



## Review

## The role of the extrapersonal brain systems in religious activity

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**Abstract**

The neuropsychology of religious activity in normal and selected clinical populations is reviewed. Religious activity includes beliefs, experiences, and practice. Neuropsychological and functional imaging findings, many of which have derived from studies of experienced meditators, point to a ventral cortical axis for religious behavior, involving primarily the ventromedial temporal and frontal regions. Neuropharmacological studies generally point to dopaminergic activation as the leading neurochemical feature associated with religious activity. The ventral dopaminergic pathways involved in religious behavior most closely align with the action-extrapersonal system in the model of 3-D perceptual-motor interactions proposed by Previc (1998). These pathways are biased toward distant (especially upper) space and also mediate related extrapersonally dominated brain functions such as dreaming and hallucinations. Hyperreligiosity is a major feature of mania, obsessive-compulsive disorder, schizophrenia, temporal-lobe epilepsy and related disorders, in which the ventromedial dopaminergic systems are highly activated and exaggerated attentional or goal-directed behavior toward extrapersonal space occurs. The evolution of religion is linked to an expansion of dopaminergic systems in humans, brought about by changes in diet and other physiological influences.

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**1. Introduction**

Religion is one of five major behavioral phenomena that evolved with modern humans and are found in all human cultures—the others being language, advanced tool-making, music, and art. Indeed, humans have been termed *homo religio* because of the near-universal belief in God (Saver & Rabin, 1997). On the basis of twin studies, there is reason to believe that religious experience and behavior have a biological basis, in that religiosity appears to be influenced by inheritance to about the same degree as intelligence (D'Onofrio, Eaves, Murrelle, Maes, & Spilka, 1999; Eaves, Martin, & Heath, 1990; Waller, Kojetin, Bouchard, Lykken, & Tellegen, 1990). Although much research has been conducted as to the neural substrate of religion—particularly in clinical populations—there has heretofore been no general theory as to why religious activity is dependent on particular brain systems that only recently evolved.

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The theory proposed here posits that religious experience and practice in humans are a consequence of the expansion of the dopamine-rich ventral brain systems that, in other mammalian species, mediate behavioral interactions with the most distant portions of the surrounding 3-D space. Specifically, it is argued that religion represents the extension of distant extrapersonal space and time into abstract and cosmic realms—e.g., heaven and eternity—even as it relies on mammalian brain pathways that ordinarily oversee whole-body, head- and oculomotor orienting and exploration in the distal portions of actual 3-D space.

After briefly discussing the key components of religion, I will review the neuroanatomy, neurochemistry, and other features of the extrapersonal brain systems. The role of these systems in dreams and hallucinations will be reviewed, and parallels between these phenomena and religious experiences will be made. The neuroanatomy and neurochemistry of religious experience and practice will then be reviewed, with an emphasis on the role of the ventromedial dopaminergic systems in four major clinical disorders associated with hyperreligiosity—mania, obsessive-compulsive disorder (OCD), schizophrenia, and temporal-lobe epilepsy (TLE). Finally, the evolutionary origins of religious activity in humans will be discussed in the context of neurochemical changes that emerged as part of a general physiological adaptation of humans and led to the final advances in human intelligence ~50,000–100,000 years ago.

## 2. Basic structure of religion in humans

As one of the few major cultural universals, there has been a considerable amount of theoretical speculation concerning the brain and religion, dating back to [James \(1902\)](#). However, empirical research into the neuropsychology of religion may not be considered especially voluminous relative to the importance of religion to individuals and society ([Goldwert, 1993](#)). One problem with trying to explain religion from a neuropsychological perspective is that that it is practiced very differently around the world. Some religions are based more on cosmological and existential themes (e.g., celestially based Gods; vivid descriptions of the afterlife), whereas others may be based more on ancestor or spirit worship ([Boyer, 2001](#)). All religions, however, invoke the concept of the “*supernatural*,” whether that involves a realm beyond death or one that is invisible to humans ([Atran & Norenzayan, 2004](#)).

Religious activity consists of three major components: beliefs, practices, and experiences.<sup>1</sup> Only religious practice can be directly observed behaviorally, although behavioral paradigms and observational techniques can be used to infer the existence of certain beliefs and practices, as will be described in later sections. While there are many differences in the three major forms of religious behavior, they are highly interrelated in that persons in societies having strong religious beliefs are more likely to interpret anomalous experiences (e.g., delusions) as religious in nature ([Klaf & Hamilton, 1961](#); [Ndeti & Vadher, 1985](#); [Verdoux et al., 1998](#)). Similarly, profound experiences may lead to religious conversions and changes in beliefs and practices ([Dewhurst & Beard, 1970](#)). Because, however, religious experiences are common to far fewer self-proclaimed religious persons than are beliefs and practices, one may presume that other aspects of religion (cultural traditions, communal relationships, extrinsic gain, etc.) sustain religious belief and/or practice among those lacking direct religious experiences (see [Batson & Ventis, 1982](#)).

Although religious beliefs vary widely across the world (see [Boyer, 2001](#)), the most prevalent beliefs involve “God” and the “afterlife.” In North American surveys, 95% of all persons stated a belief in God, 71% a belief in the afterlife, but only 53% in the existence of Hell ([Kroll & Sheehan, 1989](#)). Religious beliefs and delusions—as well as changes thereof, as in religious conversions—have been extensively studied in clinical disorders such as TLE and schizophrenia, but they have been the subject of much less neuropsychological investigation in normal populations. Religious and paranormal beliefs in normals have been occasionally studied in connection with “soft” neurological signs and tendencies, and there have been suggestions of a relationship between religiosity and certain personality traits (e.g., schizotypy, magical ideation, and obsessiveness) that may have an underlying fronto-temporal source. However, with the exception of obsessiveness, schizotypy and possibly open-mindedness (see [Batson & Ventis, 1982](#)), most personality traits show little or no overall correlation with religion. Moreover, religiosity in the general population is negatively associated with

<sup>1</sup> This categorization is similar to the “feelings, acts, and experiences” of [James \(1902, p. 42\)](#).

psychoticism, depression and other mental illness (Batson & Ventis, 1982, Chapter 7; Francis & Wilcox, 1996; Maltby, 1997; Roman & Lester, 1999), so that religion in the vast majority of individuals must be considered an outcome of normal brain tendencies. Finally, although the relationship between religious phenomena and distant space (and time) will be a major focus of this paper, little formal research currently exists as to the spatial and temporal aspects of religious beliefs.

Religious practice is carried out on two major levels: the personal and public. Personal religious practice consists of prayer, meditation and, in extreme cases, religious compulsions. There have been several studies of the neuroanatomical and neurochemical substrates of meditation, but only one study has examined the brain changes associated with simple prayer (Azari et al., 2001). The leading public form of religious practice involves the rituals and prayers observed in religious communities. Beginning with Freud (1961), religious rituals have been the topic of much theoretical speculation in relation to OCD. Certainly, religious practices bear similarities to other ritualistic behaviors that are engaged in by persons suffering from OCD (Fiske & Haslam, 1997). However, although there has been a great deal of research into the neural substrates of OCD, there understandably exists almost no neuropsychological data concerning the practice of group rituals in normal populations.

Religious experience consists of both explicit perceptions (e.g., “visions,” “voices”) and vague (numinous) perceptions that often have an emotional association. Indeed, the emotional association is important to understanding the role of cortico-limbic areas in the religious neural network. According to Hardy (1979, as cited Saver & Rabin, 1997), the most prevalent numinous experiences include: (1) a patterning of events in a person’s life that convinces him or her that in some strange way they were meant to happen; (2) an awareness of the presence of God; (3) an awareness of receiving help in answer to a prayer; (4) an awareness of being looked after or guided by a presence not called God; (5) an awareness of being in the presence of someone who has died; (6) an awareness of a sacred presence in nature; (7) an awareness of an evil presence; and (8) experiencing in an extraordinary way that all things are “One.” These beliefs are closely aligned with, or even partly subsumed under, the general category of “spiritual” or “paranormal” experiences. The experience of “oneness” with the universe is one of the most distinguishing characteristics of the mystical state (Runions, 1979).

Although religious experiences are generally rated as positive (Nielsen, 2000) and may even be associated with ecstasy and exaltation (Runions, 1979), anxiety (and its removal) also figures prominently in religion. The incorporation of both positive and negative emotionality into religious experiences is consistent with other “extrapersonal” phenomenon such as dreams and out-of-body experiences, which can be either pleasant or terrifying (Roberts & Owen, 1988). Death and the complex set of emotions (some negative) that it engenders are an important motivation for many religious rituals (Alper, 2001; Boyer, 2001, Chapter 6; Holliday, 2001; Persinger, 1984a), and “evil presences” are also commonly sensed (Persinger, 1993, 1994). Although religious experiences figure prominently in the founding and promulgation of current world religions, only about 20–60% of all religious persons actually claim to have had such experiences (Saver & Rabin, 1997). It is, therefore, difficult to make conclusions about the neuropsychology of religious behavior in the majority of self-proclaimed religious persons (see also James, 1902, Chapter 1). Abnormal sensory experiences and delusional tendencies in religious groups outside of mainstream society bear a somewhat closer resemblance with those found in clinical populations (Aronoff, Lynn, & Malinoski, 2000; Peters, Day, McKenna, & Orbach, 1999; Spencer, 1975), whose symptomatology is better understood from a neuroanatomical and neurochemical standpoint.

Because the major postulate of the theory presented in this paper is that religion is a neuropsychological phenomenon associated with distant space (and time) and the brain systems that mediate it, the following section will briefly review the neuropsychology of 3-D space and its implications for understanding dreaming, hallucinations, and religious behavior.

### **3. The neuropsychology of extrapersonal space and its relationship to dreaming, hallucinations, and religious beliefs experience and practice**

As formulated by Previc (1998), there are four major realms of 3-D space in which we interact: *peripersonal* (reaching/manipulative/consummatory) space; *focal-extrapersonal* (oculomotor scanning; object-recognition) space; *action-extrapersonal* (navigation/topographical) space; and *ambient-extrapersonal* (earth-referenced/

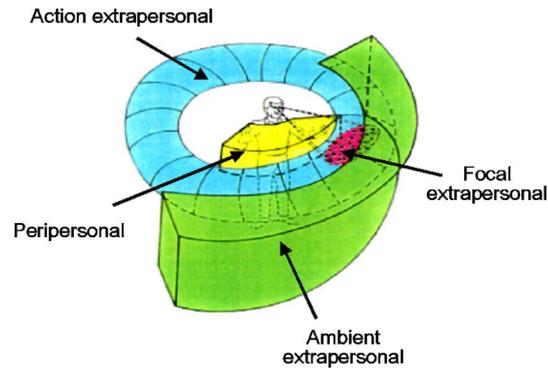


Fig. 1. The division of functional 3-D space (from Previc, 1998).

postural) space (see Fig. 1). Although the peripersonal system is the only one that relies on visual inputs that lie within arm's reach, preconscious ambient-extrapersonal visual inputs are essentially complementary to the vestibular and somatosensory/proprioceptive signals concerning the orientation of the body in earth-referenced space and may be considered as extensions of these bodily senses. Hence, the two systems whose attentional and processing resources are unambiguously directed towards distant space are the focal-extrapersonal and action-extrapersonal systems (Previc, 1998).

Section 3.1 will briefly describe the neuroanatomy of the extrapersonal brain pathways and their relationship to the major neurotransmitters. Section 3.1.2 will review the neuroanatomy and neurochemistry of two phenomena (dreaming and hallucinations) that have previously been linked to extrapersonal space (Previc, 1998) and that bear many similarities to certain religious experiences. Finally, the neuroanatomy and neurochemistry of religion will be discussed in relation to the extrapersonal brain pathways in Section 3.2.

### 3.1. Neuroanatomy and neurochemistry of the extrapersonal systems

#### 3.1.1. Neuroanatomy of the extrapersonal systems

In contrast to the peripersonal and ambient-extrapersonal systems, which are mainly housed in dorsal cortical networks extending from the dorsal visual pathways through to the lateral and medial portions of the parietal lobe and finally into the superior-lateral portions of the frontal lobe, the focal- and action-extrapersonal systems mainly course ventrally through the occipital-temporal pathways and finally on into the lateral and medial-basal portions of the frontal lobe (Previc, 1998). A diagram of the extrapersonal pathways, adapted from Previc (1998), shows the approximate location of the two ventral systems superimposed on a human brain (Fig. 2). Previc's 1998 model was an outgrowth of the original dorsal/ventral dichotomy of Ungerleider and Mishkin (1982) and is similar in many ways to the "action(dorsal)/perception(ventral)" dichotomy of Goodale and Milner (1992). However, recent brain imaging evidence suggests that the ventral pathways are foremost involved with extrapersonal space, regardless of whether perception or action is involved (Weiss, Marshall, Zilles, & Fink, 2003).

The focal-extrapersonal system is the one most dominated by vision, with its visual inputs confined to the central 30° of the visual field. This system is laterally based, extending from the occipito-temporal cortex to the lateral portion of the inferior temporal cortex and the anterior temporal lobe and onto the lateral frontal cortex anterior to the frontal eye-fields, with a branch to the superior parietal region containing the parietal eye fields. Both the posterior and anterior portions of the focal-extrapersonal system are believed to code extrapersonal perceptual-motor interactions in retinotopic coordinates (Previc, 1998) and are intimately concerned with eye movements used in searching and recognizing objects.

The action-extrapersonal system uses mainly visual and auditory information to enable us to orient, navigate, and interact in topographical space. The action-extrapersonal system is closely involved with episodic memory for places and events and the emotional associations with them, and it makes extensive use of head movements, which anticipate our bodily movements in space (Grasso, Glasauer, Takei, & Berthoz, 1996). The

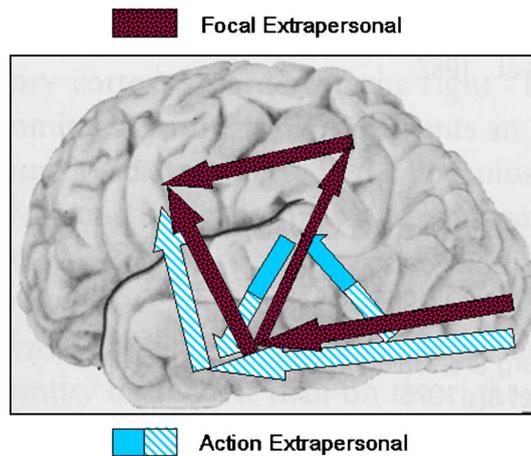


Fig. 2. The location of the focal-extraperpersonal and action-extraperpersonal brain systems. The hatched lines indicate a medial projection (adapted from Previc, 1998).

action-extraperpersonal pathways course medially through the occipital–temporal visual pathways (which are crucial for maintaining topographical memory) into ventromedial corticolimbic areas including the parahippocampal gyrus, hippocampus, orbitofrontal cortex, and anterior cingulate (Previc, 1998). The action-extraperpersonal system also performs a polymodal integration of primarily visual, auditory, and somatosensory inputs concerning the movement of the head in space in both its medial and lateral temporal portions (Previc, 1998). Posterior lesions to this system cause a neglect of extraperpersonal space (Previc, 1998) whereas anterior lesions (particularly to the anterior cingulate) cause a syndrome known as *adynamia*—an impairment of volitional actions with regards to the environment (Solms, 2000). The posterior ventromedial cortex is also important in orientation toward distant (future) time, as thinking about the future is degraded following damage to this region (Okuda et al., 2003; Rohrenbach, Regard, & Landis, 1994). By contrast, lesions to anterior ventromedial regions more degrade the execution of behaviors on the basis of future consequences, in what has been termed a “myopia for the future” (Bechara, Tranel, & Damasio, 2000).

