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A Neurotheological Perspective on Altered States of Consciousness

Abstract: *This article reviews the most recent information and data regarding brain processes associated with altered states of consciousness. It takes a neurotheological approach, seeking to blend what is known about these states, particularly as they relate to religious and spiritual experiences, in terms of brain processes and subjective elements of the experiences. The overall goal is to provide a comprehensive model that incorporates multiple brain areas including cortical, limbic, and subcortical structures, as well as considers the various neurotransmitters that might be involved. It is the hope that this framework provides a starting point for future investigations into the detailed neurophysiological and phenomenal aspects of altered states of consciousness.*

Keywords: consciousness; altered states; brain; neurotransmitters; spirituality; neurotheology.

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1. A Neurophysiological Model of Religious and Spiritual Experiences

Altered states of consciousness (ASCs) are associated with intense experiential components and are frequently interpreted in reference to religious and/or spiritual concepts. Such experiences frequently contain aspects of self-diminishment and increased feelings of connectedness making them self-transcendent experiences (STEs; Yaden *et al.*, 2017a), but other mental states are also included in this broad set (d'Aquili and Newberg, 1993). Our Survey of Spiritual Experiences and other research suggests that these ASCs can arise during near-death states, drug-induced experiences, neurological conditions such as seizures, and during intense spiritual practices such as meditation or prayer (Yaden *et al.*, 2016; 2017b,c). As one of its goals, the field of neurotheology strives to develop neurophysiological models of the underlying brain processes involved in these intense, altered states of consciousness (d'Aquili and Newberg, 1993; Newberg, 2018). Over the years, by combining qualitative and quantitative psychometric data regarding the phenomenological elements of such experiences along with the brain scan results of hundreds of individuals, we have begun to elucidate a neurophysiological model of these experiences. We hope that a robust neurophysiological model will eventually integrate the various elements and conditions associated with religious and spiritual experiences as well as other ASCs.

The model described below (please also see Figure 1) is an elaboration upon a previously described model based primarily upon attention focusing types of meditation. Such types of meditation can include various approaches based on bringing attention to a mantra (e.g. Transcendental Meditation or Kirtan Kriya meditation), an internally generated image (e.g. a sacred object such as the image of Buddha or a cross), or an external object (e.g. a candle). This model would not as specifically apply to meditation types based on open monitoring such as mindfulness, or attempts to clear one's mind of thought; however, we would expect there to be a number of brain regions that would interact in a similar manner even though the specifics might be distinct. The model presented here is still in its developmental stages, but now incorporates more recent neuroimaging, neurochemical, hormonal, and physiological data. The purpose of this model is to provide a theoretical foundation from which many different types of ASCs, especially those associated with spiritual and religious experiences, can be considered and compared. This model has continued to advance in complexity, incorporating a number of new brain structures and neurotransmitters. Dopamine, serotonin, acetylcholine, and several other neurotransmitters appear to be associated with the various phenomenal elements of such experiences and these are also considered in this model. In addition, more recent neuroimaging studies have explored specific networks such as the default mode network, salience network, and attentional network, as they relate to consciousness itself as well as ASCs (Beauregard and Paquette, 2006; Andrews-Hanna, 2012; Calabrò *et al.*, 2015; Cavanna *et al.*, 2017). It would be anticipated that, depending upon the specific practice, ritual, psychopharmacological substance, neurological disorder, spiritual tradition, or other circumstances, the specific mechanisms might be somewhat different. However, the goal of this preliminary model and integrative review is to help demonstrate both the common and unique pathways that might be associated with religious and spiritual experiences. It is also hoped that this model serves as an hypothesis generating tool for developing future studies of ASCs.

