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*Review Article*

# Neuroimaging and consciousness: applications of PET, SPECT, and advanced MRI modalities

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**Abstract:** A growing number of advanced neuroimaging studies have been used to evaluate the nature of consciousness. Such studies have focused on various states of consciousness as well as ways of inducing altered states of consciousness. Various states of consciousness include the normal waking state, sleep states, the brain under anesthesia, and the impact of disorders such as seizures or schizophrenia. The induction of altered states of consciousness includes practices such as meditation or the use of psychoactive substances leading to psychedelic effects. This paper reviews some of the relevant research and then considers some of limitations and challenges for studying consciousness with neuroimaging, particularly via positron emission tomography (PET), single photon emission computed tomography (SPECT), and advanced magnetic resonance imaging (MRI) modalities.

**Keywords:** Consciousness, cerebral metabolism, cerebral blood flow, magnetic resonance imaging (MRI), positron emission tomography (PET), single photon emission computed tomography (SPECT), meditation, brain imaging

## Introduction

Consciousness is one of the most enigmatic aspects of human life to study. Perhaps the biggest problem is introduced from the limitation that we are "trapped" within our own consciousness, making it difficult to study it from an external or objective perspective. After all, the observer and observed in any study are both operating from within their own consciousness. Given the inherently subjective nature of consciousness, the only practical method to understand another person's thoughts is often to directly ask them. However, this approach is further complicated by the fact that the very act of questioning someone about their current state of consciousness inevitably alters that state. Thus, utilizing a brain scan becomes challenging when trying to correlate neurophysiological findings with subjective experiences [1].

Consciousness itself is quite challenging to even define. Medically, consciousness typically refers to a person who is awake; if a patient comes in with a head injury or stroke, it might be observed that they are conscious. This typically means that the person presents awake and responsive to interactions. Beyond this basic medical definition of consciousness, most scholars in the field of consciousness studies, philosophy, or theology typically consider consciousness to represent the capacity to have awareness. Awareness is then the ability to experience specific things within that capacity. In human beings, consciousness more specifically refers to self-awareness [2, 3]. For example, a video camera can see the same world that our own eyes see, but we are aware that we are seeing the world. The video camera is not. For the purposes of this review, we adopt an operational definition of consciousness as a state characterized by subjective awareness and responsiveness to internal and external stimuli, which can be assessed through measurable neuroimaging correlates including changes in cerebral metabolism, blood flow, and functional connectivity patterns.

Consciousness appears to arise at a variety of levels from the biological to the psychological to the spiritual. Each of these may have underlying biological components to them as well. In prior writing, consciousness has been divided into several different types of awareness [4]. There is instinctual awareness that appears to occur primarily on an organism level. Most animals, including one-celled organisms, have some instinctual awareness of their environment, which is survival-based and encompasses sensory processing and some type of response. In animals with a nervous system, instinctual awareness most likely involves structures such as the thalamus, nucleus accumbens, periaqueductal gray, and limbic areas [5].

The next level of awareness is habitual responsiveness, characterized by some degree of learning processes leading to memory formation. An animal will learn various habits for eating, social interactions, and reproductive interactions. Areas of the brain involved in habitual


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responsiveness most likely relate to the midbrain, cerebellum, and posterior parts of the neocortex [6]. Building upon habitual responsiveness, intentional decision-making begins to enter the realm of human brain processes that include language and affective-based processing. Decision making is a form of conscious goal seeking and typically involves the dorsolateral prefrontal cortex, as well as the temporo-parietal association areas. Intentional decision-making in humans includes executive processes, such as making a daily schedule, making a grocery list, or planning a vacation. In intentional decision-making, there is an awareness of current and future events that are brought together into a decision-making process [7]. Creative imagination represents an even more advanced level of awareness, including processes such as mind wandering, daydreaming, and free, associative fantasizing. Creative imagination has been linked to the default mode network, as well as inter-hemispheric interactions. A combination of sensory processing, emotional processing, and cognitive processing come together in creative manners. Chrysikou et al. reported a complex network of brain regions in patients engaged with creativity; patients expressing higher levels of creativity had distinct patterns of activation in default mode network and executive brain regions compared to people who expressed normal levels of creativity [8].

Higher levels of consciousness include self-reflective awareness and ultimately some type of transformational awareness often considered to be an altered state of consciousness. These typically begin to fall into the realm of spiritual awareness, leading people to intuitive and symbolic processing of the self and the relationship between the self and others. Transformational awareness, specifically, pertains to profound experiences such as mystical states or enlightenment. Areas of the brain involved in these types of higher awareness include the anterior, cingulate cortex, insula, thalamus, brain stem, limbic structures, and fronto-parietal circuit. This form of higher-level consciousness typically involves the coordinated activation of multiple regions of the brain [9].

Given these complex aspects of consciousness and awareness, neuroimaging emerges as an intriguing tool for the study of its underlying mechanisms. However, this introduces the challenging philosophical and biological problem of where consciousness may arise in the context of neuronal firing, electrical activity, neurotransmitters, and the billions of neural interconnections in the brain. Today, many different parts of the brain have been considered possible “seats” of consciousness. Yet, there have been no studies which have definitively demonstrated what structures or functions of the brain produce consciousness. This is sometimes referred to as the “hard problem” of consciousness [10]. This has led many scholars in the neurosciences, as well as the field of consciousness studies, to posit that consciousness is either an emergent property, arising from a base of neurobiology, or perhaps something more than just a biological process.