The relationship between the vertical and radial representations of the visual world is important in discerning whether particular neuroanatomical or neurochemical systems have an extraperpersonal bias or not. Specifically, the more distant portion of the visual world is biased toward the upper field, given the elevated position of the eyes and the slant of the ground plane towards the horizon, whereas most peripersonal activity such as reaching is confined to the lower visual field (Previc, 1998). Hence, it may be inferred that brain systems that show a bias toward the upper visual field are probably biased toward distant space as well. Indeed, attentional neglect of upper, distant space is a frequent sequel to inferior temporal lobe damage (Kim, Yoon, Jeong, & Na, 2001; Shelton, Bowers, & Heilman, 1990), whereas proximal and lower-field attentional deficits are frequently found together following parietal-lobe damage (Mennemeier, Wertman, & Heilman, 1992; Pitzalis, Di Russo, Spinelli, & Zoccolotti, 2001; Pitzalis, Spinelli, & Zoccolotti, 1997). This parallels the oculomotor relationship in which upward eye movements result in divergence (to fixate distant targets) and downward eye movements result in convergence (to fixate on proximal targets) (Collewyn, Erkelens, & Steinman, 1988; Enright, 1989; Heuer & Owens, 1989; Knoll, 1962). Upward eye movements or upper-field biases in various tasks may, therefore, indicate a fundamental involvement of the brain systems mediating interactions with distant space (Previc, 1998), even when the task may not be overtly spatial in nature. For example, the eyes of individuals performing visual memory and mental arithmetic tasks deviate upward (Kinsbourne, 1972; Previc & Murphy, 1997; Previc, Declerck, & de Brabander, 2005), which is consistent with the notion that visual imagery and abstract reasoning tasks represent an extension of distal oculomotor space (Previc et al., 2005).

Besides the activation of the ventral pathways during attention to radially distant space (Weiss et al., 2003) and the upper-distal neglect that follows inferior temporal lobe lesions, there are several other examples of the role of the ventral pathways in distal space. For one, destruction of the hippocampus in rats results in an over-

reliance on proximal sensory cues and disturbances of scene memory for distances greater than 2 m (Miller & Best, 1980; Whishaw, 1993), whereas stimulation of the hippocampus results in a raising (dorsiflexion) of the head and enhanced orienting to extrapersonal signals (Foreman & Stevens, 1987; Kaada, Jansen, & Andersen, 1953; Previc, 1998). Damage to the superior colliculus, a structure that is important in orienting to distant objects in action-extrapersonal space and in generating the theta rhythm seen in the hippocampus during orienting behavior (Foreman & Stevens, 1987; Previc, 1998), often results in upper-field neglect and a downward head posture (Foreman & Stevens, 1987; Sprague & Meikle, 1965). The process of imagining objects and scenes (arguably a spatiotemporally distant representation) preferentially activates the occipital-temporal visual pathways (D'Esposito et al., 1997).

Along with the predominance of the ventral pathways in extrapersonal brain functions, there is an orthogonal prevalence of the left hemisphere over the right one in extrapersonal functions (see Previc, 1998). For example, right-hemispheric lesions are known to produce a neglect of the body (as in dressing apraxia), peripersonal manipulative disorders (constructional apraxia), an altered body image, impaired body orientation in space, reduced self-awareness, impaired emotional recognition and expression, and actual depersonalization (alienation or somatoparaphrenic) delusions (see Cutting, 1990; Hecaen & Albert, 1978). Many examples of the reduced self-awareness created by right-hemispheric lesions are provided by Brugger (2001), Cutting (1990), and others, such as the woman with left hemiplegia who said "... [my] hand doesn't belong to me ... [it is] just like a plastic hand" (Cutting, 1990, p. 190) or the patient who believed the left side of his body "to be evil and controlled by external agents, sometimes the devil and sometimes his deceased father in collusion with the devil" (Nightingale, 1982, p. 464). Another striking example of the loss of connectedness with one's own self or body is the failure to see oneself in morphed images of oneself and a famous person when the right but not left hemisphere is impaired (Keenan, Wheeler, Gallup, & Pascual-Leone, 2000). The attentional neglect syndrome caused by right-parietal lesions, which most studies have found to be more prevalent in near, lower space, is particularly revealing in that it is not tied to the position of the eyes (which are used to scan more distant extrapersonal space) but rather is linked to the position of the head and body in space. The advantage of the lower-left visual quadrant in global form processing, detection of crossed stereograms, and metric spatial judgments is further symptomatic of the predominance of the right hemisphere (left visual field) in the perceptual requirements of reaching and other activity in proximal (lower-field) space (Christman & Niebauer, 1997; Previc, 1998).

Conversely, the left hemisphere is important in visual search and saccadic scanning, abstract thought, and "executive" functions (which require strategizing about future space and time) (Previc, 1998, 1999). Activation of the left-hemisphere (particularly the left-temporal lobe) can cause disturbance of the self-concept and depersonalization (see Section 3.2.3), whereas damage to the left inferior temporal lobe alone can produce both upper-field and far-radial neglect characteristic of bilateral inferior temporal-lobe damage (Kim, Yoon et al., 2001). Moreover, the previously noted localization of distant scene and object imagery in the occipital-temporal pathways occurs primarily on the left side (D'Esposito et al., 1997).

### 3.1.2. Neurochemistry of the extrapersonal systems

According to Previc (1998), the behavior of humans and most other mammals in 3-D space is also governed by the relative predominance of four specific neurochemical systems. Noradrenaline (NE) and serotonin (also known as 5-hydroxytryptamine, or 5-HT) predominate in peripersonal activities, whereas dopamine (DA) and acetylcholine (ACh) mainly control extrapersonal interactions. Other key neurotransmitters such as glutamate and  $\gamma$  aminobutyric acid (GABA) interact with these four neurotransmitter systems, but there is no evidence that they are involved in perceptual, motor, and cognitive operations confined to specific portions of 3-D space.

The greatest amount of evidence concerns DA systems and their alignment with extrapersonal space (Previc, 1998). This is based on the role of DA in behavioral activation, exploratory, and incentive-motivation behavior (Berridge & Robinson, 1998; Crow, 1973; DePue & Iacono, 1989; Fink & Smith, 1980; McGuinness & Pribram, 1980; Robbins & Everitt, 1982; Tucker & Williamson, 1984), saccadic eye movements (Ho et al., 1988; Kato et al., 1995), and orienting to, attending to and associating distal cues (Blackburn, Pfaus, & Phillips, 1992; Dringenberg, Wightman, & Beninger, 2000; Horvitz, 2000; Salamone, Cousins, & Snyder, 1997; Whishaw & Dunnett, 1985). For example, DA antagonists disrupt food transport in rats, but only if the home

shelter resides in extrapersonal space (at least 2 m away from the food) (Dringenberg et al., 2000). Dopamine also is involved in orienting toward distant time, in that DA in rodents is critically involved in predicting future rewards (Schultz, Dayan, & Montague, 1997) and in both humans and animals mediates the executive intelligence (planning and strategizing) that requires alteration of future behavior on the basis of current feedback (Previc, 1999).

In line with its orientation toward distant space, DA stimulates a wide variety of upward-directed movements, including vertical rearing, climbing, jumping, and upward head and eye movements (see Previc, 1998). In humans, oculogyric crises that are characterized by a sustained conjugate upward deviation of the eyes result from DA overactivation and are often associated with delusional or hallucinogenic episodes (Leigh, Foley, Remler, & Civil, 1987; Linazasoro, Van Blercum, & Lasa, 2002; Thornton & McKenna, 1994). For example, the hyper-dopaminergic *jerker* rat—originally known as “stargazer”—makes continuous upward head movements (Truett, Brock, Lidl, & Kloster, 1994), whereas upper-field neglect, a dearth of upward eye movements, and downward reaching biases all follow damage to the DA-rich substantia nigra in Parkinson’s disease and associated animal models (Corin, Elizan, & Bender, 1972; Hotson, Langston, & Langston, 1986; Kato et al., 1995; Lee, Harris, Atkinson, Nithi, & Fowler, 2002; Poizner et al., 1998).

The role of DA in incentive-motivational behavior directed toward extrapersonal space accounts for its paramount role in sexual behavior in animals (Berridge & Robinson, 1998; Blackburn et al., 1992), especially male sexual behavior and proceptive (distally cued) sexual behavior in females (Robbins & Everitt, 1982). Dopamine also appears to be involved in actual copulatory behavior in rats, whereas it is considerably less involved in other consummatory behaviors such as feeding (Blackburn et al., 1992). Because of its involvement in sexual and self-stimulatory behavior in animals, DA has been frequently been considered the most important neurotransmitter mediating pleasurable experiences. However, such a view is contradicted by the fact that (1) DA systems are critical for registering the salience of and responding to *all* distal motivational stimuli, even aversive ones (Berridge & Robinson, 1998; Blackburn et al., 1992; Horvitz, 2000; Salamone et al., 1997), (2) excessive DA can lead to many “nonpleasurable” traits such as social withdrawal and detachment (Schlemmer, Narasimhachari, & Davis, 1980), obsessiveness and paranoia, and even anhedonia (Ellenbroek & Cools, 2000). Hence, the primary function of DA systems in the central nervous system goes far beyond mediating rewarding or hedonic experiences and behavior, as does the role of DA in extrapersonal brain phenomena such as dreams, hallucinations, and religious experiences (see later sections), which as noted earlier can have both positive and negative features associated with them.

Brain systems relying on acetylcholine are also involved in “behavioral activation” in extrapersonal space (McGuinness & Pribram, 1980; Previc, 1998; Tucker & Williamson, 1984) and in extrapersonal functions such as visual orienting, vigilance, and episodic memory (Harder, Baker, & Ridley, 1998; McGaughy, Kaiser, & Sarter, 1996; Perry, Walker, Grace, & Perry, 1999; Sarter & Bruno, 1998). Poor orienting and memory for extrapersonal space are also hallmarks of Alzheimer’s disease (Previc, 1998), in which ACh pathways are markedly degenerated (Giacometti, Davis, Alazraki, & Malko, 1994). The mostly parasympathetic actions of both ACh and DA (Burn, 1969; Velasco & Luchsinger, 1998) are consistent with the heart-rate deceleration during vigilance and orienting toward distal stimuli (Graham & Clifton, 1966). However, cholinergic systems influence striatal DA levels through a number of possible mechanisms, some of which are inhibitory (Gerber et al., 2001).

Conversely, NE and 5-HT are more involved in peripersonal or bodily functions such as sympathetic arousal, visuomotor coordination, consummatory behavior (e.g., feeding), grooming, and postural control (see Previc, 1998). Serotonergic activity, in particular, is highly inhibited during orientation to distal stimuli (Dringenberg, Dennis, Tomaszek, & Martin, 2003; Jacobs & Fornal, 1991). In contrast to DA’s role in stimulating upward behaviors, 5-HT tends to reduce rearing and related behaviors (Blanchard et al., 1997), and the loss of NE inputs from the locus coeruleus contributes to the symptoms of supranuclear palsy, which include lower-field neglect (see Previc, 1998; Steele, Richardson, & Olszewski, 1964). In accordance with the different 3-D functional specializations, there appear to be widespread, mostly inhibitory interactions between NE and 5-HT systems, on the one hand, and the DA and ACh systems, on the other (see Previc, 1996, 1998). The inhibitory action of 5-HT systems on the mesolimbic DA system in particular—which is part of the action-extrapersonal system pathways—is central to the theory presented here as well as to many other models of psychopathology and drug effects (Di Matteo, Cacchio, Di Giulio, & Esposito, 2002; Ennis, Kemp, & Cox,

1981; Gottesmann, 2002; Herve et al., 1979; Joyce, 1993; Kapur & Remington, 1996; Mandell, 1980; Micallef & Blin, 2001; Previc, 1996; Prisco & Esposito, 1995; Vollenweider, Vontobel, Hell, & Leenders, 1999; Westfall & Tittermary, 1982).

The neurochemical distributions of the extrapersonal versus body-oriented neurotransmitters in primates align reasonably well with the neuroanatomical partitioning of the peripersonal and extrapersonal brain pathways (see Previc, 1998). For example, DA is most highly concentrated in key focal-extrapersonal pathways that include the lateral prefrontal cortex and the inferior temporal lobe, although it is also heavily represented in ventral regions associated with the action-extrapersonal system, such as the medial-frontal cortex, cingulate gyrus and ventral entorhinal cortex (DePue & Iacono, 1989). Cortical ACh is most prominently found in the medial and superior temporal regions and in the medial-basal frontal lobe, all of which are key components of the action-extrapersonal system. Noradrenaline, by contrast, is located mainly in the dorsal cortex, especially in post-rolandic somatosensory areas. One seeming exception to the neurochemical–neuroanatomical alignment is the localization of the “peripersonal” transmitter 5-HT mainly to the ventral occipito-temporal “extrapersonal” pathways (Previc, 1998). However, this localization is actually consistent with the important role that 5-HT is believed to play in *inhibiting* DA transmission in the ventral posterior cortex.