2. The Prefrontal and Anterior Cingulate Cortex

Most brain imaging studies suggest that wilful acts and tasks that require sustained attention are initiated via activity in the prefrontal cortex (PFC), particularly in the right hemisphere as shown in Figure 1 (Frith *et al.*, 1991; Ingvar, 1994; Pardo, Fox and Raichle, 1991; Posner and Petersen, 1990). The cingulate gyrus has also been shown to be involved in focusing attention, probably in conjunction with the PFC, and is part of the salience network in the brain (Vogt, Finch and Olson, 1992; Peters, Dunlop and Downar, 2016). Although increased PFC activity is associated with focused attention, hypofrontality (decreased frontal lobe activity) has been more associated with ASCs such as flow states as first described by Dietrich (2004) and additionally explored by other investigators (Harris, Vine and Wilson, 2017). The model presented here supports this concept and also argues for a slightly different interpretation of the hypofrontality argument.

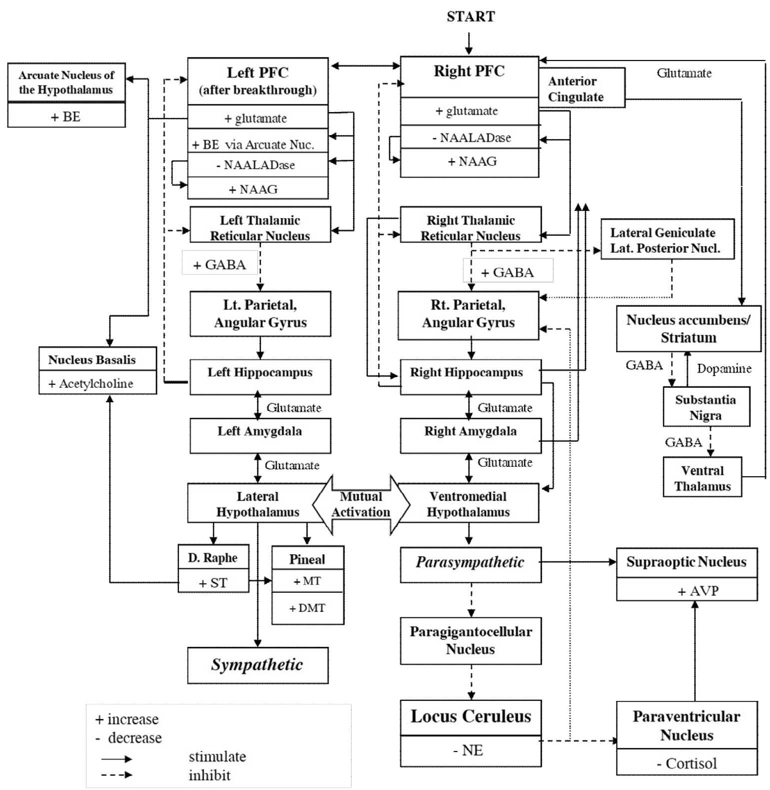

Figure 1. Schematic diagram of a neurophysiological model associated with meditation and other spiritual practices that affect various brain structures and can elicit ASCs. Please note that not all interactions and connections between the brain structures are shown, just those that are likely involved in spiritual practices and associated ASCs.

It is our contention that it is not the absolute decrease in frontal lobe activity that matters, but rather the degree (and perhaps rate) of decrease at the critical moment of the attainment of the ASC. Although this particular change has not been directly observed, several lines of evidence point to such a model for ASCs. To begin with, many meditation practices that involve intense concentration — including Transcendental Meditation, Kirtan Kriya meditation, and other mantra-based practices — are frequently associated with an initial increase in frontal lobe activity. This notion is supported by the increased activity in frontal lobe structures including the motor cortex and prefrontal cortex observed on brain imaging studies of various types of focused attention meditation in the early stages of the practice (Herzog *et al.*, 1990–91; Lou *et al.*, 1999; Lazar *et al.*, 2000; Zeidan *et al.*, 2011; 2014; Fox *et al.*, 2016). In our initial study of Tibetan Buddhist meditators, there was increased activity in the PFC bilaterally and in the cingulate gyrus during the practice in which they focused their attention on a visualized sacred object (Newberg *et al.*, 2001).

