of stress-relieving interventions in older adults.

Alternative approaches to address the complex nature of stress-related pathways are suggested by systems biology. Systems biology is a multidisciplinary approach in biomedical research with the aim of studying complex phenomena by using methods (e.g., multi-omics data integration, machine learning) that were able to integrate genetic, epigenetic, molecular, and circuit data with clinical and environmental information (Argelaguet et al., 2020; Dalvie et al., 2021). For example, this approach allowed the elucidation of multiple stress-related pathways involved in posttraumatic stress disorder and major depression, paving the way for novel therapeutics (Daskalakis et al., 2024). Notably, a recent pilot study in a twin cohort explored the physiological effects of a 7-day meditation retreat through transcriptome, metabolomic, biochemical, heart rate, and EEG analyses, which revealed changes in gene expression, metabolites, cytokines, and spectral power correlations (Zuniga-Hertz et al., 2025). Although the study did not apply multilevel integration analysis, it demonstrated the feasibility of a multidisciplinary approach for studying the mechanisms by which meditation and other MBIs can improve health (Zuniga-Hertz et al., 2025). A drawback in designing studies with this approach can include the high costs related to the large number of individuals to be recruited and multiple biomarker collection.

Conclusion

We provided preliminary support for the concept that MBIs have positive effects on physiological outcomes related to stress exposure and response in older adults. Future clinical trials including stress markers as physiological outcomes of MBIs are warranted to provide a basis of evidence for this conceptual framework. On the basis of the results of this review, we suggest that physiological measurements from EEG (event-related potentials or alpha power activity) and from saliva samples (cortisol and interleukins), along with blood pressure measurements, may represent a brief and affordable set of biomarkers to be collected in future MBI studies. In addition, the complex interplay between physiological changes and clinical outcomes should be examined. To this end, an integrated biopsychosocial research approach should be implemented to fully understand the connections among MBIs, chronic stress mechanisms and markers, and clinical improvement. This conclusive understanding may inform health care providers about the effectiveness of MBIs as a stress-relieving strategy to promote mental health in older adults.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12671-025-02718-1.

Acknowledgements The IRCCS Istituto Centro San Giovanni di Dio Fatebenefratelli acknowledges support from the Italian Ministry of Health (Ricerca Corrente).

Author Contribution Galluzzi: conceptualization, data curation, formal analysis, investigation, supervision, writing—original draft, and writing—review and editing. Singh Solorzano: formal analysis, investigation, and writing—review and editing. Marizzoni: investigation, and writing—review and editing. Gatti: investigation, and writing—review and editing. Gualco: investigation, and writing—review and editing. Lanfredi: investigation, and writing—review and editing. Rossi: investigation, and writing—review and editing. Cattaneo: investigation, and writing—review and editing. Frisoni: investigation, and writing—review and editing. Crescentini: investigation, and writing—review and editing. Di Maria: investigation, methodology, supervision, and writing—review and editing. Pievani: investigation, supervision, and writing—review and editing.

Data Availability Data used for analyses is available in a public repository (https://zenodo.org/records/17465877).

Declarations

Ethics Approval An ethics approval was not necessary for this study as we did not collect primary data.

Consent to Participate Not relevant.

Conflict of interest The authors declare no competing interests.

Use of Artificial Intelligence Artificial Intelligence was not used for editing the manuscript to improve English language.

References

Adams, J., Hillier-Brown, F. C., Moore, H. J., Lake, A. A., Araujo-Soares, V., White, M., & Summerbell, C. (2016). Searching and synthesising "grey literature" and "grey information" in public health: Critical reflections on three case studies. *Systematic Reviews, 5*(1), 164. https://doi.org/10.1186/s13643-016-0337-y

Arantes, F. S., Rosa Oliveira, V., Leão, A. K. M., Afonso, J. P. R., Fonseca, A. L., Fonseca, D. R. P., Mello, D. A. C. P. G., Costa, I. P., Oliveira, L. V. F., & da Palma, R. K. (2022). Heart rate variability: A biomarker of frailty in older adults? *Frontiers in Medicine, 9*, 1008970. https://doi.org/10.3389/fmed.2022.1008970

Argelaguet, R., Arnol, D., Bredikhin, D., Deloro, Y., Velten, B., Marioni, J. C., & Stegle, O. (2020). MOFA+: A statistical framework for comprehensive integration of multi-modal single-cell data. *Genome Biology, 21*(1), 111–121. https://doi.org/10.1186/s13059-020-02015-1

Ashton, N. J., Hye, A., Leckey, C. A., Jones, A. R., Gardner, A., Elliott, C., Wetherell, J. L., Lenze, E. J., Killick, R., & Marchant, N. L. (2017). Plasma REST: A novel candidate biomarker of Alzheimer's disease is modified by psychological intervention in an at-risk population. *Translational Psychiatry, 7*(6), e1148. https://doi.org/10.1038/tp.2017.113

Bainomugisa, C., & Mehta, D. (2022). How stress affects gene expression through epigenetic modifications. In A. Y. Nagy (Ed.), *Epigenetics of stress and stress disorders* (pp. 99–118). Academic Press.

Beard, J. R., Officer, A. M., & Cassels, A. K. (2016). The world report on ageing and health. *The Gerontologist, 56*, S163–S166. https://doi.org/10.1093/geront/gnw037

Becker, B. J. (1994). Combining significance levels. In H. Cooper & L. V. Hedges (Eds.), *Handbook of research synthesis* (pp. 215–235). The Russell Sage Foundation.