The alignment of the extrapersonal neurochemical and neuroanatomical pathways is further supported by neurochemical lateralization findings. Based on numerous direct and indirect pieces of evidence (see Flor-Henry, 1986; Previc, 1996, 1998; Tucker & Williamson, 1984, for reviews), DA and ACh are more lateralized to the left hemisphere, whereas NE and 5-HT are more lateralized to the right hemisphere. The lateralization of DA and ACh to the left hemisphere is reflected in its activational bias toward extrapersonal space (Previc, 1998) and in its predominantly parasympathetic influence on cardiac output and temperature control (Previc, 1996). Conversely, the greater innervation of the right hemisphere by NE and 5-HT can account for that hemisphere’s greater sympathetic output and its paramount role in emotional arousal and bodily/peripersonal actions (Previc, 1996; Tucker & Williamson, 1984; Wittling, 1995). Because of its greater innervation by DA, the left hemisphere is also more generally predisposed to phenomena and clinical disorders that reflect an imbalance of DA over NE and 5-HT activity—including dreams, hallucinations, and at least three of the four clinical disorders described in Section 3.4. Aside from this general neurochemical predisposition, however, there is no convincing evidence of a specific linkage between the left hemisphere and any of the behavioral phenomena and disorders to be reviewed in this paper that would reduce them to being labeled “left-hemispheric” per se.

### 3.2. *Activation of the extrapersonal brain pathways during dreams hallucinations*

#### 3.2.1. *Dreams and hallucinations and their relationship to religious experience*

In this section, two brain phenomena that bear a close relationship with the extrapersonal brain pathways—dreaming and hallucinations—will be reviewed. Many researchers have posited a fundamental similarity between dreams and hallucinations (Hobson, 1996; Hofmann, cited in Goodman, 2002; Rotenberg, 1994; Solms, 2000), which even share an etymologic root (“to wander”) e.g., hallucination from the Latin “alucinari” and dream (“reve” and “reverie”) from the French “resver.” Hallucinations bear a close relationship with dreaming, as indicated by the fact that the former frequently occur in normal individuals following sleep deprivation or during or just prior to sleep onset (“hypnogogic hallucinations”) or just after awakening (“hypnopompic hallucinations”) (Cheyne & Girard, 2004; Girard & Cheyne, 2004) and occur in clinical populations during waking near bursts of rapid-eye-movement (REM) activity, which is normally associated with dreaming (Arnulf et al., 2000). When ingested before sleep, hallucinogens such as LSD are known to potentiate dreaming (Muzio, Roffwarg, & Kaufman, 1966), and hallucinating schizophrenics themselves describe their hallucinations as dream-like (Gottesmann, 2002; Nasar, 1998, p. 351) .

According to Previc (1998), dreams and hallucinations represent the triumph of the extrapersonal systems over the body-oriented or peripersonal systems. They are both characterized by themes and experiences associated with extrapersonal space (out-of-body experiences, distant scenes, etc.), little reaching, consummatory, tactile or other peripersonal experiences, and a preponderance of upward eye movements. One type of hallucination—termed vestibular-motor—is comprised of floating, flying, and other out-of-body sensations that are more likely to occur in the upper visual field and beyond 2 m, often outside the confines of the room (Cheyne

& Girard, 2004). Many auditory hallucinations reflect an inability to monitor one's own self-generated speech by means of proprioceptive inputs (Bick & Kinsbourne, 1987; Weiss & Heckers, 1999), and some out-of-body experiences may be associated with an actual inhibition of emotionally painful signals emanating from the body (as in the case of depersonalization reactions during rape) (Sierra & Berrios, 1998). Moreover, the symptomatology of dreams and hallucinations is closely related to other disorders of extrapersonal space, most prominently schizophrenia and TLE (see Section 4).

Dreaming has long been part of various religious traditions (Gunter, 1983; Kelsey, 1976, Chapter 4; Koyama, 1995) and is considered a means of receiving messages from the supernatural. Examples of the religious elements of dreams include the meeting of ancestors in dreams (Boyer, 2001, p. 138), the significance of dreams in the Old Testament (e.g., Joseph's in the Book of Genesis), and the construction of Japanese religious temples in the past to serve as places of dreaming (Koyama, 1995). Of course, the Aboriginal religious concept of the "Dreamtime," though not alluding to normal dreaming, nevertheless represents a cosmological spirit world into which persons can transcend during religious rituals (Charlesworth, 1992).

Hallucinations during epilepsy and paranoid schizophrenia are believed to have led to experiences that have inspired many of the world's leading religions, including those of St. Paul (the founder of Catholicism), Mohammed (the founder of Islam), and Joseph Smith (the founder of the Mormon religion) (see Saver & Rabin, 1997). Hallucinations produced by psychoactive agents are also intimately tied to many religious traditions and ceremonies, especially Native American ones (Batson & Ventis, 1982; Saver & Rabin, 1997). Ingestion of hallucinogenic drugs leads to mystical experiences and religious imagery (see review by Batson & Ventis, 1982, Chapter 4; Goodman, 2002; Pahnke, 1969; Saver & Rabin, 1997), and experimentation with drugs is often a precursor to joining religious cults in college (Lansky & Pihl, 1976). One type of hallucination—namely, out-of-body experiences—is commonly experienced during near-death episodes and has assumed importance in many religions (see Section 3.2.3 and 3.3.3).

### 3.2.2. *Extrapersonal activity during dreaming*

The extrapersonal bias of dreaming is reflected in the predominantly visual and auditory nature of dreams as opposed to the relative dearth of tactile sensations. For example, only 1–2% of dreams contain tactile sensations, as opposed to 65% with auditory sensations and 100% with visual imagery (McCarley & Hoffman, 1981). The extrapersonal bias is also reflected in the preponderance of upward over downward eye movements during REM sleep (De Gennaro, Violani, & Capogna, 1984; Hansotia et al., 1990), in which most dreaming occurs (see Hobson, Pace-Schott, & Stickgold, 2000). Most dreams feature a structured narrative and fairly normal events and images, but a small percentage (5–10%) contain a bizarreness of setting that may even include adopting a viewpoint external to the dreamer (Hunt, 1982). It is these "apex" dreams—relatively more prominent in schizophrenics—that most closely resemble complex hallucinations involving full scenes (Hunt, 1982).

The neuroanatomy of dreaming has been elucidated by both lesion and functional brain imaging studies (see Hobson et al., 2000; Solms, 2000). Although REM sleep and dreaming are closely linked, they are dissociable, in that dreaming can occur without REM and REM can occur without dreaming (Solms, 2000). Dreaming is more dependent on cortical circuits, whereas REM is generated in the pons (Solms, 2000). In his analysis of 100 published cases of loss of dreaming following brain lesions, Solms (\*\*2000, Fig. 2) identified two major loci responsible for dreaming—the parietal-temporal-occipital area and the inferior ventromedial quadrant of the frontal lobes. In Hobson et al.'s (2000) review of functional brain imaging studies of REM sleep, in which the most plentiful and vivid dreaming occurs, the most consistent findings were of an activation of ventromedial and limbic areas (amygdala, anterior cingulate, hippocampus and parahippocampal gyrus, and inferior frontal lobe) as well as a de-activation of the dorsolateral prefrontal cortex and of the posterior parietal lobe (see also Braun et al., 1997; Buchsbaum, Hazlett, Wu, & Bunney, 2001; Maquet, 2000; Nofzinger, Mintun, Wiseman, Kupfer, & Moore, 1997; Nofzinger et al., 1999, for specific references). The combined result from all of these studies suggests the forebrain activation during dreaming most closely resembles that of the action-extrapersonal pathways (see also Fig. 2). The de-activation of the posterior parietal areas explains the relative dearth of peripersonal experiences during dreaming while the decrement of focal-extrapersonal and executive functions due to the dorsolateral prefrontal de-activation (Previc, 1999) accounts for the often bizarre and uncontrolled nature of the dream sequence.

Dreaming relies mainly on dopaminergic and cholinergic systems located in the cerebral cortex. These are the major neurotransmitters in the ventromedially based “action-extrapersonal” cortical network (Previc, 1998), with ACh prominent in the medial temporal lobe and hippocampus and DA in pathways coursing from the temporal visual areas to the anterior cingulate and medial-frontal cortex (Solms, 2000). Dreaming is best stimulated by both cholinergic agonists such as carbachol (see references by Hobson et al., 2000) as well as dopaminergic agents such as L-dopa (see Thompson & Pierce, 1999 and other references cited by Solms, 2000). This contrasts with the relative silence of NE and 5-HT neurons during REM sleep and the general lack of effect of NE and 5-HT agonists in promoting dreaming (Hobson et al., 2000). For example, 5-HT suppresses REM sleep and decreases dream frequency, recall, and bizarreness, although it can increase dream intensity (Pace-Schott et al., 2001). The role of DA and ACh in dreaming is further supported by the predominance of the left hemisphere in dreaming in most individuals (Greenberg & Farah, 1986; Solms, 2000) and by the parasympathetic dominance throughout the sleep cycle (Burgess, Trinder, Kim, & Luke, 1997; Miller & Horvath, 1976).

### 3.2.3. *Extrapersonal activity during hallucinations*

The cortical neuroanatomy of hallucinations has been more difficult to study than that of dreaming, because hallucinations do not ordinarily occur in normal subjects and are, therefore, more difficult to generate in a research setting. There are also many different types of hallucinations, ranging from simple perceptual ones to more complex ones involving dream-like sequences, alien presences and vestibular-motor phenomena. As with dreaming, visual and auditory hallucinations are the most common—23% and 60%, respectively, in the average of samples reviewed by Schonauer, Achtergarde, Gotthardt, and Folkerts (1998)—whereas tactile hallucinations are very rare (Schonauer et al., 1998). Hence, the use of the term hallucinations in this paper will refer to those containing complex visual and auditory experiences, unless otherwise specified.

Simple hallucinations are not located in one area of the brain, as stimulation of visual areas gives rise to visual hallucinations, stimulation of auditory areas gives rise to auditory hallucinations, etc. (Asaad & Shapiro, 1986; Hecaen & Albert, 1978; Weiss & Heckers, 1999). However, the generation of complex, dream-like associations that include full scenery is most likely to occur following stimulation of the temporal lobe (see Bancaud, Brunet-Bourgin, Chauvel, & Halgren, 1994; Hecaen & Albert, 1978, Chapter 4; Penfield & Rasmussen, 1950), either by seizures or by application of electrical current. The two most sensitive areas appear to be the medial-temporal lobe and the superior portion of the lateral temporal region (Bancaud et al., 1994).

Functional imaging studies with subjects who have ingested hallucinogenic drugs such as psilocybin and ketamine demonstrate that activations of the anterior cingulate, medial-frontal cortex, and even some lateral prefrontal regions occur during hallucinations, alongside de-activation of the primary visual cortex (Tammimga, Vogel, Gao, Lahti, & Holcomb, 2000; Vollenweider & Geyer, 2001; Weiss & Heckers, 1999). Out-of-body hallucinations are likely to be associated with prefrontal activation (Sierra & Berrios, 1998) or with damage to posterior vestibular processing areas in the parietal-temporal region, which is an important area for body perception and body cognition (Blanke, Landis, Spinelli, & Seeck, 2003). Brain imaging studies with hallucinating schizophrenics indicate that activation of the temporal-lobe, anterior cingulate, and striatum occurs along with de-activation of postcentral (parietal) activity during auditory and visual hallucinations (Cleghorn et al., 1992; Mathew, Duncan, Weinman, & Barr, 1982), although some hallucinogens do activate parietal areas (Vollenweider & Geyer, 2001). Neuroleptic treatment that helps reduce schizophrenic hallucinations and delusions (two of the most well-known “positive symptoms”) tends to decrease the frontal-parietal activation ratio (Cleghorn et al., 1992). Visual hallucinations occurring in patients suffering from a form of sensory deprivation known as the Charles Bonnet syndrome emanate from ventral visual association areas such as the fusiform gyrus, as the primary visual cortex seems particularly resistant to external visual stimulation in this syndrome (ffytche et al., 1998).

Large-scale studies have shown that lesions (i.e., under-activation) of the right hemisphere are almost twice as likely as left-sided ones to produce complex visual hallucinations (Hecaen & Angelergues, 1965; cited in Hecaen & Albert, 1978, p. 161). Similarly, epileptiform activity (i.e., overactivation) in the left hemisphere is almost twice as likely to produce hallucinations and delusions (Cutting, 1990; McAllister, 1998; Sherwin, 1984; Toone, 1981; Trimble, 1984). Some of the more prominent delusions created by either left-hemispheric overstimulation or right-hemispheric damage include denial or neglect of paralyzed limbs caused by brain

damage to the contralateral hemisphere, delusions of alien control, and other depersonalizations (Bisiach, Rusconi, & Vallar, 1991; Brugger, 2001; Cutting, 1990), particularly when the right-hemispheric damage involves the body-centered systems housed in the parietal lobe. Out-of-body hallucinations are particularly likely to involve an activation of the left hemisphere (Sierra & Berrios, 1998) and to appear predominantly in the right visual field (Cheyne & Girard, 2004; Girard & Cheyne, 2004). Conversely, hallucinations and delusions are more likely to be reduced when the epileptic focus is surgically excised from the left hemisphere than the right one (Cutting, 1990).

In terms of the pharmacology of hallucinations, most researchers have focused on the involvement of DA, ACh, and 5-HT, as well as glutamate. Unquestionably, DA is the major (if not critical) neurotransmitter responsible for hallucinations. Drugs that stimulate DA, such as amphetamine and L-dopa, are hallucinogenic whereas drugs that reduce DA transmission (such as haloperidol) tend to diminish or eliminate hallucinations (Arnulf et al., 2000; Asaad & Shapiro, 1986; Lohr & Bracha, 1988; Mandell, 1980; Rotenberg, 1994). Moreover, excessive DA is believed to lead to the positive symptoms (including hallucinations and delusions) found in schizophrenia and related disorders (e.g., Gray, Feldon, Rawlins, Hemsley, & Smith, 1991; Kapur, 2003; Swerdlow & Koob, 1987). Dopaminergic activation has also been implicated in the effects of sensory deprivation (Ridley & Baker, 1982), which frequently includes hallucinations (Siatkowski, Zimmer, & Rosenberg, 1990; Zuckerman, 1969). This makes sense in that DA is poorly represented in primary sensory areas of the cortex (Previc, 1998) and should, therefore, be relatively more active during sensory isolation and deprivation than the other three major transmitters, which are more tied to de-activated sensory processing areas.