However, more recent studies by our group and others have demonstrated decreased frontal lobe activity associated with extended practices and those that result in the experience of 'surrender' in which the individual 'releases' volitional processes and simply allows the experience to happen as part of an ASC (Newberg *et al.*, 2006; 2015). This is consistent with the model developed by Dietrich (2003) regarding transient hypofrontality associated with ASCs. To people who have these intense spiritual states or ASCs, it may feel as if the experience 'comes to them'. They are not purposely making the experience happen. A study by our group showed that activity in the PFC and anterior cingulate cortex was inversely related to the depth of the meditation practice (Wang *et al.*, 2011). And several other studies by our group have shown that intense religious and spiritual experiences, particularly those linked to trance states and a sense of surrender, are associated with decreased frontal lobe activity, as mentioned above (Newberg *et al.*, 2006; 2015). Although it is not clear how the frontal lobe function may decrease, it is possible that inhibition results via connections between the hippocampus and the frontal lobes with the former having the ability to modulate frontal lobe activity (Sotres-Bayon *et al.*, 2012; Godsil *et al.*, 2013).

It is also important to note that meditation and related practices, in and of themselves, do not represent ASCs, but rather facilitate them. Given these findings, it is reasonable to consider that the initial increase in frontal lobe activity during a practice such as meditation would be associated with a greater drop (the delta) in frontal lobe activity as the individual ends up in a hypofrontal state. Thus, we would argue that the degree of the change from a state of increased frontal lobe activity to a state of decreased activity may be what precipitates the intense ASC. Then, maintaining that reduced state of frontal lobe activity results in a persistence of that experience until frontal lobe activity is restored to baseline. It should also be noted that other states such as near-death experiences or drug-induced experiences likely are associated with a drop of activity or perfusion in the frontal lobes (Lewis *et al.*, 2017; Harris, Vine and Wilson, 2017), in addition to other cortical areas.

Furthermore, as the result of such a physiological process, the brain itself may undergo a kind of 'reorganization' leading to persistent transformative effects associated with the experience. This is a common finding described by individuals who have such experiences (Newberg and Waldman, 2016). They feel that the experience provides a new insight into knowledge about the world, and subsequently changes those people's perceptions of their relationships, jobs, spirituality, and even death. In addition, brain scan studies of long-term meditators have shown distinctions in brain structure and function compared to non-meditators (Lazar *et al.*, 2005; Engen *et al.*, 2017). Furthermore, several studies of intense spiritual practices, including longitudinal ones, also reveal alterations in brain function including changes in frontal, parietal cortices (Newberg *et al.*, 2010; Shao *et al.*, 2016; Jao *et al.*, 2016), as well as changes in dopaminergic and serotonergic levels (Newberg *et al.*, 2017).

3. Changes in Thalamic Activity

Changes in thalamic activity also likely play a prominent role in ASCs. Figure 1 shows the importance of the thalamus in regulating neuronal flow in a number of sensory, cognitive, and emotional regions. This is supported by studies showing the thalamus affected by anaesthetics (Ramani and Wardhan, 2008) as well as the overall complex relationship between thalamic activity and cortical and sub-cortical processes that support consciousness (Calabrò *et al.*, 2015; Cavanna *et al.*, 2017). In the model proposed here, it may be that initial PFC activity subsequently activates the reticular nucleus of the thalamus, particularly as part of a more global attentional network (Portas *et al.*, 1998; Zikopoulos and Barbas, 2006). Such activation may be accomplished by the PFC's production and distribution of the excitatory neurotransmitter glutamate, which the PFC neurons use to innervate other brain structures (Cheramy, Romo and Glowinski, 1987). The thalamus itself governs the flow of sensory information to cortical processing areas via its interactions with the medial and lateral geniculate (Armony and LeDoux, 2000). The lateral geniculate nucleus receives raw visual data from the optic tract and routes it to the striate cortex for processing (Andrews, Halpern and Purves, 1997). The medial geniculate nucleus receives auditory data and sends it to the primary auditory cortex in the temporal lobes. Additionally, the lateral posterior nucleus of the thalamus provides the parietal lobe with the sensory information it needs to help establish a spatial representation of the body (Bucci, Conley and Gallagher, 1999).

