ENIGMA-Meditation: Worldwide consortium for neuroscientific investigations of meditation practices

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Abstract

Meditation is a family of ancient and contemporary contemplative mind-body practices that can modulate psychological processes, awareness, and mental states. Over the last 40 years, clinical science has manualised meditation practices and designed various meditation interventions (MIs), that have shown therapeutic efficacy for disorders including depression, pain, addiction, and anxiety. Over the past decade, neuroimaging has examined the neuroscientific basis of meditation practices, effects, states, and outcomes for clinical and non-clinical populations. However, the generalizability and replicability of current neuroscientific models of meditation are yet to be established, as they are largely based on small datasets entrenched with heterogeneity along several domains of meditation (e.g., practice types, meditation experience, clinical disorder targeted), experimental design, and neuroimaging methods (e.g., preprocessing, analysis, task-based, resting-state, structural MRI). These limitations have precluded a nuanced and rigorous neuroscientific phenotyping of meditation practices and their potential benefits. Here, we present ENIGMA-Meditation, the first worldwide collaborative consortium for neuroscientific investigations of meditation practices. ENIGMA-Meditation will enable systematic meta- and mega-analyses of globally distributed neuroimaging datasets of meditation using shared, standardized neuroimaging methods and tools to improve statistical power and generalizability. Through this powerful collaborative framework, existing neuroscientific accounts of meditation practices can be extended to generate novel and rigorous neuroscientific insights, accounting for multi-domain heterogeneity. ENIGMA-Meditation will inform neuroscientific mechanisms underlying therapeutic action of meditation practices on psychological and cognitive attributes, advancing the field of meditation and contemplative neuroscience.

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Meditation encompasses contemplative mind-body practices characterized by diverse techniques, philosophies, and religious traditions (1–5). Broadly, meditation involves purposeful attention, voluntary regulation of psychological and embodied processing, and modulation of conscious awareness (6–9). Meditation practice can enable salutary psychological, psychosomatic and/or spiritual states of consciousness with acute and enduring positive impacts on mood, cognition, and general well-being (10–12). Scientific investigations of meditation have predominantly involved techniques including mindfulness, focused attention, open-monitoring, loving-kindness, compassion, mantra, non-dual awareness, and their variations (2,9,13,14). Some of these meditation forms have been incorporated directly into Western medical contexts in psychotherapies such as Mindfulness-based Stress Reduction (MBSR) (15), Mindfulness-based Cognitive Therapy (MBCT) (16), Mindfulness-Oriented Recovery Enhancement (MORE) (17), compassion meditation training (18), transcendental meditation training (19), etc. (20), and indirectly in interventions influenced by meditation traditions such as Acceptance and Commitment Therapy (ACT) (21) and Dialectical Behavior Therapy (DBT) (22) among others (20). Such psychotherapeutic meditation interventions (MIs) have transdiagnostic value (23), and can impart neuroprotective effects (24), improve stress management in medical conditions like cancer, chronic pain, and fibromyalgia, and combat psychiatric conditions including anxiety, depression, posttraumatic stress disorder (PTSD), and alcohol and substance use disorders (25–28). However, similar to other clinical interventions (29), MIs can also sometimes produce adverse events (30).

The past several decades have witnessed burgeoning neuroscientific examinations of meditation practices using magnetic resonance imaging (MRI) and electroencephalography (EEG). Meta-analyses of MRI and EEG literature suggest that meditative practices are associated with acute and enduring changes in brain structure (31,32) and function (13,33–39), including alterations in functional networks, morphology, and neural oscillations (40,41) associated with relevant cognitive and psychological processes (such as self-related processing, awareness, attentional and emotional regulation). However, the replicability and generalizability of neuroscientific findings from the meditation literature are challenged by modest sample sizes and substantial heterogeneity in experimental design, data processing techniques, and meditation practices, impeding deep neuroscientific phenotyping of meditation. Developing a more nuanced and rigorous understanding of the neural basis of meditation can potentially improve estimates of moderators and mediators of the effects of different meditation practices, and identify predictors of individual differences in brain mechanisms underlying clinical action of MIs. Such advantages can in turn enable effective patient stratification for clinical trials involving MIs, improve prognostic assessments of clinical outcomes of MIs, and inform augmentation approaches such as neuromodulation, biofeedback, and personalization.

Here we introduce Enhancing Neuroimaging Genetics through Meta Analysis (ENIGMA)-Meditation - a newly established innovative global consortium for collaborative neuroimaging of meditation that will address existing challenges and deepen the neuroscientific understanding of meditation. ENIGMA-Meditation brings together neuroimaging data from meditation researchers worldwide to facilitate large-scale meta- and mega-analysis projects using shared, strategically-planned, standardized processing, and statistical analyses. The primary goal of ENIGMA-Meditation is to systematically and reliably characterize the neuroscience of different meditation practices, evaluate commonalities and distinctions between diverse practice forms and stages, and investigate how their neuroscientific substrates relate to impact on pertinent psychological, physiological, clinical, and cognitive attributes.

Neuroimaging literature of meditation in healthy individuals

Meta-analyses of the functional MRI (fMRI) literature on cross-sectional investigations of meditation in healthy populations indicate widespread involvement and interplay between distributed brain regions spanning the default-mode network (DMN), salience network (SN), and central executive network (CEN) (13,33,35,36). These brain networks are typically thought to underpin putative neurocognitive mechanisms of meditation practice, such as self-referential processing and stimulus-independent thought (DMN), arousal and interoceptive awareness (SN), and executive function and attentional regulation (CEN) (6,8,33). Emerging evidence also highlights inter-individual variations in self-report measures of dispositional mindfulness (33,39,42–44) and differences in meditation experience between adept practitioners and novices (33,34,39,45–48) influencing functional connectivity (FC) and activation changes within and between some of these brain networks. The insula, associated with emotional processing, awareness, and interoception (49,50)) and the anterior cingulate cortex (ACC) implicated in attentional regulation and conflict monitoring (51,52) are two key SN regions commonly engaged in diverse meditation techniques (13). Similarly, while structural MRI differences between adept meditators and novices may be widespread throughout the brain (53), meta-analytic evidence from cross-sectional literature suggests these differences may be more pronounced in the insula and ACC (SN) (31,32).

Neural correlates of MI-related improvements among healthy individuals in memory (54) and executive functioning (55), emotion regulation and reactivity (56,57), and pain perception (58) are widely associated with dissociable activation and FC changes within the DMN, SN, and/or CEN, as well as the amygdala (59), thalamus, and orbitofrontal cortex (OFC) (58). Recent meta-analysis (38), review (39) and trials (60–65) examining longitudinal resting-state FC changes associated with mindfulness-focused MIs have identified modifications in these networks, implicating dorsolateral prefrontal cortex (DLPFC) (CEN), PCC (DMN) and insula (SN). Evidence on longitudinal brain structure alterations associated with MIs however remains mixed. Some studies have found distributed training-related morphometric effects within DMN and SN (66–70) but others have not replicated earlier findings (71,72).

Taken together, in healthy individuals, meditation and its outcomes demonstrate functional and structural changes in brain regions within intrinsic brain connectivity networks associated with self-referential processing, interoception and awareness, and executive functioning (i.e., DMN, SN and/or CEN), in addition to other networks. While some reviews and studies implicate DMN, SN and CEN, or a subset of these networks, others found no effects at all (e.g., with structural MRI), thus highlighting the discordance in the current literature. Notably, meditation-related changes in the insula have been most consistently reported, but there remains substantial variability across the literature.

Neuroimaging literature of meditation in individuals with clinical conditions

The neural substrates that appear to underlie impacts of MIs in transdiagnostic clinical samples also show overlap with DMN, SN and/or CEN among other brain networks and regions, as evidenced by reviews and seminal randomized control trials (RCTs).

