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Review

Is meditation associated with altered brain structure? A systematic review and meta-analysis of morphometric neuroimaging in meditation practitioners

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ABSTRACT

Numerous studies have begun to address how the brain's gray and white matter may be shaped by meditation. This research is yet to be integrated, however, and two fundamental questions remain: Is meditation associated with altered brain structure? If so, what is the magnitude of these differences? To address these questions, we reviewed and meta-analyzed 123 brain morphology differences from 21 neuroimaging studies examining ~300 meditation practitioners. Anatomical likelihood estimation (ALE) meta-analysis found eight brain regions consistently altered in meditators, including areas key to meta-awareness (frontopolar cortex/BA 10), exteroceptive and interoceptive body awareness (sensory cortices and insula), memory consolidation and reconsolidation (hippocampus), self and emotion regulation (anterior and mid cingulate; orbitofrontal cortex), and intra- and interhemispheric communication (superior longitudinal fasciculus; corpus callosum). Effect size meta-analysis (calculating 132 effect sizes from 16 studies) suggests a global 'medium' effect size (Cohen's $\bar{d} = 0.46$; $\bar{r} = .19$). Publication bias and methodological limitations are strong concerns, however. Further research using rigorous methods is required to definitively link meditation practice to altered brain morphology.

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1. Introduction

A range of effects have been associated with long- and short-term training in the mental practices broadly referred to as 'meditation.' A few striking examples include enhancement of executive functions, such as attention (Jha et al., 2007), working memory (Jha et al., 2010), and introspection (Fox et al., 2012; Sze et al., 2010); improved immune function (Davidson

Table 1
Summary of morphometric neuroimaging methods used to study meditation practitioners.

Morphometric measure	Summary	Proposed significance
Volumetry	Measures the volume (mm^3) of a particular predefined ROI (e.g., amygdala)	Larger volumetric measure → larger structure size
Concentration	Estimates the concentration of gray or white matter throughout the brain on a voxel-by-voxel basis, or in voxels within a predefined ROI	Greater concentration → greater density of tissue type within voxel or ROI
Thickness	Estimates the thickness (mm) of either cortex or other structures (e.g., corpus callosum)	Greater thickness → greater number of neurons/glia or fibers in a given region
Fractional Anisotropy	Estimates how ‘cigar-shaped’ (anisotropic) white matter fiber tracts are at a given voxel	Greater FA → greater white matter fiber density and/or coherence
Diffusivity	Estimates the coherence of water diffusion either parallel (axial diffusivity) or perpendicular (radial diffusivity) to axons	*Lower* axial and radial diffusivity → greater axonal integrity and myelination, respectively
Gyrification	Estimates the degree of folding of cortical surface on a point-by-point basis	Higher index of gyrification → greater cortical surface area (mm^2) per unit volume (mm^3)

Note: For more information, see Beaulieu (2002), May and Gaser (2006), Draganski and May (2008), Zatorre et al. (2012). FA: fractional anisotropy; ROI: region of interest.

et al., 2003; Jacobs et al., 2011); better perceptual discrimination (MacLean et al., 2010); increased prosocial (compassionate) behavior (Condon et al., 2013); and symptom improvements in clinical disorders, such as anxiety and depression (Vollestad et al., 2012). Skepticism is certainly warranted, however, when a relatively straightforward intervention demonstrates such a wide variety of benefits. With the aim of evaluating the consistency and practical significance of this body of results, a recent comprehensive meta-analysis found robust evidence that meditation practice is associated with an array of cognitive and emotional benefits that often achieve medium to large effect sizes (Sedlmeier et al., 2012). As evidence mounts that meditation may have wide-ranging and measurable effects on many aspects of brain, body, and behavior, understanding the biological mechanisms that underlie these effects is of paramount scientific and public health importance.

The study of the functional neuroanatomical bases that drive meditation’s apparently salutary effects remains in its infancy, however. This is all the more true of research examining putative differences in the *anatomical structure* of the brains of meditation practitioners. Although many studies have examined meditation with functional methods such as electroencephalography (EEG), event-related potentials (ERPs), positron emission tomography (PET), and functional magnetic resonance imaging (fMRI) (reviewed in Cahn and Polich, 2006; Hölzel et al., 2011b; Vago and Silbersweig, 2012), an understanding of potential *structural* differences via ‘morphometric’ neuroimaging remains limited (Table 1). Such an understanding is important because evidence is mounting that experience-dependent structural differences in both gray (Draganski and May, 2008; Lövdén et al., 2013) and white matter (Johansen-Berg, 2010) are fundamental to many aspects of learning and behavior in humans (though for a counterpoint, see Thomas and Baker, 2012).

1.1. Overview of the present meta-analysis

Since the first morphometric study of meditation less than a decade ago (Lazar et al., 2005), numerous studies have addressed the potential effects of meditation on brain morphology (Table 2), with over 120 results already reported (Table S1). However, the wide variety of results, sample sizes, and meditation styles makes it very difficult to readily draw a cohesive picture of meditation’s relationship to brain morphology. This difficulty is compounded by the diversity of morphometric neuroimaging methods employed (Table 1).

Supplementary Table S1 related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.neubiorev.2014.03.016.

In the absence of an overall view of what has been achieved so far, two central questions remain: (1) Is meditation associated with altered brain morphology in any consistent, replicable ways? And if so, (2) what is the magnitude (size) of these differences – i.e., are the differences potentially of any practical importance or clinical relevance? Another open question concerns whether meditation is in fact the causative factor in these brain morphology changes, because the majority of studies to date have employed cross-sectional methods, comparing long-term meditation practitioners to meditation-naïve controls. Such cross-sectional studies cannot address the critical question of whether meditation is in fact *causing* the observed structure differences, or whether pre-existing differences of brain morphology make certain people more likely to engage in intensive meditation practice (see more details in Section 6.2). A few recent studies, however, have used pre–post interventions that *can* begin to address the causal role of meditation in altering brain morphology. Another key goal, then, was to examine which regions are consistently altered after short-term meditation training, therefore suggesting a causal role for meditation – and to examine the extent to which such meditation-induced changes resemble the cross-sectional differences observed in long-term practitioners. A third, ancillary question, then, was (3) what evidence there might be for mediation as the *causative factor* in altered brain morphology.

These are all complex questions. A detailed review and meta-analysis of both neuroimaging results and effect sizes therefore seemed necessary for understanding how morphometric neuroimaging has been applied to the study of meditation, and what conclusions, if any, can be drawn from this body of work. Here, we attempt to synthesize the literature to date by performing both a systematic review and quantitative meta-analyses of all extant morphometric neuroimaging studies of meditation. Our central aim is to provide answers to the two fundamental questions posed above, and to address, so far as is possible given the limited evidence to date, the third question regarding causation.

1.1.1. Morphometric neuroimaging meta-analysis

First, of the many findings on brain morphology differences related to meditation practice, are there regions that have been repeatedly implicated in subsequent studies? To answer this question, we used anatomical likelihood estimation (ALE), a quantitative meta-analytic technique (Eickhoff et al., 2009, 2012; Laird et al., 2005; Turkeltaub et al., 2002), to identify brain regions showing consistent heterogeneities in meditation practitioners. Where use of ALE was not possible, we also ‘qualitatively’ reviewed all results to see which regions were repeatedly (in ≥ 3 studies) implicated in meditation. Neuroimaging studies typically report a ‘peak’ focus in the brain, where differences between groups (meditators vs. controls) is most statistically significant. Each study reports multiple such peaks of greatest anatomical difference; compiling all these peaks together, the ALE method seeks for statistically significant

Table 2
Summary of all morphometric studies of meditation.

Study	Meditation tradition	Sample (MED/CON)	Hand (R/L)	Meditators Age ($M \pm SD$)	Morphometric measure	Mean effect size (Cohen's *d*)	Regions showing heterogeneities
Lazar et al. (2005)	Insight	20/15	MED: 18/2 CONT: 15/0	38.2 years	Cortical thickness	–	R anterior insula; R middle and superior frontal sulci
Pagnoni and Cekic (2007)	Zen	13/13	All R (1 MED ambidex)	37.2 ± 6.9 years	Gray matter volume (VBM in SPM5)	2.14	L putamen
Hölzel et al. (2008)	Insight (BSM)	20/20	All R	34.1 ± 4.7 years	Gray matter concentration (VBM in SPM2)	1.18	L inferior temporal gyrus; R insula; R hippocampus
Vestergaard-Poulsen et al. (2009)	Tibetan Buddhist	10/10	MED:– CONT: 10/0	55.0 ± 6.2 years	Gray matter concentration and volume (VBM in SPM5)	–	Bilateral medulla; L fusiform gyrus; bilateral cerebellum; L middle and inferior frontal gyri;
Luders et al. (2009)	*Various*	22/22	MED: 22/0 CONT: 21/1	53.0 ± 11.5 years	Gray matter volume (VBM in SPM5)	0.34	R orbito-frontal cortex; R thalamus; L inferior temporal gyrus; R hippocampus
Grant et al. (2010)	Zen	19/20	–	37.6 ± 10.9 years	Cortical thickness	0.68	R dorsal anterior cingulate cortex; bilateral secondary somatosensory cortex
Hölzel et al. (2010)	MBSR	26/–	All R	35.2 ± 6.7 years	Gray matter concentration	–	Amygdala*
Tang et al. (2010)	IBMT	22/23	–	20.6 ± 1.6 years	Fractional anisotropy (DTI in FSL 4.1)	–	L anterior corona radiata; bilateral superior corona radiata; genu of CC; body of CC; L superior longitudinal fasciculus
Luders et al. (2011) Δ	*Various*	27/27	All R	51.6 ± 12.3 years	Fractional anisotropy (DTI)	0.55	18 white matter tracts throughout brain
Hölzel et al. (2011a)	MBSR	16/17	All R	38.0 ± 4.1 years	Gray matter concentration (VBM in SPM5)	1.91	L hippocampus; posterior cingulate cortex; L temporo-parietal junction; cerebellum
Luders et al. (2012a) Δ	*Various*	30/30	MED: 28/2 CONT: 28/2	47.3 ± 11.7 years	Fractional anisotropy (DTI)	0.89	Corpus callosum
Luders et al. (2012b)	*Various*	50/50	MED: 44/6 CONT: 45/5	51.4 ± 12.8 years	Cortical gyrification	0.64	Bilateral anterior insula; L precentral gyrus; R fusiform gyrus; R cuneus
Tang et al. (2012)	IBMT	34/34	–	20.5 ± 1.4 years	Fractional anisotropy, axial and radial diffusivity (DTI)	–	*Various*
Luders et al. (2012c) Δ	*Various*	30/30	MED: 28/2 CONT: 28/2	47.3 ± 11.7 years	Volume and radial distance	0.53	Bilateral hippocampus
Farb et al. (2013)	MBSR	20/16	All R	45.6 ± 13.4 years	Gray matter volume (VBM in SPM8)	1.24	L caudate nucleus
Fayed et al. (2013)	Zen	10/10	–	39.5 ± 11.1 years	Fractional anisotropy (DTI)	−2.97	L sensorimotor cortex*
Grant et al. (2013) Δ	Zen	18/18	–	37.1 ± 10.9 years	Cortical thickness	0.69	L supramarginal gyrus, L superior parietal lobule, L superior frontal gyrus
Kang et al. (2013)	BWV	46/46	All R	25.4 ± 3.3 years	Cortical thickness and fractional anisotropy (DTI)	0.60	*Various*
Kumar et al. (2013)	Soham	14/14	–	29.4 ± 2.0 years	Gray matter volume (VBM in SPM5)	0.71	L ventral palladium; L supplementary motor area; brain stem (medulla)
Leung et al. (2013)	LKM	10/15	All R	50.2 ± 10.5 years	Gray matter volume	1.69	R angular gyrus; R parahippocampal gyrus; L inferior temporal gyrus
Luders et al. (2013) Δ	*Various*	50/50	MED: 44/6 CONT: 45/5	51.4 ± 12.8 years	Gray matter concentration (VBM in SPM8)	0.26	Bilateral hippocampus/subiculum

BSM: body-scanning meditation; BWV: brain wave vibration; CC: corpus callosum; CON: controls; DTI: diffusion tensor imaging; IBMT: integrative body-mind training; L: left; LKM: loving-kindness meditation; MBSR: mindfulness-based stress reduction; MED: meditators; R: right; SPM: Statistical Parametric Mapping (Wellcome Trust Centre for Neuroimaging, London); VBM: voxel-based morphometry. – = data not reported or not applicable.

* Regions where reductions (rather than enhancements) of structure were seen after meditation training.

Δ Studies employing samples of meditation practitioners that overlap partially or entirely with prior studies.

overlaps in the peaks from independent studies. In this way, we were able to compile a list of regions that appear to be consistently altered in meditation practitioners, across many independent studies and samples (see Section 2 for detailed information).

1.1.2. Effect size meta-analysis

Knowing that certain regions are consistently different in meditation practitioners, however, does not necessarily imply that the differences are of any *practical* significance. Even if consistent and statistically significant, such brain structure differences might be too small to be considered relevant in a practical, everyday sense. Calculation of effect sizes, however, which indicate not the significance but the *magnitude* of results, can begin to address these questions of practical significance (Cumming, 2013). Simply testing whether a result is significant or not (null-hypothesis significance testing) is limited by the fact that attaining significance is very much dependent on sample size (Cumming, 2013) – and sample size is generally quite small in most neuroimaging studies, due to the high costs involved. Effect sizes, however, estimate the magnitude of differences between groups, regardless of whether the result was statistically significant (where non-significance, e.g., might be due simply to small sample size). Our effect size meta-analysis therefore allowed an overview of the apparent magnitude of brain structure differences reported in meditators. Although effect sizes are still rarely reported in neuroimaging studies, and their interpretation with respect to brain structure differences remains problematic and poorly developed at the theoretical level (Poldrack et al., 2008), we nonetheless aimed to present all quantitative effect size data and offer some preliminary interpretations of their significance.

1.2. Morphometric neuroimaging of brain structure in meditation practitioners

Brain 'morphology' refers to the structure, shape, and composition of the brain; the measurement and analysis of brain morphology via various neuroimaging techniques is generally known as 'morphometry' or 'morphometric neuroimaging' (Draganski and May, 2008; May and Gaser, 2006; Zatorre et al., 2012). Broadly speaking, morphometric neuroimaging techniques aim to characterize anatomical differences based on a variety of morphological characteristics. Some relate solely to the brain's shape or size (e.g., cortical gyrification), others take into account the relative concentration or organization of gray and white matter (e.g., gray matter concentration), and yet others combine both aspects (e.g., volumetry of predefined gray matter structures). Morphometric neuroimaging stands in contrast, then, to 'functional' neuroimaging techniques such as fMRI, EEG, and PET, which aim to characterize not brain *structure*, but brain *activity*, such as changes in electrical potentials or blood flow.

A brief overview of measures used to date in morphometric studies of meditation is presented in Table 1 (for in-depth reviews outside the field of meditation, see Draganski and May, 2008; May and Gaser, 2006; Zatorre et al., 2012; for specific methods, see Ashburner and Friston, 2000; Beaulieu, 2002; Fischl and Dale, 2000).

1.3. Does increase of structure equal enhancement of function?

A sometimes-tacit assumption underlying morphometric neuroimaging is that greater values (structural 'increase') on a given morphometric measure entail a corresponding enhancement of function. The structural increases in question could be, e.g., an increased concentration of gray matter in a given region; an increased thickness of cerebral cortex; increased integrity of white matter fibers; or any number of other measures (see Table 1). In support of this view, there are well-established connections between brain maturation and cognitive development, as well as a complementary link between neurodegenerative disease, or atrophy, and cognitive decline.