When excited, the reticular nucleus secretes the inhibitory neurotransmitter gamma aminobutyric acid (GABA) onto the lateral posterior and geniculate nuclei (Harting, Van Lieshout and Feig, 1991; von Krosigk *et al.*, 1999; Jurgens *et al.*, 2012), cutting off input to the parietal lobe and visual centres in proportion to the reticular activation (Destexhe, Contreras and Steriade, 1998). At the outset of meditation, because of the increased activity in the PFC, there should be a concomitant increase in the activity in the reticular nucleus of the thalamus. While brain imaging studies do not have the resolution to distinguish the reticular nuclei, several studies of meditation and ASCs have demonstrated initial increases in thalamic activity during meditation practices (Newberg and Iversen, 2003; Farb, Anderson and Segal, 2012). This is consistent with, but does not confirm, the specific interaction between the PFC and reticular nuclei during meditation practices.

However, if activation of the right PFC causes increased activity in the reticular nucleus of the thalamus during meditation, the result may be overall decreased sensory input entering into the parietal lobes. In fact, it is possible that as the meditation practice continues, the GABA increase might ultimately reduce thalamic activity, which has been shown to occur in several brain imaging studies of prolonged meditation practices (Fox *et al.*, 2016). It is important to note that this represents a dynamic change in thalamic activity from increased in early stages of meditation to decreased in later stages. Several studies have demonstrated an increase in brain GABA during meditation practices (Elias, Guich and Wilson, 2000; Streeter *et al.*, 2007; Guglietti *et al.*, 2013), as well as a decrease in parietal activity (Newberg *et al.*, 2001; Fox *et al.*, 2016). This functional deafferentation (or blocking of incoming neuronal input) might eventually contribute to a loss of the spatial sense of self and altered sense of objects in consciousness (see below). These are common elements of experiences associated with ASCs, particularly those that are described as spiritual. Data from our survey indicate a profound sense of oneness or interconnectedness associated with these experiences which may be related to the decrease in parietal lobe activity.

4. Parietal Lobe Deafferentation

The influence of the parietal lobe on the sense of oneness associated with ASCs has been described above. The parietal lobe is heavily involved in the analysis and integration of higher-order visual, auditory, and somaesthetic information (Adair *et al.*, 1995). It is also involved in a complex attentional network that includes the PFC and thalamus (Fernandez-Duque and Posner, 2001). These parietal lobe functions play an important role in distinguishing between the self and the external world as part of the 'normal' state of consciousness (Blanke, 2012). It should be noted that a prior study has suggested that the superior temporal lobe may play a more important role in body spatial representation, although this has not been confirmed by other reports (Karnath, Ferber and Himmelbach, 2001). Furthermore, the parietal lobe also includes structures involved in the default mode network such as the angular gyrus and precuneus which appear to be associated with various meditation practices and also with various states of consciousness (Buckner, Andrews-Hanna and Schacter, 2008). We have previously argued, and also show in Figure 1, that deafferentation of these orienting areas of the brain is the underlying neurobiological substrate for the altered sense of self and space associated with ASCs (Newberg and Iversen, 2003).