A review of FC effects of MIs found that in individuals with chronic stress and disorders including MDD and PTSD, MIs commonly modulate resting-state FC between PCC (DMN) and DLPFC (CEN) (39) which may relate to attentional control over mind wandering. Recent meta-analytic evidence of structural alterations associated with MIs in both healthy and clinical samples implicate the insula (SN) and precentral gyrus (73). A review of MIs for pain suggested that the analgesic effect of MIs involves functional changes in ACC and insula (SN), thalamus and reward/evaluation-related OFC (74). A systematic review of MIs for substance-use disorders observed therapeutic action consistently accompanied by changes in ACC (SN) and striatum (75). A recent RCT reported that emotion regulation strategies adopted by social anxiety patients after MBSR training involve differential engagement of ACC (SN), medial PFC (DMN) and DLPFC (CEN) (76). Several RCTs involving MIs for major depressive disorder (MDD) have reported that FC, activation, and structural (77) changes in DLPFC (CEN) (77–79) and amygdala (77,79) accompany clinical outcomes. An RCT involving MI for attention deficit and hyperactivity disorder (ADHD) observed dominant activation changes in the insula (SN), precuneus (DMN) and inferior parietal lobe (CEN) following the intervention, with hyperactivity symptoms linked to medial PFC and PCC (DMN) activity changes (80). Improvements associated with a 3-month MI targeting age-related mild cognitive impairment (MCI) were tracked by changes in FC dynamics primarily involving ACC (SN), PCC and superior temporal gyrus (DMN), and insula (SN) (81). Another RCT investigating white matter changes observed effects in the ACC (SN) following an MI for panic disorder (82).

Taken together, MIs targeting diverse clinical conditions also appear to commonly modulate function and structure of distinct hubs within DMN, SN and/or CEN. Additionally, studies of MIs in clinical samples have also shown evidence of involvement of other cortical and subcortical neural circuits associated with social-emotional, threat, and reward processes, including the amygdala, OFC, and striatum. Variability in the implicated neural circuits across the literature may reflect factors related to clinical studies, such as type of disorder and underlying brain network dysregulation, and specific features of the intervention and/or comparison treatment group.

Limitations in the current state of meditation neuroscience

The existing cross-sectional and longitudinal neuroimaging studies of meditation have enabled mapping of functional and structural brain changes underlying distinct meditation practices and states in clinical and non-clinical cohorts that include novices and experienced meditation practitioners. The current state of meditation neuroscience, while providing valuable insights, confronts significant variability and methodological challenges.

Although existing meta-analyses in the field find convergent activation / FC / structural changes in DMN, SN and/or CEN, the concordance between meta-analytic findings at the level of specific brain regions remains low, with changes in insula being the most consistent finding (13,31–36,38,73). Such low generalizability, specificity and discordance likely stem from inadequate statistical power driven by small study samples (< 20 studies) of meta-analyses (83) and considerable variability in sample characteristics, control conditions, task, inclusion criteria, and statistical processes. Similar challenges also hinder the generalizability of findings from reviews, many of which collapse inferences from studies involving varying meditation techniques, levels of meditation experience, and manualized MIs (32,39,75,84,85), with limited consideration of this heterogeneity across studies. Another concern is lack of adequate control for confounds (physiological responses, head motion, multiple comparisons) that can substantially contaminate fMRI signals and inferences (86). For example, less than 20% of the reviewed cross-sectional fMRI literature on focused attention meditation accounted for these confounds in their analyses (33).

Several cortical (e.g., somatomotor and attention network regions, occipital regions, OFC), subcortical (e.g., amygdala, hippocampus, thalamus, striatum) and cerebellar areas have also been implicated in the clinical and non-clinical literature, albeit variably across studies and clinical conditions. For instance, MIs can impact MDD symptoms by modulating the amygdala which is involved in affective processing (77,79), pain by modulating OFC and thalamus which are implicated in sensory evaluation and processing (58), and addiction by modulating striatal regions involved in reward-processing (75). Gaps still remain in characterizing the key brain mechanisms unique to and common across different clinical conditions and their mechanisms of action. Brain networks widely associated with meditation like the DMN, CEN and SN have also been otherwise implicated in general cognitive task demands (87,88), dysfunction across diverse psychiatric disorders (triple network model of psychopathology (89)), and other psychological processes like hypnosis (90). Greater clarity is required on the functional specificity of such brain networks pertaining to meditation practices. Meditation may also involve whole-brain distributed or multivariate effects on brain function (91–94) and structure (53,94), beyond their impact on localized regions, circuits, or networks. Robust decoding of such neural effects requires greater statistical power.

To address gaps in the literature and reliably decode the roles of diverse brain areas and complex whole-brain states unique to meditation and MIs, unified analytical methods that can increase statistical power and sensitivity, and account for confounds, are warranted. To that end, we have adopted the ENIGMA framework.

The ENIGMA framework

The ENIGMA consortium was founded in 2009 to improve the replication and generalizability of neuroimaging and genetics analyses. Early ENIGMA projects focused on genome-wide associations to detect genetic markers influencing brain morphometry, by leveraging existing worldwide brain MRI and genetic datasets and applying standardized processing, quality control, and analysis techniques (95). The ENIGMA approach differs from the classic literature-based meta-analysis (combining effects from published studies that used variable processing and analysis techniques) as it uses standardized processing, quality control and analyses shared across all the participating datasets to boost statistical power. The ENIGMA consortium now includes over fifty Working Groups (WGs) developing scalable, open-source methods to study neurological conditions such as Parkinson's disease, epilepsy and stroke, adult and adolescent onset psychiatric disorders, from schizophrenia and MDD to anxiety and Tourette syndrome, as well as normative brain variation (96–98). Today, in addition to meta-analysis, many ENIGMA Working Groups perform both federated analyses as well as pooled mega-analysis where participant-level raw or derived brain measures are centralized to facilitate more complex analyses (e.g., machine / deep learning, etc.) (99–103). Through numerous large-scale collaborative projects, ENIGMA WGs have mapped the structural and functional brain correlates of various disorders in large demographically and ancestrally diverse samples. The scale of these studies allows for the modeling of complex clinical and comorbid features (e.g., symptom severity, duration of illness, and medication) both within and across brain conditions (104).

By using pre-existing, independently collected data, the ENIGMA approach boosts sample sizes and statistical power in a cost-effective manner. The standardized application of open-source neuroimaging pipelines and analytical models used within ENIGMA improves the reliability and transparency of study findings. By pooling diverse samples from around the world, ENIGMA studies improve replication power and generalizability of results. For instance, an all-Japan cohort investigating schizophrenia independently replicated the regional gray matter volume effect sizes observed by ENIGMA-Schizophrenia (105).

An ENIGMA meta-analysis typically involves two stages: 1) estimation of site-level summary statistics (such as effect sizes, standard errors / confidence intervals) from participant-level data using standard quality checks and statistical protocols performed at participating sites, and 2) centrally performed meta-analysis of the derived summary statistics for inference across sites. Additionally, the ENIGMA framework also confers a unique capacity for world-wide "mega-analysis" involving samples much larger than individual study samples. Mega-analysis is a single-stage analysis that uses shared standard methods and computing environments to directly analyze participant-level raw data and/or derived data (e.g., brain structure volumes, or FC values) furnished by the participating sites to the central facility (106).

ENIGMA-Meditation

ENIGMA-Meditation is a recently launched WG that aims to conduct large-scale meta- and mega-analyses of globally distributed datasets using unified analytical processes to elucidate and clarify the neuroscience of meditation.

The primary goal of ENIGMA-Meditation is to advance the field of meditation neuroimaging by addressing limitations described earlier. The current literature primarily comprises small datasets with heterogeneity along several domains, including (i) meditation techniques (e.g., focused attention, open monitoring, loving-kindness, compassion), (ii) MIs (e.g., MBSR, MBCT, MORE), (iii) characteristics and meditation experience of samples (e.g., novice vs. experienced, tradition of practice, religio-cultural context, demographics) (iii) experimental design (e.g., longitudinal, RCT, cross-sectional), (iv) control conditions and comparison groups (e.g., rest or active task, exercise or relaxation for comparison intervention), (v) neuroimaging parameters (e.g., MRI scanner magnetic field strength, imaging protocols, sampling rates), (vi) analysis methods (e.g., FC, activation, multivariate), and (vii) preprocessing steps (e.g., head motion and physiological denoising, smoothing, filtering). Consequently, the generalizability and specificity of inferences drawn from existing neuroimaging reviews and meta-analyses in the field are limited.

