The Default Mode Network, the Task-Positive Network, and Serotonergic Hallucinogens: A Brief Review of Recent Findings

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In recent years, the widespread utilization of neuroimaging studies of the human brain has generated a significant body of evidence to distinguish between two primary modes of human brain activity: the brain "at rest," and the brain when focused on a task. The former has been termed the *default mode network (*DMN), and can be defined as the network of brain regions that are active when the individual is not focused on the outside world and the brain is at wakeful rest. The DMN is associated with daydreaming, envisioning the future, retrieving memories, making moral judgments, and gauging other's perspectives (Buckner, Andrews-Hanna, & Schacter, 2008; Carhart-Harris & Friston, 2010; Carhart-Harris, et al., 2013). The latter mode has been termed the *task-positive network* (TPN): a sensory orienting system activated when an individual is focused on a task, engaging in "top-down" operations (Carhart-Harris & Friston, 2010). When an individual's brain activity is monitored using functional magnetic resonance imaging (fMRI), researchers observe two distinguishable patterns of neuroanatomical activation when subjects were in the scanner: (1) when subjects were tasked with a specific goal-directed external activity (TPN activity), versus (2) when the individual was allowed to rest between tasks (DMN activity) (Buckner, Andrews-Hanna, & Schacter, 2008). Broadly, evidence suggests that DMN supports introspection, whereas the TPN supports externally focused attention.

During normal waking consciousness in healthy normal volunteers, neuroimaging research suggests that the DMN and TPN are competitive, that is, activity in one mode is associated with decreased activity in the other; the DMN and TPN are conceived as orthogonal (Carhart-Harris, et al., 2013). However, recent neuroimaging studies suggest that both modes

may be concurrently activated, a phenomenon observed in three different forms of consciousness: (1) psychosis (Shim, Oh, Jung, 2010); (2) meditative states (Brewer et al., 2011); and (3) psychedelic states of consciousness in individuals administered serotonergic hallucinogens (Carhart-Harris, et al., 2013).

This nascent body of research raises pointed questions about the phenomenological similarities among states of consciousness occasioned by psychosis, meditation, and classic hallucinogens. The advent of sophisticated neuroimaging methods offers a new inquiry tool to establish the neurobiological substrates of the psychodynamic constructs, such as Freud's articulation of the primary and secondary processes, and the mind's processing of conscious and unconscious material (Carhart-Harris, 2007; Carhart-Harris, & Friston, 2010). Finally, it suggests a preliminary neurocorrelative explanation for the experience of mystical states of consciousness, which have been shown to be occasioned by the administration of psilocybin, a serotonergic hallucinogen, resulting in positive lasting and meaningful effects on personality (MacLean, Johnson, & Griffiths, 2011; Griffiths, Richards, McCann, & Jesse, 2006; Griffiths, Richards, Johnson, McCann, & Jesse, 2008; Grob et al., 2011).

The Default Mode Network and the Task Positive Network

The DMN has been described as the "most active brain system when individuals are left to think for themselves undisturbed," perhaps not a common condition in an increasingly multi-tasking world (Buckner, Andrews-Hanna, & Schacter, 2008, p. 30). In their review of fMRI and positron emission tomography (PET) findings, Buckner, Andrews-Hanna, and Schacter (2008) concluded that the default mode network is an anatomically defined system in the brain which is active when subjects are not tasked with focusing on the external environment. They suggest that DMN activation is associated with daydreams, reveries, the retrieval of episodic memory,

envisioning the future, and theory of mind processes, such as conceiving the perspectives of others (Buckner, Andrews-Hanna, and Schacter, 2008). These rest-state spontaneous cognitions hearken back to William James' conception of the stream of consciousness (1890).

Buckner and colleagues (2008) review the body of neuroimaging evidence, which suggests that the medial temporal lobe subsystem, the medial prefrontal cortex subsystem, and the posterior cingulate cortex (the point of convergence of these two subsystems) are involved in DMN rest-state activities. These two subsystems converge on important nodes of integration including the posterior cingulate cortex. Buckner and colleagues (2008) outline the core brain regions with Brodmann's areas associated with the DMN as follows: ventral medial prefrontal cortex (24, 10 m/10 r/10 p, 32ac); posterior cingulate/retosplenial cortex (29/30, 23/31); inferior parietal lobule (39, 40) lateral temporal cortex (21); dorsal medial prefrontal cortex (24, 32ac, 10p, 9); and hippocampal formation (hippocampus proper, entorhinal cortex, parahippocampal cortex). To summarize, the medial temporal lobe subsystem and hippocampus are involved in the provision of autobiographical memories. The medial prefrontal subsystem helps to integrate these episodic data during the construction of "self-relevant mental simulations" (Buckner, Andrews-Hanna, and Schacter, 2008, p. 1).