Deafferentation of the parietal lobe is supported by findings of a more recent study of brain tumour patients undergoing surgery which found that those patients with parietal lobe lesions/surgery were more likely to report feelings of self-transcendence compared to lesions in other parts of the brain (Urgesi *et al.*, 2010). This finding is complemented by clinical observations of patients with parietal lobe damage who have difficulty orienting themselves. Deafferentation of the parietal lobe has also been supported by several imaging studies of meditation and spiritual practices demonstrating decreased activity in this region (Herzog *et al.*, 1990–91; Newberg *et al.*, 2001; 2003; 2015; Urgesi *et al.*, 2010). Finally, non-invasive brain stimulation technologies, such as transcranial magnetic stimulation (TMS), may be helpful in establishing which cortical regions are capable of enhancing or inhibiting some of meditation's effects on altered stages of consciousness (Iwry, Yaden and Newberg, 2017; Yaden and Newberg, 2014). However, more studies will be needed to determine the precise relationship between changes in each of these brain regions and the experiential elements of ASCs.

5. Hippocampal and Amygdalar Activation

Given that many of these ASCs are associated with intense emotional responses, or at least are 'labelled' as important experiences for the individual, we would expect substantial activity changes in the limbic system. Studies have shown the importance of the limbic structures such as the amygdala as part of the salience network, to be associated with experiences similar to those described during meditation (Fish *et al.*, 1993; Saver and Rabin, 1997; Newberg and Iverson, 2003).

The ability of the hippocampus to stimulate or inhibit neuronal activity in other structures probably relies upon the glutamate and GABA systems respectively (Armony and LeDoux, 2000). Deafferentation of the right parietal lobe during meditation practices may result in stimulation of the right hippocampus because of the inverse modulation of the hippocampus in relation to cortical activity. If, in addition, there is simultaneous direct stimulation of the right hippocampus via the thalamus, and mediated by glutamate, then the right hippocampus could become substantially activated. Right hippocampal activity may potentially enhance the stimulatory function of the PFC on the thalamus via the nucleus accumbens, which gates the neural input from the PFC to the thalamus via the neuromodulatory effects of dopamine (Chow and Cummings, 1999; Newman and Grace, 1999).

In addition, it seems that much of the prefrontal modulation of emotion is via the hippocampus and its connections with the amygdala (Poletti and Sujatanond, 1980; Richter-Levin and Akirav, 2000). Because of the reciprocal interaction between the amygdala and hippocampus, activation of the right hippocampus probably stimulates the right lateral amygdala as well. The results of several neuroimaging studies support the notion of increased activity in the regions of the amygdala and hippocampus during meditation and spiritual practices (Lazar *et al.*, 2000; Lutz *et al.*, 2008; Sperduti, Martinelli and Piolino, 2012).

6. Hypothalamic and Autonomic Nervous System Changes

The hypothalamus is a central structure that regulates many essential body functions including the autonomic nervous system as well as the hormonal systems. The hypothalamus also is intimately interconnected with the limbic system. As shown in Figure 1, increased activity in the right amygdala has been shown to result in activation of the ventromedial portion of the hypothalamus, with a subsequent activation of the peripheral parasympathetic system (Davis, 1992). Increased parasympathetic activity should be associated with the subjective sensation first of relaxation and, eventually, of a more profound quiescence. Activation of the parasympathetic system would also cause a reduction in heart rate and respiratory rate. All of these physiological responses have been observed during meditation and spiritual practices (Jevning, Wallace and Beidebach, 1992).

Typically, when breathing and heart rate slow down, the paragigantocellular nucleus of the medulla reduces its innervation of the locus ceruleus (LC) in the pons. The LC produces and distributes norepinephrine (or NE; Foote, 1987), a neuromodulator that increases the susceptibility of brain regions to sensory input by amplifying strong stimuli, while also gating out weaker activations that fall below the activation threshold (Waterhouse, Moises and Woodward, 1998). Decreased stimulation of the LC results in a decrease in the level of NE which has been shown during meditation practices (Infante *et al.*, 2001; Walton *et al.*, 1995). This reduction in NE would likely decrease the impact of sensory input on the parietal lobe, potentially contributing to its deafferentation. In addition, reduced NE could facilitate the ASC by reducing overall neuronal activity between brain structures.