More specifically, there exists fairly robust evidence in favor of the brain structure–function connection in both animal models and human neuroimaging. Several important studies have established relationships between structural 'increases' of both gray and white matter (for recent reviews, see Taubert et al., 2012; Zatorre et al., 2012) and beneficial outcomes, including achievement in a variety of fine motor skills, such as juggling (Draganski et al., 2004; Scholz et al., 2009) and musical instrument playing (Hyde et al., 2009). Even gross physical activities, such as aerobic exercise, show an 'enhancing' effect on brain morphology (Colcombe et al., 2006).

Importantly, such differences are observed not only in response to physical or motor skill training: some studies have recently found morphometric differences after mental training in reasoning (Mackey et al., 2012) and working memory (Takeuchi et al., 2011). Conversely, structural deterioration or deficiencies measured via morphometric neuroimaging have been linked to various forms of cognitive decline, including normal age-related cognitive decline (Good et al., 2001) and Alzheimer's disease (Frisoni et al., 2007).

The possibility remains, of course, that 'less is more' in at least some cases: the phenomenon of synaptic pruning provides a forceful example (Low and Cheng, 2006). Structural increases might also indicate functional *impairments* in at least some cases: several brain regions related to stimulus-response learning and habit formation show structural increases in obsessive compulsive disorder, for instance (Pujol et al., 2004).

Morphometric neuroimaging in meditation practitioners has generally aimed to explore whether meditation, too, is analogous to a form of (mental) skill learning, and can produce such anatomical changes. If so, brain structure increases related to meditative practice might provide at least a partial neural explanation of the numerous cognitive and emotional benefits associated with meditation (Sedlmeier et al., 2012). It should be acknowledged, however, that both in the field of morphometric neuroimaging as a whole, as well as within the smaller realm involving meditation practitioners in particular, the meaning of these brain structure differences is still very poorly understood. Very few studies have been directly replicated, and very few have correlated behavioral changes with brain structure differences. Enthusiasm about altered brain structure in meditation practitioners should therefore be tempered by the fact that the significance of these changes remains controversial (cf. Thomas and Baker, 2012); indeed, this is one of the main reasons for the present meta-analysis.

1.4. Are disparate morphometric neuroimaging methods comparable?

In collating data from multiple morphometric neuroimaging modalities, our interest is in the *regions* where differences have consistently been reported, irrespective of imaging method. The assumption is not that morphometric methods are necessarily directly comparable, but rather that particular brain regions are reliably involved in particular cognitive and emotional processes. Accordingly, alteration of a region's structure (regardless of imaging method) is presumed to entail a corresponding alteration in its function(s).

Whether a morphological difference in a single region will yield consistent results across morphometric methods is poorly understood. Since very few studies employ multiple methods simultaneously, direct comparisons are rare. However, there is preliminary evidence that results from disparate methods are comparable. For instance, Hutton et al. (2009) found broadly similar results when comparing two different-aged populations, using both gray matter concentration and cortical thickness analysis, and

Testa et al. (2004) found that volumetry methods showed results consistent with gray matter concentration analysis. Nevertheless, different methods should not be expected to produce entirely consistent results, since they likely rely on different underlying cellular changes for their outcomes (see Section 5.5). Ultimately, the differing sensitivity of various methods may prove to be a source of additional information, rather than a shortcoming (for a critical discussion, see Lemaitre et al., 2012).

1.5. *The varieties of meditative experience*

Meditation techniques vary enormously in aims, scope, difficulty, and tentatively, recruitment of brain regions (Brewer et al., 2011; Lee et al., 2012; Lou et al., 1999; Manna et al., 2010). Zen practice, for instance, tends to involve an open, undirected awareness of the present moment (Austin, 1999). Some traditions of *Vipassana* ('Insight') meditation, on the other hand, focus very explicitly on body sensations in a directed, systematic fashion (Goenka, 2000). Yet other practices involve detailed visualizations, simple awareness of the breath, or audible repetition of a particular phrase (a 'mantra') (Singh, 1979).

There are several influential attempts to find commonalities among techniques, however. The most well-known scheme categorizes practices into either 'focused attention' or 'open monitoring' meditations (Lutz et al., 2008), alternatively referred to as 'concentrative' and 'mindfulness' techniques, respectively (Cahn and Polich, 2006). Focused attention practices involve concentration of attention on a single object of meditation (e.g., the sensations of the breath, the recitation of a phrase, or the mental visualization of an image). Open monitoring practices, sometimes referred to as 'choiceless awareness,' instead involve an open, receptive, non-judgmental attitude toward any and all experience, regardless of origin (external/sensory or internal/mental) and affective tone (positive, negative, or neutral).

With respect to morphometric neuroimaging, however, it is difficult to study the neural basis of each category (much less each particular technique) independently of the others, for several reasons. Most practitioners examined to date have substantial experience with multiple categories, and more specifically, there is a dearth of studies examining only focused attention meditation practitioners (since focused attention meditation is almost always combined with, or followed by, open monitoring and compassion types of meditation). Moreover, numerous studies mix practitioners from multiple traditions in their analyses (Table 2). Therefore, despite the potential value of various classification schemes, comparative analyses based on meditation type were not undertaken here (although, where possible, a tentative discussion is offered). Whether distinct patterns of structural differences are related to particular forms of meditation practice therefore remains a question for future research.

1.6. *Prior syntheses*

Why the need for a new review and meta-analysis? Although a number of major efforts toward theoretical integration have been published in recent years (Hölzel et al., 2011b; Vago and Silbersweig, 2012; Farb et al., 2012), only a few thorough reviews of functional and morphometric neuroimaging in meditation practitioners have been undertaken (Cahn and Polich, 2006; Chiesa and Serretti, 2010; Ivanovski and Mahli, 2007; Rubia, 2009). Though generally comprehensive, several include only 'mindfulness' meditation, and only two recent studies (Sperduti et al., 2012; Tomasino et al., 2013) have conducted quantitative meta-analyses (ALE) of the burgeoning neuroimaging literature. These meta-analyses (Sperduti et al., 2012; Tomasino et al., 2013) suffer from certain limitations, such as no calculation or discussion of effect sizes, and no basic checks to ensure the robustness of the meta-analytic data (e.g., funnel plots or fail-safe *N* calculations; see Egger et al., 1997). These limitations are common to many earlier meta-analyses of meditation's cognitive and emotional effects as well (see Sedlmeier et al., 2012). Moreover, no synthesis or quantitative meta-analysis whatsoever of *morphometric* (i.e., structural) neuroimaging of meditation practitioners has yet been undertaken, despite the fact that the 21 studies examined here have already been cited more than 2200 times. Prior reviews and meta-analyses have instead tended to focus on *functional* neuroimaging results. In the present work we aim to fill this gap in the literature by providing a systematic review and quantitative meta-analysis of all morphometric neuroimaging studies of meditation.

2. Review methods

2.1. *Study selection*

2.1.1. *Search strategy*

Two of us (KCRF and SN) searched MEDLINE (http://www.pubmed.com), Google Scholar (http://scholar.google.com), and PsycINFO (http://www.apa.org/pub/databases/psycinfo/index.aspx) for all papers containing the word 'meditation' since the first morphometric study of contemplative practices was published (Lazar et al., 2005). These extensive lists of articles were then refined by searching within results for studies that contained any of the words or phrases 'magnetic resonance imaging', 'MRI,' 'neuroimaging,' 'diffusion tensor imaging,' or 'brain' within the title or abstract. Of the remaining results, every abstract was consulted to see if the study indeed employed morphometric methods to study meditation. The reference lists of each study found, as well as those of several major reviews, were also consulted, to ensure that no studies were missed.

2.1.2. *Excluded studies*

Studies examining effects of related practices on brain morphology, such as Tai Chi (Wei et al., 2013) and hatha yoga (Froeliger et al., 2012a,b), were excluded due to potential confounds and non-comparability. Studies examining morphological heterogeneities related to 'dispositional' (i.e., questionnaire-based) mindfulness measures (Taren et al., 2013; Murakami et al., 2013) were likewise excluded due to the unknown reliability of mindfulness questionnaires, and their ambiguous relationship to actual meditation practice and its effects (the widely used 'Five Facet Mindfulness Questionnaire' [FFMQ], for instance, correlates just as well with education as with meditation experience; Baer et al., 2008). We also excluded two studies investigating the relationship between meditation and brain structure that employed clinical populations with either Parkinson's disease (Pickut et al., 2013) or mild cognitive impairment (Wells et al., 2013). Although the interaction between meditation practice, neurodegenerative disease, and brain morphology is of immense interest, these clinical disorders are in themselves thought to involve significant alterations in brain structure (e.g., Jack et al., 1999; Ramirez-Ruiz et al., 2005), presenting an obvious confound if included in our meta-analyses.

2.1.3. *Included studies*

Only studies that actually involved either short-term meditation training or long-term meditation practitioners were included (Table 2); that is, studies that used questionnaire-based measures purporting to measure 'mindfulness' or some other construct were not included (see above, Section 2.1.2). Comparison groups were generally age-, sex-, and handedness-matched control subjects with no meditation experience. For short-term meditation training studies, wait-list controls with an interest in the same meditation intervention were usually employed. Evidently, random assignment is not possible when comparing long-term practitioners with meditation-naïve controls (for more on the possibility of self-selection bias in expert practitioners, see Section 6.2). All studies of short-term training, however, used random assignment to control and experimental conditions. Overall, 21 studies met our criteria and were included in the meta-analysis (Table 2).

Three of these 21 included studies used subjects who reported high levels of stress on self-report questionnaires and who voluntarily enrolled in a mindfulness-based stress reduction (MBSR) course for short-term meditation training (Farb et al., 2013; Hölzel et al., 2010, 2011a). High self-reported stress is far from a clinical diagnosis of a mental health disorder, however, and all subjects had voluntarily enrolled in such courses (vs. being enrolled by a physician or other caregiver, for example). We therefore decided that these studies warranted inclusion in the meta-analysis, and need not be excluded (as were the two clinical studies noted above; Section 2.1.2). In any case, as discussed in Section 3, overall meta-analytic results were hardly affected by whether these few short-term training studies were included or excluded (see Sections 3.1 and 3.3).

2.2. Short-term vs. long-term meditation training

For the purposes of this meta-analysis, short-term meditation refers to pre–post intervention-style studies where meditation-naïve novices were given brief meditation training, ranging between ∼5 and 60 h of actual meditation practice (Table S1). These novices undergoing training were compared to wait-list control groups who also had an interest in learning meditation. Differences in brain structure were examined by comparing brain morphology before and after this meditation intervention (compared to wait-list control groups). Of the 21 studies examined in the meta-analysis, five were *pre–post* studies involving short-term meditation training.

Studies of ‘long-term’ practitioners were instead *cross-sectional* studies comparing highly advanced meditation experts to controls with no meditation experience whatsoever. The range of practice varied enormously for long-term practitioners, but all had at least thousands of hours, or several years’ worth, of meditation experience (Table S1). Of the 21 studies included in the meta-analysis, the great majority (16/21) involved long-term practitioners (see Table S1).

2.3. Review method

As noted in the Introduction, we had two main goals: (1) to compile peak brain foci of anatomical difference between meditators and controls and examine whether there were any regions that have been consistently reported across studies; and if so, (2) to examine effect sizes for these anatomical differences and assess their magnitude.

2.3.1. Classification of primary data

To begin, we had to decide which results to include. Aside from the variety of morphometric measures employed (Table 1), there were differences in statistical significance thresholds; methods of correcting for multiple comparisons; voxel cluster size thresholds; and combinations of exploratory whole-brain (WB) and region-of-interest (ROI) analyses. We therefore followed study authors’ own criteria for a ‘significant’ result (typically, family wise error [FWE] rates of <.05 or <.01 across whole brain analyses, or within ROIs).

Many studies also reported results trending toward significance, or that were only significant before correcting for multiple comparisons. With a view toward completeness, we summarize and discuss *all* reported results, indicating statistic (t, Z, F, or r) magnitudes, cluster sizes (k), analysis type (whole-brain or ROI), trend results (designated by # symbol), and negative results (controls > meditators; designated by an asterisk [*]) whenever available (all data presented in Table S1). Both trend and stringent results were included in the main anatomical likelihood estimation (ALE) meta-analysis and qualitative review, but to ensure rigorous findings, supplemental ALE meta-analysis and qualitative review were also undertaken utilizing *only* stringently significant results.

Although we summarize every reported result to date (Table S1), we do not systematically discuss every finding, for several reasons: many results are (1) reported at lenient statistical thresholds, (2) not yet replicated by other studies or research groups, or (3) based on largely overlapping (non-independent) samples of meditation practitioners (the difficulty in recruiting highly experienced practitioners has resulted in repeated use of the same subjects in several studies; see Table 2 for details). Therefore, even though we include all reported results in our ALE and effect size meta-analyses, we focus our discussion on brain regions reported repeatedly, in multiple studies.

2.3.2. Determining consistent brain structure differences

To address our first goal of identifying brain regions consistently reported across studies, we conducted both a qualitative review and a quantitative meta-analysis (the former was necessary because not all studies provided quantitative data amenable to an ALE meta-analysis). For the qualitative review, we tabulated group (meditation practitioners vs. controls) and training (pre- vs. post-training) morphology differences reported in all studies (Table S1). In order to discern well-replicated results, we then sought regions exhibiting differences in three or more independent studies (i.e., regions suggesting substantial consistency across studies inasmuch as two broad replications have already been obtained in this relatively small body of work; cf. Kempton et al., 2008). Because some studies have used overlapping samples of meditation practitioners, however, contributing studies are not necessarily entirely independent (see Table 2 for details).

In addition to this ‘qualitative’ review, wherever possible, neuroimaging data were compiled for a quantitative ALE meta-analysis (detailed methods below). Combining results from both methods, we discuss each brain region either: (1) showing morphological differences in ≥ 3 separate studies (i.e., two replications of a given finding, as in Kempton et al., 2008), or (2) demonstrating significance in the ALE meta-analysis (methods in Section 2.4). Both methods result in a largely overlapping list of brain regions (see Sections 3 and 4).

We also performed supplemental qualitative (Table S2) and quantitative ALE (Table S3) meta-analyses in order to determine consistent brain structure differences in meditators based *only* on results reported at stringent (FWE- or FDR-corrected) statistical thresholds. There are many potential pitfalls to assuming the importance of a result based solely on null hypothesis significance testing, however (Cumming, 2013), and so we therefore conducted another ‘stringent’ ALE meta-analysis based not on p-values but instead on effect sizes (Table S4). This final ALE meta-analysis only included results that met or exceeded a ‘large’ effect size (Cohen’s $d \geq \pm 1.0$). As all of these additional analyses (Tables S2–S4) strongly parallel the results of our main neuroimaging meta-analyses (Tables 3 and 4), we report them in Supplemental Materials.

Supplementary Tables S2–S4 related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.neubiorev.2014.03.016.

Table 3
Brain regions consistently reported (in ≥3 studies), from a qualitative review of all results.