Meta- and mega-analyses using participant-level data from diverse sites enabled by ENIGMA-Meditation will boost statistical power and account for some of the heterogeneity within a tightly controlled analytical framework (Figure 1). Pooled datasets can be harmonized using shared, standardized analysis and preprocessing protocols, and the effect of different covariates (e.g., meditation experience, meditation technique, physiological confounds, key sample characteristics, clinical disorders) can be controlled for / modeled at the site-level (meta-analysis) or even participant-level (mega-analysis) as mediators or moderators. As data accumulates with ENIGMA-Meditation, subsets of the aggregated data with comparable study designs and protocols (cross-sectional or longitudinal paradigms of functional or structural MRI), and / or homogenous samples (novices or experts, patients with specific disorders or healthy populations) can also be pooled and harmonized separately to enable targeted participant-level meta- or mega-analyses that address narrower hypotheses (e.g., neuroscientific mechanisms of MBSR to improve psychological distress or MBCT for MDD, functional activation changes during open-monitoring meditation, resting-state FC changes pre-to-post meditation retreats in healthy adults, etc.). Furthermore, neurobehavioural associations underlying meditation states, self-report measures and clinical scales may potentially be examined by harmonizing distinct but related assessment scores across sites and datasets (107,108). Taken together, such collaborative well-powered approaches may help to distinguish consistent, generalizable findings from false positives and discordant outcomes that are prevalent among smaller individual studies (106,109).

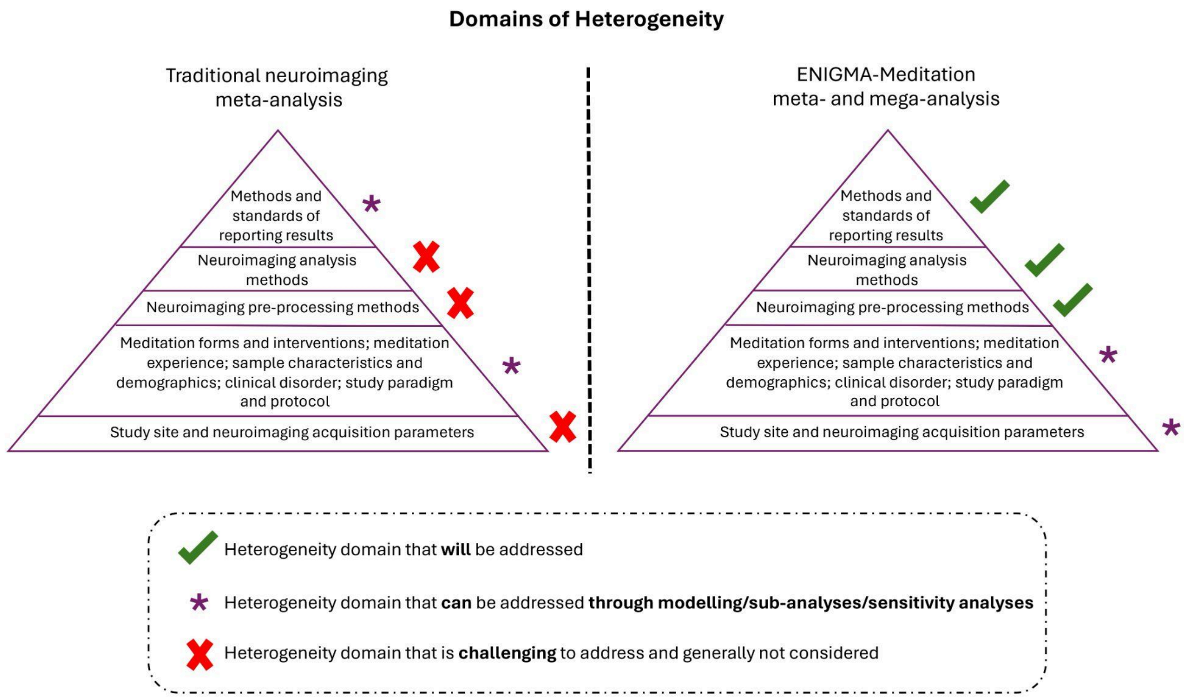

Figure 1: Comparison of the traditional meta-analytic approaches with ENIGMA-driven approaches, which can offer greater power to control for, or model, heterogeneity across multiple domains.

The main purpose of ENIGMA-Meditation is to tackle pressing neuroscientific questions surrounding meditation practices, and generate novel hypotheses. ENIGMA-Meditation will illuminate the role of complex whole-brain states and diverse cortical, subcortical and cerebellar regions in meditation practices and related states and traits. With large samples, it will examine consistent trends that may not attain statistical significance in individual underpowered studies (110). Importantly, participant-level mega-analyses can help disentangle physiological responses (e.g., changes in breathing, heart rate) and other nonspecific artifacts (e.g., head motion) from fMRI signals and inferences that are typically attributed to meditative states and effects (e.g., fMRI signals of DMN (86)). ENIGMA-Meditation will also evaluate transdiagnostic as well as disorder-specific neural mechanisms of action underlying various documented clinical effects of MIs. The statistical power of ENIGMA-Meditation analyses can generate insights into generalizable and replicable alterations of brain function and structure that are both unique to and common across meditation techniques and interventions, and levels of meditation experience among healthy and clinical populations. Recent cross-diagnostic analyses across ENIGMA WGs have successfully compared brain structural aberrations across diverse psychiatric disorders including schizophrenia, bipolar disorder, MDD, ADHD, PTSD and others (111,112). In ENIGMA-Meditation, such kinds of analyses will enable systematic comparisons between the effect sizes and brain maps associated with distinct meditation techniques and interventions, levels of meditation experience or clinical disorders targeted by MIs.

Future directions

Extensive neuroscientific mapping of meditation with ENIGMA-Meditation can potentially provide a scientific basis to understand and elucidate traditional (and often ancient) practices and contribute to their validation in modern and secular therapeutic contexts (6,8). Some of the key future directions and scope possible with ENIGMA-Meditation include:

- Different traditions and frameworks describe states and practices of meditation using varied terms and concepts (2,5,9,113,114). Reliable neural maps enabled by ENIGMA-Meditation may help to identify and harmonize common constructs across varied meditation practices and states by exploring their subjective, cultural, semantic and conceptual pluralities (9,115,116). For example, compassion, empathy, meta-awareness, equanimity, bliss, non-duality, and decentering among others are often considered essential outcomes, phenomenological dimensions and states across different meditation practices (9,14,114,117–121). Statistically empowered participant-level mega-analyses from ENIGMA-Meditation can potentially illuminate some of the relationships between these phenomenological and neuroscientific dimensions.

- In meditation research, outcomes, quality, expertise, and experience associated with meditation practices and states are often based on self-report measures, which are prone to retrospective and demand biases (122–124) especially among novices and developing practitioners (123,125). Complementing and comparing first-person self-reports with robust neuroscientific ("third-person") accounts derived from ENIGMA-Meditation findings can improve rigor by accounting for some of these biases (116,126,127), and also leverage a dimensional and multi-level approach to meditation research. Specifically, ENIGMA-Meditation will enable integration of aggregated neuroscientific datasets with their associated phenomenological and pathological measurements, which can provoke unprecedented multi-dimensional characterization of meditation practices and their effects on health and illness (similar to the Research Domain Criteria (RDoC) framework (128)).

- Several ENIGMA WGs use data-driven methods, such as non-linear, multivariate, machine and deep learning approaches to predict / determine brain-aging related abnormalities in MDD (99) and schizophrenia (129), predict alcohol dependence (100), or classify anxiety disorder cases vs. controls (101) and OCD cases vs. controls (102) based on brain structure. Similarly, ENIGMA-Meditation can develop powerful computational models that use neuroscientific data to distinguish levels of meditation experience or predict individual-level/patient-level responses to specific meditation practices and MIs (130), complementing efforts that predict meditation outcomes using self-report data (131–133). Such efforts may also help demystify the neuroscientific mechanisms and predispositions underlying various documented contraindications to meditation practice (30,134).

- Existing data-driven approaches to decode meditation states and outcomes developed using smaller datasets (91–93,135–137) can be tested and improved using the large datasets and unified analytical framework available with ENIGMA-Meditation. Well-validated data-driven neuroscientific models may then inform neural decoding algorithms in emerging non-invasive neuromodulation (138) and neurofeedback (139) technologies aimed at augmenting meditation practice.

- Neuroimaging studies of meditation have typically involved young-to-middle aged adults. However, the emergence of individual studies exploring meditation-related effects on children (140), adolescents (141) and older individuals (55) will enable large-scale aggregate analyses with ENIGMA-Meditation that dissect age-related differences and potential developmental effects of meditation on brain function and structure.

Although the current scope of ENIGMA-Meditation involves multi-modal MRI research of meditation practices, ENIGMA WGs typically expand over time and birth various subgroups (98). Therefore, the inclusion of EEG (40,41) and other contemplative practices and arts (e.g., Yoga (142), Tai-chi (143)) in ENIGMA-Meditation is imminent, as these fields are also burdened by similar challenges as in the meditation neuroscience literature.