The locus ceruleus would also deliver less NE to the hypothalamic paraventricular nucleus which normally secretes corticotropin-releasing hormone (CRH) in response to innervation by NE from the locus ceruleus (Ziegler, Cass and Herman Ziegler, 1999). Decreasing NE from the locus ceruleus during spiritual practices would be expected to decrease the production of CRH by the paraventricular nucleus, and ultimately decrease cortisol levels, a finding consistent with studies of meditation on cortisol (Walton *et al.*, 1995; Ray *et al.*, 2014). In addition, a recent study of an intense dance ritual associated with ASCs reveals significant and complex changes in cortisol depending on the type of practice and state of consciousness experienced (Lee *et al.*, 2016). Thus, further studies will be necessary to assess the relationship between various ASCs and these changes in hypothalamic response.

7. PFC Effects on Other Neurochemical Systems

As a meditation practice continues, increasing activity in the PFC could be due to the persistent focus of attention that is often required. In general, as PFC activity increases, it produces ever-increasing levels of free synaptic glutamate in the brain. This markedly increased glutamate could potentially stimulate the hypothalamic arcuate nucleus to release beta-endorphin (Kiss *et al.*, 1997). Beta-endorphin (BE) is an opioid produced primarily by the arcuate nucleus of the medial hypothalamus and distributed to the brain's subcortical areas (Yadid *et al.*, 2000). BE is known to depress respiration, reduce fear, reduce pain, and produce sensations of joy and euphoria (Janal *et al.*, 1984). That such effects have been described during ASCs may implicate some degree of BE release related to the PFC activity. However, it is also probable that BE is not solely responsible for meditative experiences, because simply taking morphine-related substances does not produce an ASC. Furthermore, one very limited study demonstrated that blocking the opiate receptors with naloxone did not affect the experience or EEG associated with meditation (Sim and Tsoi, 1992).

Glutamate activates N-methyl d-Aspartate receptors (NMDAr), but excess glutamate can kill these neurons through excitotoxic processes (Albin and Greenamyre, 1992). We have previously proposed that if glutamate levels approach excitotoxic concentrations during intense states of meditation, the brain might limit its production of N-acetylated-alpha-linked-acidic dipeptidase, which converts the endogenous NMDAr antagonist N-acetylaspartylglutamate (NAAG) into glutamate (Thomas *et al.*, 2000). Since the NMDAr inhibitor NAAG is functionally analogous to the disassociative hallucinogens ketamine, phencyclidine, and nitrous oxide (Jevtovic-Todorovic *et al.*, 2001), it might help in eliciting a variety of ASCs such as out-of-body and near-death experiences (Vollenweider *et al.*, 1997).

8. Autonomic-Cortical Activity

Based upon several lines of evidence, ASCs, especially those associated with spiritual experiences, may be associated with activation of both arms of the autonomic nervous system (ANS) (Gellhorn and Kiely, 1972; Newberg and Iversen, 2003). For example, several studies have demonstrated predominant parasympathetic activity during meditation practices associated with decreased heart rate and blood pressure (Sudsuang, Chentanez and Veluvan, 1991; Jevning, Wallace and Beidebach, 1992; Travis, 2001). However, several studies of different meditative techniques have suggested that there is a mutual activation (see Figure 1) of the parasympathetic and sympathetic systems by demonstrating an increase in heart rate variability during such practices (Peng *et al.*, 1999; 2004). The increased variation in heart rate was hypothesized to reflect activation of both arms of the ANS. Also, the notion of mutual activation of both arms of the ANS is consistent with data revealing a complex set of interactions within the ANS including mutual activations (Hugdahl, 1996). This notion also fits the characteristic description of meditative states in which there is a sense of overwhelming calmness as well as significant alertness.