Region	Approximate BA	No. of results reported (L/R)	No. of studies contributing (LTP/NOV)
Gray matter regions			
Rostrolateral prefrontal cortex	10	5 (4/1)	3 (3/0)
Anterior/mid cingulate cortex	24/32	7 (3/4)	3 (2/1)
Insular cortex	13	6 (2/4)	5 (4/1)
Somatomotor cortices	3/4/5, 40	7 (5/2)	4 (4/0)
Inferior temporal gyrus	20/21, 38	4 (4/0)	4 (4/0)
Fusiform gyrus	37	4 (3/1)	3 (3/0)
Hippocampus	–	7 (4/3)	4 (3/1)
White matter pathways			
Corpus callosum	–	9 (5/–)	5 (3/2)
Superior longitudinal fasciculus	–	4 (3/1)	3 (2/1)

In the final column, LTP and NOV indicate whether studies contributing results were of long-term practitioners or novices undergoing meditation training. Raw data available in Table S1. BA: Brodmann area; L: left hemisphere; LTP: long-term practitioners; NOV: novice practitioners; R: right hemisphere.

2.3.3. *Determining the magnitude of differences*

To address our second goal of assessing the magnitude of these brain structure differences, wherever possible we calculated effect sizes for individual results (both stringent and trend) and tabulated mean effect sizes for each study included in the meta-analysis (Table 2). Detailed methods and equations for our effect size meta-analysis are presented below (Section 2.5).

2.4. *Anatomical likelihood estimation (ALE) neuroimaging meta-analysis*

We used a quantitative, random-effects meta-analytic method known as 'anatomical' or 'activation' likelihood estimation (ALE) (Eickhoff et al., 2009, 2012; Laird et al., 2005; Turkeltaub et al., 2002) implemented in the software program GingerALE 2.1 (San Antonio, TX: UT Health Science Center Research Imaging Institute). Aside from being the most commonly used meta-analytic technique for morphometric neuroimaging studies (Bora et al., 2010; Eickhoff et al., 2009; Salimi-Khorshidi et al., 2009), ALE is the coordinate-based meta-analytic method that most closely matches findings from more ideal *image-based* meta-analyses, which meta-analyze original empirical neuroimaging datasets, not just published peak coordinates of difference (Salimi-Khorshidi et al., 2009).

The most recent ALE algorithm tests for above-chance clustering of peak foci from different experiments included in the meta-analysis, by comparing *actual* activation foci locations with a null distribution created by distributing the same number of foci randomly throughout the brain through several thousand iterations (Eickhoff et al., 2009, 2012). Analogous to behavioral studies of meditation, where statistics typically represent differences in *performance* between meditation practitioners and control subjects, peak foci of anatomical difference represent points or clusters in the brain where significant differences in *brain structure* were observed. These significant differences were either between the experimental (meditator) and control (meditation-naïve) groups, or, in the case of short-term meditation training, differences within the same subjects at pre- and post-intervention time periods.

Included anatomical foci were smoothed using a full-width half maximum (FWHM) Gaussian kernel dependent on the sample size (number of participants) of the experiment from which foci were drawn (larger sample → smaller smoothing kernel; empirically determined by Eickhoff et al., 2009, 2012). Resulting statistical maps show clusters where convergence between anatomical foci is greater than would be expected by chance, i.e., if foci from each experiment were distributed independently. GingerALE 2.1 uses more conservative random-effects (vs. fixed-effects) analyses, which also allow the results to be generalized to the population at large (Eickhoff et al., 2009). Further, it controls for the number of foci contributed by a given study, such that studies reporting many foci (e.g., Kang et al., 2013) do not disproportionately affect the meta-analytic results (Turkeltaub et al., 2012).

A total of 78 anatomical foci drawn from 14 experiments were meta-analyzed. The remaining 7 studies either did not provide, or did not use methods amenable to the reporting of, peak foci of anatomical difference. Statistical maps provided meta-analytic loci of maximal likely anatomical difference between meditation practitioners and controls, and were thresholded using a false discovery rate (FDR; Genovese et al., 2002) of $q = .05$ and a cluster threshold of $k = 40\,\text{mm}^3$. To display results, we used template brain images from GingerALE 2.1 displayed in the 'Mango' software package.

In order to delineate only the most well-replicated results, we also performed a supplemental ALE meta-analysis, using the same settings and thresholds as above, but including *only* anatomical foci that met stringent statistical thresholds. These results consisted of 42 FWE- or FDR-corrected foci drawn from 14 experiments (results *not* marked with a '#' symbol in Table S1). Stringent ALE results are reported in Table S3.

As noted above, because there are many potential pitfalls in null hypothesis significance testing (Cumming, 2013), we also conducted another 'stringent' ALE meta-analysis based not on p-values but instead on effect sizes (Table S4). This final ALE meta-analysis

Table 4
Anatomical likelihood estimation meta-analysis results: structural differences in meditators > controls.

Region (BA)	Peak focus in MNI space (x, y, z)	Cluster size (mm^3)	Peak ALE value
L anterior/mid cingulate cortex (32/24)	−18, 21, 25	664	0.01607
R mid-cingulate cortex/MFG (24/6)	19, 4, 43	488	0.01490
Midline anterior precuneus (7)	−4, −53, 56	384	0.01842
L fusiform/ITG (20)	−47, −9, −28	328	0.01615
R orbitofrontal cortex (11/32)	16, 30, −16	240	0.01277
L ITG (21)	−41, −1, −38	232	0.01308
L somatomotor cortices (4/6)	−25, −13, 66	176	0.01121
L anterior insula white matter (13)	−29, 9, 20	56	0.01103

Note: Meta-analysis results: regions showing structural heterogeneities in meditation practitioners (meditators > controls) at a cluster threshold $k = 40\,\text{mm}^3$. See also Fig. 2. BA: Brodmann area; ITG: inferior temporal gyrus; L: left; MFG: middle frontal gyrus; MNI: Montreal Neurological Institute; R: right.

only included results that met or exceeded a ‘large’ effect size (Cohen’s $d \geq \pm 1.0$). This ALE meta-analysis included 34 foci from 10 studies. Large effect size ALE results are reported in Table S4.

2.5. Effect size meta-analysis

2.5.1. General method

In addition to determining which brain regions were consistently altered in meditation practitioners, we sought to evaluate the magnitude of these differences, i.e., their effect size (Cohen, 1992; Lipsey and Wilson, 1993; Sedlmeier et al., 2012). In all, 16 of 21 studies provided sufficient data to allow calculation of effect sizes (see Table 2 for the mean effect size of each study). Wherever possible, we used studies’ t-statistics of group differences between brain morphology of meditators vs. controls, or of meditation practitioners before and after short-term training, to calculate effect size (Cohen’s d) for each result using Eq. (1) (Ray and Shadish, 1996):

$$d = t\sqrt{\frac{1}{n_e} + \frac{1}{n_c}}, \tag{1}$$

where t is the value of the reported peak t-statistic, and n_e and n_c are the sample sizes for experimental (meditation) and control groups, respectively. Where means and standard deviations were available instead, we used Eq. (2):

$$d = \frac{M_e - M_c}{s_p}, \tag{2}$$

where M_e and M_c are the means of the experimental and control groups, respectively, and s_p is the pooled standard deviation from both groups. Occasionally, where only F-statistics were provided, effect sizes were calculated using the online Practical Meta-Analysis Effect Size Calculator (Lipsey and Wilson, 2001). After calculating effect sizes for 132 unique results, a mean effect size was calculated for each of the 16 studies (Table 2). Further, we compared mean effect sizes by brain tissue type examined (gray matter vs. white matter) to investigate whether meditation has differential effects on given tissue types.

To facilitate comparability with prior meta-analyses, we converted Cohen’s d scores to r, following the formula used in Sedlmeier et al. (2012). In line with the recommendations of Schmidt et al. (2009), we calculated 95% confidence intervals for mean effect sizes, to provide an estimate of their precision, following Eqs. (8) and (10) in Sedlmeier et al. (2012).

Negative effect sizes (results of controls > meditators) were also included in the above statistical meta-analysis, except where the authors interpreted *decreased* morphometric measure values as structural *increase*. This was the case with, for instance, axial and radial diffusivity (see Table 1). In these cases, the sign of negative t-statistics was reversed to correctly count the result as a ‘positive’ or increasing effect on brain structure.

2.5.2. Adjusting for potential inflation of effect sizes

The standard procedure in neuroimaging literature is to report peak t- or F-statistics only, which by definition are the extreme values for a given significant cluster of difference between groups. Mean t-statistics for an entire cluster of difference are rarely reported. Our calculated effect sizes thus represent the peak, *extreme* effects for each given result. On the other hand, mean t-statistics for given clusters are guaranteed to be lower. As such, our results necessarily overestimate the effect size of the cluster as a whole. This caveat should be kept in mind when interpreting these findings.

In an effort to address the problem of inflated effect sizes, we examined studies where both effect sizes based on peak t-statistics and those based on mean t-statistics for the entire cluster of significant difference were reported. Our aim was to get a sense of the inflationary bias caused by reporting of only peak t-statistics (vs. t-statistics for entire clusters of significant difference), and then adjust (deflate) mean effect sizes from other studies accordingly. Unfortunately, only a single study (Kang et al., 2013) provided both peak and mean cluster t-statistics. This study reported a large number of results ($n = 44$), however, adding some validity to the comparison. As cluster mean effect sizes were found to be much smaller (about 57% as large as effect size from peak foci only), we adjusted other studies’ mean effect sizes accordingly, assuming a comparable difference between cluster and peak effect sizes (see Section 3.7). Though ideally, of course, such a deflation of effect sizes would be based on more data from multiple studies, no further data were available to us. This method of adjusting mean effect sizes for this peak vs. cluster bias therefore seemed to us the best available method, given the limited data at our disposal.

2.5.3. Other caveats regarding effect sizes in neuroimaging

A further problem is that meta-analysis of mean effect sizes should also include all null (non-significant) results. Standard procedure in neuroimaging studies is to set a significance threshold and report only differences that exceed the threshold, i.e., attain significance. Null results are therefore rarely reported, except where ROIs are investigated. This introduces an unknown amount of inflationary bias in the mean effect sizes for the remaining studies, a bias for which, to our knowledge, there is no correction as of yet. That said, of the 16 studies contributing effect sizes, a fair number (six) did provide some null results. This yielded 41 null result-based effect sizes (out of a total of 132 effect sizes calculated) in our effect size meta-analysis. Even including these many null results, and after the adjustments mentioned above, mean effect sizes here for each study should probably still be considered to be overestimates to some extent (because many studies here report no null or negative [controls > meditators] results whatsoever).

Another concern is interpretation of effect sizes: the interpretive guidelines laid down by Cohen (1992) were intended for the behavioral sciences, not neuroimaging. Although it seems reasonable to us to use similar guidelines (i.e., the general assumption that a one-half standard deviation difference between groups is meaningful and of practical significance), rigorous discussion and elaboration of these ideas has, to our knowledge, not yet been undertaken in the field of neuroimaging. Indeed, even in the behavioral and social sciences, the interpretation of effect sizes as ‘small,’ ‘medium,’ or ‘large’ is ultimately arbitrary (Cohen, 1992).

Despite these limitations, effect sizes have been profitably employed in prior meta-analyses of morphometric neuroimaging studies (e.g., Kempton et al., 2008). The benefits of reporting effect size information appear to us to outweigh the drawbacks inherent in their calculation and interpretation for neuroimaging studies. We therefore calculate and report effect sizes here for completeness and in order to get a general sense of the magnitude of brain structure differences reported in meditation practitioners, but we emphasize the need for caution in interpreting these results.

2.6. Estimating publication bias in meta-analytic results

The bias toward publication of only positive results (the ‘file drawer’ problem) is a serious concern (Rosenthal, 1979). We constructed a funnel plot (scatterplot of effect size against sample size) to test for potential publication bias in our sample of studies (Egger et al., 1997). Effect sizes were calculated as described above, and plotted against total sample size (meditators + controls). For detailed discussion of funnel plots see Egger et al. (1997); for an example of their use in a meta-analysis of psychological effects of meditation, and further discussion, see Sedlmeier et al. (2012).

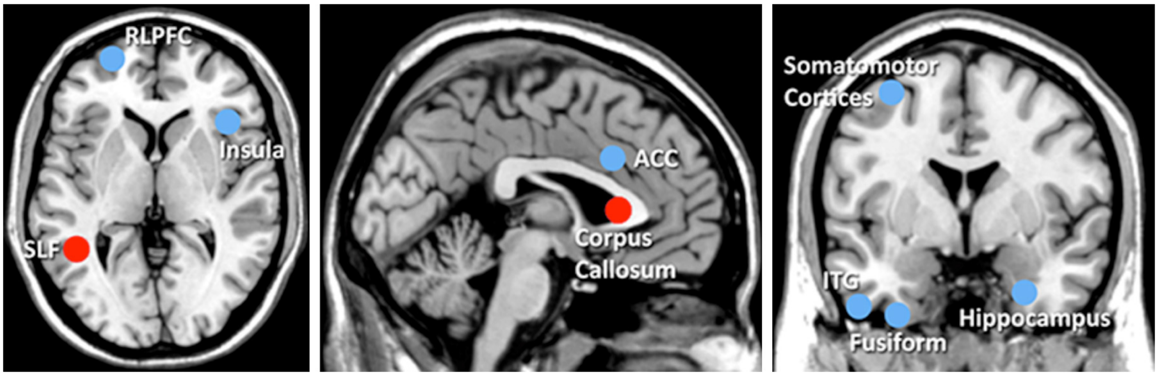

Fig. 1. Convergent brain structure differences in meditation practitioners. *Note*: Convergent findings from all morphometric studies of meditation practitioners (from both long-term practitioners and novices undergoing short-term training). Regional labels are approximate, and are shown for illustrative purposes only. Blue circles: gray matter regions; red circles: white matter pathways. ACC: anterior/mid cingulate cortex; ITG: inferior temporal gyrus; RLPFC: rostrolateral prefrontal cortex; SLF: superior longitudinal fasciculus.

2.7. *Reporting and classification of results*

All peak voxel coordinates are reported in Montreal Neurological Institute (MNI) space (Table S1). For one paper where peak voxels were reported in Talairach coordinates (Kang et al., 2013), we used the WFU Pickatlas software package (Maldjian et al., 2003) to perform a nonlinear transformation of Talairach coordinates to MNI space for consistency. In most cases, results are classified under the same brain region originally identified by the authors (usually either a major gyrus or Brodmann area [BA]). For meta-analytic ALE results, region classifications follow those indicated in the Multi-Image Analysis GUI ('Mango') image-viewing software (UT Health Science Center Research Imaging Institute) used to display results (see below). For additional precision, the Duvernoy neuroanatomical atlas was also consulted to verify results (Duvernoy, 1999).

3. Results

3.1. *Qualitative review of group differences in long-term practitioners and novices*

Among all group differences (Table S1), we found 9 regions to be consistently (in ≥3 studies) reported (Table 3 and Fig. 1): rostrolateral prefrontal cortex (RLPFC)/BA 10, anterior/mid-cingulate cortex, insular cortex, somatomotor cortices, inferior temporal gyrus, fusiform gyrus, hippocampus, corpus callosum, and superior longitudinal fasciculus. We pool all results together in Table 3 to obtain an overview of consistent brain differences associated with meditation generally, not only long-term practice.

Expert practitioners have been studied much more extensively than novices and contribute most of the available data. Accordingly, restricting results to long-term practitioners only (i.e., excluding results from short-term training) yields an almost identical list of regions. Only the anterior/mid-cingulate cortex and superior longitudinal fasciculus, each reported twice in studies of long-term practitioners, would be removed from Table 3.