Philosophical and spiritual traditions throughout the world have frequently considered consciousness to be the primary substance of the universe, from which matter itself is derived. Buddhist and Hindu thought strongly suggest consciousness as the most fundamental aspect of the universe [11]. However, even if consciousness is primary, it clearly must interact with the biology of the brain. Hence, there is always some value for using neuroimaging as an approach to help understand the concepts of consciousness as it relates to the biology of the brain. Some of these topics also arise within a field of study called *neurotheology*. Neurotheology seeks to understand the relationship between the brain and religious and spiritual phenomena [12]. Some of the most profound religious and spiritual phenomena, such as mystical or enlightenment experiences, are typically regarded as altered states of consciousness [13]. Thus, a neurotheological investigation of consciousness may be an important intermediary in the neuroimaging study of consciousness. Specifically, neurotheology provides a framework for understanding how altered states of consciousness induced by spiritual practices can be systematically studied using neuroimaging techniques such as positron emission tomography (PET), single photon emission computed tomography (SPECT), and functional magnetic resonance imaging (fMRI), thereby bridging phenomenological reports with objective brain measures.

## Neuroimaging of consciousness

There are numerous applications of neuroimaging in the study of consciousness. These approaches can track the various ways in which consciousness can be affected (e.g., enhanced or inhibited). The most commonly used neuroimaging techniques for the study of consciousness include MRI, PET, and SPECT.

fMRI has been used to evaluate several physiological processes, including functional connectivity, cerebral blood flow, and even neurotransmitter concentrations with MR spectroscopy (MRS) [14]. Since many studies that use fMRI include some type of resting scan as a baseline, it is relatively easy to compare such scans across individuals, including those that have altered states of consciousness [15-21]. In doing so, differences in cerebral blood flow or functional connectivity can be observed. More recent work with MRI has been to develop the “connectome” to observe the more global interconnectedness of various brain structures. This has also led to concepts of network neuroscience focusing on larger scale networks that underlie specific functions. Well known networks include the default mode network, salience network, and attention network, among others.

MRS evaluates the concentration of neurotransmitter molecules that can be involved in the experience of consciousness. Primary neurotransmitters that can be evaluated are glutamate (main excitatory neurotransmitter in the brain); gamma-aminobutyric acid (GABA; the main