One other area of the brain that might be particularly related to the intense emotional experiences associated with ASCs would be the insula. The insula, which is part of the salience network and rests between the limbic system and cortex, appears to be involved a number of meditative practices (Fox *et al.*, 2016). It may be that the intense activity in the insula helps to not only permit the individual to feel strong emotions but actually increases the intensity of the entire experience.

9. Serotonergic and Dopaminergic Activity

Activation of the ANS can result in intense stimulation of structures in the lateral hypothalamus and median forebrain bundle, which are known to produce both ecstatic and blissful feelings when directly stimulated (Olds and Forbes, 1981). Stimulation of the lateral hypothalamus can also result in changes in serotonergic activity. In fact, several studies have shown that there is increased serotonin during meditation and spiritual practices (Walton *et al.*, 1995; Yu *et al.*, 2011). Serotonin (ST) is a neuromodulator that densely supplies the visual centres of the temporal lobe, where it strongly influences the flow of visual associations generated by this area (Foote, 1987). The cells of the dorsal raphe produce and distribute ST when innervated by the lateral hypothalamus (Aghajanian, Sprouse and Rasmussen, 1987) and also when activated by the prefrontal cortex (Juckel, Mendlin and Jacobs, 1999).

When cortical ST receptors (especially in the temporal lobes) are activated, the stimulation can result in an hallucinogenic effect. Tryptamine psychedelics such as psylocybin and LSD take advantage of this mechanism to produce ASCs and intense mystical or religious experiences (Aghajanian and Marek, 1999; Griffiths *et al.*, 2006). The mechanism by which this appears to occur is that ST inhibits the lateral geniculate nucleus, greatly reducing the amount of visual information that can pass through (Funke and Eysel, 1995; Yoshida, Sasa and Takaori, 1984). If combined with reticular nucleus inhibition of the lateral geniculate, ST may increase the fluidity of temporal visual associations in the absence of sensory input, possibly resulting in the internally generated imagery that has been described during certain altered states.

Increased ST levels can affect several other neurochemical systems. An increase in ST has a modulatory effect on dopamine, suggesting a link between the serotonergic and dopaminergic system, which may enhance feelings of euphoria (Vollenweider *et al.*, 1999). ST, in conjunction with increased glutamate, has been shown to stimulate the nucleus basalis to release acetylcholine, which has important effects throughout the cortex (Manfridi, Brambilla and Mancia, 1999; Zhelyazkova-Savova, Giovannini and Pepeu, 1997). Increased acetylcholine in the frontal lobes has been shown to augment the attentional system, and in the parietal lobes to enhance orienting without altering sensory input (Fernandez-Duque and Posner, 2001). While no studies have evaluated the specific role of acetylcholine in meditation, it appears that this neurotransmitter may enhance the attentional component as well as the orienting response in the face of progressive deafferentation of sensory input into the parietal lobes, possibly resulting in intense experiences of oneness.

Increased ST combined with lateral hypothalamic innervation of the pineal gland may lead the latter to increase production of several neurotransmitters. Under circumstances of heightened activation, pineal enzymes can also endogenously synthesize the powerful hallucinogen 5-methoxy-dimethyltryptamine (DMT) (Monti and Christian, 1981). Several studies have linked DMT to a variety of ASCs, including out-of-body experiences, distortion of time and space, and interaction with supernatural entities (Strassman and Clifford, 1994; Strassman *et al.*, 1996; Gallimore and Strassman, 2016). Hyperstimulation of the pineal at this step, then, could also lead to DMT production, which can be associated with the wide variety of mystical-type experiences that occur under that hallucinogen.