Current state

As of April 2024, several research groups have expressed interest to contribute data to ENIGMA-Meditation from published studies as well as prospective trials, which span over 65 investigators across North America, Oceania, Asia and Europe. Figure 2 shows a map illustrating the current geographic diversity of ENIGMA-Meditation.

Figure 2: Geographical distribution of the current ENIGMA-Meditation membership (as of April 2024).

The currently available datasets include multimodal MRI neuroimaging data already or imminently acquired pre-to-post interventions (resting-state fMRI, structural MRI) and during meditation-related tasks (task-fMRI) associated with a variety of samples (healthy individuals, individuals with clinical conditions, novice meditator and expert meditator), contemplative practices (mindfulness, focused attention, compassion / loving-kindness, Vipassana, Yoga, Zen) and MIs (e.g., MBSR, MBCT, MORE, retreats). A number of resting-state and task-based EEG datasets have also been identified for future inclusion. Most of the datasets also include standardized self-report measurements such as Five Facet Mindfulness Questionnaire (FFMQ), Mindful Attention Awareness Scale (MAAS), State Mindfulness Scale (SMS), Cognitive Affective Mindfulness Scale (CAMS), etc. Supplementary Table 1 lists neuroimaging datasets currently available to ENIGMA-Meditation. Overall, ENIGMA-Meditation currently has access to MRI data from >200 expert meditators, >1300 healthy beginner-level individuals, and >600 patients with different psychiatric disorders, including MDD, PTSD, dissociation, social anxiety and early-life adversity.

There is an ongoing call for additional groups / investigators to join ENIGMA-Meditation. Information on how to participate is available on the ENIGMA-Meditation website (https://enigma.ini.usc.edu/ongoing/enigma-meditation/). ENIGMA-Meditation aspires to expand its membership which will increase the size and diversity of its datasets, samples, investigators, and studies.

Some of the initial projects being planned by ENIGMA-Meditation broadly include meta- and / or mega-analyses of enduring structural MRI and resting-state FC changes associated with MIs in healthy and clinical populations, fMRI activation / FC correlates of MRI meditation tasks, and associations between brain function / structure and self-reported meditation expertise.

Challenges with ENIGMA-Meditation

Although ENIGMA-Meditation and the broader ENIGMA framework offer scope and opportunities for advancement as a field, some challenges remain.

ENIGMA's projects are limited by the type and quality of data originally acquired by participating sites. While legacy datasets acquired years ago may have poor data quality due to technological and methodological limitations at the time of data acquisition, higher quality datasets acquired using newer neuroimaging techniques (e.g., multi-band, 7T, etc.) or other modalities (e.g., functional near infrared spectroscopy (fNIRS), MEG, etc.) are currently fewer. It can hence be challenging to fully account for heterogeneity in data quality, neuroimaging site, and depth of phenotyping (98). However, the global ENIGMA framework has been consistently developing methods and tools to address some of these limitations (144–147), such as harmonization of distinct symptom / neuropsychological scales, self-report measures, and site and protocol effects (107). This aspect is vital for ENIGMA-Meditation, since assessments of subjective experience and compliance with meditation instructions are often lacking, biased, or inconsistent across meditation neuroimaging studies (113). Data aggregated by ENIGMA-Meditation will not be sufficiently large or powered for reliable population-level inferences that are possible with prospectively-sampled large-scale neuroimaging databases like UK biobank (N>500,000) (148). However, findings from ENIGMA-Meditation can motivate large-scale prospective data collection efforts specific to meditation in the future.

Meditation and contemplative practices are culturally and geographically sensitive. Due to the expense of MRI scanning, representation from low- and middle-income countries with limited scientific resources will be impeded (149,150). Consequently, ENIGMA-Meditation might not fully capture the wide spectrum of meditation practices globally. Future inclusion of less expensive and more accessible neuroimaging data such as EEG can guide ENIGMA-Meditation to foster a more globally inclusive approach to meditation research, embracing a diverse range of practices, voices and perspectives from across the world.

Conclusions

We present a global collaborative consortium - ENIGMA-Meditation - which currently comprises >65 neuroimaging research groups across four continents. This consortium aims to perform rigorous neuroscientific examinations of meditation and other contemplative practices while accounting for key issues of multi-domain heterogeneity and modest sample sizes prevalent in the current literature. By enabling large-scale integration of meditation neuroimaging datasets across continents and cultures, this initiative will set out to test and elaborate on the prevailing neuroscientific models of meditation practices with high analytical power. ENIGMA-Meditation will rigorously examine nuanced and novel neurocognitive and neuroplastic mechanisms that subserve the assortment of meditation practices, states, and their documented effects on psychopathology, health, and wellness. The standardized processing and statistical protocols along with advancements in big data analytics developed and tested over a decade by the ENIGMA framework and neuroimaging community will empower ENIGMA-Meditation to systematically elucidate and demystify the links between neuroscientific processes and meditation practices, experience, expertise, states, and outcomes. Consequently, the global consortium would help to illuminate the modern and secular therapeutic value of ancient contemplative practices through rigorous neuroscience research. By ensuring transparency, cultural sensitivity, humility, and inclusivity in its research practices, ENIGMA-Meditation is well-positioned to advance the field of meditation and contemplative neuroscience in a respectful, culturally informed, and scientifically rigorous manner.

References

1. Matko K, Ott U, Sedlmeier P (2021): What Do Meditators Do When They Meditate? Proposing a Novel Basis for Future Meditation Research. *Mindfulness* 12: 1791–1811.

2. Matko K, Sedlmeier P (2019): What Is Meditation? Proposing an Empirically Derived Classification System. *Front Psychol* 10: 2276.

3. Katyal S, Lumma A-L, Goldin PR, Roy S (2023): Editorial: The varieties of contemplative experiences and practices. *Front Psychol* 14: 1232999.

4. Woods TJ, Windt JM, Brown L, Carter O, Van Dam NT (2023): Subjective Experiences of Committed Meditators Across Practices Aiming for Contentless States. *Mindfulness* 14: 1457–1478.

5. Sparby T, Sacchet MD (2021): Defining Meditation: Foundations for an Activity-Based Phenomenological Classification System. *Front Psychol* 12: 795077.

6. Lutz A, Slagter HA, Dunne JD, Davidson RJ (2008): Attention regulation and monitoring in meditation. *Trends Cogn Sci* 12: 163–169.

7. Shapiro SL, Walsh R (2003): An analysis of recent meditation research and suggestions for future directions. *The Humanistic Psychologist* 31: 86–114.

8. Hölzel BK, Lazar SW, Gard T, Schuman-Olivier Z, Vago DR, Ott U (2011): How Does Mindfulness Meditation Work? Proposing Mechanisms of Action From a Conceptual and Neural Perspective. *Perspect Psychol Sci* 6: 537–559.

9. Lutz A, Jha AP, Dunne JD, Saron CD (2015): Investigating the phenomenological matrix of mindfulness-related practices from a neurocognitive perspective. *Am Psychol* 70: 632–658.

10. Galante J, Friedrich C, Dawson AF, Modrego-Alarcón M, Gebbing P, Delgado-Suárez I, *et al.* (2021): Mindfulness-based programmes for mental health promotion in adults in nonclinical settings: A systematic review and meta-analysis of randomised controlled trials. *PLoS Med* 18: e1003481.

11. Bowles NI, Davies JN, Van Dam NT (2022): Dose-response Relationship of Reported Lifetime Meditation Practice with Mental Health and Wellbeing: a Cross-sectional Study. *Mindfulness* 13: 2529–2546.

12. Chiesa A, Calati R, Serretti A (2011): Does mindfulness training improve cognitive abilities? A systematic review of neuropsychological findings. *Clin Psychol Rev* 31: 449–464.

13. Fox KCR, Dixon ML, Nijeboer S, Girn M, Floman JL, Lifshitz M, *et al.* (2016): Functional neuroanatomy of meditation: A review and meta-analysis of 78 functional neuroimaging investigations. *Neurosci Biobehav Rev* 65: 208–228.

14. Laukkonen RE, Slagter HA (2021): From many to (n)one: Meditation and the plasticity of the predictive mind. *Neurosci Biobehav Rev* 128: 199–217.

15. Kabat-Zinn J (1982): An outpatient program in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: theoretical considerations and preliminary results. *Gen Hosp Psychiatry* 4: 33–47.