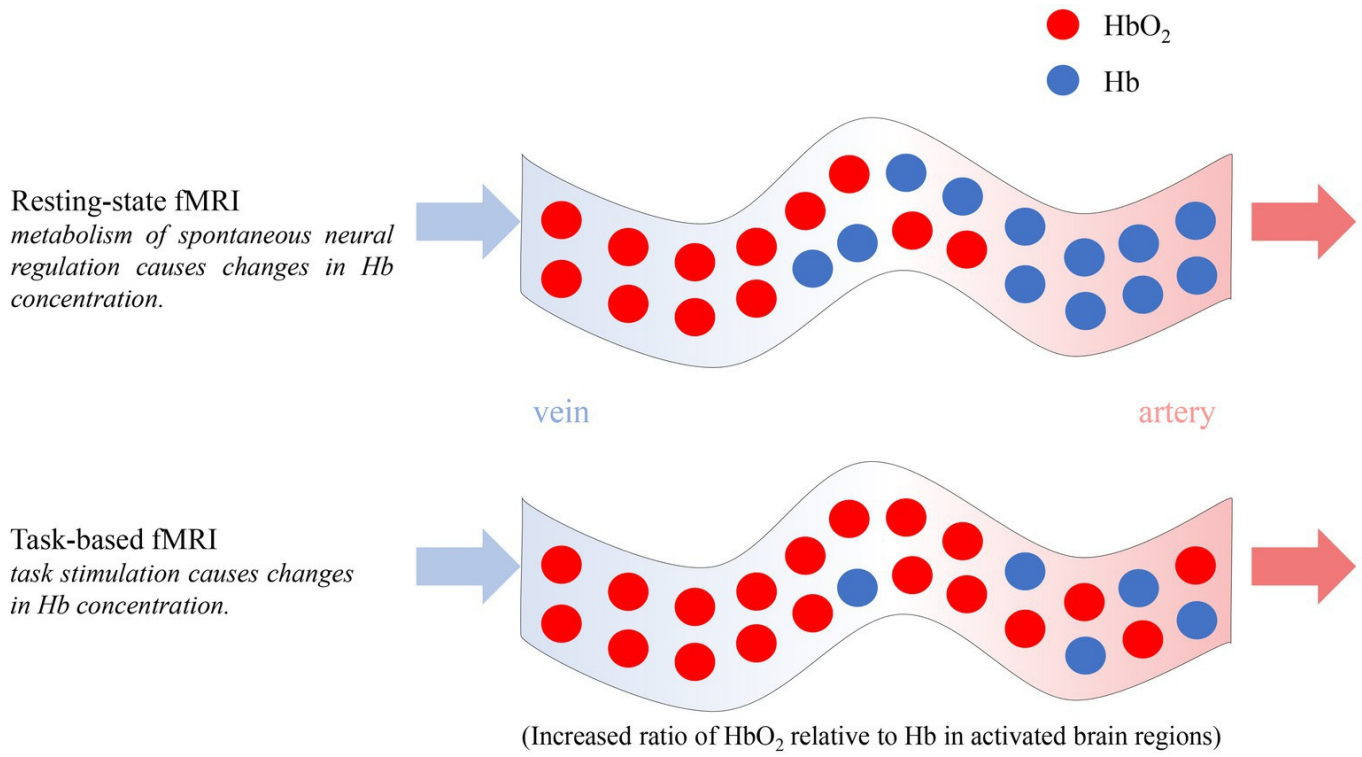


**Figure 1.** Changes in hemoglobin oxygenation ratios associated with different states of consciousness. Reproduced with permission from Wang et al. [23].

inhibitory neurotransmitter in the brain; glutamine (Gln; a precursor to glutamate and GABA); N-acetylaspartylglutamate (NAAG; a neuropeptide and a metabolite related to glutamate; and glycine (another inhibitory neurotransmitter). MRS focuses primarily on the concentration or amount of these neurotransmitters in various brain regions. However, this is different than measuring receptor concentrations, binding, or affinity which is typically performed with PET or SPECT.

While these techniques are generally well-established, there are some important limitations when it comes to the evaluation of consciousness. Firstly, it remains unclear if functional connectivity or cerebral blood flow "at rest" truly represents the resting state of the brain and whether that is reflective of a person's state of consciousness. Some researchers have suggested, based on fMRI data, that the most likely model of consciousness involves dynamic changes in core networks that are fundamental to the underlying nature of consciousness, particularly as it shifts from state to state [22]. **Figure 1** shows a representation of fMRI-detectable ratio shifts of oxygenated to deoxygenated hemoglobin among different states of consciousness [23]. Morphometric studies do not have the problem of needing to define the resting state but do have the issue of clearly delineating brain structures, motion artifact, and appropriate segmentation of brain structures. An additional limitation to the use of neuroimaging is that structural brain imaging (e.g., MRI) is less likely to capture the dynamic changes in the brain during different states of consciousness [24].

A related approach implements fMRI to evaluate certain states or tasks that might be different in different states of consciousness. For example, people can be evaluated while performing an emotional task or cognitive task to observe differences between the two states. Such an approach would demonstrate whether specific states of consciousness or awareness might affect certain functional processes in the brain.

A further premise of the field studying consciousness is that aspects of consciousness are associated with specific brain functions. In other words, if one feels an emotion, it is related to activity in the limbic system. However, it is also possible that mental processes and consciousness itself are fully dynamic, and thus not related to a specific state of brain activity, but rather the shifts in such activity. In this way, it is the increase itself that is associated with an emotion rather than the state of being increased. Future studies will need to explore how dynamic brain processes are associated with consciousness. fMRI is likely to be the most useful technique for evaluating such a hypothesis.

PET and SPECT imaging are nuclear medicine techniques that can also be used to evaluate states of consciousness. The most common approach is to perform scans with the injection of a radioactive tracer that measures either cerebral glucose metabolism in PET or cerebral blood flow in SPECT [25, 26]. As with MRI, there is a similar problem in PET/SPECT imaging in clearly establishing the subjective resting state. These two nuclear medicine