In recent years, a greater proportion of functional connectivity magnetic resonance imaging (fcMRI) studies have assessed brain activity in subjects in a "resting-state," or when they "rest quietly in the scanner" (Greicius, Supekar, Menon, & Dougherty, 2009). A review of fcMRI studies of the resting state found that resting-state functional connectivity reflects structural connectivity in bilateral hippocampus clusters, and that while it is deactivated by most cognitive tasks, the introduction of episodic memory tasks activates these structures (Greicius, Supekar, Menon, & Dougherty, 2009). This is noteworthy, as the neural maps overlap

considerably with those associated with Alzheimer's disease, "the quintessential disorder of episodic memory" (Greicius et al. 2004; Buckner et al. 2005).

In their influential review, Fox and colleagues (2005) marshal the growing body of neuroimaging evidence to articulate the case that the human brain is "intrinsically organized into dynamic, anticorrelated functional networks" (p. 9673). They argue that activity in the TPN is associated with decreased activity in the DMN. Specifically, when subjects are given an attention-demanding cognitive task, activity in the frontal and parietal cortical regions are activated, including the dorsal-lateral and ventral prefrontal regions, insula, and supplementary motor area (Fox et al., 2005). The TPN comprises regions previously termed the "endogenous" or "dorsal attention system" active during directed attention (Fox et al., 2005). Activity in these areas is conceived as "*top-down* modulation of attention and working memory" (p. 9673, emphasis added), however, even during task administration, decreases in TPN activity are associated with the occurrence of emotion, episodic memory, or thoughts unrelated to the assigned task, all processes associated with the DMN, or what the authors term the task-negative network (Fox et al., 2005). There are conceptual implications for the naturally occurring modes of the human brain. The authors encourage "shifting one's perspective of brain function from the view of a system simply responding to changing contingencies to one *operating on its own*, intrinsically, with sensory information *modulating* rather than *determining* the operation of the system" (Fox et al., 2005, p. 9677, emphases added).

Neural Correlates of Psychedelic States of Consciousness

In the last ten years, there has been a renaissance of research studies evaluating the safety and efficacy of classical hallucinogens, such as psilocybin, a naturally occurring compound found in a specific type of mushroom that has been used in mystical or spiritual states of

consciousness in religious and healing practices for centuries (Griffiths, Richards, McCann, & Jesse, 2006; Grob et al., 2011). Psilocybin is active at multiple serotonin (5-HT) receptor sites, especially at the 5-HT2A receptor sites (Kometer, Schmidt, Jäncke, and Vollenweider, 2013). In a series of double-blind placebo controlled trials, the administration of this serotonergic hallucinogen has been associated with significant and lasting decreases in anxiety and improvements among cancer patients (Grob et al., 2011); significant lasting changes in personality through increases in the domain of Openness (to new experience) (MacLean, Johnson, & Griffiths, 2011); and profound spiritual and mystical experiences (Griffiths, Richards, McCann, & Jesse, 2006; Griffiths, Richards, Johnson, McCann, & Jesse, 2008). In one study, Griffiths and colleagues (2006) reported that at 67% of the subjects rated the psilocybin experiences to be either the single most meaningful experience or among the top five most meaningful experiences of his or her life---an experience described as on par with the birth of a child or death of a parent. While a comprehensive review of these findings is beyond the scope of this paper, they raise a host of questions concerning the neurocorrelative underpinnings of such profoundly meaningful and spiritual experiences, how such experiences ameliorate dysphoric clinical symptoms, and how they may foster personality changes that last for years after only a single, discrete administration of a substance.