3.2. *Anatomical likelihood estimation (ALE) meta-analysis*

Significant, consistent clusters of difference were found via ALE meta-analysis in anterior/mid cingulate cortex bilaterally, midline anterior precuneus, left fusiform/inferior temporal gyrus, right orbitofrontal cortex, left somatomotor cortices, and in white matter bordering the left anterior insula (Table 4 and Fig. 2). ALE results were generally consonant with those of the qualitative review (compare Table 4 with Table 3, and Fig. 2 with Fig. 1). Most disparities appear to be due to the lack of activation foci available for inclusion in ALE for certain regions (e.g., BA 10 and corpus callosum; see Table S1) – recall that not all studies used methods amenable to inclusion of their data in an ALE meta-analysis. A summary of significant meta-analytic clusters is provided in Table 4, and illustrated in Fig. 2. These clusters are discussed in detail in Section 4.

3.3. *Qualitative review of structural differences after short-term meditation training*

There were not enough morphometric studies of short-term meditation training to apply the more rigorous standard of including only regions where ≥3 studies have reported a result (cf. Kempton et al., 2008). Nonetheless, here we summarize all regions identified in short-term training studies because of their inherent interest: pre–post morphometric studies of meditation-naïve subjects provide the best available evidence regarding the causal effect of meditation on brain morphology.

Structural differences in a total of 7 gray matter regions and 5 white matter tracts were identified in novice (meditation-naïve) practitioners after having undergone brief (5–60 h) meditation training. Gray matter regions included anterior and posterior cingulate cortices, insular cortex, temporoparietal junction, hippocampus, caudate nucleus, and cerebellum (Table 5). White matter pathways included the corpus callosum, superior longitudinal fasciculus, sagittal stratum, thalamic radiation, and corona radiata (Table 5). Importantly, similar differences were observed in long-term practitioners in all of these regions except the caudate nucleus and the latter two white matter tracts (Table S1).

Table 5
Regions that show brain structure differences after brief meditation training in novices.

Region	Approximate BA
Gray matter regions	
Anterior cingulate cortex	24/32
Posterior cingulate cortex	31
Insular cortex	13
Temporoparietal junction	39/40, 22
Cerebellum	–
Hippocampus	–
Caudate nucleus	–
White matter pathways	
Corpus callosum	–
Superior longitudinal fasciculus	–
Sagittal stratum	–
Thalamic radiation	–
Corona radiata	–

Regions reported (in one or more studies) in novices after brief meditation training, from a qualitative review of all results (Table S1). BA: Brodmann area.

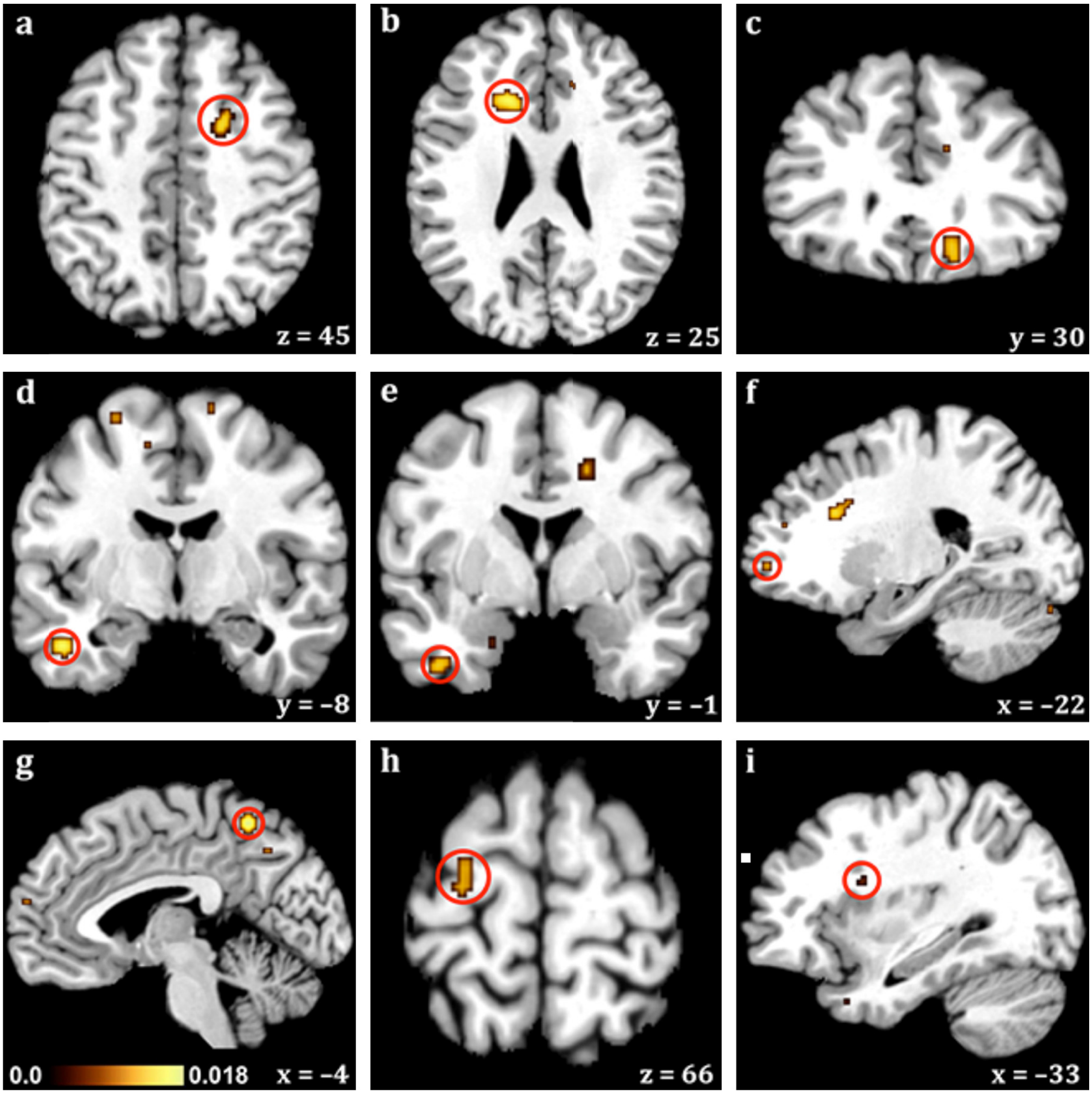

Fig. 2. Anatomical likelihood estimation (ALE) meta-analysis of significant brain morphology differences (meditators > controls). *Note:* Significant meta-analytic clusters of morphological difference were found in 8 regions, and one additional trend-level cluster. (a) Right mid-cingulate cortex/middle frontal gyrus (BA 24/6). (b) White matter near the left anterior/mid-cingulate cortex (BA 32/24). (c) Right orbitofrontal cortex (BA 11/32). (d) Left fusiform gyrus (BA 20). (e) Left inferior temporal gyrus (BA 21). (f) Trend-level cluster in rostrolateral prefrontal cortex (BA 10). (g) Midline anterior precuneus (BA 7). (h) Left somatomotor cortex (BA 4/6). (i) White matter near the left anterior insula (BA 13). Color bar indicates likelihood that peaks represent actual peaks of difference at a given voxel (see Section 2). *x*, *y*, *z* coordinates in MNI space. See Table 4 for complete listing. BA: Brodmann area.

3.4. Hemispheric asymmetries

Of all lateralized findings (118 results), a somewhat greater number were reported in the left (69) vs. right (49) hemisphere (Table S1). However, the difference was not statistically significant $\chi^2(1) = 3.39$, $p = .066$.

3.5. Correlations between brain structure and meditation experience or behavioral measures

We found 16 correlations between meditation experience and brain structure differences, reported in 8 studies (Table 6). Overall, correlations were not strong. Of the 16 reported correlations, only 6 were significant at stringent statistical thresholds, whereas 10 trended toward significance or did not survive correction for multiple comparisons. Moreover, very few relationships (2 of 16) were based on whole-brain analyses. The great majority of results (14/16) rely on ROI analyses based on either a priori assumptions, or peak group difference results from the same study (Table S1). That is, almost all correlation analyses are non-independent (Vul et al., 2009).

In four studies, a further 9 correlations were observed between various behavioral measures and structural heterogeneities (Table 7). Though all correlations were significant at stringent statistical thresholds, all also relied on ROI analyses based on a priori assumptions or group-difference results – i.e., again, all were non-independent (Vul et al., 2009).

3.6. Controls > meditators

Several results (16/124), restricted to three of 21 studies (Fayed et al., 2013; Kang et al., 2013; Tang et al., 2012), showed an apparent pattern of structural increase in controls vs. meditators (results indicated with an asterisk [*] in Table S1). In Tang et al. (2012),

Table 6
Regions where brain structure differences correlate with meditation experience level.

Region name, peak voxel in MNI space (*x*, *y*, *z*), BA	*T* at peak voxel or *r*	Side	Cluster size (*k*)	Analysis type	Morphometric measure	Experience (*M* ± *SD*)	Age (*M* ± *SD*)	Study
Visual cortex								
Inferior occipitotemporal[*]	Partial *r* = .63	R	–	ROI	CT	9.1 ± 7.1 years	38.2 years	Lazar et al. (2005)
Middle temporal gyrus								
–[#]	*r* = −.59	L	–	ROI	GMV	6456.2 ± 6040.6 h	50.2 ± 10.5 years	Leung et al. (2013)
Inferior temporal gyrus								
–	*r* = .40	L	–	ROI	GMC	6254.0 ± 4529.0 h	34.1 ± 4.7 years	Hölzel et al. (2008)
Inferior temporal lobe								
–	*t* ≅ 3.5	R	–	ROI	CG	19.8 ± 11.4 years	51.4 ± 12.8 years	Luders et al. (2012b)
Insula								
–[#]	*r* = .36	R	–	ROI	GMC	6254.0 ± 4529.0 h	34.1 ± 4.7 years	Hölzel et al. (2008)
–[#]	*t* ≅ 3.5	R	–	ROI	CG	19.8 ± 11.4 years	51.4 ± 12.8 years	Luders et al. (2012b)
Orbitofrontal cortex								
1, 45, −16 (BA 11)[#]	*t* = 4.28	R	185	WB	GMC	6254.0 ± 4529.0 h	34.1 ± 4.7 years	Hölzel et al. (2008)
Somatosensory cortices								
33, −26, 59 (BA 1–3)	*t* = 5.42	R	–	WB	CT	6404.0 ± 8522.0 h	37.6 ± 7.9 years	Grant et al. (2010)
−8, −42, 60 (BA 1–3)[#]	*t* = 3.28	L	–	ROI	CT	6404.0 ± 8522.0 h	37.6 ± 7.9 years	Grant et al. (2010)
Anterior cingulate								
7, 22, 31[#]	*t* = 2.01	R	–	ROI	CT	14.4 ± 8.4 years	37.6 ± 7.9 years	Grant et al. (2010)
−6, −3, 42[#]	*t* = 1.82	L	–	ROI	CT	14.4 ± 8.4 years	37.6 ± 7.9 years	Grant et al. (2010)
Angular gyrus								
–	*r* = −.76	R	–	ROI	GMV	6456.2 ± 6040.6 h	50.2 ± 10.5 years	Leung et al. (2013)
Cingulate cortex hippocampus								
–[#]	*r* = .40	L	–	ROI	FA	23.3 ± 12.2 years	51.6 ± 12.3 years	Luders et al. (2011)
Cingulate cortex cingulum								
–[#]	*r* = .36	R	–	ROI	FA	23.3 ± 12.2 years	51.6 ± 12.3 years	Luders et al. (2011)
Premotor cortex								
BA 6[#]	*r* = .31	L	–	ROI	CT	3.4 ± 2.3 years	25.4 ± 3.3 years	Kang et al. (2012)
Hippocampus								
−18, −37, −11	Partial *r* = .33	L	–	ROI	GMC	19.8 ± 11.4 years	51.4 ± 12.8 years	Luders et al. (2013)

BA: Brodmann area; CT: cortical thickness; GMC: gray matter concentration; L: left; MNI: Montreal Neurological Institute; R: right; ROI: region of interest; WB: whole-brain.

[*] Significant after controlling for age and average hemisphere thickness.

[#] Results trending toward significance and/or uncorrected for multiple comparisons.

Table 7
Regions where brain structure differences correlate with behavioral measures in meditation practitioners.

Region name, peak voxel in MNI space (*x*, *y*, *z*), BA	*T* at peak voxel or *r*	Side	Cluster size (*k*)	Analysis type	Morphometric measure	Behavioral measure	Study
Visual cortex							
Inferior occipitotemporal	*r* = .72	R	–	ROI	CT	Respiration rate	Lazar et al. (2005)
Insula							
–[*]	Partial *r* = .48	R	–	ROI	CT	Respiration rate	Lazar et al. (2005)
51, 2, 6 (BA 13/14)	*t* = 3.57	R	–	ROI	CT	Pain sensitivity	Grant et al. (2010)
Operculum							
51, −27, 25 (BA 52)	*t* = 3.37	R	–	ROI	CT	Pain sensitivity	Grant et al. (2010)
Anterior cingulate							
4, 12, 27 (BA 24)	*t* = 3.53	R	–	ROI	CT	Pain sensitivity	Grant et al. (2010)
Parahippocampal gyrus							
20, −3, −11 (BA 28)	*t* = 4.94	R	–	ROI	CT	Pain sensitivity	Grant et al. (2010)
Amygdala							
32, 0, −26[**]	*t* = 3.18	R	10	ROI	GMC	Perceived stress	Hölzel et al. (2010)
Posterior corona radiata							
–	*r* = .41	R	–	ROI	AD	Mood disorder	Tang et al. (2012)
Sagittal stratum							
–	*r* = .45	L	–	ROI	AD	Mood disorder	Tang et al. (2012)

AD: axial diffusivity; BA: Brodmann area; CT: cortical thickness; df: degrees of freedom; GMC: gray matter concentration; L: left; MNI: Montreal Neurological Institute; R: right; ROI: region of interest.

[*] After controlling for age.

[**] Negative correlation between morphometric measure and behavioral measure.

however, *lower* axial diffusivity as measured with DTI is interpreted as structural *enhancement* of white matter (see Table 1). Therefore, following this interpretation, *higher* axial diffusivity in controls vs. meditators suggests white matter *increases* in meditation practitioners. Accordingly, only Fayed et al. (2013) and Kang et al. (2013) actually report results of controls > meditators, and only one such result is reported by Fayed et al. (2013). Of 10 such results reported by Kang et al. (2013), half (5) were significant at stringent statistical thresholds. Brain regions showing structure differences of controls > meditators included somatomotor cortices, anterior and posterior cingulate cortices, temporoparietal junction, middle temporal gyrus, angular gyrus, precuneus, and cuneus (for detailed information, see results indicated with an asterisk [*] in Table S1).

3.7. *Global mean effect sizes for morphometric studies of meditation*

Overall, we were able to calculate 132 unique effect sizes from 16 studies. Mean effect sizes, weighted by sample size, were also calculated for each study (Table 2). We report our effect sizes as both Cohen's *d* (Cohen, 1992) as well as *r* to facilitate comparison with prior meta-analyses. Global mean effect size ($\bar{d}$) across all studies, i.e., the average of all studies' mean effect sizes weighted by study sample size, was medium-to-large by Cohen's (1992) criteria ($\bar{d}_{\text{global}} = 0.77 \pm 0.11$; $\bar{r}_{\text{global}} = .34$). One extreme, unduly influential study effect size ($d = -2.97$) based on only a single result (from Fayed et al., 2013) was excluded from the averages.