16. Teasdale JD, Segal ZV, Williams JM, Ridgeway VA, Soulsby JM, Lau MA (2000): Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. *J Consult Clin Psychol* 68: 615–623.

17. Garland EL (2013): *Mindfulness-Oriented Recovery Enhancement for Addiction, Stress, and Pain*. NASW Press.

18. Pace TWW, Negi LT, Adame DD, Cole SP, Sivilli TI, Brown TD, *et al.* (2009): Effect of compassion meditation on neuroendocrine, innate immune and behavioral responses to psychosocial stress. *Psychoneuroendocrinology* 34: 87–98.

19. Schneider RH, Carr T (2014): Transcendental Meditation in the prevention and treatment of cardiovascular disease and pathophysiological mechanisms: An evidence-based review. *Adv Integr Med* 1: 107–112.

20. Creswell JD (2017): Mindfulness Interventions. *Annu Rev Psychol* 68: 491–516.

21. Hayes SC, Strosahl KD, Wilson KG (1999): *Acceptance and Commitment Therapy*, vol. 6.

Guilford press New York.

22. Linehan MM (1993): Cognitive-behavioral treatment of borderline personality disorder. *Diagnosis and treatment of mental disorders* 558. Retrieved from https://psycnet.apa.org/fulltext/1993-97864-000.pdf

23. Greeson JM, Zarrin H, Smoski MJ, Brantley JG, Lynch TR, Webber DM, *et al.* (2018): Mindfulness Meditation Targets Transdiagnostic Symptoms Implicated in Stress-Related Disorders: Understanding Relationships between Changes in Mindfulness, Sleep Quality, and Physical Symptoms. *Evid Based Complement Alternat Med* 2018: 4505191.

24. Luders E, Cherbuin N (2016): Searching for the philosopher's stone: promising links between meditation and brain preservation. *Ann N Y Acad Sci* 1373: 38–44.

25. Goldberg SB, Tucker RP, Greene PA, Davidson RJ, Wampold BE, Kearney DJ, Simpson TL (2018): Mindfulness-based interventions for psychiatric disorders: A systematic review and meta-analysis. *Clin Psychol Rev* 59: 52–60.

26. Creswell JD, Lindsay EK, Villalba DK, Chin B (2019): Mindfulness Training and Physical Health: Mechanisms and Outcomes. *Psychosom Med* 81: 224–232.

27. Goldberg SB, Riordan KM, Sun S, Davidson RJ (2022): The Empirical Status of Mindfulness-Based Interventions: A Systematic Review of 44 Meta-Analyses of Randomized Controlled Trials. *Perspect Psychol Sci* 17: 108–130.

28. Kim D-Y, Hong S-H, Jang S-H, Park S-H, Noh J-H, Seok J-M, *et al.* (2022): Systematic Review for the Medical Applications of Meditation in Randomized Controlled Trials. *Int J Environ Res Public Health* 19. https://doi.org/10.3390/ijerph19031244

29. Linden M, Schermuly-Haupt M-L (2014): Definition, assessment and rate of psychotherapy side effects. *World Psychiatry* 13: 306–309.

30. Farias M, Maraldi E, Wallenkampf KC, Lucchetti G (2020): Adverse events in meditation practices and meditation-based therapies: a systematic review. *Acta Psychiatr Scand* 142: 374–393.

31. Pernet CR, Belov N, Delorme A, Zammit A (2021): Mindfulness related changes in grey matter: a systematic review and meta-analysis. *Brain Imaging Behav* 15: 2720–2730.
32. Fox KCR, Nijeboer S, Dixon ML, Floman JL, Ellamil M, Rumak SP, *et al.* (2014): Is meditation associated with altered brain structure? A systematic review and meta-analysis of morphometric neuroimaging in meditation practitioners. *Neurosci Biobehav Rev* 43: 48–73.
33. Ganesan S, Beyer E, Moffat B, Van Dam NT, Lorenzetti V, Zalesky A (2022): Focused attention meditation in healthy adults: A systematic review and meta-analysis of cross-sectional functional MRI studies. *Neurosci Biobehav Rev* 141: 104846.
34. Boccia M, Piccardi L, Guariglia P (2015): The Meditative Mind: A Comprehensive Meta-Analysis of MRI Studies. *Biomed Res Int* 2015: 419808.
35. Tomasino B, Fregona S, Skrap M, Fabbro F (2012): Meditation-related activations are modulated by the practices needed to obtain it and by the expertise: an ALE meta-analysis study. *Front Hum Neurosci* 6: 346.
36. Kim JJ, Cunnington R, Kirby JN (2020): The neurophysiological basis of compassion: An fMRI meta-analysis of compassion and its related neural processes. *Neurosci Biobehav Rev* 108: 112–123.
37. Josipovic Z (2014): Neural correlates of nondual awareness in meditation. *Ann N Y Acad Sci* 1307: 9–18.
38. Rahrig H, Vago DR, Passarelli MA, Auten A, Lynn NA, Brown KW (2022): Meta-analytic evidence that mindfulness training alters resting state default mode network connectivity. *Sci Rep* 12: 12260.
39. Sezer I, Pizzagalli DA, Sacchet MD (2022): Resting-state fMRI functional connectivity and mindfulness in clinical and non-clinical contexts: A review and synthesis. *Neurosci Biobehav Rev* 135: 104583.
40. Lee DJ, Kulubya E, Goldin P, Goodarzi A, Girgis F (2018): Review of the Neural Oscillations

Underlying Meditation. *Front Neurosci* 12: 178.

41. Kora P, Meenakshi K, Swaraja K, Rajani A, Raju MS (2021): EEG based interpretation of human brain activity during yoga and meditation using machine learning: A systematic review. *Complement Ther Clin Pract* 43: 101329.
42. Lim J, Teng J, Patanaik A, Tandi J, Massar SAA (2018): Dynamic functional connectivity markers of objective trait mindfulness. *Neuroimage* 176: 193–202.
43. Shaurya Prakash R, De Leon AA, Klatt M, Malarkey W, Patterson B (2013): Mindfulness disposition and default-mode network connectivity in older adults. *Soc Cogn Affect Neurosci* 8: 112–117.
44. Ganesan S, A Moffat B, Van Dam NT, Lorenzetti V, Zalesky A (2023): Meditation attenuates default-mode activity: A pilot study using ultra-high field 7 Tesla MRI. *Brain Res Bull* 203: 110766.
45. Guidotti R, D'Andrea A, Basti A, Raffone A, Pizzella V, Marzetti L (2023): Long-Term and Meditation-Specific Modulations of Brain Connectivity Revealed Through Multivariate Pattern Analysis. *Brain Topogr* 36: 409–418.
46. Lutz A, Brefczynski-Lewis J, Johnstone T, Davidson RJ (2008): Regulation of the neural circuitry of emotion by compassion meditation: effects of meditative expertise. *PLoS One* 3: e1897.
47. Kral TRA, Lapate RC, Imhoff-Smith T, Patsenko E, Grupe DW, Goldman R, *et al.* (2022): Long-term Meditation Training Is Associated with Enhanced Subjective Attention and Stronger Posterior Cingulate-Rostrolateral Prefrontal Cortex Resting Connectivity. *J Cogn Neurosci* 34: 1576–1589.
48. Garrison KA, Scheinost D, Constable RT, Brewer JA (2014): BOLD signal and functional connectivity associated with loving kindness meditation. *Brain Behav* 4: 337–347.
49. Uddin LQ, Nomi JS, Hébert-Seropian B, Ghaziri J, Boucher O (2017): Structure and Function of the Human Insula. *J Clin Neurophysiol* 34: 300–306.

50. Khalsa SS, Adolphs R, Cameron OG, Critchley HD, Davenport PW, Feinstein JS, *et al.* (2018): Interoception and Mental Health: A Roadmap. *Biol Psychiatry Cogn Neurosci Neuroimaging* 3: 501–513.

51. Posner MI, Rothbart MK, Sheese BE, Tang Y (2007): The anterior cingulate gyrus and the mechanism of self-regulation. *Cogn Affect Behav Neurosci* 7: 391–395.

52. Ebitz RB, Hayden BY (2016, September 27): Dorsal anterior cingulate: a Rorschach test for cognitive neuroscience. *Nature Neuroscience*, vol. 19. pp 1278–1279.

53. Luders E, Kurth F (2019): The neuroanatomy of long-term meditators. *Curr Opin Psychol* 28: 172–178.

54. Greenberg J, Romero VL, Elkin-Frankston S, Bezdek MA, Schumacher EH, Lazar SW (2019): Reduced interference in working memory following mindfulness training is associated with increases in hippocampal volume. *Brain Imaging Behav* 13: 366–376.