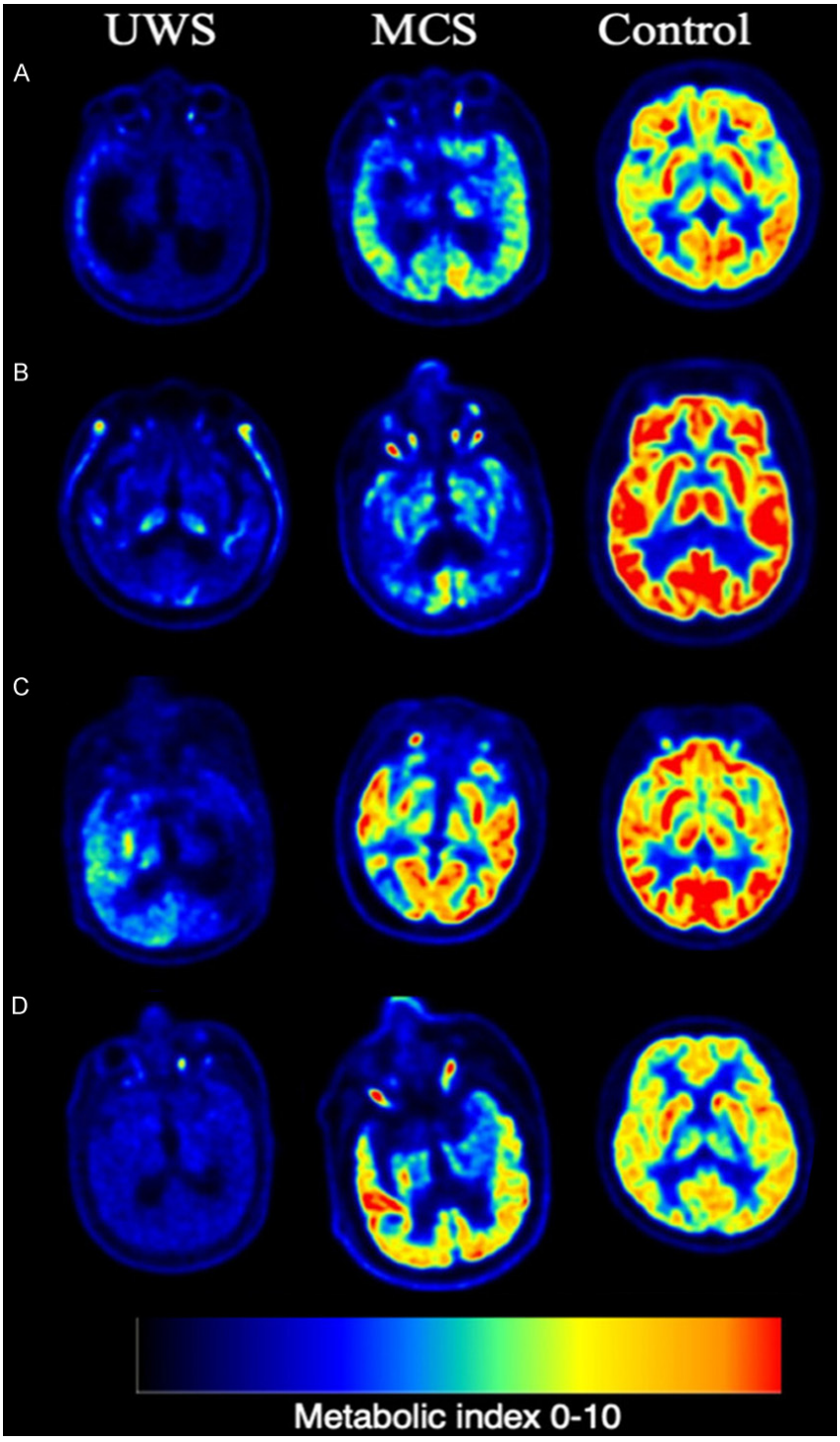


**Figure 2.** Representative examples of FDG PET images in unresponsive wakefulness syndrome (UWS), minimally conscious state (MCS), and controls. A. Cerebral trauma. B. Ischemic hypoxic encephalopathy. C. Cerebral hemorrhage. D. Brain stem hemorrhage. Reproduced with permission from Liu et al. [28]. Each panel illustrates the distinct metabolic profiles associated with different etiologies. A. The figure (cerebral trauma) shows focal hypometabolism corresponding to contusion sites with preserved metabolism in non-injured regions, correlating with potential for recovery of specific functions. B. The figure (ischemic hypoxic encephalopathy) demonstrates diffuse cortical hypometabolism often sparing the brainstem, associated with poor prognosis when global metabolism falls below 42% of normal values. C. The figure (cerebral hemorrhage) reveals peri-hematomal metabolic depression with variable recovery potential depending on the extent of secondary injury. D. The figure (brain stem hemorrhage) shows relatively preserved cortical metabolism despite impaired arousal, suggesting intact cortical processing capacity that may be masked by disrupted ascending activation.

techniques are nevertheless well-established in their ability to quantify physiological measures. While the primary downside of PET and SPECT imaging is the administration of a radioactive material, these diagnostic scans are generally regarded as safe and can also be used as part of functional studies to assess specific states of consciousness that might not be amenable to being induced in the MRI scanning environment [25, 26]. Such states might occur during various spiritual practices that involve various movements or postures that help induce altered states of consciousness.

PET has shown promising clinical application in the assessment of disorders of consciousness, particularly in distinguishing the minimal conscious state (MCS) from unresponsive wakefulness syndrome (UWS). In a study of 41 patients with UWS, 4 with locked-in syndrome, and 81 in MCS, Stender et al. achieved a high sensitivity (93%) for identification of MCS with $^{18}$F-fluorodeoxyglucose (FDG) PET, superior to fMRI methods (45%) [27]. Liu et al. achieved similar results by measuring global cerebral $^{18}$F-FDG PET uptake, achieving a sensitivity of 88% and specificity of 81% for MCS (**Figure 2**) [28].

Boly et al. analyzed pain perception via $^{15}$O-radiolabelled water PET in 5 patients in MCS, 15 controls, and 15 patients in a persistent vegetative state (VS) [29]. In patients in MCS and controls, they found that noxious stimulation activated the thalamus, primary somatosensory cortex, and the secondary somatosensory or insular, frontoparietal, and anterior cingulate cortices (referred to as the pain matrix). Cortical pain matrix activation was significantly greater in patients in MCS relative to patients in persistent VS.

Perhaps one of the more intriguing uses of PET and SPECT imaging is the evaluation of neurotransmitter changes in the brain during different states of consciousness. There are nuclear medicine tracers to evaluate virtually every neurotransmitter system, including the serotonin, dopamine, GABA, and opiate systems [30]. Furthermore, PET and SPECT tracers have been developed that can assess a variety of receptor types, including pre- and post-synaptic receptors,

transporters, and glial cell receptors [30]. Such tracers might be useful in the evaluation of various pharmacological agents that alter consciousness including anesthetics and psychedelics. These agents alter various neurotransmitters as well as consciousness itself which might be correlated phenomena.