Dopamine is also implicated in the near-death experiences that, despite variations in content across cultures, appear to be a universal phenomenon among humans (Kellehear, 1993; Roberts & Owen, 1988). The near-death experience typically involves a transport into a “different world,” encounters with “different beings,” or some even more direct form of an out-of-body experience (e.g., autoscapy, the experience of looking at oneself from above) (Kellehear, 1993; Roberts & Owen, 1988). These experiences are more likely to be interpreted in a spiritual context by religious individuals (Roberts & Owen, 1988). One explanation for the near-death experience is that it represents an adaptation to a situation in which reduced oxygen and/or extreme stress may be present (Alper, 2001; Roberts & Owen, 1988). Increased DA transmission is a major feature of the brain during hypoxia (Buyukuysal & Mete, 1999), and hypoxia at birth is one of several early-developmental risk factors for schizophrenia (Dalman et al., 2001), in which DA levels are elevated. Upward eye movements and auditory and visual hallucinations are additional correlates of hypoxia (Lempert, Bauer, & Schmidt, 1994). For example, intense and bizarre dreams and hallucinations frequently occur during loss of consciousness in pilots exposed to high-G forces (Forster & Whinnery, 1988) and during hypoxia induced at high altitude in mountain climbers (Brugger, Regard, Landis, & Oelz, 1999). The putative roles of glutamate and possibly the endorphins in the near-death experience (Alper, 2001) may also be mediated by their actions on DA. Phencyclidine (PCP) and ketamine, two drugs that can lead to out-of-body and mystical experiences (Hansen, Jensen, Chandresh, & Hilden, 1988; Rosse et al., 1994), bind with opioid, glutamatergic, D<sub>2</sub> dopaminergic and other receptors (Kapur & Seeman, 2002), with the glutamatergic and other non-DA actions ultimately expressed via DA pathways (Ault & Werling, 1999; Irifune et al., 1997; Kapur & Seeman, 2002; Lonart & Zigmund, 1991).

Finally, it must be noted that DA not only exerts a parasympathetic cardiovascular action (Velasco & Luchsinger, 1998) but also has analgesic properties (Altier & Stewart, 1999). The parasympathetic dominance that has been observed during out-of-body experiences (Schuman, 1980; Sierra & Berrios, 1998) is consistent with a link between such experiences and a need to reduce metabolic activity. Conversely, greater sympathetic activation caused by adopting a standing versus supine position diminishes the probability of perceiving hallucinations during sensory deprivation (Zuckerman, 1969).

In contrast to DA, ACh is more likely to inhibit most hallucinatory behavior, even though cholinergic activation stimulates dreaming and even mild hypnopompic hallucinations (Yorston & Gray, 2000) and may contribute to the positive symptoms of schizophrenia (Sarter & Bruno, 1998). Anticholinergic drugs (e.g., atropine, the psychoactive agent in the hallucinogenic Jimson Weed plant) stimulate hallucinations (Perry & Perry, 1995) whereas anticholinesterase agents such as physostigmine (which increase the supply of ACh at the synapse) block the hallucinations created by the reduced cholinergic activity found in Parkinson's disease, Alzheimer's disease and Lewy Body disease (Ballard et al., 2000; Perry et al., 1999). Cholinergic

inhibitory interactions with DA both in the basal ganglia (Yeomans, 1995) and the septohippocampal region (Mandell, 1980) may underlie the role of ACh in blocking hallucinations.

An anti-hallucinogenic role for 5-HT in general has been suggested by several researchers (Asaad & Shapiro, 1986; Goodman, 1982; Tissot, 1975) and is supported by evidence that: (1) 5-HT and its precursor (tryptophan) help prevent the positive symptoms of schizophrenia (Irwin, Marder, Fuentenebro, & Yuwiler, 1987; Kapur & Remington, 1996; Tissot, 1975); (2) 5-HT administration or elevation counters the effects of hallucinogens (Aghajanian & Marek, 2000); (3) decreased 5-HT activity potentiates the hallucinogenic effects of sensory deprivation and LSD (Appel, Sheard, & Freedman, 1970; Goodman, 1982); and (4) hallucinations and other LSD effects are reduced by the administration of antidepressants that boost serotonergic activity (Davis, Gallager, & Aghajanian, 1977; Dilsaver, 1994). Although classical hallucinogens such as LSD and psilocybin have both agonistic and antagonistic serotonergic properties (Aghajanian & Marek, 2000; Glennon, 1990; Pierce & Peroutka, 1990), depending on the specific 5-HT receptor, inhibitory action at least one receptor (e.g., the 5-HT<sub>2A</sub>) may actually lead to a greater synaptic serotonin transmission (Aghajanian & Marek, 2000). Further complicating the effects of 5-HT on hallucinatory experiences is the fact that serotonergic systems are also known to modulate DA transmission, predominantly by inhibiting the latter in the striatum and elsewhere (Di Matteo et al., 2002; Ennis et al., 1981; Herve et al., 1979; Joyce, 1993; Kapur & Remington, 1996; Mandell, 1980; Nicolaou, Garcia-Munoz, Arbuthnott, & Eccleston, 1979; Prisco & Esposito, 1995; Vollenweider et al., 1999; Westfall & Tittermary, 1982). Indeed, classic hallucinogens such as LSD and mescaline that are believed to reduce serotonergic activity and increase DA levels in general accordance with their hallucinogenic potential (Trulson, Stark, & Jacobs, 1977). Reduced or otherwise altered 5-HT activity may also accompany the glutamatergic effects of hallucinogens such as ketamine (Aghajanian & Marek, 2000; Irfune et al., 1997; Kapur & Seeman, 2002; Vollenweider & Geyer, 2001).

In summary, dreams and complex hallucinations share extrapersonal themes and a neural substrate that involves predominantly the ventromedial pathways. Parietal and primary sensory areas are relatively less active in dreaming and in some hallucinations, and both phenomena exhibit varying degrees of left-hemispheric predominance. Both dreaming and hallucinations are associated with elevated DA transmission and, in most cases, reduced 5-HT transmission, but the roles of NE (reduced in dreaming; unclear during most hallucinations) and ACh (increased during dreaming; reduced during hallucinations) appear divergent. The most obvious common denominator in these phenomena appears to be a selective activation of DA in the ventromedial pathways, particularly beyond the primary and secondary sensory areas where DA is relatively under-represented. Dopamine is itself hallucinogenic, is either directly or indirectly elevated in response to virtually all hallucinogens that affect other neurotransmitter systems, and is elevated during hallucinatory activity in schizophrenia, dreaming, sensory isolation, hypoxia, and near-death experiences. Finally, the elevation of DA transmission helps account for the predominance of upward eye movements and parasympathetic autonomic influences during dreaming and hypoxia-induced hallucinations.

The next section will discuss how religious activity and its various facets may also be considered extrapersonal phenomena, with a neural substrate similar to that of dreams and hallucinations.

### 3.3. *Activation of the extrapersonal brain systems during religious activity*

#### 3.3.1. *Religious activity in relationship to distant space and time*

As noted earlier, all religious concepts involve the “supernatural.” Religious belief is associated with a general belief in paranormal phenomena,<sup>2</sup> in which distantly related or even purely coincidental encounters and events are causally linked by the believer, often using the framework of a powerful, cosmic force. Hence, one

<sup>2</sup> Although differing in some respects (Persinger, 1993), paranormal beliefs (e.g., magical ideation) and traditional religious beliefs are often significantly correlated (Peltzer, 2003; Persinger, 1984a). Magical ideation is also associated with the trait of schizotypy, which is in turn positively associated with religiosity (see next section), and mystical experiences and felt presences are commonly experienced among persons who engage in normal religious practice (Fenwick, Galliano, Coate, Rippere, & Brown, 1985). These positive relationships exist despite modern Christian prohibitions against the same paranormal experiences that were so important in its development and promulgation (Kelsey, 1976; Peltzer, 2003).

of the most crucial elements in understanding the neural basis of religion is the relationship of religious activity in humans to distant space and time.

Inherent to most religions are the concepts of God, Heaven, soul, and the after-life. The soul is an extension of corporeal space, God and Heaven extend the concept of space beyond the most distant sensorial realm, and the after-life extends time beyond the finite period of our own lives. The concepts of God and Heaven are also inextricably linked to upper space—e.g., the Hebrew word “El Elyon” for God refers to “Most High,” “exalt” has as its Latin root “alt” for high, “transcendence” connotes an upward movement; “supernatural” denotes a higher plane of existence. Jesus reputedly talked to the spirits of Abraham and Moses on a mountaintop, Mohammed purportedly was lifted by Gabriel’s chariot into the sky, the Nordic Gods lived in the heights of Valhalla, and Nirvana represents the highest stage of enlightenment (seventh heaven), in which bodily pleasures and pains no longer matter. The relationship between the sacred and the celestial dates at least as far back as the Aboriginal “sky-world,” but it is more clearly evidenced by later religions. The Egyptians bestowed great status on astronomer-priests and created the pyramids, one of many famous structures on different continents with both astronomical and religious significance. Large mosques, temples, and cathedrals of all major religions protrude into the sky, and monasteries are much more likely to be built on top of hills rather than in deep valleys. Many famous mountains throughout the world, such as Fuji, Kilimanjaro, Olympus, Sinai, and Shasta, have been imbued with sacred properties, while angelic and other positive supernatural figures typically associated with upper space invoke flight. The upward bias of modern religions is not as apparent in less structured religions, but even in these cases upward biases may be present. In examples provided by Boyer (2001), a shaman in the Cuna tribe in Panama may attempt to send spirits back into the sky (p. 1), the personal spirits of the Buid people may fly over mountaintops to visit them (p. 266), witches in the Fang tradition of West Africa are believed to be able to fly or to have special organs that fly (p. 297), etc.

The religious significance of upper space is further reflected in upward oriented behaviors and orientations during individual religious experience and practice. Upward eye shifts (eye-rolling) have been shown to accompany meditation, hypnosis and seizures (Rosenow et al., 1998; Tebecis, 1976; Tebecis & Provins, 1975), similar states that are frequently associated with religious experience (e.g., Hood, 1973; Saver & Rabin, 1997). Indeed, upward eye deviations promote generation of the EEG alpha rhythm characteristic of the initial meditative state (Schuman, 1980), and concentration on the “third eye” (an area on the forehead above the eyes and midway between them) is a common meditative technique leading to mystical experiences (Leskowitz, 1988; Schuman, 1980). Upward ocular deviations also commonly occur in mystical states induced by magnetic stimulation of the brain (Persinger, 2004) [personal communication, July].

The religious connotations of upper space are consistent with the association of positive affect with upper space (Meier & Robinson, 2004) and a higher cultural valuation of upper space, at least in Western cultures. A few of the many examples of this bias in the English language are shown in Table 1. In addition to the upward bias, a bias towards distant space is also evidenced by such distinctions as “farsighted” versus “myopic” and “unlimited” versus “limited” thinking, and there are frequent positive metaphorical linkages between upward and right-sided space (e.g., “uprightness”).

Conversely, negative aspects of religion often exhibit a downward orientation. The most prominent of these negative religious concepts is that of Hell, which is a widely held but less universal concept than Heaven. Bats, snakes, and other creatures that move low to the ground or emerge from underground frequently have negative religious connotations, as does darkness (which, by virtue of the vertical luminance gradient of the ambient visual world, is more prevalent in lower space). There are also negative connotations for leftward space, both generally (e.g., “sinister” derives the French word for left) and in religious contexts (Fabbro, 1994; Tan, 1998). For example, Persinger (1994) found in 83% of his subjects that “sensed presences” in the left visual field were associated with negative experiences (e.g., fear), where 83% of right-visual field presences were associated with pleasant experiences (e.g., angels).<sup>3</sup>

The relationship of religion and distant, upper space may partly account for the religious experiences and conversions frequently found in pilots and astronauts while flying high above the ground (Gawron, 2004; Pon-

<sup>3</sup> The angelic visions of Swedenborg in the mid-1700s appeared in his upper-right quadrant and helped to transform him from scientist to spiritual leader (Bradford, 1999).

Table 1  
Cultural valuations of upper and lower space

| Upper space           | Lower space             |
|-----------------------|-------------------------|
| Heaven                | Hell                    |
| <i>Exalt</i>          | <i>Debase</i>           |
| Shoot for the stars   | Get down to earth       |
| Hold your head high   | Hang your head low      |
| Take the high road    | Below the belt/low-blow |
| Upwardly mobile       | In a downward spiral    |
| Going uptown          | Heading downriver       |
| Raise oneself up      | Dig oneself into a hole |
| Climbing the mountain | Hitting rock bottom     |
| High-class            | The pits                |
| Uplifted              | Downtrodden             |
| Above the fray        | Down and dirty          |

omarenko, 2000), as well as other depersonalization experiences such as the “breakoff” phenomenon, in which pilots at high-altitude actually feel like they have left the aircraft (Benson, 1973). Ponomarenko states that:

“... cosmonauts have noted the rush of an unusual, positive energy, a sense of the soul’s freedom as never before, also an exceptional awareness of their second ‘Ego,’ a connection to all peoples and mainly a feeling of love for mankind in general. It is remarkable that mainly in space, people recall the past, and realize that inner freedom is life’s essence” (Ponomarenko, 2000, p. 141) .

Besides reflecting the orientation toward upper space at high altitudes, the mystical experiences of pilots and cosmonauts could also be caused by reduced oxygen intake or the reduced sensory environment of space,<sup>4</sup> all of which have been associated with elevations in DA activity. Certainly, the experiences of Ponomarenko’s cosmonauts are strikingly similar to the mystical states produced by drugs (Hansen et al., 1988) and by experienced meditators, such as one in the study of Newberg et al. (2001):

“There was a feeling of energy centered within me . . . going out into infinite space and returning . . . There was a relaxing of the dualistic mind, and an intense feeling of love. I felt a profound letting of the boundaries around me, and a connection with some kind of energy and state of being that had a quality of clarity, transparency and joy. I felt a deep and profound sense of connection to everything, recognizing that there never was a true separation at all.” (Michael Baime, as cited in Underwood, 2001, p. 53).

### 3.3.2. Neuroanatomy of religious activity

Although religion is difficult to study from a neuropsychological perspective in normal populations, two major approaches have been used in this regard. The first has involved correlating measures of religiosity, magical ideation, and belief in paranormal events with behavioral and other indicants of activation of certain brain regions. This general approach has been most widely used by Persinger and Brugger and their colleagues. The second major line of research into the neuropsychology of religion has been to directly record electroencephalographic and metabolic brain activity during meditation, trances, and other quasi-religious events.