Belliveau, C., Nagy, C., Escobar, S., Mechawar, N., Turecki, G., Rej, S., & Torres-Platas, S. G. (2021). Effects of mindfulness-based cognitive therapy on peripheral markers of stress and inflammation in older-adults with depression and anxiety: A parallel analysis of a randomized controlled trial. *Frontiers in Psychiatry, 12*, 804269. https://doi.org/10.3389/fpsyt.2021.804269

Benzies, K. M., Premji, S., Hayden, K. A., & Serrett, K. (2006). State-of-the-evidence reviews: Advantages and challenges of including grey literature. *Worldviews on Evidence-Based Nursing, 3*(2), 55–61. https://doi.org/10.1111/j.1741-6787.2006.00051.x

Billot, B., Bocchetta, M., Todd, E., Dalca, A. V., Rohrer, J. D., & Iglesias, J. E. (2020). Automated segmentation of the hypothalamus and associated subunits in brain MRI. *NeuroImage, 223*, 117287. https://doi.org/10.1016/j.neuroimage.2020.117287

Black, D. S., & Slavich, G. M. (2016). Mindfulness meditation and the immune system: A systematic review of randomized controlled trials. *Annals of the New York Academy of Sciences, 1373*(1), 13–24. https://doi.org/10.1111/nyas.12998

Brown, K. W., & Ryan, R. M. (2003). The benefits of being present: Mindfulness and its role in psychological well-being. *Journal of Personality and Social Psychology, 84*(4), 822–848. https://doi.org/10.1037/0022-3514.84.4.822

Brown, K. W., Weinstein, N., & Creswell, J. D. (2012). Trait mindfulness modulates neuroendocrine and affective responses to social evaluative threat. *Psychoneuroendocrinology, 37*(12), 2037–2041. https://doi.org/10.1016/j.psyneuen.2012.04.003

Buric, I., Farias, M., Jong, J., Mee, C., & Brazil, I. A. (2017). What is the molecular signature of mind-body interventions? A systematic review of gene expression changes induced by meditation and related practices. *Frontiers in Immunology, 8*, 670. https://doi.org/10.3389/fimmu.2017.00670

Campbell, M., McKenzie, J. E., Sowden, A., Katikireddi, S. V., Brennan, S. E., Ellis, S., Hartmann-Boyce, J., Ryan, R., Shepperd, S., Thomas, J., Welch, V., & Thomson, H. (2020). Synthesis without meta-analysis (SWiM) in systematic reviews: Reporting guideline. *British Medical Journal, 368*, l6890. https://doi.org/10.1136/bmj.l6890

Cardoner, N., Andero, R., Cano, M., Marin-Blasco, I., Porta-Casteràs, D., Serra-Blasco, M., Via, E., Vicent-Gil, M., & Portella, M. J. (2024). Impact of stress on brain morphology: Insights into structural biomarkers of stress-related disorders. *Current Neuropharmacology, 22*(5), 935–962. https://doi.org/10.2174/1570159X21666230703091435

Chambers, R., Gullone, E., & Allen, N. B. (2009). Mindful emotion regulation: An integrative review. *Clinical Psychology Review, 29*(6), 560–572. https://doi.org/10.1016/j.cpr.2009.06.005

Chen, S., Lin, H., Atherton, J. J., MacIsaac, R. J., & Wu, C. J. (2020). Effect of a mindfulness programme for long-term care residents with type 2 diabetes: A cluster randomised controlled trial measuring outcomes of glycaemic control, relocation stress and depression. *International Journal of Older People Nursing, 15*(3), e12312. https://doi.org/10.1111/opn.12312

Chiesa, A., & Serretti, A. (2009). Mindfulness-based stress reduction for stress management in healthy people: A review and meta-analysis. *Journal of Alternative and Complementary Medicine, 15*(5), 593–600. https://doi.org/10.1089/acm.2008.0495

Chiesa, A., Serretti, A., & Jakobsen, J. C. (2013). Mindfulness: Top-down or bottom-up emotion regulation strategy? *Clinical Psychology Review, 33*(1), 82–96. https://doi.org/10.1016/j.cpr.2012.10.006

Cinar, O., & Viechtbauer, W. (2022). The poolr package for combining independent and dependent p values. *Journal of Statistical Software, 101*, 1–42.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Erlbaum.

Corona, G., Rastrelli, G., Giagulli, V. A., Sila, A., Sforza, A., Forti, G., Mannucci, E., & Maggi, M. (2013). Dehydroepiandrosterone supplementation in elderly men: A meta-analysis study of placebo-controlled trials. *The Journal of Clinical Endocrinology and Metabolism, 98*(9), 3615–3626. https://doi.org/10.1210/jc.2013-1358

Creswell, J. D., Lindsay, E. K., Villalba, D. K., & Chin, B. (2019). Mindfulness training and physical health: Mechanisms and outcomes. *Psychosomatic Medicine, 81*(3), 224–232. https://doi.org/10.1097/PSY.0000000000000675

Dalvie, S., Chatzinakos, C., Al Zoubi, O., Georgiadis, F., PGC-PTSD Systems Biology workgroup, Lancashire, L., & Daskalakis, N. P. (2021). From genetics to systems biology of stress-related mental disorders. *Neurobiology of Stress, 15*, 100393. https://doi.org/10.1016/j.ynstr.2021.100393