We reiterate, however, that effect sizes are based on peak difference results within larger clusters. They therefore represent extreme values and necessarily overestimate the effect size for a given cluster of significant anatomical difference (see Section 2.5.2 for more information). To provide a more conservative estimate of effect size, we used results ($n = 44$) from a single study (Kang et al., 2013) where both peak and mean cluster *t*-statistics were reported to compare mean effect sizes for both cases. As expected, we found that mean effect size for peak *t*-statistics was much greater ($\bar{d}_{\text{peak voxels}} = 0.60$) than mean *t*-statistics for clusters of difference ($\bar{d}_{\text{cluste means}} = 0.34$). The average effect size for cluster means is therefore approximately 57% of that for peak voxels only ($0.34/0.60 = \sim 56.67\%$). Cluster mean effect sizes, then, are clearly the more conservative estimates. Assuming a similar cluster–peak effect size differential for other morphometric neuroimaging studies, we recalculated more conservative ('adjusted') mean effect sizes at ∼57% of each study's raw mean effect size (Table 2). This yields $\bar{d}_{\text{global adjusted}} = 0.44 \pm 0.04$, and $\bar{r}_{\text{global adjusted}} = .19$. With these conservative adjustments, effect sizes for morphometric neuroimaging in meditators fall between the 'small' and 'medium' effect size level ($r = .1$–$.3$; Cohen, 1992).

3.8. *Mean effect sizes by tissue type (gray vs. white matter)*

To examine whether meditation is differentially associated with greater morphology differences in given brain tissue types, we also compared mean effect sizes for studies examining gray matter ($\bar{d}_{\text{gray}} = 0.81 \pm 0.15$; $\bar{r}_{\text{gray}} = .35$) vs. white matter ($\bar{d}_{\text{white}} = 0.73 \pm 0.02$; $\bar{r}_{\text{white}} = .34$) results separately (Fig. 3). One study (Kang et al., 2013) was not included in this analysis because results for both tissue types were mixed in their results. Levene's test for heterogeneity of variance was significant, $F(679) = 71.56$, $p < .001$. Therefore, not assuming equal variances, we found a significant difference between mean effect sizes for the two tissue types, $t(557) = 2.84$, $p = .005$, suggesting that meditation may affect gray matter more strongly than white matter (Fig. 3). Nevertheless, in practical terms the effect sizes for both tissue types are very similar, and can be considered 'moderate' or 'medium' ($r = .3$; Cohen, 1992). The significant difference between effect sizes by tissue type is likely due to the very large sample size employed in this test.

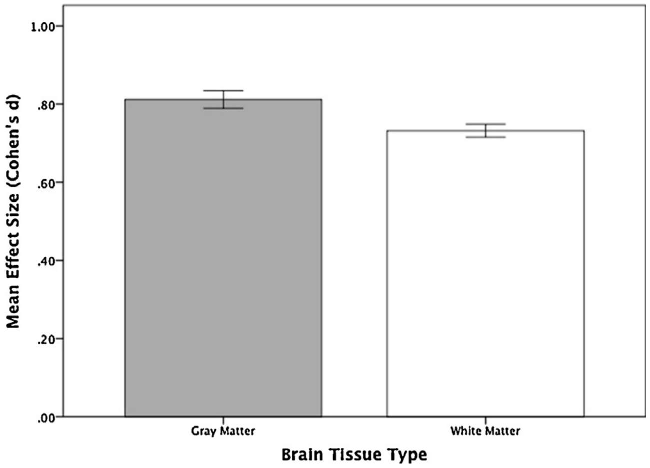

Fig. 3. Mean effect size as a function of brain tissue type (gray vs. white matter). *Note*: Effect sizes for morphological differences in meditation practitioners appear significantly stronger in gray matter ($n = 567$ subjects) vs. white matter ($n = 114$ subjects). Error bars: ±SEM.

3.9. *Mean effect size as a function of meditation experience*

When examining the relationship between length of practice time (how experienced practitioners were) and effect sizes for morphological differences between meditators and controls, we found that the two showed a negative linear relationship, $r(14) = -.56$, $p < .001$ (Fig. 4). At first glance, such a result suggests rather counter-intuitively that the magnitude of differences decreases with increasing meditation experience. Several other factors are relevant, however, particularly the fact that increasing meditation experience entails increased age, with a high likelihood of concomitant brain structure attenuation. See Section 5.1 for further discussion of this finding.

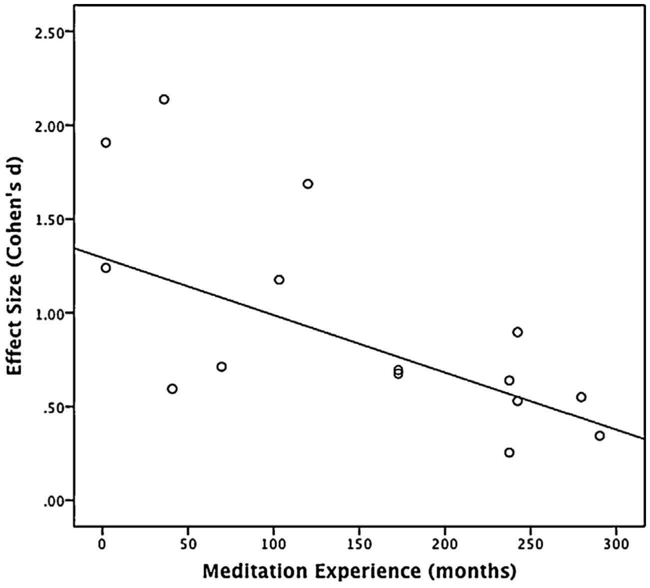

Fig. 4. Mean study effect size as a function of meditation experience. Linear correlation shows a significant negative relationship ($r = -.56$) between effect size and meditation experience.

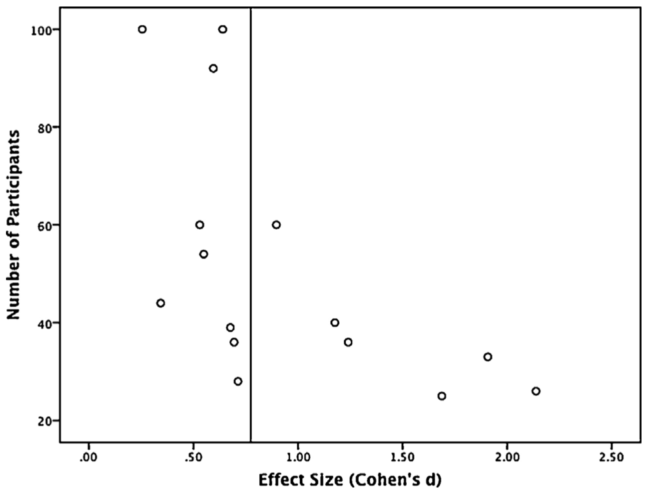

Fig. 5. Funnel plot of mean effect sizes for morphometric neuroimaging studies. Funnel plot of mean effect sizes for each study ($k = 15$) plotted against sample size. Vertical bar indicates weighted (by sample size) mean of the study mean effect sizes (Cohen's $\bar{d}$). See Section 2 for more information.

3.10. *Assessment of publication bias*

Visual inspection of a funnel plot (Egger et al., 1997) showed considerable deviation from the idealized inverted funnel shape. This suggests a fair degree of publication bias, i.e., non-publication of negative findings and/or preferential publication of large positive results (Fig. 5). For instance, very large mean effect sizes (Cohen's $d > 1.0$) were found exclusively in studies with relatively small sample sizes ($n < 40$). This could be because only small-n studies with large effects (and a higher chance of achieving significance) have been published, whereas many or all of the small-n studies with smaller effects are missing because they could not be published (a classic case of publication bias, or the 'file drawer' problem; Rosenthal, 1979). On the other hand, well-powered studies with larger ($n > 40$) samples (Lieberman and Cunningham, 2009; Murphy and Garavan, 2004) generally had moderate mean effect sizes (Fig. 5).

3.11. *Stringent meta-analyses of brain regions implicated in meditation*

In addition to the qualitative and ALE meta-analyses of brain regions involved in meditation reported above, we performed a supplemental qualitative review in which we included only raw data that met stringent statistical thresholds correcting for multiple comparisons (FWE- or FDR-correction). Results from the stringent qualitative review (Table S2) were consonant with the results reported in the non-stringent review (Table 3 and Fig. 1), albeit less numerous (compare Tables 3 and S2).

As with the qualitative review, we also conducted a supplemental ALE meta-analysis in which we included *only* peak foci that met stringent statistical thresholds (FWE- or FDR-corrected, usually at $p < .05$). Results from the stringent ALE meta-analysis (Table S3) are basically similar to those of the more exploratory ALE reported in the non-stringent ALE meta-analysis (Table 4 and Fig. 2) and the qualitative review of findings (Table 3 and Fig. 1). This includes significant clusters in the anterior/mid cingulate cortex, RLPFC/BA 10, left inferior temporal gyrus, and anterior insula (Table S3). However, as expected, some clusters are absent, and the significant clusters tend to be less extensive (i.e., smaller in size; compare Tables 4 and S3).

There are numerous problems with null hypothesis significance testing, however, and many fields are now moving toward greater reliance on other statistical measures, such as effect sizes (Cumming, 2013). We therefore conducted another supplemental ALE meta-analysis including only results that had large effect sizes (Cohen's $d \geq 1.0$). We used this large threshold because (as discussed in detail in Section 2.5.2) neuroimaging effect sizes will tend to be inflated; therefore a 'large' effect size threshold of 1.0 is better considered a roughly 'moderate' threshold of Cohen's $d \cong 0.50$. This more stringent ALE meta-analysis based only on results with large effect sizes again yielded results (Table S4) that were highly consonant with our central meta-analyses (Tables 3 and 4), and are therefore presented in Supplementary Materials (Table S4).

4. Convergent findings

In this section we discuss brain regions that have shown structural differences in multiple ($\geq$3) studies (Table 3), and/or show significant clusters in the ALE meta-analysis (Table 4). We relate morphometric findings to relevant functional neuroimaging research in meditators and non-meditators, as well as anatomical investigations in non-human primates. We offer overviews of the putative functionality of each region along with hypotheses regarding how structural increases in a region might advance the ostensible goals of meditation practices, and account, at least in part, for the associated behavioral and affective benefits reported in studies of meditation practitioners.

4.1. *Gray matter regions*

4.1.1. *Insular cortex*

Six structural differences in the insular cortex of meditation practitioners have been reported in five studies to date (Table 3). We also found a significant cluster near the insula in our ALE meta-analysis (Table 4 and Fig. 2i). Structural differences in the insula are among the most well-replicated findings in morphometric studies (Table S1), consistent with the many fMRI studies showing differential insula activation related to meditation (Brefczynski-Lewis et al., 2007; Dickenson et al., 2012; Engström and Söderfeldt, 2010; Farb et al., 2007, 2010, 2013; Froeliger et al., 2012a,b; Gard et al., 2012; Grant et al., 2011; Ives-Deliperi et al., 2011; Kakigi et al., 2005; Lutz et al., 2009, 2013; Manna et al., 2010; Monti et al., 2012; Wang et al., 2011; Zeidan et al., 2011).

The insula is consistently linked to interoception – awareness of the body's internal and visceral states, including respiration, heart rate, etc. (Craig, 2004; Critchley et al., 2004) – but has also been implicated in a host of other activities, including emotional self-awareness (Craig, 2004), and potentially, metacognitive awareness (Fleming and Dolan, 2012). Interestingly, the studies reporting insula differences involved practitioners with an intensive, explicit focus on body awareness, including attention to body posture, respiration, ambient tactile sensations, temperature sensations, etc. (Hölzel et al., 2008; Kang et al., 2013; Lazar et al., 2005; Tang et al., 2010). One further study mixed practitioners from various meditative backgrounds (Luders et al., 2012b), but nearly half the participants (24/50) practiced *Vipassana* (Insight) meditation, which typically involves a strong focus on body awareness.

We propose that structural differences in insular cortex are tied to the particular type of body-centered meditations that are practiced. Insula structural differences might also relate to apparent enhancements in body awareness in *Vipassana* practitioners observed in behavioral (Fox et al., 2012), physiological (Sze et al., 2010), magnetoencephalographic (Kerr et al., 2011, 2013), and functional neuroimaging research (Farb et al., 2007, 2010; but for disparate results see Khalsa et al., 2008). Insula involvement in enhanced body awareness appears to be the most parsimonious explanation for these consistent structural findings (Hölzel et al., 2008; Lazar et al., 2005; Luders et al., 2012b).

Many psychological disorders, such as depression and anxiety, involve problems with the perception of the body and the emotions engendered by various interoceptive signals (Brausch and Gutierrez, 2009; Michalak et al., 2012) – and importantly, these problems may be related to structural declines in the insula (e.g., Soriano-Mas et al., 2011). A greater ability to accurately represent the body (Fox et al., 2012), potentially mediated by brain structure changes in the insula, may play a role in the emotional and clinical benefits apparently engendered by meditation (Chiesa and Serretti, 2009, 2010; Sedlmeier et al., 2012).

4.1.2. Somatomotor cortices

Primary and secondary somatomotor cortices are the main cortical hubs for processing of tactile information (touch, pain, conscious proprioception). The common differences found in these areas (six findings in four studies; Tables 3 and 4; Fig. 2h) in the present work complement the results in insular cortex. The preponderance of studies involving practitioners with an explicit focus on body awareness (three of four studies; Kang et al., 2013; Lazar et al., 2005; Luders et al., 2012b) should again be emphasized. Although causal claims are as yet unwarranted, the connection between meditation type and structural findings is suggestive of a meaningful association. Other meditation styles, too, may lead to ancillary benefits in terms of enhanced awareness of the body. Recent work testing meditators by using a body-scanning meditation practice (in the *Vipassana* tradition) found that the introspective reports of mental experiences during meditation were more objective in long-term practitioners than in controls – even when practitioners had little or no prior experience with body-awareness practices (Fox et al., 2012). These differences are consistent with numerous fMRI studies showing differential somatomotor cortex activation during various (not just body-centered) forms of meditation (Baerentsen et al., 2001; Engström et al., 2010; Farb et al., 2007, 2010; Kirk et al., 2011; Lazar et al., 2000; Lutz et al., 2009). Related work with the Chinese contemplative exercise Tai Chi has shown enhanced tactile acuity in long-term practitioners compared to controls (Kerr et al., 2008). Importantly, like the body-centered meditations discussed here, Tai Chi predominantly involves an increased *focusing* of attention on tactile inputs (as opposed to an increase in sensory input itself), suggesting that mental practice alone can enhance tactile sensory acuity.

Long-term meditators have also been shown to have higher pain tolerance (or perhaps equivalently, lower pain sensitivity) than non-meditators (e.g., Grant and Rainville, 2009), and mindfulness meditation training can reduce the perceived unpleasantness of painful stimuli (Zeidan et al., 2011). Both these effects are related to altered function or structure in somatosensory cortices (Grant et al., 2010, 2011; Zeidan et al., 2011). A related possibility, then, is that structural differences in somatomotor cortices underlie the apparent ability of meditation practitioners to focus on the sensory qualities of painful and unpleasant stimuli, rather than the affective (emotional) and self-related cognition that might be engendered by them (cf. Grant et al., 2010, 2011).