The medial temporal lobe (see below) and, to a lesser extent, the medial frontal cortex (Muramoto, 2004), are the regions that have been most implicated in religious activity in humans. Many researchers have reported a greater number of temporal-lobe “signs,” similar to those associated with TLE, in normal individuals who hold above-average beliefs in spiritual and paranormal phenomena and/or are more prone to paranormal or transcendental experiences (Britton & Bootzin, 2004; Brugger & Graves, 1997; Fenwick et al., 1985; MacDonald & Holland, 2002; Mohr, Graves, Gianotti, Pizzagalli, & Brugger, 2001; Morneau, MacDonald,

<sup>4</sup> It is also noteworthy that many important religious traditions emerged out of behaviors associated with the sparse desert landscape of the Middle East (e.g., Moses hearing voices on Mt. Sinai, Paul’s blinding on the road to Damascus, Jesus’ spiritual conversations with Moses and Abraham during his sojourn in the wilderness, Mohammed’s encounters with Gabriel, etc.)

& Holland, 1996; Persinger, 1984a; Persinger, 1991; Persinger & Fisher, 1990; Persinger & Makarec, 1987). Indeed, Brugger and Graves (1997) observed a correlation of +0.69 between temporal-lobe signs and paranormal (magical-ideation) scores. It should be noted that while most of the “temporal-lobe signs” in these studies consisted of minor epileptiform activity or responses to nonreligious questions or tests (e.g., olfactory and visual illusions, feelings of being spatially lost), others involved questions related to paranormal experience themselves (e.g., feelings of invisible “presences”). For example, one of Persinger’s temporal signs was agreeing with the statement “When I have a tough decision to make a sign will be given and I will know what to do” (Persinger, 1984a, p. 967).

It is also noteworthy that schizotypy, a trait that is linked to both temporal-lobe dysfunction (Dinn, Harris, Aycicegi, Greene, & Andover, 2002) and magical ideation (Taylor, Zach, & Brugger, 2002), has been found to be higher in religious persons (Diduca & Joseph, 1997; White, Joseph, & Neil, 1995), primarily males (Diduca & Joseph, 1997).<sup>5</sup> Feldman and Rust (1989) showed a significant positive relationship between schizotypy and religiosity in schizophrenic patients but not normals. Although delusional, schizoid thinking has been shown to occur more frequently in members of religious cults (Peters et al., 1999; Spencer, 1975), there does not appear to be a positive correlation between psychosis among religious practitioners in general. Rather, psychoticism and religiosity have repeatedly been shown to be negatively correlated in the 0.1–0.3 range (Francis & Wilcox, 1996; Maltby, 1997; Roman & Lester, 1999).

The other major source of evidence concerning the neuroanatomy of religion in normals are studies that measure brain activity during deep meditation in trained individuals, religious persons reading religious passages, or other types of religious/transcendental experience. Nine published studies in this area (Aftanas & Golocheikine, 2001; Azari et al., 2001; Herzog et al., 1990; Jevning, Anand, Biedebach, & Fernando, 1996; Lazar et al., 2000; Lehmann et al., 2001; Lou et al., 1999; Newberg et al., 2001; Persinger, 1984b) all investigated brain activity at multiple sites or across the entire cortex using electrophysiological or functional brain imaging techniques (Table 2).<sup>6</sup> Three of the studies assessed topographical EEG activity (Aftanas & Golocheikine, 2001; Lehmann et al., 2001; Persinger, 1984b), while the others measured cerebral blood flow or cerebral metabolism. There were many other differences among the studies, in that six studied brain changes during active (self-generated) meditation (Aftanas & Golocheikine, 2001; Herzog et al., 1990; Jevning et al., 1996; Lehmann et al., 2001; Newberg et al., 2001; Persinger, 1984b), two studied the effects of meditation using auditory instructions (Lazar et al., 2000; Lou et al., 1999), one studied changes during reading of a Biblical passage (Azari et al., 2001), and one additionally measured brain activity during a dissociative religious experience (glossolalia) (Persinger, 1984b).

It is also not easy to compare these studies in terms of their neuroanatomical loci, because electrophysiological experiments may show activations in an electrode that picks up from a large or distant cortical site whereas functional imaging studies may observe highly localized regions of activation and de-activation in the same overall brain region. Nevertheless, it proved possible in most cases to determine broadly whether activations occurred in the temporal lobe, occipital lobe, dorsolateral prefrontal cortex, anterior cingulate/medial frontal cortex, or parietal lobe. Notwithstanding the differences in methodology and the obvious inconsistencies across studies, a slight pattern emerges in that the frontal, temporal, and anterior cingulate/medial frontal cortices are more likely to be activated during meditation or religious experience than are the parietal and occipital lobes, since

<sup>5</sup> The greater religiosity–schizotypy link in males as opposed to females could be caused by a greater DA activation in males, given that other disorders associated with DA overactivation show a male predominance (see Section 4.1). On the other hand, women tend to have more paranormal experiences overall (Batson & Ventis, 1982, Chapter 2; Peltzer, 2003).

<sup>6</sup> Aftanas did not measure anterior cingulate activity directly, but it has been shown that the frontal theta rhythm they recorded is generated in the anterior cingulate and medial prefrontal cortex (Ishii et al., 1999). Lazar et al. (2000) did not show their de-activations and, because of other inconsistencies in the way they analyzed their data, only their significant results from the meditation vs. control comparison are shown. Lehmann et al. (2001) and Lou et al. (1999) measured brain activity under multiple meditation conditions, but the condition considered most representative of the deep “meditative” experience—“abstract joy” in Lou et al. (1999) and “self-dissolution” in Lehmann et al. (2001)—were included in Table 2. Also, because significant subcortical activations were listed only in the Lazar et al. (2000) and Newberg et al. (2001) studies, no subcortical sites are included in Table 2. Finally, a study by Kubota et al. (2001) also showed midline frontal-theta activation during meditation, but it only measured theta and alpha activity at two sites (midline frontal and occipital) and did not use experienced meditators/practitioners, as was the case of the other nine studies included in Table 2. It is likely, therefore, that Kubota et al.’s results pertain more to the state of relaxed concentration than to a deep-meditative/religious state.

Table 2  
Brain activity during religious practice<sup>a</sup>

| Study   | Temporal | Occipital | Prefrontal<br>(dorsolateral) | Anterior cingulate/<br>medial-frontal | Parietal |
|---|----------|-----------|------------------------------|---------------------------------------|----------|
| Aftanas and Golocheikine (2001)<br>Meditation (long-term) <i>EEG alpha &amp; theta</i> ( $n = 16$ ) | +        | o         | +                            | +                                     | o        |
| Azari et al. (2001)<br>Religious recitation <i>PET</i> ( $n = 6$ )                                  | o        | o         | +                            | +                                     | +        |
| Herzog et al. (1990)<br>Yoga mediation <i>PET</i> ( $n = 8$ )                                       | o        | o         | o                            | o                                     | o        |
| Jevning et al. (1996)<br>Meditation (long-term) <i>Cerebral Blood Flow Impedance</i>                | x        | +         | +                            | x                                     | o        |
| Lazar et al. (2000)<br>Meditation <i>fMRI</i> ( $n = 5$ )   | +        | o         | o                            | +                                     | o        |
| Lehmann et al. (2001)<br>Mediation (self-dissolution) <i>EEG gamma tomography</i> ( $n = 1$ )       | o        | o         | +                            | o                                     | o        |
| Lou et al. (1999)<br>Meditation (abstract joy) <i>PET</i> ( $n = 9$ )                               | +        | +         | o                            | o                                     | +        |
| Newberg et al. (2001)<br>Meditation <i>SPECT ROI</i> ( $n = 8$ )                                    | o        | o         | +                            | +                                     | o        |
| Persinger (1984a, 1984b)<br>Mediation/glossalia <i>EEG</i> ( $n = 2$ )                              | +        | o         | o                            | x                                     | x        |

<sup>a</sup> Note. Symbols refer to activation (+); no change (o); not measured (x).

at least half of the studies showed activations in the former regions as compared to less than half in the latter regions (see Table 2). Except for the prefrontal cortex, the areas activated during meditation are also very active during dreams (see Section 3.2.2), an indication that the prefrontal activation may be at least partly related to the intense focusing of attention during meditation (Newberg & Iversen, 2003).

In terms of laterality, functional imaging, electrophysiological, and behavioral findings have not yet clearly demonstrated a greater involvement of one hemisphere versus the other during religious behavior. Although Bear and Fedio (1977) argued that hyperreligiosity is more likely to occur in left-sided TLE, their findings were only marginally significant and subsequent replications have not consistently demonstrated the left-sided bias (see review by Csernansky, Leiderman, Mandabach, & Moses, 1990). More recently, however, Wuerfel et al. (2004) found a significant correlation between reduced right (but not left) hippocampal volume and religiosity scores in TLE, and Britton and Bootzin (2004) confirmed that left-temporal epileptiform activity is more likely to be associated with transcendental (“near-death”) experiences. Aftanas and Golocheikine (2001) and Newberg et al. (2001) observed a greater activation of the left prefrontal cortex during meditation, but Lehmann et al. (2001) observed greater right-frontal activation and the other meditation studies either did not investigate laterality trends or did not report consistent hemispheric asymmetries in brain activity. In further support of the left-hemisphere-religiosity link is the subtle right-hemispheric dysfunction in normals with either paranormal or even traditional religious beliefs (Fenwick et al., 1985). Whereas 47% and 35% of Fenwick et al.’s paranormal and religious groups, respectively, showed evidence of right-hemispheric impairment, not a single subject in either group showed evidence of reduced left-hemispheric activity. This is consistent with the results of at least one behavioral study suggesting schizotypy—related to both religiosity and paranormal beliefs—reflects a selective activation of the left hemisphere (Raine & Manders, 1988).

Other behavioral studies have inferred greater right-hemispheric activity in clinically normal individuals disposed to magical ideation and paranormal beliefs (e.g., Barnett & Corballis, 2002; Brugger, Gamma, Muri, Schafer, & Taylor, 1993; Leonhard & Brugger, 1998; Mohr et al., 2001; Mohr, Rohrenbach, Laska, & Brugger, 2001; Persinger, 1993, 1994; Taylor et al., 2002), but most of these results are difficult to interpret. Some of the above studies (e.g., Brugger et al., 1993; Taylor et al., 2002) assessed laterality using measures of parietal-lobe function, such as lateralized visuospatial attention. Evidence of relatively diminished left-parietal activity

during spiritual experiences and practice is actually consistent with heightened activity in the left lateral frontal area, due to reciprocal inhibition of the extrapersonal (frontal) and peripersonal (parietal) systems (see D'Aquili & Newberg, 1993). Use of lateralized olfactory performance to infer greater right-hemispheric activation in paranormally inclined populations (Mohr et al., 2001) is also somewhat problematic in that the higher-order projections of the olfactory system show both contralateral and ipsilateral predominance in humans, depending on the specific brain region activated (Savic & Gulyas, 2000). The observation of Persinger (1994) that presences are more likely to be reported in the left visual field is also of limited value, because his patients evidently suffered at least mild brain trauma, whose lateralization was never specified.<sup>7</sup> Finally, the notion that mixed-handedness (i.e., reduced left-hemispheric dominance) is more likely to be associated with paranormal ideas (Barnett & Corballis, 2002) is somewhat contradicted by the finding that mixed-handers are less likely to believe in religious dogma such as Creationism (Niebauer, Christman, & Reid, 2002).

### 3.3.3. *Neurochemistry of religious activity*

The literature concerning the neurochemistry of religious behavior, including meditation and trances and mystical experiences, has mainly focused on the role of DA and 5-HT, while more limited evidence exists concerning the roles of ACh, NE, and a variety of other transmitters in religious activity.

In a recent functional imaging study, Kjaer et al. (2002) provided direct evidence for activation of DA receptors in the striatum during meditation using [<sup>11</sup>C]raclopride, which attaches to DA receptors. A significant (7.9%) decrease in binding of injected [<sup>11</sup>C]raclopride during meditation was attributed to the fact that DA receptors were more greatly occupied in the meditative relative to control periods.<sup>8</sup> Kawai et al. (2001) showed an increase in both DA and NE (as well as beta-endorphin) during Balinese religious trances, but this could have been due to the fact that their subjects were quite active during the ceremony. Joseph et al. (1981) and Swinyard et al. (1974) showed reductions in adrenaline or in the enzyme that transforms DA to NE (dopamine *B*-hydroxylase), which when diminished leads to higher DA activity and lowered NE activity (Robinson, Schutz, Macciardi, White, & Holden, 2001). By contrast, Infante et al. (2001) showed a significant decrease of NE levels but no overall change in DA levels in regular practitioners of transcendental meditation, because DA levels were elevated in the evening but decreased in the morning in the meditation group. This result was similar to that of Bujatti and Riederer (1976), who observed a decrease in vanillic-mandelic acid (the major metabolite of NE) but no change in homovanillic acid (the major metabolite of DA).

The reports of elevated DA during meditation and trance states are consistent with the auditory and visual hallucinations and the heightened awareness of environmental stimuli found in these states (Buckley, 1981; Castillo, 2003), both of which are found in other hyperdopaminergic states (Kapur, 2003). It is also in line with the faster perceived passage of time during transcendental experiences (Goodman, 2002), given that DA is known to speed up the internal clock (Meck, 1996). Finally, it is consistent with the finding of Comings, Gonzales, Saucier, Johnson, and MacMurray (2000) that “spiritual acceptance” is by far the most highly correlated ( $p < .001$ ) personality trait with the number of repeat alleles of the dopamine D<sub>4</sub> receptor gene (DRD4).

Inhibition of 5-HT activity may also be an important in fostering religious experience. In a recent brain imaging study, Borg, Andree, Soderstrom, and Farde (2003) showed that reduced 5-HT receptor density, as reflected in serotonergic binding, correlated inversely in both cortical and subcortical regions with scores on “self-transcendence,” a personality trait associated with spirituality. Serotonergic deficiencies appear to be associated with extreme religious beliefs and practices that resemble OCD symptoms (Fallon et al., 1990), and drugs with predominantly anti-serotonergic influences readily create mystical states and religious experiences (see reviews by Batson & Ventis, 1982, Chapter 4; Goodman, 2002; Mandell, 1980; Pahnke, 1969). Many such drugs—including peyote (mescaline) and ayahuasca—are widely used by Native Americans in their religious rituals (Appel & Callahan, 1989; Riba et al., 2002). However, one study (Bujatti & Riederer, 1976) that actually measured 5-HT levels during meditation reported an increase in 5-hydroxyindole-3-acetic acid (the major metabolite of 5-HT) during and after meditation.

<sup>7</sup> Based on other studies (e.g., Ardila & Gomez, 1988), it is likely that the sensed presence actually was associated with right-hemispheric damage, left-sided neglect, and *left-hemispheric activation*.

<sup>8</sup> The 7.9% decrease in DA binding potential is much greater than than the 4% average difference observed between the left and right hemispheres (Larisch et al., 1998) and is believed to represent an increase in endogenous DA release of 65% (Kjaer et al., 2002).