Daskalakis, N. P., Iatrou, A., Chatzinakos, C., Jajoo, A., Snijders, C., Wylie, D., DiPietro, C. P., Tsatsani, I., Chen, C. Y., Pernia, C. D., Soliva-Estruch, M., Arasappan, D., Bharadwaj, R. A., Collado-Torres, L., Wuchty, S., Alvarez, V. E., Dammer, E. B., Deep-Soboslay, A., Duong, D. M., … & Ressler, K. J. (2024). Systems biology dissection of PTSD and MDD across brain regions, cell types, and blood. *Science, 384*(6698), eadh3707. https://doi.org/10.1126/science.adh3707

Dee, G., Ryznar, R., & Dee, C. (2023). Epigenetic changes associated with different types of stressors and suicide. *Cells, 12*(9), 1258. https://doi.org/10.3390/cells12091258

Dion, A., Muñoz, P. T., & Franklin, T. B. (2022). Epigenetic mechanisms impacted by chronic stress across the rodent lifespan. *Neurobiology of Stress, 17*, 100434. https://doi.org/10.1016/j.ynstr.2022.100434

Dragoş, D., & Tănăsescu, M. D. (2010). The effect of stress on the defense systems. *Journal of Medicine and Life, 3*(1), 10–18.

Dunn, T. J., & Dimolareva, M. (2022). The effect of mindfulness-based interventions on immunity-related biomarkers: A comprehensive meta-analysis of randomised controlled trials. *Clinical Psychology Review, 92*, 102124. https://doi.org/10.1016/j.cpr.2022.102124

Epel, E. S., Blackburn, E. H., Lin, J., Dhabhar, F. S., Adler, N. E., Morrow, J. D., & Cawthon, R. M. (2004). Accelerated telomere shortening in response to life stress. *Proceedings of the National Academy of Sciences of the United States of America, 101*(49), 17312–17315. https://doi.org/10.1073/pnas.0407162101

Fam, J., Sun, Y., Qi, P., Lau, R. C., Feng, L., Kua, E. H., & Mahendran, R. (2020). Mindfulness practice alters brain connectivity in community-living elders with mild cognitive impairment. *Psychiatry and Clinical Neurosciences, 74*(4), 257–262. https://doi.org/10.1111/pcn.12972

Fisher, V., Li, W. W., & Malabu, U. (2023). The effectiveness of mindfulness-based stress reduction (MBSR) on the mental health, HbA1C, and mindfulness of diabetes patients: A systematic review and meta-analysis of randomised controlled trials. *Applied Psychology: Health and Well-Being, 15*(4), 1733–1749. https://doi.org/10.1111/aphw.12441

Fox, K. C. R., Dixon, M. L., Nijeboer, S., Girn, M., Floman, J. L., Lifshitz, M., Ellamil, M., Sedlmeier, P., & Christoff, K. (2016). Functional neuroanatomy of meditation: A review and meta-analysis of 78 functional neuroimaging investigations. *Neuroscience and Biobehavioral Reviews, 65*, 208–228. https://doi.org/10.1016/j.neubiorev.2016.03.021

GBD 2019 Ageing Collaborators. (2022). Global, regional, and national burden of diseases and injuries for adults 70 years and older: Systematic analysis for the Global Burden of Disease 2019 Study. *British Medical Journal, 376*, e068208-068208. https://doi.org/10.1136/bmj-2021-068208

Geiger, C., Cramer, H., Dobos, G., & Kohl-Heckl, W. K. (2023). A systematic review and meta-analysis of mindfulness-based stress reduction for arterial hypertension. *Journal of Human Hypertension, 37*(3), 161–169. https://doi.org/10.1038/s41371-022-00764-z

Geiger, P. J., Boggero, I. A., Brake, C. A., Caldera, C. A., Combs, H. L., Peters, J. R., & Baer, R. A. (2016). Mindfulness-based interventions for older adults: A review of the effects on physical and emotional well-being. *Mindfulness, 7*(2), 296–307. https://doi.org/10.1007/s12671-015-0444-1

Godoy, L. D., Rossignoli, M. T., Delfino-Pereira, P., Garcia-Cairasco, N., & de Lima Umeoka, E. H. (2018). A comprehensive overview on stress neurobiology: Basic concepts and clinical implications. *Frontiers in Behavioral Neuroscience, 12*, 127. https://doi.org/10.3389/fnbeh.2018.00127

González-Martín, A. M., Aibar-Almazán, A., Rivas-Campo, Y., Marín-Gutiérrez, A., & Castellote-Caballero, Y. (2023). Effects of