55. Sevinc G, Rusche J, Wong B, Datta T, Kaufman R, Gutz SE, *et al.* (2021): Mindfulness Training Improves Cognition and Strengthens Intrinsic Connectivity Between the Hippocampus and Posteromedial Cortex in Healthy Older Adults. *Front Aging Neurosci* 13: 702796.

56. Magalhaes AA, Oliveira L, Pereira MG, Menezes CB (2018): Does Meditation Alter Brain Responses to Negative Stimuli? A Systematic Review. *Front Hum Neurosci* 12: 448.

57. Kral TRA, Schuyler BS, Mumford JA, Rosenkranz MA, Lutz A, Davidson RJ (2018): Impact of short- and long-term mindfulness meditation training on amygdala reactivity to emotional stimuli. *Neuroimage* 181: 301–313.

58. Zeidan F, Baumgartner JN, Coghill RC (2019): The neural mechanisms of mindfulness-based pain relief: a functional magnetic resonance imaging-based review and primer. *Pain Rep* 4: e759.

59. Leung M-K, Lau WKW, Chan CCH, Wong SSY, Fung ALC, Lee TMC (2018): Meditation-induced neuroplastic changes in amygdala activity during negative affective

processing. *Soc Neurosci* 13: 277–288.

60. Bremer B, Wu Q, Mora Álvarez MG, Hölzel BK, Wilhelm M, Hell E, *et al.* (2022): Mindfulness meditation increases default mode, salience, and central executive network connectivity. *Sci Rep* 12: 13219.
61. Smith JL, Allen JW, Haack C, Wehrmeyer K, Alden K, Lund MB, Mascaro JS (2021): The Impact of App-Delivered Mindfulness Meditation on Functional Connectivity and Self-Reported Mindfulness Among Health Profession Trainees. *Mindfulness* 12: 92–106.
62. Kral TRA, Imhoff-Smith T, Dean DC, Grupe D, Adluru N, Patsenko E, *et al.* (2019): Mindfulness-Based Stress Reduction-related changes in posterior cingulate resting brain connectivity. *Soc Cogn Affect Neurosci* 14: 777–787.
63. Vishnubhotla RV, Radhakrishnan R, Kveraga K, Deardorff R, Ram C, Pawale D, *et al.* (2021): Advanced Meditation Alters Resting-State Brain Network Connectivity Correlating With Improved Mindfulness. *Front Psychol* 12: 745344.
64. Guu S-F, Chao Y-P, Huang F-Y, Cheng Y-T, Ng H-YH, Hsu C-F, *et al.* (2023): Interoceptive awareness: MBSR training alters information processing of salience network. *Front Behav Neurosci* 17: 1008086.
65. Taren AA, Gianaros PJ, Greco CM, Lindsay EK, Fairgrieve A, Brown KW, *et al.* (2017): Mindfulness Meditation Training and Executive Control Network Resting State Functional Connectivity: A Randomized Controlled Trial. *Psychosom Med* 79: 674–683.
66. Kang D-H, Jo HJ, Jung WH, Kim SH, Jung Y-H, Choi C-H, *et al.* (2013): The effect of meditation on brain structure: cortical thickness mapping and diffusion tensor imaging. *Soc Cogn Affect Neurosci* 8: 27–33.
67. Valk SL, Bernhardt BC, Trautwein F-M, Böckler A, Kanske P, Guizard N, *et al.* (2017): Structural plasticity of the social brain: Differential change after socio-affective and cognitive mental training. *Sci Adv* 3: e1700489.
68. Gotink RA, Meijboom R, Vernooij MW, Smits M, Hunink MGM (2016): 8-week Mindfulness

Based Stress Reduction induces brain changes similar to traditional long-term meditation practice - A systematic review. *Brain Cogn* 108: 32–41.

69. Hölzel BK, Carmody J, Vangel M, Congleton C, Yerramsetti SM, Gard T, Lazar SW (2011): Mindfulness practice leads to increases in regional brain gray matter density. *Psychiatry Res* 191: 36–43.

70. Lenhart L, Steiger R, Waibel M, Mangesius S, Grams AE, Singewald N, Gizewski ER (2020): Cortical reorganization processes in meditation naïve participants induced by 7 weeks focused attention meditation training. *Behav Brain Res* 395: 112828.

71. Kral TRA, Davis K, Korponay C, Hirshberg MJ, Hoel R, Tello LY, *et al.* (2022): Absence of structural brain changes from mindfulness-based stress reduction: Two combined randomized controlled trials. *Sci Adv* 8: eabk3316.

72. Chételat G, Lutz A, Klimecki O, Frison E, Asselineau J, Schlosser M, *et al.* (2022): Effect of an 18-Month Meditation Training on Regional Brain Volume and Perfusion in Older Adults: The Age-Well Randomized Clinical Trial. *JAMA Neurol* 79: 1165–1174.

73. Siew S, Yu J (2023): Mindfulness-based randomized controlled trials led to brain structural changes: an anatomical likelihood meta-analysis. *Sci Rep* 13: 18469.

74. Zeidan F, Vago DR (2016): Mindfulness meditation-based pain relief: a mechanistic account. *Ann N Y Acad Sci* 1373: 114–127.

75. Lorenzetti V, Gaillard A, Beyer E, Kowalczyk M, Kamboj SK, Manning V, Gleeson J (2023): Do mindfulness-based interventions change brain function in people with substance dependence? A systematic review of the fMRI evidence. *BMC Psychiatry* 23: 407.

76. Goldin PR, Thurston M, Allende S, Moodie C, Dixon ML, Heimberg RG, Gross JJ (2021): Evaluation of Cognitive Behavioral Therapy vs Mindfulness Meditation in Brain Changes During Reappraisal and Acceptance Among Patients With Social Anxiety Disorder: A Randomized Clinical Trial. *JAMA Psychiatry* 78: 1134–1142.

77. Li H, Yan W, Wang Q, Liu L, Lin X, Zhu X, *et al.* (2022): Mindfulness-Based Cognitive

Therapy Regulates Brain Connectivity in Patients With Late-Life Depression. *Front Psychiatry* 13: 841461.

78. van der Velden AM, Scholl J, Elmholdt E-M, Fjorback LO, Harmer CJ, Lazar SW, *et al.* (2023): Mindfulness Training Changes Brain Dynamics During Depressive Rumination: A Randomized Controlled Trial. *Biol Psychiatry* 93: 233–242.

79. Barnhofer T, Reess TJ, Fissler M, Winnebeck E, Grimm S, Gärtner M, *et al.* (2021): Effects of Mindfulness Training on Emotion Regulation in Patients With Depression: Reduced Dorsolateral Prefrontal Cortex Activation Indexes Early Beneficial Changes. *Psychosom Med* 83: 579–591.

80. Bachmann K, Lam AP, Sörös P, Kanat M, Hoxhaj E, Matthies S, *et al.* (2018): Effects of mindfulness and psychoeducation on working memory in adult ADHD: A randomised, controlled fMRI study. *Behav Res Ther* 106: 47–56.

81. Fam J, Sun Y, Qi P, Lau RC, Feng L, Kua EH, Mahendran R (2020): Mindfulness practice alters brain connectivity in community-living elders with mild cognitive impairment. *Psychiatry Clin Neurosci* 74: 257–262.

82. Bang M, Kim B, Lee KS, Choi TK, Lee S-H (2023): Long-term benefits of mindfulness on white matter tracts underlying the cortical midline structures in panic disorder: A 2-year longitudinal study. *Psychiatry Clin Neurosci* 77: 355–364.

83. Eickhoff SB, Nichols TE, Laird AR, Hoffstaedter F, Amunts K, Fox PT, *et al.* (2016): Behavior, sensitivity, and power of activation likelihood estimation characterized by massive empirical simulation. *Neuroimage* 137: 70–85.

84. Chaudhary IS, Shyi GC-W, Huang S-TT (2023): A systematic review and activation likelihood estimation meta-analysis of fMRI studies on arousing or wake-promoting effects in Buddhist meditation. *Front Psychol* 14: 1136983.

85. Young KS, van der Velden AM, Craske MG, Pallesen KJ, Fjorback L, Roepstorff A, Parsons CE (2018): The impact of mindfulness-based interventions on brain activity: A systematic

review of functional magnetic resonance imaging studies. *Neurosci Biobehav Rev* 84: 424–433.