Other techniques that have been used to study practices associated with altered states of consciousness include electroencephalography (EEG), near infrared imaging (NIR), and magnetoencephalography (MEG) [31-34]. EEG is perhaps the oldest technique for studying meditators, typically during the practice of meditation [34]. EEG renders itself useful for this purpose due to its excellent temporal resolution and simplicity of measurement, as a simple head cap is unlikely to interfere with many meditation practices [34, 35]. However, EEG becomes problematic with regards to clearly delineating the anatomy from the electrical activity that might arise [33-35].

The greater challenge with many of these neuroimaging techniques is the study of specific states while they are being experienced. Meditation practices that induce various states of consciousness, or the use of various psychedelic compounds, can sometimes be performed while laying down in a scanner, and thus can be evaluated with MRI techniques [1]. However, some states of consciousness may not be amenable to being in the scanner and may require the use of nuclear medicine techniques, EEG, or NIR.

## Studying specific aspects of consciousness

There are many conditions in which consciousness is impaired. Injuries to the brain that include traumatic injury, tumors, stroke, or inflammatory processes can all affect a person's consciousness. Neuroimaging can elucidate the areas of the brain that are affected by the injury and consequently help understand how these regions are associated with consciousness itself [36]. In a similar manner, neurodegenerative diseases, such as Alzheimer's or Parkinson's, can affect consciousness. Seizure disorders can affect consciousness, with a particularly intriguing connection between temporal lobe epilepsy and unusual spiritual experiences [37].

Psychiatric disorders such as schizophrenia also can affect consciousness in unusual ways. People with schizophrenia might hallucinate or experience delusions that are associated with altered consciousness. Further, these symptoms can have religious or spiritual elements. Perhaps one of the more intriguing psychological problems is dissociative identity disorder, previously called multiple personality disorder, in which a person appears to embody different consciousnesses at different times. Brain scans of such occurrences could be particularly important for understanding how consciousness can shift [38].

Psychedelic drug use is known to alter consciousness, and current research is focusing on the therapeutic use of psychedelic compounds for patients with depression, anxiety, and post-traumatic stress disorder. These compounds illicit unusual states of consciousness which can lead to a variety of sensory, cognitive, effective, and ego-self changes [39]. As the mechanism of action of many psychedelic drugs is not fully understood, neuroimaging may provide insight into the neuropsychiatric mechanisms by which these drugs affect consciousness. Several studies have now begun to look at the effects on brain physiology of these compounds [40, 41]. Studies have also considered comparing such psychedelic states to other altered states of consciousness such as those produced through hypnosis [42].

Perhaps one of the most widely studied approaches to altering consciousness is the study of various spiritual practices, such as meditation or prayer. Interestingly, these practices can induce altered states of consciousness in the moment of the practice but can also lead to long-term effects on the brain and on the individual [43-47]. In this way, the concept of spiritual enlightenment applies to both a state as well as a treat. There is the moment of enlightenment, and then there is the persistent change in the individual who is now considered to be enlightened. Many studies of meditation practices, both in the short term and long-term, have helped to understand how these practices affect people and affect their consciousness.

One study has reported structural and functional differences in the brain of meditators who frequently experience alterations in consciousness associated with their practice [48]. These findings offer deeper insight into the brain regions and networks associated with different meditation practices. **Figure 3** shows an extraction of such model features using fMRI-based measures of resting state activity [49]. Brain regions linked to spiritual practices include areas within the frontal and parietal lobes, limbic structures, and broader networks such as the salience network and default mode network (DMN). Other studies have demonstrated that different meditation programs can influence consciousness, cognition, emotion, and other neural processes over extended periods. Such findings are related to neurological changes that occur during the meditation practice itself [50]. For instance, multiple studies have shown that meditation practice can be associated with changes in the brain's response to different emotional and cognitive tasks [51-54]. Other studies [47-49, 55] have reported differences in brain volume, especially in the frontal lobes, as well as increased prefrontal cortical thickness, when comparing long-term meditators to non-meditators using MRI morphometry, as demonstrated in **Figure 4** [56]. This has been shown for specific types of meditation as well as meditation practices across different traditions [34]. Previously, Newberg et al. demonstrated differences in cerebral blood flow within regions such as the midbrain, thalamus, putamen,