mindfulness-based cognitive therapy on older adults with sleep disorders: A systematic review and meta-analysis. *Frontiers in Public Health, 11*, 1242868. https://doi.org/10.3389/fpubh.2023.1242868
Gotink, R. A., Meijboom, R., Vernooij, M. W., Smits, M., & Hunink, M. G. M. (2016). 8-week mindfulness based stress reduction induces brain changes similar to traditional long-term meditation practice - A systematic review. *Brain and Cognition, 108*, 32–41. https://doi.org/10.1016/j.bandc.2016.07.001
Grasmann, J., Almenräder, F., Voracek, M., & Tran, U. S. (2023). Only small effects of mindfulness-based interventions on biomarker levels of inflammation and stress: A preregistered systematic review and two three-level meta-analyses. *International Journal of Molecular Sciences, 24*(5), 4445. https://doi.org/10.3390/ijms24054445
Guidi, J., Lucente, M., Sonino, N., & Fava, G. A. (2021). Allostatic load and its impact on health: A systematic review. *Psychotherapy and Psychosomatics, 90*(1), 11–27. https://doi.org/10.1159/000510696
Harrison, S., Jones, H. E., Martin, R. M., Lewis, S. J., & Higgins, J. P. T. (2017). The albatross plot: A novel graphical tool for presenting results of diversely reported studies in a systematic review. *Research Synthesis Methods, 8*(3), 281–289. https://doi.org/10.1002/jrsm.1239
Hashizume, S., Nakano, M., Kubota, K., Sato, S., Himuro, N., Kobayashi, E., Takaoka, A., & Fujimiya, M. (2021). Mindfulness intervention improves cognitive function in older adults by enhancing the level of miRNA-29c in neuron-derived extracellular vesicles. *Scientific Reports, 11*(1), 21848. https://doi.org/10.1038/s41598-021-01318-y
Hazlett-Stevens, H., Singer, J., & Chong, A. (2019). Mindfulness-based stress reduction and mindfulness-based cognitive therapy with older adults: A qualitative review of randomized controlled outcome research. *Clinical Gerontologist, 42*(4), 347–358. https://doi.org/10.1080/07317115.2018.1518282
Heckenberg, R. A., Eddy, P., Kent, S., & Wright, B. J. (2018). Do workplace-based mindfulness meditation programs improve physiological indices of stress? A systematic review and meta-analysis. *Journal of Psychosomatic Research, 114*, 62–71. https://doi.org/10.1016/j.jpsychores.2018.09.010
Heo, S., Kang, J., Umeakunne, E., Lee, S., Bertulfo, T. F., Barbé, T., Kim, J., Black, V., An, M., & Randolph, J. (2023). Effects of meditation intervention on self-management in adult patients with type 2 diabetes: A systematic literature review and meta-analysis. *Journal of Cardiovascular Nursing, 38*(6), 581–592. https://doi.org/10.1097/JCN.0000000000000973
Higgins, J. P. T., & Green, S. (2019). *Cochrane handbook for systematic reviews of interventions* (2nd ed.). The Cochrane Collaboration and John Wiley & Sons.
Hölzel, B. K., Lazar, S. W., Gard, T., Schuman-Olivier, Z., Vago, D. R., & Ott, U. (2011). How does mindfulness meditation work? Proposing mechanisms of action from a conceptual and neural perspective. *Perspectives on Psychological Science, 6*(6), 537–559. https://doi.org/10.1177/1745691611419671
Jørgensen, M. A., Pallesen, K. J., Fjorback, L. O., & Juul, L. (2021). Effect of mindfulness-based stress reduction on dehydroepiandrosterone-sulfate in adults with self-reported stress. A randomized trial. *Clinical and Translational Science, 14*(6), 2360–2369. https://doi.org/10.1111/cts.13100
Juster, R., McEwen, B. S., & Lupien, S. J. (2010). Allostatic load biomarkers of chronic stress and impact on health and cognition. *Neuroscience and Biobehavioral Reviews, 35*(1), 2–16. https://doi.org/10.1016/j.neubiorev.2009.10.002
Kabat-Zinn, J. (2003). Mindfulness-based interventions in context: Past, present, and future. *Clinical Psychology: Science and Practice, 10*, 144–156. https://doi.org/10.1093/clipsy.bpg016
Kaliman, P. (2019). Epigenetics and meditation. *Current Opinion in Psychology, 28*, 76–80. https://doi.org/10.1016/j.copsyc.2018.11.010
Kirkwood, T. B. (2008). A systematic look at an old problem. *Nature, 451*(7179), 644–647. https://doi.org/10.1038/451644a
Kriakous, S. A., Elliott, K. A., Lamers, C., & Owen, R. (2021). The effectiveness of mindfulness-based stress reduction on the psychological functioning of healthcare professionals: A systematic review. *Mindfulness, 12*(1), 1–28. https://doi.org/10.1007/s12671-020-01500-9
Kunimatsu, A., Yasaka, K., Akai, H., Kunimatsu, N., & Abe, O. (2020). MRI findings in posttraumatic stress disorder. *Journal of Magnetic Resonance Imaging, 52*(2), 380–396. https://doi.org/10.1002/jmri.26929
Kurth, F., Cherbuin, N., & Luders, E. (2017). Promising links between meditation and reduced (brain) aging: An attempt to bridge some gaps between the alleged fountain of youth and the youth of the field. *Frontiers in Psychology, 8*, 860. https://doi.org/10.3389/fpsyg.2017.00860
Lavretsky, H., & Newhouse, P. A. (2012). Stress, inflammation, and aging. *The American Journal of Geriatric Psychiatry, 20*(9), 729–733. https://doi.org/10.1097/JGP.0b013e31826573cf
Leggett, A., & Zarit, S. H. (2014). Prevention of mental disorder in older adults: Recent innovations and future directions. *Generations, 8*(3), 45–52.
Lenart-Bugla, M., Szcześniak, D., Bugla, B., Kowalski, K., Niwa, S., Rymaszewska, J., & Misiak, B. (2022). The association between allostatic load and brain: A systematic review. *Psychoneuroendocrinology, 145*, 105917. https://doi.org/10.1016/j.psyneuen.2022.105917
Lenze, E. J., Voegtle, M., Miller, J. P., Ances, B. M., Balota, D. A., Barch, D., Depp, C. A., Diniz, B. S., Eyler, L. T., Foster, E. R., Gettinger, T. R., Head, D., Hershey, T., Klein, S., Nichols, J. F., Nicol, G. E., Nishino, T., Patterson, B. W., Rodebaugh, T. L., … Wetherell, J. L. (2022). Effects of mindfulness training and exercise on cognitive function in older adults: A randomized clinical trial. *JAMA Internal Medicine, 328*(22), 2218–2229. https://doi.org/10.1001/jama.2022.21680
Li, H., Yan, W., Wang, Q., Liu, L., Lin, X., Zhu, X., Su, S., Sun, W., Sui, M., Bao, Y., Lu, L., Deng, J., & Sun, X. (2022). Mindfulness-based cognitive therapy regulates brain connectivity in patients with late-life depression. *Frontiers in Psychiatry, 13*, 841461. https://doi.org/10.3389/fpsyt.2022.841461
Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Ioannidis, J. P. A., Clarke, M., Devereaux, P. J., Kleijnen, J., & Moher, D. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. *PLoS Medicine, 6*(7), e1000100. https://doi.org/10.1371/journal.pmed.1000100
Lim, H., Saw, W., Feng, L., Lee, Y., Mahendran, R., Cheah, I. K., Rawtaer, I., Kumar, A. P., Kua, E., Mahendran, R., & Tan, E. (2018). Dataset on gene expression in the elderly after mindfulness awareness practice or health education program. *Data in Brief, 18*, 902–912. https://doi.org/10.1016/j.dib.2018.03.086
Lindsay, E. K., Creswell, J. D., Stern, H. J., Greco, C. M., Dutcher, J. M., Lipitz, S., Walsh, C. P., Wright, A. G. C., Brown, K. W., & Marsland, A. L. (2021). Mindfulness-based stress reduction buffers glucocorticoid resistance among older adults: A randomized controlled trial. *Psychosomatic Medicine, 83*(6), 641–649. https://doi.org/10.1097/PSY.0000000000000928
Lindsay, E. K., Creswell, J. D., Stern, H. J., Greco, C. M., Walko, T. D., Dutcher, J. M., Wright, A. G. C., Brown, K. W., & Marsland, A. L. (2022). Mindfulness-based stress reduction increases stimulated IL-6 production among lonely older adults: A randomized