Taken together, these results suggest that attention to the body – whether the body is focused upon directly through body-awareness meditations, or indirectly through present-moment-centered awareness – may have significant effects on tactile acuity and introspective body-awareness, as well as on brain morphology and function in somatomotor regions. These structural differences in meditators parallel studies showing considerable functional and structural plasticity of somatomotor regions in humans after various forms of motor learning and tactile discrimination (e.g., Draganski et al., 2004; Hyde et al., 2009). Alteration of somatomotor cortical structure by mental training alone is further consistent with research showing that merely imagining (deCharms et al., 2004) or dreaming of (Dresler et al., 2011) somatomotor activities (e.g., fist-clenching) results in higher blood-oxygen level dependent (BOLD) signal in these regions, even without any muscle activity or explicit sensory input. As such, these studies suggest that attention alone is sufficient to significantly modulate activity, and thereby, potentially structure, in these brain areas. As with insula changes and enhanced interoceptive body awareness, changes in somatosensory cortices and enhanced exteroceptive body awareness may play a role in meditation's apparent benefits for a variety of clinical disorders involving altered attention to the body or bodily sensations.

4.1.3. Anterior precuneus (BA 7)

Our ALE meta-analysis detected a large significant cluster in the sensorimotor anterior region of the precuneus (BA 7; Table 4 and Fig. 2g). This finding is consistent with activations of precuneus found in several fMRI studies (Baerentsen et al., 2010; Ives-Deliperi et al., 2011; Manna et al., 2010), although few morphometric studies directly reported results in this area (Table S1). Precuneus is often thought to be part of the so-called 'default mode network,' but careful and thorough reviews suggest that this notion is mistaken and a result of overly broad anatomical generalizations (cf. Buckner et al., 2008; Fox et al., 2014). Though it remains a relatively poorly understood region, the putative roles suggested for the anterior precuneus in higher-order body image, self-related processing, and attentional shifting (Cavanna and Trimble, 2006) are consistent with the practices and goals of many meditations. As such, this meta-analytic cluster in the sensorimotor anterior region of the precuneus may be related to the strong emphasis on present moment-centered, body-oriented awareness cultivated in many meditation traditions, particularly *Vipassana* ('Insight') meditation. In line with our meta-analytic results in the insula and somatosensory regions, this subregion of the precuneus shows strong functional (and, based on macaque tracing studies, probably also anatomical) connectivity with primary and secondary somatomotor cortices, insula, and superior parietal cortex (Margulies et al., 2009). Structural differences here may therefore be involved in higher-order integration of heightened interoceptive and exteroceptive attention, potentially mediated by insula and somatomotor cortices, or other forms of self-processing and evaluation. Such integration may aid in achieving the greater present-centered awareness, and transformed view of the self, advocated in many meditation traditions (Analayo, 2003; Austin, 1999; Goenka, 2000).

4.1.4. Rostrolateral prefrontal cortex (RLPFC)/BA 10

Three studies reported findings in BA 10/rostrolateral prefrontal cortex (RLPFC) (Tables 3 and S1), and we also found a trend-level cluster in BA 10 in our quantitative meta-analysis (Fig. 2f). The three structural studies where BA 10 results were reported involved practitioners from disparate meditative backgrounds: Insight (Lazar et al., 2005), Tibetan Buddhist (Vestergaard-Poulsen et al., 2009), and Brain Wave Vibration (BWV) meditation (Kang et al., 2013). Given the diversity in meditative training type, structural differences in RLPFC/BA 10 may be generalizable beyond any particular meditative practice. Consistent with this notion, RLPFC has also been implicated in fMRI studies of various meditative traditions. RLPFC becomes more active at the onset of a meditation session (Baerentsen et al., 2001), as well as during both focused attention and open awareness (Manna et al., 2010), and Zen (Ritskes et al., 2003) meditations.

RLPFC/BA10 is hypothesized to be involved in introspection and metacognition (Christoff and Gabrieli, 2000; Fleming et al., 2010; McCaig et al., 2011), the evaluation of self-generated information (Christoff et al., 2003), processing of complex, abstract information (Christoff et al., 2001, 2009b), and the integration of multiple separate cognitive processes in the service of higher-order behavioral goals (Ramnani and Owen, 2004). Considering the highly introspective nature of meditative practices, results in BA 10 across meditation styles are consistent with the idea that meditation engages, and possibly trains, metacognitive awareness. Although difficult to assess, efforts have been made to measure the 'accuracy' of introspection (Corallo et al., 2008; Fleming et al., 2010). Typically, subjective reports of an experience are contrasted with some measure (behavioral, physiological, or neural) purported to be an objective measure of that same experience. The degree of correlation represents a participant's 'introspective accuracy.' These structural differences in BA 10 are consonant with evidence (and may in part provide a neural basis) for enhancements of introspection observed in meditators (Fox et al., 2012; Sze et al., 2010). These changes may also enhance the ability to observe thoughts and emotions in a detached, dispassionate manner (Fox and Christoff, 2014).

If meditation indeed trains metacognition, enhancements of metacognitive skill may have implications beyond personal interest and insight for practitioners. For instance, researchers have argued that metacognitive awareness (either dispositional, or intervention-enhanced with mindfulness-based cognitive therapy) might be a key mechanism in the prevention of depression relapse (Teasdale, 1999). Further, enhanced introspective accuracy may make expert meditators more reliable reporters of inner experience – a crucial step toward a better understanding of the neural correlates of higher cognitive functions and subjective experiences not amenable to study in animal models (Lutz and Thompson, 2003; Fox et al., 2012).

4.1.5. *Anterior cingulate cortex (ACC) and mid-cingulate cortex (MCC)*

Seven structural differences were found in the anterior cingulate cortex (ACC) and mid-cingulate cortex (MCC) (Table 3), and two significant clusters were found in the ACC/MCC in the ALE meta-analysis (Table 4; Fig. 2a and b). These findings are consistent with many fMRI studies showing differential ACC/MCC activity in relation to meditation practices (Baerentsen et al., 2001; Dickenson et al., 2012; Engström and Söderfeldt, 2010; Engström et al., 2010; Gard et al., 2012; Grant et al., 2011; Hölzel et al., 2007; Ives-Deliperi et al., 2011; Lazar et al., 2000; Lutz et al., 2013; Manna et al., 2010; Orme-Johnson et al., 2006; Xue et al., 2011; Zeidan et al., 2011). One unifying framework of the ACC/MCC argues for its involvement in the general process of 'self-regulation' (Bush et al., 2000; Posner et al., 2007). Complementary theories view it as a region crucial for self-control, focused problem-solving, and adaptive behavioral responses under changing conditions (Allman et al., 2001). These processes are considered goals of the utmost importance in many meditation traditions. Special emphasis is placed on self-control, emotion regulation, and behavioral flexibility in both traditional meditation training manuals (e.g., Analayo, 2003; Iyengar, 1996; Singh, 1979) and the works of contemporary teachers (e.g., Goenka, 2000). Moreover, behavioral evidence is accumulating that shows improvements in many of these functions in long-term meditation practitioners (or in novices after meditation training). Examples include pain regulation (Grant et al., 2010), emotional awareness (Sze et al., 2010), emotion regulation (Condon et al., 2013; Desbordes et al., 2012), and insightful problem solving (Ostafin and Kassman, 2012).

Consistent with a role in decision-making and adaptively selecting actions based on anticipated outcomes (Morecraft and Tanji, 2009; Rushworth et al., 2007; Shackman et al., 2011), the ACC/MCC is activated during reward processing, conflict monitoring, error detection, and pain (Beckmann et al., 2009; Shackman et al., 2011; Vogt, 2005). The ACC/MCC may be particularly important when the value of actions is uncertain or rapidly changing, and when multiple pieces of information must be considered to discern the optimal behavior (Behrens et al., 2007; Shackman et al., 2011). Meditation practice may lead to more conscious (i.e., less automatic) action selection, greater attention to thoughts and other information entering into the decision-making process, and also increased attention to the actual movement of the body during action execution. Although speculative, such changes in the conscious control of action could potentially activate ACC/MCC and create a positive feedback loop wherein such conscious action becomes more frequent. Such frequent recruitment of ACC/MCC for conscious action control might relate to the consistently observed differences in ACC and MCC structure.

4.1.6. *Orbitofrontal cortex (OFC/BA 11/13/47)*

We found a sizable (240 mm^3) meta-analytic cluster (Table 4 and Fig. 2c) of anatomical difference in the right orbitofrontal cortex (OFC), in an area sometimes referred to as ventromedial prefrontal cortex. Also activated in several fMRI studies of meditation (Klimecki et al., 2012; Westbrook et al., 2013; Zeidan et al., 2011), the OFC is richly connected to primary sensory regions as well as the limbic system, including the amygdala, striatum, and hypothalamus (Barbas, 2000; Ongur and Price, 2000). Consistent with these anatomical connections, the OFC is critical for discerning the precise relationship between stimuli and motivational outcomes (Gottfried et al., 2003; Wallis, 2007; Walton et al., 2011). Notably, whereas the amygdala and striatum may store relatively automatic, inflexible stimulus-reward associations reflecting past experience, the OFC may generate more flexible, 'online' assessments of stimuli and experience (Schoenbaum and Esber, 2010; Wallis, 2007). We agree with others (Luders et al., 2009) that meditative training may eventually lead to greater reliance on the OFC and its dynamic predictions of the current value of stimuli to guide behavior, instead of relying on static stimulus-reward associations from the past. Structural heterogeneities in OFC may thus relate to the stated goals of meditation in that they may facilitate more conscious and flexible behavior.

OFC is implicated not only in online, integrative decision-making, but also in emotion regulation, specifically in down-regulating (Ochsner et al., 2004) and reappraising (Goldin et al., 2008) negative emotional states. This regulatory function may be part of a broader role for OFC in self-monitoring and integration of cognitive and emotional cues in decision-making (Beer et al., 2006). Heightened self-monitoring, as well as a better ability to regulate negative emotion, are consistent with meditation's apparently salutary effects on disorders such as depression, anxiety, and stress (Chiesa and Serretti, 2009, 2010; Sedlmeier et al., 2012; Teasdale et al., 2002).

4.1.7. *Fusiform and inferior temporal gyri (BA 20/21)*

Our meta-analysis revealed significant clusters in the area of the fusiform gyrus/inferior temporal gyrus (FG/ITG; Tables 3 and 4; Figs. 1 and 2d and e). Numerous studies suggest that FG and ITG are activated during various forms of meditation (e.g., Brefczynski-Lewis et al., 2007; Goldin and Gross, 2010; Lou et al., 1999; Pagnoni et al., 2008). Other researchers (Hölzel et al., 2008; Luders et al., 2009) have highlighted the possible role of the ITG in the 'mystical' states associated with meditation, and/or the experience of enhanced well-being and 'bliss' often reported by advanced practitioners. In general, however, findings in the FG/ITG appear puzzling and have been little discussed (e.g., Vestergaard-Poulsen et al., 2009).

Inferior temporal lobe structures are most strongly implicated in detailed, high-level visual processing, however (Joseph, 2001). As a growing body of research has demonstrated enhanced visual processing in meditation practitioners (Brown et al., 1984; Hodgins and Adair, 2010; Jha et al., 2007; Kozhevnikov et al., 2009; MacLean et al., 2010; Tloczynski et al., 2000), the most parsimonious explanation for our meta-analytic clusters is that structural heterogeneities in FG and IFG are related to these apparent enhancements of visual attention and perception. As many meditation practices, including Zen (Austin, 1999) and *Vipassana*/'Insight' (Goenka, 2000), are typically conducted with eyes open, with a simultaneous and strong emphasis on sustained attention, such enhanced sensory acuity is reasonable.

A complementary explanation relates to visual *imagery*, as opposed to perception. Eyes-closed and even eyes-open meditations are often associated with an intense degree of visual imagery accompanying spontaneously arising thoughts, memories, and so on (e.g., Austin, 1999), particularly during lengthy sessions of practice and retreats. A related possibility, then, is that structural changes in these regions underlie the visual imagery commonly accompanying the mind wandering processes prevalent during meditation (cf. Hamamé et al., 2012; Ranganath and D'Esposito, 2005).

4.1.8. *Hippocampus*

We found several studies ($n = 5$) that reported structural differences in the hippocampal formation in meditators (Tables 3, 4 and S1; Fig. 1). This finding complements the frequently observed activations of the hippocampus and associated medial temporal lobe structures during meditation in functional neuroimaging studies using PET (Lou et al., 1999) and fMRI (Dickenson et al., 2012; Engström et al., 2010; Hölzel et al., 2007; Lazar et al., 2000; Monti et al., 2012).

The hippocampus appears to be critical for contextualized emotional learning, i.e., facilitating emotional responses that take into account the current context, as opposed to a single salient cue. Diminished hippocampal functioning, for instance, is associated with inappropriate expression of stress (Kaouane et al., 2012). Moreover, research with rodents has demonstrated that environmental factors (e.g., a supportive rearing environment) can lead to structural changes in the hippocampus (e.g., increased density of glucocorticoid receptors) that have a protective effect *against* stress (Davidson et al., 2000). One possibility is that meditation training enhances stress resilience via similar structural alterations. Further evidence for this notion comes from a 'negative' viewpoint: hippocampal atrophy is associated with numerous clinical disorders involving stress, anxiety, and depression (e.g., Gurvits et al., 1996; Watanabe et al., 1992; cf. Hölzel et al., 2011a). Many such clinical disorders are also associated with problems of concentration and memory (Millan et al., 2012).

Another possibility, then (Luders et al., 2012c), is that structural hippocampal increases relate to meditation's potential amelioration of such clinical conditions (Chiesa and Serretti, 2010) and reduction of stress (Chiesa and Serretti, 2009).

A related possibility revolves around the idea of memory reconsolidation. Although, traditionally, memories have been seen as only temporarily dependent on the hippocampus, then later *consolidated* to other cortical regions (and thereafter hippocampus-independent), recent research suggests that the reactivation of memories puts them again into a labile state requiring *re*consolidation by the hippocampus, and possibly other structures (e.g., Debiec et al., 2002; Nader et al., 2000). Though based largely on animal models, similar behavioral results have been demonstrated in humans and suggest that one function of reconsolidation may be to integrate new information with older memory traces (e.g., Hupbach et al., 2007; Winocur and Moscovitch, 2011). Many meditative practices place a strong emphasis on re-evaluating past behavioral patterns and default emotional reactions to events. Differences in hippocampus, then, may play a role in both seeing past experiences in a new light, and allowing for greater flexibility in present behavior – in line with the possible role of anterior cingulate and orbitofrontal cortices (discussed above).

The hippocampus also appears to be centrally involved in the arising of spontaneous thoughts (Andrews-Hanna, 2012; Christoff et al., 2004; Fox et al., 2014), the generation of creative ideas (Ellamil et al., 2012; Fox and Christoff, 2014), and the simulation of imagined future scenarios (Addis et al., 2007). The arising of many such spontaneous thoughts and imagined future scenarios is a ubiquitous experience during meditation (Goenka, 2000; Thera, 1954). Hippocampal structural differences may be related to the high levels of attention given to such spontaneous thought processes, memories, and simulations, and the effort involved in re-contextualizing them, during meditation practice.