Dr. Carhart-Harris, at Imperial College, London, and colleagues have developed a cogent explanation of the neural correlates of the psychedelic state, drawing primarily from fMRI studies with psilocybin. In a recent study, Carhart-Harris and colleagues (2012a) administered psilocybin to fifteen healthy volunteers and fifteen controls in a task-free fMRI setting, in order to assess transitions from "normal waking consciousness to the psychedelic state of consciousness" (p. 2138). They found decreased activity in the posterior cingulate cortex and

medial prefrontal cortex. This decreased activity was correlated with the intensity of the phenomenological effects reported by participants. These brain structures are associated with the DMN and receive more blood flow and consume more energy as compared to other areas of the brain; as such, these areas constitute an important "connector hub" in the brain (Carhart-Harris, et al., 2012a, p. 2142; Carhart-Harris, et al., 2013). Interestingly, these areas have been associated with constructs such as the "self" or the "ego" (Carhart-Harris, et al., 2012a, p. 2142). The authors suggest that their findings are consistent with the model of the human brain as a "reducing valve," (Huxley, 1954) in which the purpose of the mind/brain is to filter down "unimportant" internal and external stimulus. Deactivation in these regions suggests that the administration of psilocybin promotes an "unconstrained style of cognition" which may allow the human mind to "experience a thing fully" (Carhart-Harris, et al., 2012a, p. 2142; Huxley, 1954).

In a similar fMRI study, Carhart-Harris and colleagues (2012b) administered psilocybin to ten healthy participants. Findings suggest that psilocybin improves autobiographical recollection and may enhance emotional insight by lowering psychological defenses. The authors conclude that psilocybin may be useful as an adjunct to psychosocial interventions such as therapy. In a previous literature review, Carhart-Harris (2007) assembled evidence to suggest that the dream state, the dreamy state of temporal lobe epilepsy and temporal lobe stimulation, the acute psychotic state, and the psychedelic state involve common neural structures, and that phenomenological, subjective reports suggest that these four states all involve the emergence of unconscious material into consciousness. Carhart-Harris argues that "bursts of electrical activity spreading from the medial temporal lobes to the association cortices are…experienced on a subjective level as the emergence of unconscious material into consciousness" (p. 183). Such a

fanciful hypothesis linking psychodynamic theories and neurocorrelative fMRI findings might be dismissed as ambitious, at best, however, subsequent research findings continues to add evidence for the proposed argument.

In a functional connectivity study utilizing fMRI with fifteen volunteers, Carhart-Harris and colleagues (2013) measured the effects of psilocybin on thalamocortical functional connectivity with a resting-state protocol. After outlining that spontaneous activity in the DMN is independent of spontaneous activity in the TPN, the authors found increased DMN-TPN functional connectivity and so decreased DMN-TPN orthogonality after psilocybin administration. This pattern is similar to the effects found in psychosis and meditative states, which share some subjective similarities with states of consciousness induced by psilocybin (Carhart-Harris, et al., 2013). Carhart-Harris has suggested that under psilocybin, the DMN is effectively "shut down," therefore allowing for the subjective experience of dissolving ego boundaries; he suggests that diminished activity in the posterior cingulate cortex (critical in the DMN) is a correlate of ego disintegration experience frequently reported in the phenomenological literature regarding psychedelic states of consciousness (Carhart-Harris, 2013).

This brief review outlines how the research convergence of neuroimaging studies and psilocybin studies has afforded a glimpse into previously unchartered territories of the human experience. As William James wrote in 1902 in *The Varieties of Religious Experience*:

> But just as our primary wide-awake consciousness throws open our senses to the touch of this material, so it is logically conceivable that if there be higher spiritual agencies that can directly touch us, the psychological condition of their doing so might be *our possession of a subconscious region* which alone should yield access

> to them. The hubbub of the waking life might close a door which in the dreamy Subliminal might remain ajar or open" (James, 1902/1999, p. 266-267, emphasis added).

The recent convergent findings from the neuroimaging studies and psychedelic research suggest a hypothetical model to elucidate the neurobiological substrates of mental phenomena experienced outside of everyday waking consciousness. These phenomena are, by definition, not easily amenable to assessment, and include meditative states, reverie, daydreaming, spiritual insight, ego-dissolution, psychosis, and mystical-type experiences. Both domains of inquiry are at a germinal point of development, and further research is warranted to address lacunae in the existing literature base and to chart the predicted “subconscious region” which may yield access to them.

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