The role of acetylcholine in religious activity is less certain. The evidence for elevated ACh or acetylcholinesterase during meditation is mixed (Joseph et al., 1981; Udupa, Singh, & Yadav, 1973), and both cholinergic activation and de-activation caused by pharmacological agents can lead to intense religious experiences (Perry & Perry, 1995; Sarter & Bruno, 1998). However, anti-ACh (particularly antimuscarinic) hallucinogenic agents from various plant sources such as jimson weed have been more widely used in religious and magical ceremonies throughout history (Perry & Perry, 1995).

The role of ketamine and PCP in mystical experiences further illuminates the role of the major transmitters in religious experience. Ketamine and PCP are known to affect multiple transmitter systems, principally as glutamatergic antagonists, that in the end stimulate DA transmission (Deutsch, Mastropaolo, Schwartz, Rosse, & Morihisa, 1989; Olney & Farber, 1995). These drugs also strongly affect 5-HT transmission, but their action is complicated (Aghajanian & Marek, 2000; Kapur & Seeman, 2002), and they are also believed to modulate DA activity by their actions on cholinergic and sigma receptors (Ault & Werling, 1999; Castellani, Giannini, & Adams, 1982). These drugs are powerful hallucinogens that frequently induce mystical and out-of-body effects (Hansen et al., 1988), perhaps even more so than classical stimulants such as cocaine (Rosse et al., 1994), and their actions constitute a leading pharmacological model of schizophrenia (Deutsch et al., 1989; Olney & Farber, 1995; Rosse et al., 1994). The delusions and hallucinations produced by these drugs are greatly reduced both by DA antagonists (e.g., haloperidol) and the cholinesterase-inhibiting (and ACh-enhancing) drug physostigmine (Castellani et al., 1982), which is consistent with the putative role of ACh in inhibiting DA-induced hallucinations (Mandell, 1980; Yeomans, 1995).<sup>9</sup>

Additional evidence for the role of DA in religion is the effect of DA agents on paranormal beliefs and related behaviors (e.g., superstitions). Krummenacher, Brugger, Fahti, and Mohr (2002) demonstrated that the DA-precursor L-dopa administered to skeptics decreased their perceptual sensitivity to the level of paranormal believers. The reduced perceptual sensitivity caused by L-dopa is hypothesized to occur because of an increase in “internal noise” that distorts the actual extrapersonal sensory input. The greater effect of L-dopa on the skeptical subjects was interpreted as due to a ceiling effect in the paranormal group caused by their reputedly high baseline DA levels (Krummenacher et al., 2002). This finding is consistent with the hypothesis that DA produces less constrained firing patterns in mesolimbic neurons and promotes internal noise, loosened associations, and superstitious beliefs (Shaner, 1999), a hallmark of paranormal thought (Brugger, 2001; Brugger, Dowdy, & Graves, 1994).

Paranormal believers are more likely than others to believe in their power to control events, consistent with the critical role of DA in maintaining control over the external environment in challenging situations (Previc, 2004), and they also correspondingly underestimate the role of chance (Blackmore & Troscianko, 1985; Brugger & Graves, 1997; Brugger, Landis, & Regard, 1990; Brugger, Regard, & Landis, 1991). Even the average person is likely to develop superstitious beliefs in certain paradigms in which the reinforcement contingencies are sporadic, random or otherwise not readily apparent, such as differential reinforcement of low rates of responding or response-independent (e.g., variable-interval) reinforcement schedules (Brugger & Graves, 1997; Ono, 1987). In rodents encountering such schedules, superstitious or stereotypical behaviors occur after amphetamine administration, especially after DA-inhibitory inputs from the prefrontal cortex are removed (Sokolowski & Salamone, 1994; Wiley, Compton, & Golden, 2000). Superstitious behavior is also much easier to elicit in avians than rodents (Davenport & Holloway, 1980), possibly because of the higher DA content of the avian brain (see Previc, 1999). Finally, superstitious behavior is greatly increased following hippocampal lesions (Davenport & Holloway, 1980), arguably because of the loss of the normal inhibitory influence of the medial temporal lobe and its cholinergic and serotonergic signal processing on mesolimbic DA activity (see Gray et al., 1991; Weiner, 2003).<sup>10</sup>

<sup>9</sup> The fact that PCP leads to more powerful mystical experiences than cocaine could be due to the fact that cocaine also alters the re-uptake of NE (see earlier section) or to PCP's stimulation of primarily medial DA systems by means a variety of indirect routes (e.g., glutamatergic, serotonergic, and cholinergic interactions).

<sup>10</sup> Dopamine-inspired insensitivity to actual feedback from the distal environment is also manifested in the effects of hippocampal lesions, DA excitation, and 5-HT depletion to all decrease the contrasting phenomenon known as latent inhibition—i.e., the effect of a previous non-reinforced stimulus to delay conditioning when subsequently paired with a reinforcer (Gray et al., 1991; Weiner, 2003). Interestingly, the effect of DA-blocking drugs to enhance latent inhibition occurs mainly for those with schizotypal/paranormal inclinations and presumably high DA levels to begin with (Kumari et al., 1999; Williams et al., 1997).

One final piece of evidence indirectly suggests an involvement of DA—or at least a relative increase in DA and ACh relative to NE and 5-HT—in meditation and other religious behaviors in normal individuals. Most studies (e.g., Bowman et al., 1997; Hoffman et al., 1982; Joseph et al., 1981; Newberg & Iversen, 2003; Schuman, 1980) have shown that meditation leads to an increase in primarily parasympathetic activity in the autonomic nervous system, reflected in lowered heart rate, blood pressure, and core body temperature. Similarities between the use of meditation and DA-enhancing drugs in controlling hypertension have even been noted (*British Medical Journal*, 1976). The DA-mediated parasympathetic effect is consistent with the increase in parasympathetic activity during sleep and dreaming (Miller & Horvath, 1976), depersonalization reactions (Sierra & Berrios, 1998), and possibly schizophrenia (Kudoh, Ishihara, & Matsuki, 1999). The contribution of DA to elevated parasympathetic tone is further consistent with the paramount role of the DA-rich left hemisphere both in parasympathetic activation (Oppenheimer, Gelb, Girvin, & Hachinski, 1992; Previc, 1996; Zamrini et al., 1990) and in dreaming, hallucinations, and schizophrenia (see Section 3.2). It is possible that elevated ACh may contribute to the increased parasympathetic tone, but as noted earlier, the evidence for elevated ACh or acetylcholinesterase during meditation is mixed (Joseph et al., 1981; Udupa et al., 1973).

### 3.4. Summary

A review of the neuroanatomy and neurochemistry of dreaming, hallucinations, and religious beliefs, practices and experiences in normal humans indicates that there may be a common neural substrate of all behavioral phenomena that reflect a predominance of extrapersonal brain system activity and a reduction of bodily (self-oriented) activity (see also D'Aquili & Newberg, 1993). In terms of their neuroanatomy, dreams, hallucinations, and religious experiences may all be mediated by ventromedial (cortico-limbic) pathways extending from the medial temporal lobe to the anterior cingulate and prefrontal cortex. Conversely, there appears to be little activation or even de-activation of the parietal-occipital areas during these phenomena. There may be additional involvement of the lateral prefrontal cortex during certain spiritual practices such as meditation and possibly some depersonalization/out-of-body reactions, which suggests a greater conscious control in these situations than in the case of dreams and hallucinogenic states. A greater involvement of the left hemisphere has been demonstrated for dreams and hallucinations but not as convincingly for religious experience.

The most consistent neurochemical change associated with all of these behaviors is the elevation of DA, particularly in the ventromedial cortical areas. By contrast, ACh is elevated during dreaming, decreased during most hallucinations, and inconsistently affected during meditation, while NE transmission is reduced during dreaming, largely unaffected during hallucinations, and possibly decreased during religious behaviors. Serotonin is also decreased during dreaming, hallucinations, and mystical behavior, but direct empirical evidence for its role in religious activity is not as impressive as for DA.<sup>11</sup>

The above evidence from normal subjects suggests that elevated DA in the ventromedial cortex and striatum plays a major role in religious experiences. However, much more evidence needs to be obtained concerning the neuroanatomy of religious and paranormal beliefs, as lesion data in these areas is almost totally lacking. The theory presented here suggests that there should be positive relationships among paranormal beliefs, paranormal behaviors (e.g., superstitious behaviors, misattribution of chance results), and upward/

<sup>11</sup> It has been argued that activation of DA-rich fronto-temporal regions during meditation and other religious activities may be related to the pleasurable nature of these activities (D'Aquili & Newberg, 1993). It is well-documented that DA is associated with sexual behavior (Blackburn et al., 1992) and the pleasurable sensations associated with brain self-stimulation and cocaine ingestion (Volkow, Fowler, & Wang, 2002), and many religious rituals are intertwined with fertility or other sexual themes (Alper, 2001). However, religious obsessions certainly cannot be described as pleasant, just as other obsessions and addiction itself are associated with disturbing thoughts and anhedonia over time (Peoples, 2002). Indeed, religious practice in many cultures is anxiety-producing (Boyer, 2001; Pfeifer & Waeltly, 1995), despite its overall positive rating. Also, religious experiences can be both ecstatic and terrifying, and religious delusions with ecstatic themes are reputedly rare in clinical disorders such as temporal-lobe epilepsy (Morgan, 1990; but see Mandell, 1980). Finally, it has already been noted earlier that DA's role in reward behavior has less to do with hedonic aspects than with attending to distal, motivationally salient stimuli.

extrapersonal biases in bisection and other perceptual–motor tasks. It further predicts that an increase in the ratio of 5-HT to DA and/or lesions of the ventral pathways (particularly on the left side) should decrease all of the above behaviors, whereas an increase in the DA to 5-HT ratio and/or lesions to the dorsal pathways (particularly on the right side) should increase them.

In the next section, research concerning religious experiences and practices in clinical disorders will be presented, which will further confirm the important relationship between religion, DA, and the extrapersonal brain pathways.

#### 4. Religiosity in selected clinical disorders and its relationship to the extrapersonal brain pathways

Although, religion is associated with a normal psychological profile in the vast majority of practitioners, an elevated level of religiosity has been noted in clinical populations dating back to antiquity. For example, the original meaning of the Hebrew word “nabi” (“those carried away by religious visions”) was “insanity” (Herschel, as cited in Goldwert, 1993). Similarly, the ancient Greeks viewed epilepsy as a “sacred disease” brought about by a visitation from the Gods (Saver & Rabin, 1997).

The four clinical disorders most studied in terms of religious activity are bipolar disorder (mania/hypomania), OCD, schizophrenia, and TLE. All of these disorders are associated with heightened religiosity, religious experiences, and/or religious practices. One disorder—Alzheimer’s disease—associated with degeneration of the ACh-rich medial and superior/lateral temporal lobe—is reputedly associated with reduced religiosity (Saver & Rabin, 1997), although there are no published data to support this conclusion.

##### 4.1. *Mania, obsessive-compulsive-disorder, schizophrenia, and temporal-lobe epilepsy: General relationships and underlying pathology*

Bipolar mania, OCD schizophrenia, and TLE psychosis have a high degree of genetic, epidemiological, and behavioral linkage (Bearden, Hoffman, & Cannon, 2001; Sachdev, 1998). For example, psychotic delusions are a common feature of mania, TLE psychosis, and paranoid schizophrenia, which makes it difficult to distinguish them in the acute phase (Gonzalez-Pinto et al., 1998; Sachdev, 1998). All of these disorders are to varying degrees associated with overactivity of the fronto-temporal pathways (mostly on the left side), elevated DA, and a bias toward extrapersonal space. In line with the roles of testosterone and estrogen to facilitate and inhibit, respectively, brain DA levels (Hull et al., 1999; Lindamer, Lohr, Harris, & Jeste, 1997), males are more likely to develop severe schizophrenic symptoms (Aleman, Kahn, & Selten, 2003), TLE (Briellmann, Berkovic, & Jackson, 2000), and mania (Leibenluft, 1996), along with an earlier onset of OCD (Castle, Deale, & Marks, 1995; Noshirvani, Kasvikis, Marks, Tsakiris, & Monteiro, 1991).

Paranoid schizophrenia bears the closest relationship to TLE, occurring in up to 10% of postical or interictal (between-seizure) periods, with the seizures and psychotic symptoms frequently alternating (Hyde & Weinberger, 1997; McAllister, 1998; Sachdev, 1998; Sherwin, 1984). Both disorders involve physical damage and/or heightened electrical activity in the medial-basal temporal lobe, although these are greater in the case of TLE (Hyde & Weinberger, 1997). Bipolar mania and OCD show an overlap in the 10–15% range (Freeman, Freeman, & McElroy, 2002), which is far greater than their respective occurrences in the general population. The probability of having delusions, hallucinations, and other schizophrenic symptoms in conjunction with OCD is 14% (Eisen & Rasmussen, 1993), while the probability of having OCD symptoms in schizophrenia is at least 10% (Fabisch, Fabisch, Langs, Huber, & Zapotoczky, 2001; Reznik & Sirota, 2000); again, these overlaps are far higher than the percentages of OCD and schizophrenia in the general population (1–2%). Epilepsy and OCD are less strongly linked, although TLE and, in some cases, anterior-cingulate epilepsy do present OCD symptoms (Bear & Fedio, 1977; Kettle & Marks, 1986; Levin & Duchowny, 1991; Sorenson et al., 1989). Bipolar mania and epilepsy exhibit the lowest co-morbidity (Kanemoto, 1995), which makes sense in that mania is arguably the disorder most predominantly linked to neurochemical imbalances whereas TLE is the disorder most closely tied to neuroanatomical damage.

Mania, schizophrenia, TLE, and OCD are all associated with activation of the frontal and/or temporal pathways, with mania and OCD involving primarily a greater frontal lobe and cingulate activation (Adler et al., 2000; Blumberg et al., 2000; Joseph, 1999) and chronic schizophrenia and TLE involving greater temporal-lobe activation (Bogerts, 1997; Gur & Chin, 1997). There is certainly no evidence for reduced dorsolateral prefrontal cortical function in OCD and mania (Abbruzzese, Ferri, & Scarone, 1995; Adler et al., 2000; Rosenberg et al., 1997), as has been alleged for schizophrenia (Bunney & Bunney, 2000; Joseph, 1999). Nor is there any widespread evidence of temporal-lobe overactivation or dysfunction in OCD and mania (Bearden et al., 2001), as in schizophrenia and TLE. There is also little evidence for parietal or other dorsal overactivation in any of these disorders; rather, parietal-lobe activity may actually be diminished in schizophrenia (Buchanan, Kirkpatrick, Heinrichs, & Carpenter, 1990) and during schizophrenic hallucinations (Cleghorn et al., 1992). Moreover, psychosis is rarely a consequence of epilepsy originating outside of the temporal lobe (McAllister, 1998; Sherwin, 1984).