controlled trial. *Brain, Behavior, and Immunity, 104*, 6–15. https://doi.org/10.1016/j.bbi.2022.05.001

Liu, W., Li, H., Lin, X., Li, P., Zhu, X., Su, S., Shi, J., Lu, L., Deng, J., & Sun, X. (2022). Blunted superior temporal gyrus activity to negative emotional expression after mindfulness-based cognitive therapy for late-life depression. *Frontiers in Aging Neuroscience, 14*, 1001447. https://doi.org/10.3389/fnagi.2022.1001447

Lomas, T., Ivtzan, I., & Fu, C. H. Y. (2015). A systematic review of the neurophysiology of mindfulness on EEG oscillations. *Neuroscience and Biobehavioral Reviews, 57*, 401–410. https://doi.org/10.1016/j.neubiorev.2015.09.018

Luo, J., Beam, C. R., & Gatz, M. (2023). Is stress an overlooked risk factor for dementia? A systematic review from a lifespan developmental perspective. *Prevention Science, 24*(5), 936–949. https://doi.org/10.1007/s11121-022-01385-1

Lutz, A., Chételat, G., Collette, F., Klimecki, O. M., Marchant, N. L., & Gonneaud, J. (2021). The protective effect of mindfulness and compassion meditation practices on ageing: Hypotheses, models and experimental implementation. *Ageing Research Reviews, 72*, 101495. https://doi.org/10.1016/j.arr.2021.101495

Lutz, A., Jha, A. P., Dunne, J. D., & Saron, C. D. (2015). Investigating the phenomenological matrix of mindfulness-related practices from a neurocognitive perspective. *American Psychologist, 70*(7), 632–658. https://doi.org/10.1037/a0039585

Maragkakis, M., Malla, S., Hatzoglou, M., Trifunovic, A., Glick, A. B., Finkel, T., Longo, V. D., Kaushik, S., Muñoz-Cánoves, P., Lithgow, G. J., Naidoo, N., Booth, L. N., Payea, M. J., Herman, A. B., de Cabo, R., Wilson, D. M., Ferrucci, L., & Gorospe, M. (2023). Biology of stress responses in aging. *Aging Biology, 1*, 20230002. https://doi.org/10.59368/agingbio.20230001

McKenzie J. E., & Brennan, S. E. (2023). Chapter 12: Synthesizing and presenting findings using other methods. In: J. P. T. Higgins, J. Thomas, J. Chandler, M. Cumpston, T. Li, M. J. Page, & V. A. Welch (Eds.), *Cochrane handbook for systematic reviews of interventions version 6.4 (Updated August 2023)*. Cochrane.