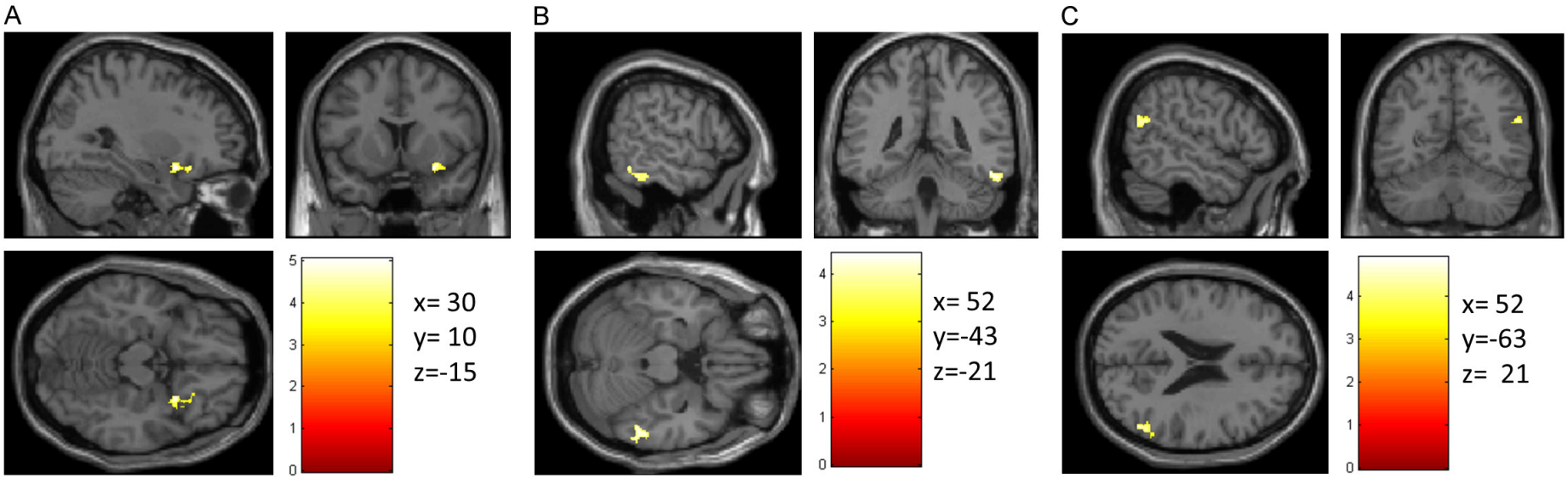


**Figure 3.** Meditators demonstrate areas of larger Gray Matter Volume (GMV) relative to non-meditators in the (A) right insula/vmOFC, (B) right inferior temporal gyrus, and (C) right angular gyrus. The color intensity represents T-statistic values at the voxel level. Reproduced with permission from Hernández et al. [49].

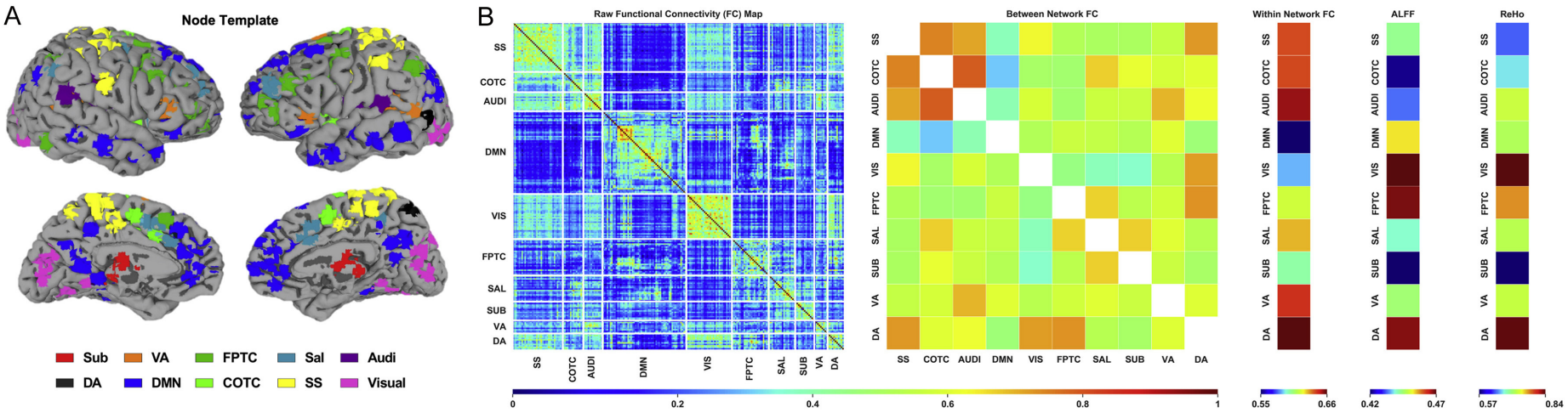


**Figure 4.** Extraction of model features using fMRI-based measures of resting state activity. A. Node template representing anatomical location of 226 seed regions of interest (ROIs) consolidated into 10 networks (Power et al., 2011): subcortical (Sub), ventral attention (VA), frontoparietal task control (FPTC), salience (Sal), auditory (Audi), dorsal attention (DA), default mode (DMN), cinguloopercular task control (COTC), sensory/somatomotor (SS), visual (Visual). B. Raw functional connectivity map (left) generated from seed-based pairwise Pearson correlations between 226 ROIs. Activity was averaged according to network template yielding measures of between network (off-diagonal) and within network (on-diagonal) functional connectivity (middle). Two additional measures of functional segregation, the amplitude of low-frequency fluctuations (ALFF) and regional homogeneity (ReHo), were calculated independently using the network templates. Reproduced with permission from Campbell et al. [56].

caudate, prefrontal cortex, and parietal cortex when comparing long-term meditators to non-meditators [57]. Most of these studies, however, have not specifically evaluated how these practices alter or affect consciousness itself.

Several studies have grouped subjects who perform different types of practices together and compared them to non-mediating controls, thereby allowing a comparison between a heterogeneous group of meditators and non-meditators. For example, Luders et al. combined approximately 50 subjects who performed a multitude of different practices such as Zen Buddhist, Kriya, Vipassana, Yoga, and Kundalini to examine the relationship between age and cerebral gray matter in long-term meditators and control subjects [58].