4.2. *White matter pathways*

4.2.1. *Corpus callosum*

Several studies (mostly using diffusion tensor imaging; Table 1) reported structural differences in the corpus callosum of meditation practitioners (Tables 3 and S1; Fig. 1). The human corpus callosum is thought to follow a broad anterior–posterior topographical connectivity pattern, with anterior corpus callosum connecting frontal brain regions, posterior corpus callosum connecting early visual cortices at the back of the brain, and so on (Zarei et al., 2006). Among meditation practitioners, structural differences observed in the corpus callosum are mostly localized to its anterior portions (e.g., genu, forceps minor), which are thought to preferentially connect prefrontal brain regions (Hofer and Frahm, 2006; Zarei et al., 2006). The simplest explanation of these results, therefore, relates them to the consistent findings of structural differences in the prefrontal cortical regions discussed above, including RLPFC/BA 10, anterior insula, OFC, and anterior and mid-cingulate cortices. Prefrontal structural increases might result in, or alternatively, follow, alterations of particular corpus callosum areas that reciprocally connect bilateral prefrontal gray matter structures. Hypothetically, increased prefrontal gray matter might in turn require more or larger connective fibers to facilitate communication among, and synchronization of, regions in opposite hemispheres (Luders et al., 2012a). This interpretation is also consistent with the general lack of hemispheric asymmetry observed in the results (see above).

4.2.2. *Superior longitudinal fasciculus (SLF)*

Several studies reported morphological differences in the SLF (Tables 3 and S1; Fig. 1). The superior longitudinal fasciculus (SLF) is present bilaterally and represents one of the brain's major rostrocaudal fiber pathways (Makris et al., 2005). Imaging of SLF in vivo in humans with diffusion tensor imaging has led to a broad division into three major subcomponents, connecting more dorsal temporoparietal areas with numerous (mostly lateral) prefrontal regions (Makris et al., 2005).

The posterior projection areas of the SLF are implicated in higher-order spatial processing, including the representation of the body in three-dimensional space, as well as in the directing of attentional focus in space (Table 8). Accordingly, differences in the SLF are consonant with the robust findings in anterior precuneus, insular and somatomotor cortices, as well as RLPFC and ACC regions (discussed above). Together, these results support the preliminary hypothesis that differences in the SLF relate to increased connectivity between parietal body awareness and attention areas, and prefrontal executive regions.

5. Discussion

5.1. *Is meditation associated with altered brain structure?*

Evidence for meditation practice as the *causative* factor in structural brain change remains tenuous, and much further work is needed before such a relationship is either established or disconfirmed. Several regions show *consistent* differences in advanced

Table 8
Subcomponents, connectivity, and putative functional roles of the superior longitudinal fasciculus in humans.

	Caudal projection areas		Rostral projection areas	Putative functional role
SLF I	Superior parietal lobule/precuneus (BA 7); postcentral gyrus (BA 5);	⇌	Secondary motor cortex (M II); SMA (BA 6); superior frontal gyrus (BA 8/9)	Higher-order proprioception (sense of body in space); execution of appropriate motor acts
SLF II	Caudal inferior parietal lobule; angular gyrus (BA 39); supramarginal gyrus (BA 40); postcentral gyrus (BA 3,1,2); precentral gyrus (BA 4)	⇌	Middle frontal gyrus (BA 6 and 46)	Spatial attention; top-down control of attentional focus
SLF III	Rostral inferior parietal lobule/supramarginal gyrus (BA 40);	⇌	Middle frontal gyrus (BA 6 and 46); pars opercularis (BA 44); mid-insula (BA 43)	Higher-order somatosensation; working memory

Note: BA: Brodmann area; M II: secondary motor cortex; SLF: superior longitudinal fasciculus; SMA: supplementary motor area. For more information see Makris et al. (2005). '⇌' denotes reciprocal (bidirectional) connections between caudal and rostral projection areas.

practitioners vs. meditation-naïve controls (Section 4), but the possibility remains that pre-existing brain structure heterogeneities explain the observed group differences. Other findings bear on the question of causality, however, particularly pre–post examinations of meditation-naïve subjects undergoing brief meditation training with comparable wait-list control groups.

One of the most interesting results to emerge from the nascent literature on brain structure and meditation is just how few hours of training seem necessary to induce neuroplastic changes (cf. Hölzel et al., 2011a; Tang et al., 2010, 2012). Further, differences similar to those after brief training have also been observed in long-term practitioners in almost all the same brain regions (compare Tables 3 and 4 with Table 5). This substantial overlap suggests that short-term training may engage and modify many of the same regions that show heterogeneities in long-term practitioners. Early-onset structural changes might persist after initial training, be sustained by continuous practice, or some combination of the two (see Section 5.2).

A straightforward prediction, assuming that meditation indeed alters brain structure, might be that effect size will scale with the length of time participants have been engaged in meditation practice. However, overall, we found a negative correlation between meditation experience and effect size (Fig. 4), suggesting that this is not the case. The apparent decline in effect size with further meditation experience may be related to the fact that long-term practitioners are very often older in age than short-term practitioners, and thus, normal age-related declines in gray and white matter may interact with any potential gains due to meditation and reduce effect sizes (cf. Lazar et al., 2005; Pagnoni and Cekic, 2007). Another possibility is that larger structural differences are required for the initial acquisition and execution of meditative skills such as emotion- and attention-regulation. With increased practice, functional benefits may persist without any further structural change. However, correlations are extremely unstable with such small sample sizes ($n = 15$ in this case); any firm conclusions about the relation of meditation experience to effect size are premature.

Although perhaps implausible at first glance, significant differences in brain structure resulting from only a few hours of meditation practice (e.g., Hölzel et al., 2011a,b; Tang et al., 2010, 2012) parallel results reported after relatively brief motor skill learning (e.g., Draganski et al., 2004). For instance, a recent study found that only 2 h of spatial learning was sufficient to induce DTI-detectable changes in white matter microstructure in both humans and rats (Sagi et al., 2012). The notion that a largely mental practice, such as meditation, can equally produce such changes is further supported by studies showing structural differences after short-term mental training of working memory (Takeuchi et al., 2011) and reasoning abilities (Mackey et al., 2012). Nevertheless, we reiterate that evidence for meditation as the causative factor in brain structure change remains very limited.

5.2. *Persistence or transience of structural differences*

The apparently rapid induction of changes in brain structure naturally invites the question of whether such differences disappear equally rapidly in the absence of continued practice. Gray matter changes related to motor skill learning (juggling), for instance, have been found to diminish without continued practice (Draganski et al., 2004). Long-term follow-up studies are both difficult and expensive to execute, but would be the ideal paradigm for demonstrating either persistent or cumulative effects of intensive or continuing meditation practice, respectively.

Even assuming meditation is indeed a causative factor, several important questions regarding structural brain plasticity in meditators remain to be answered, including: (1) Do morphological differences persist in the absence of further training? (2) Is there a ceiling beyond which further training results in no further significant structural alterations? (3) Is there a 'dose-dependent' relationship between practice and structural change, and if so, does this relationship follow a linear, logarithmic, or other distinct trend? It has been suggested in the case of motor skill learning that the initial phase of learning is more critical for inducing gray matter changes than the later maintenance of the skill (Driemeyer et al., 2008). We suspect the same may be true of the acquisition of mental skills such as meditation, although this remains to be studied.

Although several studies have pioneered longitudinal analyses of anatomical differences (Farb et al., 2013; Hölzel et al., 2010, 2011a; Tang et al., 2010, 2012), much work is needed to firmly establish the putative causal effects of meditation on brain structure. Extensive longitudinal pre–post training studies, ideally with long-term follow-ups, can begin to address these key questions in the future.

5.3. *Distinctive morphological differences with different meditation practices?*

Several functional neuroimaging studies have now examined multiple types of meditation practice within the same practitioners (e.g., Lou et al., 1999; Manna et al., 2010; Brewer et al., 2011), and a recent meta-analysis has examined peak activations across different meditation styles (Tomasino et al., 2013). Overall, results from these studies consistently support the notion that distinctive neural activity underlies disparate categories of meditation. The present study collapsed data across many distinct contemplative traditions and meditation practice types due to challenges that tend to arise in research of this kind. For example, long-term practitioners typically combine multiple types of practice throughout their lifetimes, and may alternate between focused and open attentional stances, as well as emotion-regulation practices, within a single practice session. As a result, testing for structural heterogeneities related to specific forms of mental practice was not feasible in the present meta-analysis. That said, some practitioners adhere

Table 9
Candidate cellular mechanisms putatively underlying macroscale structural differences in gray and white matter.

Cellular mechanism	Tissue type affected	Morphometric methods putatively affected
Dendritic arborization/synaptogenesis	GM	GMC, GMV
Neurogenesis	GM	CT, GMC, GMV
Angiogenesis	GM/WM	CT, GMC, GMV, WMV
Axon sprouting	GM/WM	CT, GMC, GMV, FA
Gliogenesis	GM	CT, GMC, GMV
Fiber reorganization	WM	FA
Myelin formation	WM	FA
Myelin remodeling	WM	FA
Astrocyte changes	WM	WMV

Note: CG: cortical gyrification; CT: cortical thickness; FA: fractional anisotropy; GM: gray matter; GMC: gray matter concentration; GMV: gray matter volume; WM: white matter; WMV: white matter volume. Based on Anderson (2011), Zatorre et al. (2012), and Lövdén et al. (2013).

firmly to a single practice or tradition only, and may therefore serve as suitable subjects for future work distinguishing structural heterogeneities unique to particular forms of mental training.

5.4. *Structural decrease in meditation practitioners?*

As noted in Section 3.6, 11 structural differences to date show increases in controls vs. meditators (Fayed et al., 2013; Kang et al., 2013), which are alternately interpretable as structural declines or decreases in meditation practitioners. Only half of these results were significant at stringent statistical thresholds, and importantly, many were in regions related to the default mode network, such as the posterior cingulate cortex, angular gyrus, precuneus, and temporoparietal junction (Buckner et al., 2008). Given that default mode network activity is linked to mind wandering and spontaneous thought (Christoff et al., 2009; Fox et al., 2013; Mason et al., 2007), the authors (Kang et al., 2013) suggest these results indicated a weakening of default mode network function, possibly reflecting reduced mind wandering and discursive thought in long-term meditation practitioners – or potentially reduced ‘chaining’ of the thoughts that initially arise. This idea is consistent with a recent fMRI study that shows reduced activation and functional connectivity in default mode network regions in long-term meditation practitioners (Brewer et al., 2011). A preliminary interpretation of these structural declines in meditators vs. controls, then, is that they may indicate functional benefits to meditators (Kang et al., 2013), but such an interpretation remains highly speculative (cf. Fox et al., 2014).

5.5. *Underlying cellular basis of macroscale differences in brain structure*

The underlying cellular-level changes that putatively give rise to the many gross structural differences reported here remain very poorly understood, particularly in humans. Nonetheless, numerous candidate cellular mechanisms have been identified (Anderson, 2011; Zatorre et al., 2012; Lövdén et al., 2013) and are tentatively summarized in Table 9. Although most of these relationships remain highly speculative, some first steps have been taken toward understanding cellular-level changes that might give rise to macroscopically observable brain morphology differences. Preliminary evidence from a mouse model (Lerch et al., 2011), for instance, found that volumetric changes as measured by morphometric MRI methods correlated most strongly with the presence of axon growth cones (as opposed to neuron size or number). What this suggests is that axon sprouting and reorganization may be a more important factor than, for example, neuron soma growth or neurogenesis proper. In contrast, neurogenesis – which results in the addition of relatively few total neurons, remains equivocal in humans, and seems mostly restricted to hippocampus (Zatorre et al., 2012) – is a very unlikely cellular mechanism (for detailed discussion, see the reviews noted above). Determining the cellular candidates for changes observed in meditation practitioners faces the additional challenge that direct animal models are not possible, whereas motor skill or spatial learning, for instance, can be plausibly simulated in rodents and monkeys and compared concurrently with human results (e.g., Sagi et al., 2012).

5.6. *Correlations between structural measures and experience or behavior*

Although we report all correlational results for completeness (Section 3.5; Tables 6 and 7), we feel any further speculation is premature at this time. Nearly all correlations were obtained at lenient statistical thresholds, and/or in a priori-defined ROIs, and/or using non-independent statistical analyses – rendering their reliability questionable (Fiedler, 2011; Vul et al., 2009). Moreover, very few correlations are consistent across studies (unlike group difference results) – though there are suggestive overlaps in correlations in the insula (Tables 6 and 7) and somatomotor cortices (Table 6). We acknowledge, however, that weak and/or inconsistent correlations may be due to a number of factors, such as the masking of training-related effects by age-related declines in gray matter concentration and volume (Lazar et al., 2005). Future work should continue to address experience– and behavior–structure correlations to build on the present tentative results.

5.7. *Integration of anatomical investigations with behavioral measures*

Several studies so far have integrated measures of structural differences in the brains of meditators with a behavioral measure (Table 7). For instance, Grant et al. (2010) correlated cortical thickness in long-term Zen meditation practitioners with pain sensitivity, and Hölzel et al. (2010) correlated self-reported stress levels with amygdala gray matter concentration. As already noted, however, these correlations are based on statistically lenient ROI analyses. Further work is required to demonstrate the behavioral and/or clinical relevance of these results. In particular, structural differences need to be related not only to self-report questionnaires, but also to objective measures of relevant behaviors, such as attention and emotion regulation, body awareness, and so on. Ultimately, brain morphology differences are of importance only inasmuch as they relate to altered behavior and subjective well-being. Establishing such relationships should therefore be a paramount concern in future research.

5.8. *Integration of anatomical investigations with functional neuroimaging*

To our knowledge, no study has related structural brain differences with functional MRI activation differences in meditators.

Function and structure differences can corroborate one another when correlated with the same behavioral task, as has been elegantly demonstrated with insula structure and function as related to interoceptive awareness (Critchley et al., 2004). Such functional–structural integration of results represents a major challenge – and opportunity – for future research in the cognitive neuroscience of meditation.

6. Meta-analytic methods, reliability, and limitations

In the present section we discuss in more detail the validity of the present meta-analysis, the checks of its robustness, and the limitations imposed both by our meta-analytic techniques and the methodology of the primary research reviewed.

6.1. *Reliability of meta-analyses*

Although we included all available morphometric neuroimaging studies of meditation to date, nonetheless, the sample size for our meta-analysis was fairly small (21 studies total). Only 14 studies could be included in quantitative ALE meta-analysis, and only 16 studies provided data that enabled calculation of effect sizes. There were also too few studies to test separately among different meditation traditions, and too few peak foci reported to conduct a separate ALE for short-term meditation training results only.

6.1.1. *Determining consistent brain structure differences*

Aside from seven studies not contributing to the ALE meta-analysis, some studies (especially Kang et al., 2013) contributed far more foci than others (Table S1). The latest ALE algorithms, however, correct for this bias, reducing the influence of studies that contribute disproportionate numbers of foci (Turkelbaub et al., 2012). ALE also uses random-effects analyses, which are more conservative than fixed-effects analyses. In addition, these analyses are generalizable to the population at large, which is the theoretical population of 'all meditation practitioners,' or at least all practitioners within a given school of practice. As a further check, we conducted an ALE meta-analysis of stringent statistical results only (Table S3) and of large effect size results only (Table S4); both by and large paralleled our primary results (Table 4).

There are also other drawbacks to our meta-analytic techniques for determining consistent brain regions across studies that should be kept in mind when interpreting our results. In our 'qualitative' review, the criterion of three reports for a given brain region (i.e., two replications of a given result), though used to advantage by others (Kempton et al., 2008), is somewhat arbitrary. A more or less stringent criterion could just as well be imposed, resulting in shorter or longer lists of brain regions, respectively. Further, the regional labels reported by the source studies are always approximate; three findings reported in the 'same' region or Brodmann area may in fact differ considerably in location across studies.