Menon, V. (2011). Large-scale brain networks and psychopathology: A unifying triple network model. *Trends in Cognitive Sciences, 15*(10), 483–506. https://doi.org/10.1016/j.tics.2011.08.003

Monin, J. K., Sperduto, C. M., Manigault, A. W., Dutton, A., Ali, A., Clark, M. S., & Jastreboff, A. M. (2020). Mindfulnes-based stress reduction for older couples with metabolic syndrome: A pilot randomized controlled trial. *Mindfulness, 11*(4), 917–927. https://doi.org/10.1007/s12671-019-01301-9

Moynihan, J. A., Chapman, B. P., Klorman, R., Krasner, M. S., Duberstein, P. R., Brown, K. W., & Talbot, N. L. (2013). Mindfulness-based stress reduction for older adults: Effects on executive function, frontal alpha asymmetry and immune function. *Neuropsychobiology, 68*(1), 34–43. https://doi.org/10.1159/000350949

Ng, T. K. S., Fam, J., Feng, L., Cheah, I. K., Tan, C. T., Nur, F., Wee, S. T., Goh, L. G., Chow, W. L., Ho, R. C., Kua, E. H., Larbi, A., & Mahendran, R. (2020). Mindfulness improves inflammatory biomarker levels in older adults with mild cognitive impairment: A randomized controlled trial. *Translational Psychiatry, 10*(1), 21. https://doi.org/10.1038/s41398-020-0696-y

Ng, T. K. S., Slowey, P. D., Beltran, D., Ho, R. C. M., Kua, E. H., & Mahendran, R. (2021). Effect of mindfulness intervention versus health education program on salivary Aβ-42 levels in community-dwelling older adults with mild cognitive impairment: A randomized controlled trial. *Journal of Psychiatric Research, 136*, 619–625. https://doi.org/10.1016/j.jpsychires.2020.10.038

Ouzzani, M., Hammady, H., Fedorowicz, Z., & Elmagarmid, A. (2016). Rayyan-a web and mobile app for systematic reviews. *Systematic Reviews, 5*(1), 210–214. https://doi.org/10.1186/s13643-016-0384-4

Palix, C., Chauveau, L., Felisatti, F., Chocat, A., Coulbault, L., Hébert, O., Mézenge, F., Landeau, B., Haudry, S., Fauvel, S., Collette, F., Klimecki, O., Marchant, N. L., De La Sayette, V., Vivien, D., Chételat, G., Poisnel, G., & Medit-Ageing Research Group. (2025). Allostatic load, a measure of cumulative physiological stress, impairs brain structure but not beta-accumulation in older adults: An exploratory study. *Frontiers in Aging Neuroscience, 17*, 1508677. https://doi.org/10.3389/fnagi.2025.1508677

Palta, P., Page, G., Piferi, R. L., Gill, J. M., Hayat, M. J., Connolly, A. B., & Szanton, S. L. (2012). Evaluation of a mindfulness-based intervention program to decrease blood pressure in low-income African-American older adults. *Journal of Urban Health, 89*(2), 308–316. https://doi.org/10.1007/s11524-011-9654-6

Pascoe, M. C., Thompson, D. R., Jenkins, Z. M., & Ski, C. F. (2017). Mindfulness mediates the physiological markers of stress: Systematic review and meta-analysis. *Journal of Psychiatric Research, 95*, 156–178. https://doi.org/10.1016/j.jpsychires.2017.08.004

Pernet, C. R., Belov, N., Delorme, A., & Zammit, A. (2021). Mindfulness related changes in grey matter: A systematic review and meta-analysis. *Brain Imaging and Behavior, 15*(5), 2720–2730. https://doi.org/10.1007/s11682-021-00453-4

Polsky, L. R., Rentscher, K. E., & Carroll, J. E. (2022). Stress-induced biological aging: A review and guide for research priorities. *Brain, Behavior, and Immunity, 104*, 97–109. https://doi.org/10.1016/j.bbi.2022.05.016

Priovoulos, N., Jacobs, H. I. L., Ivanov, D., Uludağ, K., Verhey, F. R. J., & Poser, B. A. (2018). High-resolution in vivo imaging of human locus coeruleus by magnetization transfer MRI at 3T and 7T. *NeuroImage, 168*, 427–436. https://doi.org/10.1016/j.neuroimage.2017.07.045

R Core Team. (2023). *R: A language and environment for statistical computing*. R Foundation for Statistical Computing.

Reive, C. (2019). The biological measurements of mindfulness-based stress reduction: A systematic review. *Explore, 15*(4), 295–307. https://doi.org/10.1016/j.explore.2019.01.001

Rogerson, O., Wilding, S., Prudenzi, A., & O'Connor, D. B. (2024). Effectiveness of stress management interventions to change cortisol levels: A systematic review and meta-analysis. *Psychoneuroendocrinology, 159*, 106415. https://doi.org/10.1016/j.psyneuen.2023.106415

Rossiello, F., Jurk, D., Passos, J. F., & d'Adda di Fagagna, F. (2022). Telomere dysfunction in ageing and age-related diseases. *Nature Cell Biology, 24*(2), 135–147. https://doi.org/10.1038/s41556-022-00842-x

Sanada, K., Montero-Marin, J., Alda Díez, M., Salas-Valero, M., Pérez-Yus, M. C., Morillo, H., Demarzo, M. M. P., García-Toro, M., & García-Campayo, J. (2016). Effects of mindfulness-based interventions on salivary cortisol in healthy adults: A meta-analytical review. *Frontiers in Physiology, 7*, 471. https://doi.org/10.3389/fphys.2016.00471