While this heterogeneous approach allows for larger sample sizes and broader generalizations, it is important to acknowledge that different meditation practices may engage distinct neural mechanisms. Future studies would benefit from stratifying participants by practice type or conducting within-practice analyses to better characterize the specific neural correlates of each tradition.

Neuroimaging studies of heterogeneous groups of meditators have revealed notable findings on the impact of this practice on the brain. One analysis reported increased cortical gyrification in meditators within the left precentral gyrus, right fusiform gyrus, right cuneus, and both the left and right anterior dorsal insula [59]. These increases in cortical gyrification correlated with the number of years of mediation practice. An analysis of similar mediators revealed larger gray matter volumes in meditators in the right orbito-frontal cortex, the right thalamus, left inferior temporal gyrus, and right hippocampus [46]. Hippocampal volume and cytoarchitecture have also been observed to be significantly different in long-term meditators compared to non-meditators [60].

Studies utilizing diffusion tensor imaging, an advanced MRI modality, revealed increased structural connectivity in long term meditators compared to controls throughout the entire brain and particularly between the two hemispheres [61, 62]. The largest group differences were observed within the corticospinal tract, the superior longitudinal fasciculus, and the uncinate fasciculus. These findings suggest meditation practice leads to heightened structural connectivity due to enhanced cognitive functioning during meditation.

Mindfulness meditation, rooted in ancient contemplative traditions, has garnered increasing attention in contemporary scientific and medical research for its potential to induce beneficial changes in brain function and structure. Mindfulness specifically works to obtain a heightened awareness of the present moment, and therefore consciousness, typically through practices such as focused attention on the breath, mentally scanning the body for various sensations, or loving-kindness meditation. Studies utilizing morphometric MRI have shown that long-term mindfulness practitioners exhibit increased grey matter density and volume in brain regions associated with self-awareness, introspection, and emotional regulation [63]. Notably, the hippocampus, implicated in learning and memory, has been found to show structural changes associated with mindfulness meditation [64].

Long-term mindfulness-based practice has been associated with increased cortical thickness, particularly in frontal lobes, hippocampus, and right insula [55]. It should be noted that while these cross-sectional findings are compelling, they do not establish causality. Longitudinal studies that track structural and functional brain changes from baseline through extended meditation training periods are needed to determine whether observed differences are a result of practice or reflect pre-existing traits that predispose individuals to sustained meditation engagement. Mindfulness meditation has been linked to alterations in the functional connectivity of the DMN, a network associated with self-referential thinking and mind-wandering. Long-term practitioners exhibit enhanced connectivity within the DMN, suggesting a shift towards more present-focused and less self-referential mental states [65]. An additional study observed that long-term mindfulness practitioners exhibit altered activity in the amygdala and prefrontal cortex, suggesting enhanced emotion regulation and reduced emotional reactivity [66].

The burgeoning field of contemplative neuroscience provides compelling evidence for the enduring impact of meditation on both brain structure and function. Long-term practitioners demonstrate structural changes indicative of enhanced cognitive and emotional regulation, coupled with functional alterations aligning with improved attention and self-awareness. As research in this domain continues to unfold, understanding the sustained effects of meditation offers valuable insights into the potential neuroplasticity of the human brain and the transformative power of contemplative practices on consciousness itself.

## Neuroimaging, anesthesia, and consciousness

Anesthesia provides a powerful and ethically permissible model for exploring the neural correlates of consciousness by enabling the controlled and reversible suppression of awareness [17, 67]. Unlike many pathological conditions that impair consciousness unpredictably, general anesthesia allows researchers to induce unconsciousness with high temporal precision, making it ideal for imaging-based investigation [67-71]. Neuroimaging studies have consistently demonstrated that anesthetic agents such as propofol, sevoflurane, and isoflurane disrupt functional connectivity across large-scale brain networks, particularly the DMN, fronto-parietal network, and

thalamo-cortical circuits [17, 72-74]. These disruptions are often characterized by decreased integration and increased modularity, which are hypothesized to impair information transfer and integration, both of which are considered essential for conscious awareness [17, 68, 75]. Theories such as the Global Neuronal Workspace and Integrated Information Theory draw support from such findings, as they propose that consciousness arises from the capacity of the brain to integrate information across distributed regions [70, 72].

PET imaging further complements these observations by revealing robust reductions in cerebral glucose metabolism during anesthetic-induced unconsciousness. Specifically, studies have shown decreased metabolism in key hubs of consciousness such as the thalamus, precuneus, posterior cingulate cortex, and medial prefrontal cortex [69]. These are areas which overlap significantly with the DMN and are known to be involved in self-referential thinking and wakeful awareness. Different anesthetic agents produce variable patterns of disruption, suggesting that consciousness is not tied to a single structure or neurotransmitter system but rather emerges from the dynamic interaction of multiple brain regions and neurochemical pathways [73]. For example, ketamine, a dissociative anesthetic, tends to preserve or even increase activity in some cortical regions, providing an altered but not absent form of consciousness, whereas agents like propofol produce profound reductions in cortical activity [75]. These differential effects have important implications for theories of consciousness. According to Integrated Information Theory (IIT), consciousness corresponds to integrated information (phi), which requires both differentiation and integration of neural activity [76]. Propofol, which produces widespread cortical suppression and reduced thalamo-cortical connectivity, dramatically decreases phi by disrupting both differentiation and integration [77]. Ketamine, by contrast, appears to preserve certain cortical activity patterns while inducing a dissociative state, potentially maintaining some degree of differentiated activity even as the normal integration of information is disrupted [78]. PET studies have demonstrated that propofol produces a dose-dependent global reduction in cerebral glucose metabolism of approximately 15-55%, whereas ketamine may paradoxically increase metabolism in certain frontal and limbic regions [79-82]. These contrasting metabolic signatures, when combined with fMRI connectivity analyses showing disrupted fronto-parietal integration under propofol versus preserved posterior cortical activity under ketamine, provide complementary neuroimaging perspectives on the mechanistic basis of anesthetic-induced unconsciousness.