86. Birn RM, Diamond JB, Smith MA, Bandettini PA (2006): Separating respiratory-variation-related fluctuations from neuronal-activity-related fluctuations in fMRI. *Neuroimage* 31: 1536–1548.

87. Dosenbach NUF, Fair DA, Miezin FM, Cohen AL, Wenger KK, Dosenbach RAT, *et al.* (2007): Distinct brain networks for adaptive and stable task control in humans. *Proc Natl Acad Sci U S A* 104: 11073–11078.

88. Sridharan D, Levitin DJ, Menon V (2008): A critical role for the right fronto-insular cortex in switching between central-executive and default-mode networks. *Proc Natl Acad Sci U S A* 105: 12569–12574.

89. Menon V (2011): Large-scale brain networks and psychopathology: a unifying triple network model. *Trends Cogn Sci* 15: 483–506.

90. Sim S, Maldonado IL, Castelnau P, Barantin L, Hage WE, Andersson F, Cottier J-P (2023): Neural correlates of mindfulness meditation and hypnosis on magnetic resonance imaging: similarities and differences. A scoping review. *J Neuroradiol*. https://doi.org/10.1016/j.neurad.2023.11.002

91. Escrichs A, Sanjuán A, Atasoy S, López-González A, Garrido C, Càmara E, Deco G (2019): Characterizing the Dynamical Complexity Underlying Meditation. *Front Syst Neurosci* 13: 27.

92. Weng HY, Lewis-Peacock JA, Hecht FM, Uncapher MR, Ziegler DA, Farb NAS, *et al.* (2020): Focus on the Breath: Brain Decoding Reveals Internal States of Attention During Meditation. *Front Hum Neurosci* 14: 336.

93. Zuo ZX, Price CJ, Farb NAS (2023): A machine learning approach towards the differentiation between interoceptive and exteroceptive attention. *Eur J Neurosci* 58: 2523–2546.

94. Valk SL, Kanske P, Park B-Y, Hong S-J, Böckler A, Trautwein F-M, *et al.* (2023): Functional and microstructural plasticity following social and interoceptive mental training. *Elife* 12: e85188.

95. Stein JL, Medland SE, Vasquez AA, Hibar DP, Senstad RE, Winkler AM, *et al.* (2012): Identification of common variants associated with human hippocampal and intracranial volumes. *Nat Genet* 44: 552–561.

96. van den Heuvel OA, Boedhoe PSW, Bertolin S, Bruin WB, Francks C, Ivanov I, *et al.* (2022): An overview of the first 5 years of the ENIGMA obsessive-compulsive disorder working group: The power of worldwide collaboration. *Hum Brain Mapp* 43: 23–36.

97. Ocklenburg S, Güntürkün O (2024): *The Lateralized Brain: The Neuroscience and Evolution of Hemispheric Asymmetries*. Elsevier.

98. Thompson PM, Jahanshad N, Ching CRK, Salminen LE, Thomopoulos SI, Bright J, *et al.* (2020): ENIGMA and global neuroscience: A decade of large-scale studies of the brain in health and disease across more than 40 countries. *Transl Psychiatry* 10: 1–28.

99. Han LKM, Dinga R, Hahn T, Ching CRK, Eyler LT, Aftanas L, *et al.* (2021): Brain aging in major depressive disorder: results from the ENIGMA major depressive disorder working group. *Mol Psychiatry* 26: 5124–5139.

100. Hahn S, Mackey S, Cousijn J, Foxe JJ, Heinz A, Hester R, *et al.* (2022): Predicting alcohol dependence from multi-site brain structural measures. *Hum Brain Mapp* 43: 555–565.

101. Bruin WB, Zhutovsky P, van Wingen GA, Bas-Hoogendam JM, Groenewold NA, Hilbert K, *et al.* (2024): Brain-based classification of youth with anxiety disorders: transdiagnostic examinations within the ENIGMA-Anxiety database using machine learning. *Nature Mental Health* 2: 104–118.

102. Kim B-G, Kim G, Abe Y, Alonso P, Ameis S, Anticevic A, *et al.* (2024): White matter diffusion estimates in obsessive-compulsive disorder across 1653 individuals: machine learning findings from the ENIGMA OCD Working Group. *Mol Psychiatry*.

https://doi.org/10.1038/s41380-023-02392-6

103. Petrov D, Gutman BA, Kuznetsov E, Ching CRK, Alpert K, Zavaliangos-Petropulu A, *et al.* (2018): Deep Learning for Quality Control of Subcortical Brain 3D Shape Models. *Shape in Medical Imaging* 268–276.

104. McWhinney SR, Abé C, Alda M, Benedetti F, Bøen E, Del Mar Bonnin C, *et al.* (2023): Mega-analysis of association between obesity and cortical morphology in bipolar disorders: ENIGMA study in 2832 participants. *Psychol Med* 53: 1–11.

105. Hashimoto N, Ito YM, Okada N, Yamamori H, Yasuda Y, Fujimoto M, *et al.* (2018): The effect of duration of illness and antipsychotics on subcortical volumes in schizophrenia: Analysis of 778 subjects. *Neuroimage Clin* 17: 563–569.

106. Zugman A, Harrewijn A, Cardinale EM, Zwiebel H, Freitag GF, Werwath KE, *et al.* (2022): Mega-analysis methods in ENIGMA: The experience of the generalized anxiety disorder working group. *Hum Brain Mapp* 43: 255–277.

107. Kennedy E, Vadlamani S, Lindsey HM, Lei P-W, Jo-Pugh M, Adamson M, *et al.* (2023): Bridging Big Data: Procedures for Combining Non-equivalent Cognitive Measures from the ENIGMA Consortium. *bioRxiv*. https://doi.org/10.1101/2023.01.16.524331

108. van Erp TGM, Preda A, Nguyen D, Faziola L, Turner J, Bustillo J, *et al.* (2014): Converting positive and negative symptom scores between PANSS and SAPS/SANS. *Schizophr Res* 152: 289–294.

109. Boedhoe PSW, Heymans MW, Schmaal L, Abe Y, Alonso P, Ameis SH, *et al.* (2018): An Empirical Comparison of Meta- and Mega-Analysis With Data From the ENIGMA Obsessive-Compulsive Disorder Working Group. *Front Neuroinform* 12: 102.

110. Kong X-Z, Mathias SR, Guadalupe T, ENIGMA Laterality Working Group, Glahn DC, Franke B, *et al.* (2018): Mapping cortical brain asymmetry in 17,141 healthy individuals worldwide via the ENIGMA Consortium. *Proc Natl Acad Sci U S A* 115: E5154–E5163.

111. Cheon E-J, Bearden CE, Sun D, Ching CRK, Andreassen OA, Schmaal L, *et al.* (2022):

Cross disorder comparisons of brain structure in schizophrenia, bipolar disorder, major depressive disorder, and 22q11.2 deletion syndrome: A review of ENIGMA findings. *Psychiatry Clin Neurosci* 76: 140–161.

112. Boedhoe PSW, van Rooij D, Hoogman M, Twisk JWR, Schmaal L, Abe Y, *et al.* (2020): Subcortical Brain Volume, Regional Cortical Thickness, and Cortical Surface Area Across Disorders: Findings From the ENIGMA ADHD, ASD, and OCD Working Groups. *Am J Psychiatry* 177: 834–843.
113. Engström M, Willander J, Simon R (2022): A Review of the Methodology, Taxonomy, and Definitions in Recent fMRI Research on Meditation. *Mindfulness* 13: 541–555.
114. Dahl CJ, Lutz A, Davidson RJ (2015): Reconstructing and deconstructing the self: cognitive mechanisms in meditation practice. *Trends Cogn Sci* 19: 515–523.
115. Wright MJ, Sanguinetti JL, Young S, Sacchet MD (2023): Uniting Contemplative Theory and Scientific Investigation: Toward a Comprehensive Model of the Mind. *Mindfulness* 14: 1088–1101.
116. Lutz A, Dunne JD, Davidson RJ (2007): Meditation and the neuroscience of consciousness: an introduction. *The Cambridge Handbook of Consciousness*. Cambridge University Press.
117. Desbordes G, Gard T, Hoge EA, Hölzel BK, Kerr C, Lazar SW, *et al.* (2014): Moving beyond Mindfulness: Defining Equanimity as an Outcome Measure in Meditation and Contemplative Research. *Mindfulness* 2014: 356–372.
118. Galante J, Grabovac A, Wright M, Ingram DM, Van Dam NT, Sanguinetti JL, *et al.* (2023): A Framework for the Empirical Investigation of Mindfulness Meditative Development. *Mindfulness* 14: 1054–1067.
119. Franquesa A, Cebolla A, García-Campayo J, Demarzo M, Elices M, Pascual JC, Soler J (2017): Meditation Practice Is Associated with a Values-Oriented Life: the Mediating Role of Decentering and Mindfulness. *Mindfulness* 8: 1259–1268.