Sanada, K., Montero-Marin, J., Barceló-Soler, A., Ikuse, D., Ota, M., Hirata, A., Yoshizawa, A., Hatanaka, R., Valero, M. S., Demarzo, M., Campayo, J. G., & Iwanami, A. (2020). Effects of mindfulness-based interventions on biomarkers and low-grade inflammation in patients with psychiatric disorders: A meta-analytic review. *International Journal of Molecular Sciences, 21*(7), Article 2484. https://doi.org/10.3390/ijms21072484

Schneider, M., & Schwerdtfeger, A. (2020). Autonomic dysfunction in posttraumatic stress disorder indexed by heart rate variability: A meta-analysis. *Psychological Medicine, 50*(12), 1937–1948. https://doi.org/10.1017/S003329172000207X

Seeman, T. E., McEwen, B. S., Rowe, J. W., & Singer, B. H. (2001). Allostatic load as a marker of cumulative biological risk: MacArthur studies of successful aging. *Proceedings of the National*

Academy of Sciences of the United States of America, 98(8), 4770–4775. https://doi.org/10.1073/pnas.081072698

Segal, Z. V., Williams, J. M., & Teasdale, J. D. (2002). *Mindfulness-based cognitive therapy for depression: A new approach to preventing relapse*. Guilford Press.

Segerstrom, S. C., Boggero, I. A., Smith, G. T., & Sephton, S. E. (2014). Variability and reliability of diurnal cortisol in younger and older adults: Implications for design decisions. *Psychoneuroendocrinology, 49*, 299–309. https://doi.org/10.1016/j.psyneuen.2014.07.022

Sevinc, G., Rusche, J., Wong, B., Datta, T., Kaufman, R., Gutz, S. E., Schneider, M., Todorova, N., Gaser, C., Thomalla, G., Rentz, D., Dickerson, B. D., & Lazar, S. W. (2021). Mindfulness training improves cognition and strengthens intrinsic connectivity between the hippocampus and posteromedial cortex in healthy older adults. *Frontiers in Aging Neuroscience, 13*, 702796. https://doi.org/10.3389/fnagi.2021.702796

Sezer, I., Pizzagalli, D. A., & Sacchet, M. D. (2022). Resting-state fMRI functional connectivity and mindfulness in clinical and non-clinical contexts: A review and synthesis. *Neuroscience and Biobehavioral Reviews, 135*, 104583. https://doi.org/10.1016/j.neubiorev.2022.104583

Shenkin, S. D., Harrison, J. K., Wilkinson, T., Dodds, R. M., & Ioannidis, J. P. A. (2017). Systematic reviews: Guidance relevant for studies of older people. *Age and Ageing, 46*(5), 722–728. https://doi.org/10.1093/ageing/afx105

Sipe, W. E. B., & Eisendrath, S. J. (2012). Mindfulness-based cognitive therapy: Theory and practice. *The Canadian Journal of Psychiatry, 57*(2), 63–69. https://doi.org/10.1177/070674371205700202

Smart, C. M., & Segalowitz, S. J. (2017). Respond, don't react: The influence of mindfulness training on performance monitoring in older adults. *Cognitive, Affective, & Behavioral Neuroscience, 17*(6), 1151–1163. https://doi.org/10.3758/s13415-017-0539-3

Smart, C. M., Segalowitz, S. J., Mulligan, B. P., Koudys, J., & Gawryluk, J. R. (2016). Mindfulness training for older adults with subjective cognitive decline: Results from a pilot randomized controlled trial. *Journal of Alzheimer's Disease, 52*(2), 757–774. https://doi.org/10.3233/JAD-150992

Snyder, A. Z., Nishino, T., Shimony, J. S., Lenze, E. J., Wetherell, J. L., Voegtle, M., Miller, J. P., Yingling, M. D., Marcus, D., Gurney, J., Rutlin, J., Scott, D., Eyler, L., & Barch, D. (2022). Covariance and correlation analysis of resting state functional magnetic resonance imaging data acquired in a clinical trial of mindfulness-based stress reduction and exercise in older individuals. *Frontiers in Neuroscience, 16*, 825547. https://doi.org/10.3389/fnins.2022.825547

Sterne, J. A. C., Savović, J., Page, M. J., Elbers, R. G., Blencowe, N. S., Boutron, I., Cates, C. J., Cheng, H., Corbett, M. S., Eldridge, S. M., Emberson, J. R., Hernán, M. A., Hopewell, S., Hróbjartsson, A., Junqueira, D. R., Jüni, P., Kirkham, J. J., Lasserson, T., Li, T., McAleenan, A.,…, Higgins, J. P. T. (2019). RoB 2: a revised tool for assessing risk of bias in randomised trials. *British Medical Journal, 366*, l4898. https://doi.org/10.1136/bmj.l4898

Szeszko, P. R., & Yehuda, R. (2019). Magnetic resonance imaging predictors of psychotherapy treatment response in post-traumatic stress disorder: A role for the salience network. *Psychiatry Research, 277*, 52–57. https://doi.org/10.1016/j.psychres.2019.02.005