Though ALE avoids the latter problem by using precise coordinates (rather than general regional labels) as its input, nonetheless these peak coordinate foci are highly imperfect indicators of the location of a significant anatomical difference. The peak coordinates usually represent the weighted center of a cluster of significant difference, but they provide no information about the size of the cluster (number of voxels) or its shape. Even when this information is provided, however, ALE as yet has no means of integrating this information into its meta-analysis. Finally, ALE attempts to find overlapping clusters of difference by averaging across different peak coordinates. There is therefore the risk that, with two or more relatively nearby peak foci, ALE will find an average, 'significant' cluster somewhere between these foci, in a brain region not actually reported in any of the source studies.

6.1.2. *Effect sizes in morphometric neuroimaging*

Despite the finding that the overall mean effect size across 15 studies was 'medium' ($\bar{d}_{\text{global}} = 0.77$; $\bar{r}_{\text{global}} = .34$), these effect sizes are based on peak *t*-statistics, as commonly reported in the neuroimaging literature (see Sections 2 and 3). After attempting to adjust for this bias and estimate effect sizes based on mean *t*-statistics for entire clusters of significant anatomical difference (instead of only *peak* voxels of difference), our results suggest that the effect sizes can be more conservatively estimated at approximately 57% of their reported value (see Section 3). This adjustment places our mean effect size in the realm of 'moderate' or 'medium' ($\bar{d}_{\text{global adjusted}} = 0.44$ and $\bar{r}_{\text{global adjusted}} = .19$). Such effects are comparable to the mean effect sizes for studies of meditation's influence on attentional, cognitive, and emotional factors (overall $\bar{r} = .27$; Sedlmeier et al., 2012). Nonetheless, this resemblance should not be over-interpreted: as already noted, the interpretation of effect sizes in neuroimaging studies remains poorly developed (e.g., Poldrack et al., 2008).

6.1.3. *Publication bias*

Funnel plots (Egger et al., 1997) can indicate the probable degree of publication bias (Sedlmeier et al., 2012). Although a quantitative Egger test (Egger et al., 1997) of funnel plot asymmetry was precluded by the lack of data on standard error provided in the original studies meta-analyzed, visual inspection suggested that a fairly large degree of bias was present in averaged effect sizes by study (Fig. 5). Almost all large effect sizes have been reported in studies with the smallest sample sizes ($n < 40$), whereas studies with larger ($n > 40$) samples tend to yield mean effect sizes around or below the field-wide mean of $\bar{d}_{\text{global}} = 0.77$. The trend toward more reasonable effect sizes in well-powered, large sample size studies (Fig. 5) could be interpreted as evidence that true effects are being converged upon. However, the lack of publication of almost any negative results in morphometric neuroimaging of meditation to date suggests a fair degree of publication bias, and indicates a strong chance of there being a 'file-drawer problem' in this literature (Rosenthal, 1979).

6.2. *Selection bias and preexisting brain structure differences*

Even short-term meditation training can be very demanding, and consistent, long-term practice involving thousands of hours of commitment is obviously so. The possibility of a selection bias in favor of participants predisposed to such regimens, and/or already possessing higher trait levels of body awareness, sustained attention, metacognitive awareness, and so on, is clearly a major potential confound. Such initial differences in personality and cognitive ability would likely be reflected in brain structure and function. A recent study, for instance, found that differential baseline activation in certain brain regions predicted subsequent practice time of both mindfulness and compassion forms of meditation (Mascaro et al., 2013). Longitudinal morphometric studies in meditation-naïve novices (Hölzel et al., 2011a,b; Farb et al., 2013; Tang et al., 2010, 2012) have begun to mitigate this problem, but extensive research will be necessary to address whether preexisting differences explain, or perhaps interact with, apparently experience-dependent changes in brain structure. The use of active control groups requiring substantial time and commitment (vs. simple wait-list controls) can also help to limit this potential confound.

6.3. *Divergent findings*

Convergent findings aside (Section 4), there are many brain structure differences observed in only a single study included in this meta-analysis. There are many reasons why a result might have been found in only a single study. First, a great variety of meditation practices were examined. Although the small number of studies precluded practice-specific analyses, techniques differed markedly (e.g., loving-kindness meditation focused on interpersonal emotional training vs. body-scanning *Vipassana* meditation focused on tactile sensations). Practitioners focusing on highly disparate techniques should not be expected to exhibit identical or even necessarily similar structural differences.

Second, different practices are related to differing lifestyle variables that may in turn affect brain structure. Some meditation regimens, for instance, are particularly strict and austere (e.g., Zen; Austin, 1999), whereas others take a more relaxed approach. These differing styles influence numerous lifestyle variables ostensibly peripheral (but arguably critical) to the mental meditation practice itself, including fasting, sleep deprivation, dietary restrictions (e.g., vegetarianism), overall mood and levels of stress, etc. Any of these lifestyle factors may interact synergistically or antagonistically with the putative influence on brain structure of the mental practices themselves. Studies to date have typically controlled for only age, sex, and handedness. Ideally, future questionnaire-based research would establish demographic models of meditation practitioners, and subsequent neuroimaging work could attempt to control for the relevant individual difference factors when selecting control groups.

Third, error and inconsistencies related to the variety of morphometric measures employed (Table 1) is a likely contributor to inconsistent results across studies. Fourth, and finally, some results may simply be the product of chance or error. Considering the lenient statistical thresholds often used in the reviewed studies, the rate of Type I (false positive) error is evidently heightened. That said, the relative paucity of studies of brain structure and meditation makes any conclusions about not-yet-replicated results somewhat premature. Future research can more definitively distinguish results that replicate consistently from anomalous or chance findings.

6.4. *Few research groups and overlapping samples*

The majority of the studies conducted so far have been from only a few research groups, and several studies have used largely or entirely overlapping samples of meditation practitioners (marked with a Δ symbol in Table 2). This is partly because it is often difficult to recruit subjects with high levels of expertise. Although these facts in no way invalidate the results obtained, we emphasize them because it is possible that the samples of practitioners studied by these groups are atypical in some way (e.g., in having particularly effective teachers and practices, or abnormally large structural brain differences). Further, overlapping samples used in multiple studies (published in multiple papers) may suggest completely independent results whereas findings are, to an unknown degree, dependent. Until larger and more independent samples of practitioners are studied by a wider variety of research groups, generalizing from the present results to conclusions about brain structure of meditation practitioners as a *population* should be undertaken with considerable caution.

6.5. *Lack of exploratory analyses (controls > meditators)*

Beyond stringent statistical tests showing differences for meditators > controls, many studies reported results of exploratory analyses examining structural increases in meditators at much more lenient statistical thresholds (marked with a # symbol in Table S1). Structural increases for controls > meditators are almost entirely absent at stringent thresholds (for exceptions, see Fayed et al., 2013; Kang et al., 2013), but are rarely tested for at more lenient thresholds. This presents a potential problem because many meditators > controls differences *are*reported at lenient thresholds. Although exploratory analyses for controls > meditators may be of less interest to researchers, we suggest that in future exploratory contrasts of meditators > controls, the reverse contrast should be conducted as well. Such an approach would allow researchers to test for potential trend differences in controls > meditators that are typically overlooked, providing a more balanced and comprehensive understanding of differences between meditators and non-meditators.

7. Conclusions and directions for future research

At the outset of this review, we asked two fundamental questions about the morphometric neuroimaging of meditation practitioners: (1) Is meditation associated with altered brain morphology in any consistent, replicable way? And if so, (2) what is the magnitude of these differences? In this final section we present what we consider the best available answer to each question, and also provide some suggestions for future work along these lines.

7.1. *Is meditation associated with consistent alterations of brain structure?*

Morphometric studies of the brains of meditation practitioners show promising preliminary results, but should be interpreted with caution given many methodological limitations in both the original source literature and the meta-analyses employed here. Any firm claims about whether meditation truly *causes* differences in brain structure are still premature. That said, we do find that meditation is consistently *associated* with changes in brain morphology, though the limitations of a qualitative review, and the ALE method (see above), should be kept in mind. Findings converge on several brain regions hypothesized to be involved in meditation based on results from functional neuroimaging, behavioral and clinical research, and phenomenological reports of meditative experience. These include regions key to meta-awareness and introspection (RLPFC/BA 10), exteroceptive and interoceptive body awareness (sensory cortices and insular cortex, respectively), memory consolidation and reconsolidation (hippocampus), self and emotion regulation (anterior and mid-cingulate, and orbitofrontal cortex), and finally intra- and interhemispheric communication (superior longitudinal fasciculus and corpus callosum, respectively). Notably, with the exception of primary and secondary somatomotor regions, consistent differences were found almost exclusively in higher-order ('downstream') executive and association cortices. This suggests that meditation preferentially recruits such general, higher-order brain regions.

In contrast to differences between groups, correlations between structural differences and either total meditation practice time, or other behavioral measures, are mostly statistically non-independent or marginal. No strong conclusions about these correlational analyses can yet be drawn. However, results after short-term training of novices closely parallel those observed when comparing long-term practitioners to meditation-naïve controls. Importantly, this supports the notion that mental training via meditation is the causal source of differences observed in expert practitioners, but we acknowledge that a great deal of further research is needed using longitudinal, experimental designs to confirm this still tenuous relationship.

7.2. *What is the magnitude of brain morphology differences in meditators?*

The overall effect sizes from morphometric neuroimaging studies, after correcting for inflation, are 'moderate' ($\bar{d} = 0.44$; $\bar{r} = .19$). However, a funnel plot (Fig. 5) suggests that a fair degree of bias and unreliability is present in these studies, particularly with results reported at lenient statistical thresholds and in studies with small sample sizes ($N < \sim 40$). Nevertheless, our fairly conservative estimate of the global effect size for all morphometric studies compares favorably with the effects of hundreds of other interventions – behavioral, educational, psychological, and therapeutic – which, on average, yield effect sizes of roughly $d = 0.50$ (Lipsey and Wilson, 1993). More recent meta-analyses of various (non-meditation) interventions similarly show mean/global effect sizes in the 'moderate' to 'large' range (cf. Butler et al., 2006; Morley et al., 1999; Westen and Morrison, 2001). Interestingly, cognitive and emotional effects of meditation, based on a meta-analysis of 163 behavioral studies, show a mean effect size in a similar range ($d = 0.56$; Sedlmeier et al., 2012), as does a recent meta-analysis of studies using the meditation-derived 'mindfulness-based therapy' as an intervention for anxiety and depression (Hoffman et al., 2010).

We hasten to add, however, that the interpretation of effect sizes is based largely on behavioral research; a comparable mean effect size based on neuroimaging results is not necessarily equivalent, and even in the behavioral sciences, interpretation of effect sizes is ultimately arbitrary (Cohen, 1992). Moreover, the reporting and interpretation of effect sizes in neuroimaging is still novel and poorly developed (e.g., Poldrack et al., 2008). Nevertheless, we report these mean and global effect sizes here to give an indication of the magnitude of brain structure differences in meditation practitioners, and to make future meta-analyses more convenient. Future research and statistical theory can improve on our understanding of neuroimaging-based effect sizes and their interpretation.

7.3. Directions for future research

Many concerns have been raised throughout this paper with respect to proper control groups, methods, confounding demographic variables, etc. In the interest of beginning to address these concerns and establishing morphometric neuroimaging of meditation on a firmer footing, we propose the following directions for future research:

- Collect more detailed demographic information about practitioners, so that relevant variables (e.g., education level, income, number of offspring, dietary preferences, etc.) can be better controlled for in comparison groups
- Integrate morphometric analyses with concurrent behavioral measures and functional neuroimaging to begin to establish the functional relevance of morphological differences
- Place greater emphasis on longitudinal (vs. cross-sectional) studies of novices, which can better address the question of whether meditation is indeed *causing* the observed morphological differences
- Conduct long-term follow-up studies after termination of meditation training, to see if induced changes (if any) persist in the absence of continued practice, or are transient and dependent on continued practice
- Directly compare long-term practitioners of disparate meditation styles (e.g., Zen vs. compassion meditation) to investigate whether distinct meditation styles show differing effects on brain morphology; attempt to control for associated lifestyle variables that may influence such results
- Calculate and report appropriate effect sizes for all results, so that the magnitude (and not just significance) of differences between meditators and controls is known, and in order to facilitate future meta-analyses (Poldrack et al., 2008)
- When conducting exploratory (lenient statistical threshold) analyses in mediators > controls, conduct similar analyses for controls > meditators. Brain deactivations during functional neuroimaging studies of meditation seem to be nearly as prevalent, and important, as activations (e.g., Brewer et al., 2011). Exploratory morphometric analyses for controls > meditators may reveal relevant brain regions showing structural *diminution* in meditation practitioners. Such structure diminutions could potentially indicate functional benefits (cf. Kang et al., 2013)

Table 10
Most consistently altered brain regions in meditation practitioners, across all meta-analyses.

Most consistently altered brain regions
Left rostrolateral prefrontal cortex
Anterior/mid cingulate cortex
Anterior insula
Primary/secondary somatomotor cortices
Inferior temporal gyrus
Hippocampus

7.4. Conclusions

Such methodologically ideal (and often, costly) studies may not be implemented for some time, however. What can we conclude at present? Are there regions that we can confidently claim to have altered brain morphology in meditation practitioners? In all, we conducted five different versions of our neuroimaging meta-analysis (Tables 3 and 4; Tables S2–S4). Taking the most conservative approach, we can list regions found in the majority (i.e., at least three) of these five meta-analyses: qualitative review (Table 3); ALE meta-analysis (Table 4); and stringent versions of both of the former (Tables S2–S4). This convergent approach suggests that at present, the most dependable morphological differences are in the left rostrolateral prefrontal cortex (BA 10), anterior/mid-cingulate cortex, anterior insula, primary/secondary somatomotor cortices, left inferior temporal gyrus, and hippocampus (Table 10).

Although we feel that this consistency across multiple meta-analytic methods makes our neuroimaging results in meditation practitioners notable and fairly reliable, we acknowledge that morphometric neuroimaging in mediators suffers from all the same limitations as morphometric studies of other phenomena (e.g., motor skill learning; cf. Thomas and Baker, 2012). We therefore underscore the need for future research to both modify and enrich the preliminary conclusions drawn here (Table 10). That said, our combined neuroimaging-based and effect size meta-analyses suggest that the results to date show a fair degree of regional consistency and relatively large magnitude – and, potentially, practical significance. A major challenge for the future is to better understand how, and to what extent, meditation is associated with differences in brain morphology, and whether the magnitude of these differences indicates any practical significance.

One of us (Sedlmeier et al., 2012) recently concluded, after a comprehensive meta-analysis, that meditation does indeed have positive effects on cognitive and emotional processes. In the present study, we conclude that meditation appears to be reliably associated with altered anatomical structure in several brain regions (Table 10). Moreover, these differences appear to be about 'medium' in magnitude (as measured by effect size). These effect sizes are comparable to the roughly 'medium' effects of many other behavioral, educational, and psychological interventions (Lipsey and Wilson, 1993), and may therefore indicate practical significance – though this remains a difficult issue to be resolved by future research and statistical theory in neuroimaging. The great challenge ahead will be to relate apparent morphological brain differences to the complex and subtle psychological and behavioral changes evident in meditation practitioners (Sedlmeier et al., 2012).

Conflicts of interest

The authors declare no conflicts of interest.

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