The bizarre hallucinations and delusions (including depersonalizations and body-schema distortions) associated with these four disorders reflect their greater affinity to extrapersonal than to peripersonal space. Schizophrenia is the best-studied disorder in this regard, and the upward ocular deviations (Thornton & McKenna, 1994), upper-field hallucinations (Bracha, Cabrera, Karson, & Bigelow, 1985), flattened appearance of the world (Chapman, 1966), and neglect of proprioceptive and other signals emanating from the body (Bick & Kinsbourne, 1987; Frith, Blakemore, & Wolpert, 2000) all suggest an excessive orientation toward distant space (Previc, 1993). An upward conjugate deviation of the eyes (“oculogyric crisis”) is also a prominent feature of seizures (Rosenow et al., 1998) and Tourette’s syndrome (Frankel & Cummings, 1984), a hyperdop-aminergic disorder closely related to OCD. In OCD and mania, the heightened motivation and goal-directedness—“deranged planning,” according to Boyer (2001)—further reflect a heightened concern or anxiety about future (temporally distant) events.

The neural changes in schizophrenia, TLE, and mania also interact with and, to varying degrees, resemble the mechanisms of REM sleep, in which NE and 5-HT activity is diminished relative to that of DA and ACh. Seizures decrease the amount of subsequent REM sleep, presumably because they produce a compensatory increase in low pre-seizure levels of NE and 5-HT (Pompeiano, 1969). Schizophrenia is associated with a shorter REM latency (Gillin, 1983), which is consistent with a compounding of relative DA and ACh activation in REM by a similar neurochemical imbalance in schizophrenia. The similarities between the positive symptoms of schizophrenia and dreaming and hallucinations, in which a similar predominance of DA over 5-HT occurs, have been noted by many researchers (Gottesmann, 2002; Hobson, 1996; Kleinman, Gillin, & Wyatt, 1977; Tamminga et al., 2000; Vollenweider & Geyer, 2001). Finally, sleeplessness and bizarre dreaming also characterize hypomania (Beauchemin & Hays, 1995), with the elevated NE found in this disorder presumably decreasing the need for REM sleep and the elevated DA responsible for the bizarre dreams.

As originally formulated by Flor-Henry and colleagues in the late 1970s (see Flor-Henry, 1986), all of these disorders predominantly involve overactivation of the DA-rich left hemisphere. Certainly, TLE predominantly afflicts the left hemisphere, because large-scale investigations and reviews have documented between a 2:1 and 4:1 predominance of left-sided over right-sided temporal-lobe seizures (Cutting, 1990; McAllister, 1998; Sherwin, 1984; Toone, 1981; Trimble, 1984). The notion of a left-hemispheric overactivation for at least the positive symptoms of schizophrenia (delusions, hallucinations, and thought disorder) has consistently been supported by comprehensive reviews of the functional imaging and brain lesion literatures over the past two decades (Bogerts, 1997; Cutting, 1990, Chapter 19; Gruzelier, 1999; Gur & Chin, 1999; Rotenberg, 1994), and this view is consistent with the greater right-field (left-hemispheric) locus of schizophrenic visual and auditory hallucinations (Bracha et al., 1985; Nayani & David, 1996; Sommer, Aleman, & Kahn, 2003). The overactivation of the left hemisphere in TLE and schizophrenia is particularly interesting in that left-sided lesions to treat TLE are relatively more successful in diminishing psychotic symptoms than are right-sided lesions (Sachdev, 1998; Sherwin, 1984; Stevens, 1990). The relative right-hemispheric underactivation is consistent with schizophrenic deficits in emotional interpretation, prosody, proverb interpretation, global processing, and space perception (Carpenter & Chapman, 1982; Cutting, 1990, Chapter 20; Goodarzi, Wykes, & Hemsley, 2000; Mitchell & Crow, 2005; Rotenberg, 1994), processes dependent on right-hemispheric function (Perry et al., 2001; Wymer, Lindman, & Booksh,

2002; Weintraub & Mesulam, 1983).<sup>12</sup> Evidence for a relatively greater left-hemispheric activation in mania is also provided by numerous lesion and functional imaging studies (Blumberg et al., 2000; Braun, Larocque, Daigneault, & Montour-Proulx, 1999; Cummings, 1997; Cutting, 1990; Joseph, 1999; Robinson, Boston, Starkstein, & Price, 1988), although not all researchers accept the notion of left-hemispheric overactivation (Bearden et al., 2001). Finally, despite early indications of left-hemispheric overactivation in OCD (Flor-Henry, Yeudall, Koles, & Howarth, 1979), the literature on OCD lateralization remains inconclusive. Although one review concluded on the basis of functional brain imaging and behavioral data that left-hemispheric overactivation is present in OCD (Otto, 1992), a more recent meta-analysis of the functional imaging literature (Whiteside, Port, & Abramowitz, 2004) did not find a clear lateralization trend.

Excessive DA levels are found in all of these disorders, with the possible exception of TLE. Schizophrenia, at least as regards its positive symptoms, has classically been viewed as a hyperdopaminergic disorder (see Gray et al., 1991; Kapur, 2003; Swerdlow & Koob, 1987, for key reviews). However, the recent therapeutic successes with atypical antipsychotic drugs that affect a variety of other neurotransmitter systems demonstrate that other neurotransmitters (especially 5-HT) may be important in schizophrenia as well (see Vollenweider & Geyer, 2001). Mania is generally associated with elevated NE and DA, with DA precursors and agonists potentiating manic symptoms and DA antagonists offering therapeutic value (DePue & Iacono, 1989; Freeman et al., 2002; Goodwin & Jamison, 1990, Chapter 17; Swerdlow & Koob, 1987). A common mechanism for a variety of drugs that are effective against mania is the inhibition of DA transmission, even when the direct effect of the drug may be on a different system, such as the cholinergic one (Bymaster & Felder, 2002). Elevated DA levels are also present in OCD and Tourette's syndrome (Carpenter, McDougle, Epperson, & Price, 1996; Goodman et al., 1990; Micallef & Blin, 2001; Rosenberg & Keshavan, 1998), and DA overactivation is known to produce stereotypy in animals (Ridley & Baker, 1982), which is considered the single-best animal model for these disorders (Szechtman, Culver, & Eilam, 1999). Although 5-HT re-uptake blockers are currently the most commonly used therapeutic agents against OCD, anti-DA drugs (and especially the atypical DA blockers) are also effective in treating this disorder (Carpenter et al., 1996; Goodman et al., 1990; Micallef & Blin, 2001).

The relationship between DA levels and TLE is more complex than in the case of the other three disorders. Dopamine generally exerts an anticonvulsant action, although this is true more for the D<sub>2</sub> receptor than the D<sub>1</sub> receptor, which has proconvulsant properties (Starr, 1996). Dopamine levels are more elevated in the brains of those with mesial TLE than in those with neocortical TLE (Pacia, Doyle, & Broderick, 2001), but the significance of this finding is not clear. One hypothesis is that the anticonvulsant action of DA is mounted to counteract the seizure, just as seizures trigger elevations in NE and 5-HT and subsequently diminish REM activity (Pompeiano, 1969). Dopamine then remains elevated during the interictal and postictal periods, thereby triggering psychoses that can be successfully treated by DA antagonists such as haloperidol (Kanemoto, Kawasaki, & Kawai, 1996; So, Savard, Andermann, Olivier, & Quesnay, 1990).

The role of the other three major neurotransmitters is less consistent in these four disorders than is that of DA. For example, NE is elevated in mania (Freeman et al., 2002; Goodwin & Jamison, 1990, Chapter 17), decreased in epilepsy (see Previc, 1996, for a review), and of uncertain status in schizophrenia and OCD—e.g., both clonidine, an  $\alpha$ -2 NE receptor agonist that acts to decrease synaptic NE levels as well as various antidepressants that boost NE transmission have been used to treat Tourette's syndrome (Jimenez-Jimenez & Garcia-Ruiz, 2001). Acetylcholine is also inconsistently involved, as elevated ACh levels counter mania

<sup>12</sup> Left-hemispheric overactivation in schizophrenia is not universally accepted, because schizophrenics can show left-hemispheric deficits on some perceptual tasks (e.g., Posner, Early, Reiman, Pardo, & Dhawan, 1988). However, some of these deficits may reflect reduced *parietal* function, which may be diminished in schizophrenia (Buchanan et al., 1990). The parietal deficits may be more evident on the right side because the left parietal lobe may be more inhibited by the left-ventral overactivation (e.g., the reciprocal frontal–parietal model discussed in Section 3.3.2 in reference to religiosity). Evidence of left-temporal atrophy in schizophrenia is also not indicative of underactivation of the left hemisphere, since chronic overactivation of the medial temporal lobe and hippocampus leads to long-term damage of these structures (McEwen, 2001). Finally, evidence of increased right-hemispheric activity in certain language areas suggests that, in addition to a general left-hemispheric overactivation, increases in “left-hemispheric”-type processing typified by schizophrenic deficits in social and communicative aspects of language may partly stem from an increase in DA levels—ordinarily higher in the left hemisphere—in *both* hemispheres (Sommer, Ramsey, & Kahn, 2001).

(Bymaster & Felder, 2002), potentiate seizures (see Previc, 1996, for a review), are positively associated with schizophrenic symptoms (Sarter & Bruno, 1998), and are of little relevance to OCD. Serotonin seems somewhat more consistently to be involved in all of these disorders, but in an opposite manner to DA. Serotonin levels are reduced in epilepsy (see Previc, 1996, for a review) and OCD (see Carpenter et al., 1996; Freeman et al., 2002; Micallef & Blin, 2001; Rosenberg & Keshavan, 1998), but their relationship to mania is less clear and consistent (Freeman et al., 2002). It is likely that deficits in 5-HT transmission contribute to the pathophysiology of schizophrenia (Joyce, 1993; Kapur & Remington, 1996; Vollenweider et al., 1999; Weiner, 2003), given that (1) positive symptoms of schizophrenia resemble dreams and hallucinogenic states, in which 5-HT activity is diminished, (2) 5-HT deficits probably contribute to the high rate of depression and suicide among schizophrenics (Joyce, 1993), and (3) drugs that increase 5-HT transmission have proven effective against depression and OCD in schizophrenia (Reznik & Sirota, 2000; Silver, 2001). Although atypical antipsychotics such as clozapine have 5-HT<sub>2</sub> receptor antagonist properties (Meltzer, 1989), it has previously been noted that antagonism at the 5-HT<sub>2</sub> receptor may actually increase overall synaptic 5-HT levels (Section 3.2.3).

In summary, the best characterization of mania, OCD, schizophrenia, and the psychosis of TLE is that they all reflect varying amounts and locations of frontal-temporal overactivity, they all show or have been postulated to show a left-hemispheric predominance, and they all reflect to varying degrees a heightened ratio of extrapersonal (DA) to peripersonal (5-HT) neurochemical activity.

#### *4.2. Religiosity in mania, obsessive-compulsive disorder, schizophrenia, and temporal-lobe epilepsy*

##### *4.2.1. Mania*

Although mania has been the least-studied of the four clinical disorders in relationship to religiosity, the limited evidence to date indicates that persons suffering from mania are much more likely than normals to profess a belief in major religious tenets (e.g., almost all report a belief in God and in Biblical miracles). Religious delusions and hallucinations were reported by 90% of bipolar manic patients in the survey of Brewerton (1994), and over half (55%) of the manic patients responded positively to the statement “I have had a personal religious experience” in the survey by Kroll and Sheehan (1989). In both cases, manic patients were second only to schizophrenics in their religious experiences and ranked ahead of patients with seizure disorders, depression, personality disorders, and anxiety disorders. In terms of delusions of grandiosity (e.g., the patient thinks they are the messiah or that God speaks through them), persons suffering from mania scored higher than any clinical population, including schizophrenics (Brewerton, 1994; Kroll & Sheehan, 1989). Manic patients also reportedly experience a 2.5-fold increase in religious conversions relative to normals (Gallemore, Wilson, & Rhoads, 1969).

##### *4.2.2. Obsessive-compulsive disorder*

The relationship between OCD and religiosity was the subject of Freud’s first essay on religion entitled “Obsessive Actions and Religious Practices” and a subject of a later book entitled “Totem and Taboo” (see Freud, 1961). There is undeniably at least a moderate relationship between OCD and religiosity, in that obsessive traits are much more common in highly religious persons, with correlations ranging from +.15 to +.40 (see review by Lewis, 1994). Finally, religious obsessions are very common in OCD, ranging from 5% to 30% in Europe, North America, and East Asia to ~50% in the Middle East (Tek & Ulug, 2001).

Whether there is an intrinsic relationship between religion and OCD is controversial, however. On the one hand, patients with religious obsessions do not fundamentally differ from those with nonreligious obsessions in terms of their religious practice and OCD symptoms (e.g., severity, frequency, and type) (Tek & Ulug, 2001) and their response to 5-HT re-uptake inhibitors (Fallon et al., 1990). On the other hand, patients with religious obsessions do tend to have more obsessions overall and to have higher loadings on magical ideation and related perceptual distortions (Tek & Ulug, 2001; Tolin, Abramowitz, Kozak, & Foa, 2001). Moreover, there are more features of OCD than any other psychological disorder found in religious rituals, and more OCD features are found in rituals than in other societal activities (Fiske & Haslam, 1997). Thus, it is reasonable to conclude that at least a mild relationship between obsessive-compulsive traits and religious practice and beliefs exists in the general population.

#### 4.2.3. Schizophrenia

Schizophrenia, especially of the paranoid variety, is the clinical disorder most clearly linked to hyperreligiosity. As noted earlier, there exist fundamental similarities between the mystical, meditative, and schizophrenic states (Buckley, 1981; Castillo, 2003). Schizophrenia is also the best-studied disorder, for which a voluminous literature exists concerning its neuroanatomical, neurochemical, and behavioral profiles. Because schizophrenia additionally represents the disorder most closely aligned with extrapersonal space, it is arguably the most valuable disorder for understanding the relationship between religious activity and extrapersonal brain mechanisms.