120. Luberto CM, Shinday N, Song R, Philpotts LL, Park ER, Fricchione GL, Yeh GY (2018): A Systematic Review and Meta-analysis of the Effects of Meditation on Empathy, Compassion, and Prosocial Behaviors. *Mindfulness* 9: 708–724.

121. Brahm (2006): *Mindfulness, Bliss, and Beyond: A Meditator's Handbook*. Simon and Schuster.

122. Van Dam NT, van Vugt MK, Vago DR, Schmalzl L, Saron CD, Olendzki A, *et al.* (2018): Mind the Hype: A Critical Evaluation and Prescriptive Agenda for Research on Mindfulness and Meditation. *Perspect Psychol Sci* 13: 36–61.

123. Davidson RJ, Kaszniak AW (2015): Conceptual and methodological issues in research on mindfulness and meditation. *Am Psychol* 70: 581–592.

124. Goldberg SB, Wielgosz J, Dahl C, Schuyler B, MacCoon DS, Rosenkranz M, *et al.* (2016): Does the Five Facet Mindfulness Questionnaire measure what we think it does? Construct validity evidence from an active controlled randomized clinical trial. *Psychol Assess* 28: 1009–1014.

125. Fox KCR, Zakarauskas P, Dixon M, Ellamil M, Thompson E, Christoff K (2012): Meditation experience predicts introspective accuracy. *PLoS One* 7: e45370.

126. Lutz A, Thompson E (2003): Neurophenomenology Integrating Subjective Experience and Brain Dynamics in the Neuroscience of Consciousness. *Journal of Consciousness Studies* 10: 31–52.

127. Garrison KA, Scheinost D, Worhunsky PD, Elwafi HM, Thornhill TA 4th, Thompson E, *et al.* (2013): Real-time fMRI links subjective experience with brain activity during focused attention. *Neuroimage* 81: 110–118.

128. Morris SE, Sanislow CA, Pacheco J, Vaidyanathan U, Gordon JA, Cuthbert BN (2022): Revisiting the seven pillars of RDoC. *BMC Med* 20: 220.

129. Constantinides C, Han LKM, Alloza C, Antonucci LA, Arango C, Ayesa-Arriola R, *et al.* (2022): Brain ageing in schizophrenia: evidence from 26 international cohorts via the

ENIGMA Schizophrenia consortium. *Mol Psychiatry* 28: 1201–1209.

130. Fingelkurts AA, Fingelkurts AA, Kallio-Tamminen T (2015): EEG-guided meditation: A personalized approach. *J Physiol Paris* 109: 180–190.

131. Webb CA, Hirshberg MJ, Davidson RJ, Goldberg SB (2022): Personalized Prediction of Response to Smartphone-Delivered Meditation Training: Randomized Controlled Trial. *J Med Internet Res* 24: e41566.

132. Webb CA, Swords CM, Lawrence HR, Hilt LM (2022): Which adolescents are well-suited to app-based mindfulness training? A randomized clinical trial and data-driven approach for personalized recommendations. *J Consult Clin Psychol* 90: 655–669.

133. Kambolis DM (2017): Predictors of Meditation Success: A Literature Review. *https://www.semanticscholar.org › paper › Predictors-of..https://www.semanticscholar.org › paper › Predictors-of.* Retrieved February 29, 2024, from https://pdfs.semanticscholar.org/7133/1990b6c29fb67be6ecd1a2c0badeb04fd2dc.pdf

134. Schlosser M, Sparby T, Vörös S, Jones R, Marchant NL (2019): Unpleasant meditation-related experiences in regular meditators: Prevalence, predictors, and conceptual considerations. *PLoS One* 14: e0216643.

135. Escrichs A, Perl YS, Uribe C, Camara E, Türker B, Pyatigorskaya N, *et al.* (2022): Unifying turbulent dynamics framework distinguishes different brain states. *Communications Biology* 5: 1–13.

136. De Filippi E, Escrichs A, Càmara E, Garrido C, Marins T, Sánchez-Fibla M, *et al.* (2022): Meditation-induced effects on whole-brain structural and effective connectivity. *Brain Struct Funct* 227: 2087–2102.

137. Guidotti R, Del Gratta C, Perrucci MG, Romani GL, Raffone A (2021): Neuroplasticity within and between Functional Brain Networks in Mental Training Based on Long-Term Meditation. *Brain Sci* 11. https://doi.org/10.3390/brainsci11081086

138. Cain JA, Brandmeyer T, Simonian N, Sanguinetti J, Young S, Sacchet M, Reggente N

(2024): Facilitating meditation with focused ultrasound neuromodulation : A first investigation in experienced practitioners. osf.io. Retrieved February 29, 2024, from https://osf.io/3bzg6/download

139. Zhang J, Raya J, Morfini F, Urban Z, Pagliaccio D, Yendiki A, *et al.* (2023): Reducing default mode network connectivity with mindfulness-based fMRI neurofeedback: a pilot study among adolescents with affective disorder history. *Mol Psychiatry* 28: 2540–2548.

140. Hafeman DM, Ostroff AN, Feldman J, Hickey MB, Phillips ML, Creswell D, *et al.* (2020): Mindfulness-based intervention to decrease mood lability in at-risk youth: Preliminary evidence for changes in resting state functional connectivity. *J Affect Disord* 276: 23–29.

141. Kirlic N, Cohen ZP, Tsuchiyagaito A, Misaki M, McDermott TJ, Aupperle RL, *et al.* (2022): Self-regulation of the posterior cingulate cortex with real-time fMRI neurofeedback augmented mindfulness training in healthy adolescents: A nonrandomized feasibility study. *Cogn Affect Behav Neurosci* 22: 849–867.

142. van Aalst J, Ceccarini J, Demyttenaere K, Sunaert S, Van Laere K (2020): What Has Neuroimaging Taught Us on the Neurobiology of Yoga? A Review. *Front Integr Neurosci* 14: 34.

143. Yu AP, Tam BT, Lai CW, Yu DS, Woo J, Chung K-F, *et al.* (2018): Revealing the Neural Mechanisms Underlying the Beneficial Effects of Tai Chi: A Neuroimaging Perspective. *Am J Chin Med* 46: 231–259.

144. Tate DF, Dennis EL, Adams JT, Adamson MM, Belanger HG, Bigler ED, *et al.* (2021): Coordinating Global Multi-Site Studies of Military-Relevant Traumatic Brain Injury: Opportunities, Challenges, and Harmonization Guidelines. *Brain Imaging Behav* 15: 585–613.

145. Olsen A, Babikian T, Bigler ED, Caeyenberghs K, Conde V, Dams-O'Connor K, *et al.* (2021): Toward a global and reproducible science for brain imaging in neurotrauma: the ENIGMA adult moderate/severe traumatic brain injury working group. *Brain Imaging Behav*

15: 526–554.

146. Larivière S, Paquola C, Park B-Y, Royer J, Wang Y, Benkarim O, *et al.* (2021): The ENIGMA Toolbox: multiscale neural contextualization of multisite neuroimaging datasets. *Nat Methods* 18: 698–700.

147. Radua J, Vieta E, Shinohara R, Kochunov P, Quidé Y, Green MJ, *et al.* (2020): Increased power by harmonizing structural MRI site differences with the ComBat batch adjustment method in ENIGMA. *Neuroimage* 218: 116956.

148. Miller KL, Alfaro-Almagro F, Bangerter NK, Thomas DL, Yacoub E, Xu J, *et al.* (2016): Multimodal population brain imaging in the UK Biobank prospective epidemiological study. *Nat Neurosci* 19: 1523–1536.

149. Hilabi BS, Alghamdi SA, Almanaa M (2023): Impact of Magnetic Resonance Imaging on Healthcare in Low- and Middle-Income Countries. *Cureus* 15: e37698.

150. Murali S, Ding H, Adedeji F, Qin C, Obungoloch J, Asllani I, *et al.* (2023): Bringing MRI to low- and middle-income countries: Directions, challenges and potential solutions. *NMR Biomed* e4992.