EEG studies support these findings by showing characteristic patterns of slow-wave activity and burst suppression correlating with loss and recovery of consciousness under anesthesia [74]. MEG and transcranial magnetic stimulation (TMS)-EEG approaches have also been used to measure perturbational complexity, which tends to collapse during anesthesia and re-emerge as consciousness returns [71]. These findings suggest that anesthesia does not merely "turn off" the brain but rather alters the complexity and structure of its dynamic activity. As such, the study of anesthetic-induced unconsciousness offers a replicable and mechanistically rich framework for probing the boundaries and mechanisms of human consciousness, as well as for testing competing theoretical models.

## Study of neurotransmitters in meditation practices

Neurotransmitters are chemical messengers that play a crucial role in communication between nerve cells. The balance and function of neurotransmitter systems are integral to various cognitive processes, mood regulation, and overall mental health. Meditation practices encompass a spectrum of techniques, and understanding their impact on neurotransmitters provides insights into the neurobiological underpinnings of the observed psychological and physiological benefits.

Meditation practices have been associated with increased serotonin levels. Research suggests that meditation may enhance serotonin production and availability, contributing to improvements in mood and emotional well-being [83, 84]. In support of this view, a limited number of neuroimaging studies have demonstrated acute changes in neurotransmitters during meditation practices. One study showed that dopamine was increased during a Yoga Nidra meditation using [$^{11}$C] raclopride PET imaging [85]. Farb et al. found that mindfulness meditation training led to increased dopamine D2 receptor density in areas associated with self-awareness and attention [86]. GABA has also been found to increase following meditation. A study by Streeter et al. using MRS reported increased GABA levels in the brains of individuals after an 8-week mindfulness meditation program [87].

Glutamate undergoes modulation during meditation as well. Fayed et al. using MRS showed that there is a decrease in glutamate in the brain of long-term Zen meditators [88]. This could have important implications for understanding how meditation affects the brain suggesting an ability of the brain to downregulate its excitatory system, or at least increasing the efficiency with which the brain operates.

Finally, Newberg et al. performed a study of a spiritual retreat program that included intensive meditation practices and found significantly reduced serotonin and dopamine transporter binding after the one-week program [89]. Many participants described changes in their sense of self and self-awareness as the result of performing a week-long meditation and spiritual practice retreat. Although this does not reflect long term changes, it does indicate that such changes last beyond merely performing these practices.

## Conclusions and future directions

The discussed neuroimaging studies permit an assessment of specific states of consciousness and various methods for attaining altered states of consciousness. In addition, neuroimaging can evaluate the effects of neurological and psychiatric disorders that affect consciousness. Whether neuroimaging, and more broadly neuroscience, can ever find an answer to the hard problem of where consciousness arises in the brain, is uncertain. Nonetheless, neuroimaging will play a key role in future research endeavors into the evaluation of consciousness.

Several priorities should guide future research in this domain. First, standardization of imaging protocols across studies would enhance comparability and reproducibility, particularly for altered states induced by meditation, anesthesia, or psychedelic compounds. Establishing consensus guidelines for acquisition parameters, preprocessing pipelines, and analytical approaches would strengthen the field's methodological foundation. Second, multimodal imaging approaches combining PET, fMRI, and EEG/MEG offer complementary temporal and spatial resolution that may better capture the dynamic nature of consciousness. Simultaneous PET-MRI acquisitions, for example, could correlate moment-to-moment changes in neurotransmitter binding with functional connectivity patterns during transitions between conscious states. Third, longitudinal studies are essential to establish causal relationships between contemplative practices and observed brain changes. Current cross-sectional designs cannot distinguish whether structural differences in long-term meditators reflect neuroplastic adaptation or pre-existing traits that facilitate sustained practice. Fourth, advancing our understanding of disorders of consciousness through neuroimaging may improve prognostic accuracy and guide clinical decision-making. Developing validated biomarkers that reliably distinguish minimally conscious from unresponsive states remains a clinical priority with profound ethical implications for patient care. Finally, the expanding use of psychedelics in research and therapeutic contexts necessitates careful ethical consideration. While neuroimaging studies of psychedelic-induced states provide unique insights into consciousness, researchers must navigate regulatory frameworks, ensure appropriate participant screening and support, and consider the societal implications of this research. As these compounds move from research to clinical application, establishing ethical guidelines for their study and use becomes increasingly important.

## Disclosure of conflict of interest

None.

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