In addition to serotonergic involvement, it is likely that dopamine also plays a role in spiritual practices that result in ASCs. For example, it should also be noted that the dopaminergic system, via the basal ganglia, is believed to participate in regulating the glutamatergic system and the interactions between the prefrontal cortex and subcortical structures. Several studies point to the involvement of dopamine in these practices. For example, a PET study utilizing 11C-Raclopride to measure the dopaminergic tone during Yoga Nidra meditation demonstrated significantly increased dopamine levels during the practice (Kjaer *et al.*, 2002). The authors hypothesized that this increase may be associated with the gating of cortical–subcortical interactions that leads to an overall decrease in readiness for action associated with this particular type of meditation.

Our group recently published data of the effects of a one-week intensive spiritual retreat on dopamine activity (Newberg *et al.*, 2017). In this study, participants were initially scanned using ioflupane single photon emission computed tomography (called DaTscan) which observes changes in dopamine transporter (DAT) binding. They then underwent a one-week spiritual retreat based on the spiritual exercises of St. Ignatius (the founder of the Jesuit Church). The retreat is performed primarily in silence and incorporates intensive prayer, meditation, and personal reflection. Shortly after completing the retreat, participants were scanned again. The results demonstrated significantly reduced DAT binding. Since the DAT removes excess dopamine from the synapse after neuronal transmission, the decreased amount of DAT binding implies that the neurons would be more sensitive to dopamine release in the synapse. A higher response to dopamine would potentially result in a more intense euphoric spiritual experience. Thus, the results of our retreat study support the notion that spiritual practices affect the dopaminergic system in such a way as to predispose individuals to having ASCs.

10. Final Pathways for ASCs

With the above described brain regions and processes, we can try to elucidate the final pathway related to ASCs. Given that consciousness is associated with a complex set of brain processes that involve frontal lobe executive functions, thalamic mediation of various cortical and subcortical pathways, limbic and salience networks, sensory perception, and memory and cognition, it seems likely that many brain structures are affected in ASCs. Whether these structures change which subsequently results in the ASC or whether the ASC causes the brain changes is not yet clear. More detailed studies evaluating the timing of the altered states and their associated brain processes will be necessary to better determine the causal arrow between brain functions and consciousness.

Meditation and other spiritual practices frequently have the goal of eliciting ASCs and it might even be possible to develop a taxonomy of such practices based upon the goals of those studies (Nash and Newberg, 2013). With that in mind, it would seem that the initiation point might be frontal lobe modulation of the thalamus, sensory processing areas, and parietal lobe functions. Although studies of meditation practices typically show increased frontal lobe activity, it is likely that a rapid decrease in frontal lobe function occurs at the time of ASCs. The magnitude of the decrease and the resulting hypofrontality would affect many other structures and brain processes. It appears that there may be concomitant decreases in thalamic, parietal, and temporal lobe functions which, again, have been observed in a number of states of altered consciousness including those under meditation or various psychedelic substances (Fox *et al.*, 2016; Lewis *et al.*, 2017). The neurotransmitter changes appear to affect sensory perceptions, cognitions, and even the perceived level of consciousness itself. However, it is also important to state that the relationship between ASCs associated with meditation practices and psychedelic experiences might be different, and certainly do not inherently reflect the societal or spiritual importance of many meditation practices.

Since such experiences are also associated with intense limbic activity and autonomic activity, they are perceived as intensely real (Yaden *et al.*, 2017b), as maintaining a strong sense of clarity, and a profound sense of unity or connectedness (Yaden *et al.*, 2017a). The decreased frontal lobe function also enables such experiences to be perceived as flowing through the person or even surrendering to some source outside the person (e.g. God if it is a religious experience). The end result of these mental states can, in some cases, amount to a transformative experience that changes many brain processes and ultimately many fundamental traits of the person.

11. Conclusion

The neurophysiology of religious and spiritual experiences is continuing to make progress. More sophisticated neuroimaging technology and increased research attention has allowed the field of neurotheology to make substantial advances since its inception. However, the field remains in the early stages of its development. Many existing studies require replication and newer studies should make use of more robust psychometric tools and larger sample sizes. The neurotheological study of religious and spiritual experiences remains an important field of study.

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