Tafet, G. E., & Nemeroff, C. B. (2016). The links between stress and depression: Psychoneuroendocrinological, genetic, and environmental interactions. *Journal of Neuropsychiatry and Clinical Neurosciences, 28*(2), 77–88. https://doi.org/10.1176/appi.neuropsych.15030053

Tang, Y., Hölzel, B. K., & Posner, M. I. (2015). The neuroscience of mindfulness meditation. *Nature Reviews Neuroscience, 16*(4), 213–225. https://doi.org/10.1038/nrn3916

Taylor, A. G., Goehler, L. E., Galper, D. I., Innes, K. E., & Bourguignon, C. (2010). Top-down and bottom-up mechanisms in mind-body medicine: Development of an integrative framework for psychophysiological research. *Explore, 6*(1), 29–41. https://doi.org/10.1016/j.explore.2009.10.004

Thoms, H. C., & Stark, L. A. (2021). The NF-κB nucleolar stress response pathway. *Biomedicines, 9*(9), 1082. https://doi.org/10.3390/biomedicines9091082

Tomlinson, E. R., Yousaf, O., Vittersø, A. D., & Jones, L. (2018). Dispositional mindfulness and psychological health: A systematic review. *Mindfulness, 9*(1), 23–43. https://doi.org/10.1007/s12671-017-0762-6

Tong, R. L., Kahn, U. N., Grafe, L. A., Hitti, F. L., Fried, N. T., & Corbett, B. F. (2023). Stress circuitry: Mechanisms behind nervous and immune system communication that influence behavior. *Frontiers in Psychiatry, 14*, 1240783. https://doi.org/10.3389/fpsyt.2023.1240783

Van Dam, N. T., van Vugt, M. K., Vago, D. R., Schmalzl, L., Saron, C. D., Olendzki, A., Meissner, T., Lazar, S. W., Kerr, C. E., Gorchov, J., Fox, K. C. R., Field, B. A., Britton, W. B., Brefczynski-Lewis, J. A., & Meyer, D. E. (2018). Mind the hype: A critical evaluation and prescriptive agenda for research on mindfulness and meditation. *Perspectives on Psychological Science, 13*(1), 36–61. https://doi.org/10.1177/1745691617709589

Venditti, S., Verdone, L., Reale, A., Vetriani, V., Caserta, M., & Zampieri, M. (2020). Molecules of silence: Effects of meditation on gene expression and epigenetics. *Frontiers in Psychology, 11*, 1767. https://doi.org/10.3389/fpsyg.2020.01767

Wallensten, J., Ljunggren, G., Nager, A., Wachtler, C., Bogdanovic, N., Petrovic, P., & Carlsson, A. C. (2023). Stress, depression, and risk of dementia - A cohort study in the total population between 18 and 65 years old in Region Stockholm. *Alzheimer's Research & Therapy, 15*(1), 161–164. https://doi.org/10.1186/s13195-023-01308-4

Wetherell, J. L., Hershey, T., Hickman, S., Tate, S. R., Dixon, D., Bower, E. S., & Lenze, E. J. (2017). Mindfulness-based stress reduction for older adults with stress disorders and neurocognitive difficulties: A randomized controlled trial. *Journal of Clinical Psychiatry, 78*(7), e734–e743. https://doi.org/10.4088/JCP.16m10947

Whitlock, M. C. (2005). Combining probability from independent tests: The weighted Z-method is superior to Fisher's approach. *Journal of Evolutionary Biology, 18*(5), 1368–1373. https://doi.org/10.1111/j.1420-9101.2005.00917.x

World Health Organization. (2022). *Facts and sheets on ageing and health*. Retrieved March 5, 2024, from https://www.who.int/news-room/fact-sheets/detail/ageing-and-health

World Health Organization. (2023). *Facts and sheets on mental health of older adults*. Retrieved April 29, 2024, from https://www.who.int/news-room/fact-sheets/detail/mental-health-of-older-adults

Young, K. S., van der Velden, A. M., Craske, M. G., Pallesen, K. J., Fjorback, L., Roepstorff, A., & Parsons, C. E. (2018). The impact of mindfulness-based interventions on brain activity: A systematic review of functional magnetic resonance imaging studies. *Neuroscience and Biobehavioral Reviews, 84*, 424–433. https://doi.org/10.1016/j.neubiorev.2017.08.003

Yu, J., Rawtaer, I., Feng, L., Fam, J., Kumar, A. P., Kee-Mun Cheah, I., Honer, W. G., Su, W., Lee, Y. K., Tan, E. C., Kua, E. H., & Mahendran, R. (2021). Mindfulness intervention for mild cognitive impairment led to attention-related improvements and

neuroplastic changes: Results from a 9-month randomized control trial. *Journal of Psychiatric Research, 135*, 203–211. https://doi.org/10.1016/j.jpsychires.2021.01.032
Zuniga-Hertz, J. P., Simpson, S., Chitetti, R., Hsu, C. F., Huang, H. P., Jinich-Diamant, A., Chernov, A. V., Onton, J. A., Cuomo, R., Dispenza, J., Davis, D., Christov-Moore, L., Reggente, N., Gu, W., Kong, M., Bonds, J. A., Maree, J., Simonson, T.S., Ahn, A. C., Poirier, M. A., … & Patel, H. H. (2025). Multidimensional analysis of twin sets during an intensive week-long meditation retreat: A pilot study. *Mindfulness, 16*(6)*,* 1634–1655. https://doi.org/10.1007/s12671-025-02584-x