Both the surveys of Brewerton (1994) and Kroll and Sheehan (1989) found schizophrenics to have stronger religious beliefs and more religious experiences than normals.<sup>13</sup> Other researchers have also found a high percentage of schizophrenics with religious delusions (nine of 24, in Cothran & Harvey, 1986), a positive correlation between religious delusions, psychoticism and religiosity in schizophrenics (Feldman & Rust, 1989; Getz, Fleck, & Strakowski, 2001), or a larger number of schizophrenics in cult religions (Peters et al., 1999; Spencer, 1975). The playwright August Strindberg (Brugger, 2001) and the Nobel laureate and mathematician John Nash (Nasar, 1998) are two of the more famous schizophrenics reputed to have suffered religious delusions, a group that may have also included the prophet Ezekial (Goldwert, 1993). It must be reiterated, however, that the correlation between psychoticism and religiosity in the general population has consistently been shown to be negative (Francis & Wilcox, 1996; Maltby, 1997; Roman & Lester, 1999).

Schizophrenic religious delusions range from the “messiah complex” (Goldwert, 1993) to the “passivity” (alien-control) delusion, in which the schizophrenic feels his actions and thoughts to be controlled by God or some other powerful entity (Frith et al., 2000). In general, these experiences are part of what has long been regarded as a hallmark of schizophrenic thought—the emphasis on the mystical and cosmic:

“The cosmic experience is characteristic of schizophrenic experience. The end of the world is here, the twilight of the gods. A mighty revolution is at hand in which the patient plays a major role. He is the center of all that is coming to pass. He has immense tasks to perform, of vast powers. Fabulous distant influences, attractions, and obstructions are at work. ‘Everything’ is always involved: all the peoples of the earth, all men, all the gods, etc. The whole of human history is experienced at once. The patient lives through infinite millennia. The instant is an eternity to him. He sweeps through space with immense speed, to conduct mighty battles; he walks safely by the abyss” (Jaspers, 1964, p. 295).

As with schizophrenia in general, functional imaging studies point to a left-temporal predominance for delusions of a religious nature (Puri, Lekh, Nijran, Bagary, & Richardson, 2001). However, cultural and other factors determine to a great extent whether schizophrenic delusions take on a religious flavor or not. For example, grandiosity delusions may be supplanted with religious ones as the patient ages (Verdoux et al., 1998), religious delusions may give way to nonreligious ones as a society becomes less religious (Klaf & Hamilton, 1961), and (3) religious delusions may be much more common in more religious or magical societies (e.g., religious delusions are low in China but are higher in Korea and Jamaica and are significantly more prevalent among Protestants than Catholics) (Getz et al., 2001; Kim, Hwu et al., 2001; Ndeti & Vadher, 1985).

#### 4.2.4. Temporal-lobe epilepsy

The relationship between TLE and religiosity has been recognized scientifically since the mid-1800s, although informally the relationship dates back to antiquity. As reviewed by Saver and Rabin (1997), epilepsy is a disorder that has afflicted many of the greatest religious prophets and leaders throughout history.

The issue of religiosity and TLE was raised in 1970 by Dewhurst and Beard (1970), who reviewed the cases of six TLE patients who experienced sudden religious conversions. In an influential paper, Waxman and Geschwind (1975) considered the trait of hyperreligiosity to be a cardinal feature of interictal TLE, based on their own clinical experience. Bear and Fedio (1977) and Bear, Levin, Blumer, Chetham, and Reider (1982) later empirically confirmed that TLE is associated with hyperreligiosity and further argued the

<sup>13</sup> In Kroll and Sheehan’s study, 70% of schizophrenics claimed to have had a religious experience, with those schizophrenics with additional EEG abnormalities reporting the highest percentage of religious delusions.

hyperreligiosity was more likely to occur in left-sided TLE (but see Section 3.3.2). Kanemoto et al. (1996) further reported that a high percentage (23%) of religious delusions are associated with postictal psychosis in TLE. However, Tucker, Novelly, and Walker (1987) later questioned the specific link between hyperreligiosity and TLE, and it is certainly true that hyperreligiosity is common to other types of epilepsy (Kroll & Sheehan, 1989). Nevertheless, Csernansky et al. (1990) and Saver and Rabin (1997) both concluded from their reviews that the preponderance of studies have provided support for a greater hyperreligiosity in TLE. Moreover, Wuerfel et al. (2004) recently reported that religiosity in TLE is more likely to be accompanied by reduced medial-temporal (hippocampal) volumes on the right side, thereby confirming the original assertion of Bear and colleagues that religiosity is a function of greater left-sided activation.

#### 4.3. Summary

There is clear evidence of hyperreligiosity, albeit in varying degrees, in the four clinical disorders reviewed here that are affiliated with extrapersonal space. Table 3 contains a more complete depiction of the relationship between these disorders and the behavioral phenomena of dreaming, hallucinations, and religious experience/practice, on the one hand, and eight indicants of extrapersonally oriented brain function on the other. The eight extrapersonal criteria, extracted from the theoretical model presented of Previc (1998) and described in Section 3.1, are: (1) ventral frontal-temporal activation; (2) dorsal frontal–parietal relative deactivation; (3) & (4) elevated DA and ACh; (5) & (6) diminished NE and 5-HT; (7) upward spatial biases; and (8) left-hemispheric activation. The relationships are denoted as positive (+), negative (–), or uncertain because of inconsistent or insufficient data (?). For example, most hallucinations are associated with ventral cortical activation, left-hemispheric activation, DA activation, and 5-HT inhibition. They are also associated with ACh inhibition (hence, the minus sign in the ACh activation column), and an uncertain relationship with the upper visual field, noradrenergic activity, and dorsal cortical deactivation.

As evidenced, all of the disorders except mania prove positive for at least four of the eight extrapersonal signs. Schizophrenia represents the clinical disorder most convincingly tied to extrapersonal space, although other disorders may prove be more linked as additional data become available. Dreams clearly represent the most extrapersonally oriented of the three widespread phenomena (i.e., dreams, hallucinations, and religious behavior), with religious activity less stringently linked to extrapersonal space mainly because of incomplete or equivocal data for four of the eight extrapersonal criteria. Overall, only the inhibitory role of ACh in hallucinations and mania clearly differ from their predicted extrapersonal roles, but that may partly stem from the inhibitory action of ACh systems over DA systems. Elevated NE in mania also contradicts its putative personal role, but there is no evidence that NE contributes to the delusions and hallucinations often found in mania.

### 5. Religious activity in relation to the evolution of the extrapersonal systems in humans

The evolution of religion in modern humans remains poorly understood. Primitive religious concepts (such as the concept of death) were already present in *Homo Sapiens Neanderthalis*, while the first clear evidence of

Table 3  
Various functions and extrapersonal brain activity<sup>a</sup>

|  | Ventral cortex ↑ | Dorsal cortex ↓ | DA ↑ | ACh ↑ | NE ↓ | 5-HT ↓ | UVF bias | LH > RH |
|--|------------------|-----------------|------|-------|------|--------|----------|---------|
| Extrapersonal spatial interaction (Previc, 1998) | +                | +               | +    | +     | +    | +      | +        | +       |
| Dreaming   | +                | +               | +    | +     | +    | +      | +        | +       |
| Hallucinations                                   | +                | ?               | +    | –     | ?    | +      | ?        | +       |
| Religious belief/ experience/practice            | +                | ?               | +    | ?     | ?    | +      | +        | ?       |
| Mania  | +                | ?               | +    | –     | –    | ?      | ?        | +       |
| Obsessive- compulsive disorder                   | +                | ?               | +    | ?     | ?    | +      | ?        | ?       |
| Schizophrenia                                    | +                | +               | +    | +     | ?    | +      | +        | +       |
| Temporal-lobe epilepsy                           | +                | ?               | ?    | +     | +    | +      | ?        | +       |

<sup>a</sup> Note. Symbols refer to: supportive evidence (+); conflicting evidence (–); and evidence unclear or not sufficiently general (?).

mythical creatures in cave drawings (e.g., half-man; half-god) appeared approximately 40,000 years ago (Mithen, 1996). The origin of religion has been postulated to coincide with the beginnings of advanced tool making and art, in what has been termed the human evolutionary “Big Bang” (Mithen, 1996). More recent findings push the beginnings of symbolic drawings and advanced tool-making to 77,000 years ago (McBrearty & Brooks, 2000), but there is still no evidence of religious art dating back this far.

The oldest examples of supernatural art in cave paintings are mythical animals that were drawn as part human or as a composite of two or more animals (Mithen, 1996). It is likely that the earliest religious themes and customs dealt with predation, as is still the case with many current hunter-gatherer populations (Boyer, 2001). The emergence of cosmological/celestial religions emerged later, although the “dreamtime” and “sky-world” concepts date back to ancient Australian aboriginal practices (Charlesworth, 1992).

The gap that exists between the development of anatomically modern humans—now placed at ~200,000 years ago (McDougall, Brown, & Fleagle, 2005)—and the “Big Bang” (whether that be 50,000 or 80,000 years ago) raises the possibility that other factors besides brain size and shape may have played a role in the evolution of all human culture, including religion. A recent evolutionary theory (Previc, 1999) proposed that the driving force behind the attainment of the modern human intellect was an expansion of dopaminergic brain systems. This expansion began early in primate evolution and produced a more homogenous distribution of DA throughout the brain, particularly in its upper layers where relatively more intracortical circuitry is housed (Berger, Gaspar, & Verney, 1991). One reflection of the continued expansion of DA systems in humans is the large increase (near-doubling, relative to body weight) of the DA-rich neostriatum of humans relative to chimpanzees (Rapoport, 1990), who spend the majority of their day in peripersonal activities (Wrangham, 1977; as cited in Whiten, 1990). In contrast to the DA expansion, other key neurotransmitter systems such as glutamate and acetylcholine have remained the same or even decreased in relative terms during human evolution (Perry & Perry, 1995; Rapoport, 1990).

The initial rise of DA during hominid evolution coincided with and helped lead to an increased tolerance to heat (Previc, 1999). A precursor to the final stages of human brain evolution about 100,000 years ago appears to have been an increase in the consumption of shellfish and other marine fauna (Crawford et al., 1999; Dobson, 1998; McBrearty & Brooks, 2000), which are rich in essential fatty acids and iodine that stimulate DA activity, overall brain development, and human intellectual achievement (Previc, 2002; Wainwright, 2002).

The final expansion of DA could have prompted the rise in abstract reasoning, human creativity in the form of art and music, and religious behavior. There is no convincing evidence that any of these intellectual capabilities were directly selected for in and of themselves, independent of the generic DA expansion. Both abstract reasoning and religious thought involve an emphasis on nonvisible (distant) space and time, and both are linked to the upper field (see Kinsbourne, 1972; Previc & Murphy, 1997; Previc et al., 2005; and Section 3.2).<sup>14</sup> The final DA expansion may have also led to the onset of clinical disorders in which DA is overactive, such as schizophrenia. Horrobin (1998), among others, has argued that the same processes that led to schizophrenia must have led to advances in human reasoning and religion, because of the higher incidence of creativity and religiosity in first-degree relatives of schizophrenics (Karlsson, 1974). It might seem strange that “genius and madness” should be so closely linked, especially since the intellectual quotient of schizophrenics is generally below normal (Crawford et al., 1993). However, one needs to consider the higher (sometimes extremely high) premorbid intellectual capability of many schizophrenics (Crawford et al., 1993; Isohanni, Jarvelin, Jones, Jokelainen, & Isohanni, 1999), the better relationship between the “positive,” DA-linked symptoms of schizophrenia and intelligence (Frith, 1996), the high prevalence of “giftedness” found in families of schizophrenics (Karlsson, 1974), and the positive relationship between mania and intellectual achievement (Goodwin & Jamison, 1990, Chapter 14).

It might also seem strange that two ostensibly antagonistic processes—religious behavior and abstract (scientific) reasoning—may have co-evolved. However, both phenomena are concerned with abstract concepts and comprehensive frameworks with which to comprehend spatio-temporal events in the external environment. One of these processes (abstract reasoning) is clearly left hemispheric (see Previc, 1999), while the other

<sup>14</sup> The fact that *Homo Sapiens Sapiens* built their cave dwellings on much higher ground than did *Homo Sapiens Neanderthalis* (Apsell, 1997) is an indication of a greater exploitation and valuation of upper space in the final stages of human evolution.

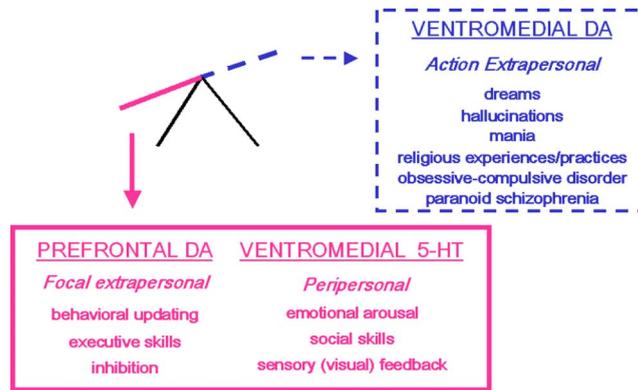


Fig. 3. The balance of brain activity during dreams, hallucinations, religious experience and paranormal behaviors, and various clinical disorders associated with hyper-religiosity. The ventromedial action extrapersonal system is freed from the inhibition of the prefrontal (focal-extrapersonal or executive) dopaminergic system and/or posterior serotonergic (peripersonal) inputs.

(religion) has been postulated to be. A common element in these two mental phenomena is suggested by an experiment by [Wolford, Miller, and Gazzaniga \(2000\)](#) involving split-brain patients. When randomly presented with keys to the left and right that are rewarded differentially (e.g., 70% to right; 30% to the left), the isolated right hemisphere will maximize rewards by mostly pressing the higher-percentage key. By contrast, the isolated left hemisphere continues to “search” for patterns in the randomness and ends up performing worse than the right one. Searching for the scientific “truth” is a hallmark of the DA-rich left hemisphere, but in a random environment such searching begins to resemble the superstitious behavior seen in animals (see also [Brugger, 2001](#)).

According to [Previc et al. \(2005\)](#), the same dopaminergic mechanisms that stimulate exploratory locomotion and vertical climbing in rodents and oculomotor exploratory behavior in lower primates facilitate the search for abstract patterns and meaning in humans in a space that is internally generated but distally oriented (“off-line” in the words of [Bickerton, 1995, Chapter 3](#)). The off-line capability of human thought has provided us with enormous powers of abstract reasoning, generativity and creativity, but the failure to anchor these thought processes with feedback from the external world can lead to bizarre consequences. When sensory or motor feedback from the posterior cortex is diminished or eliminated—due to stress (which depletes 5-HT and potentiates a wide range of psychological disorders in which DA activity is excessive), drugs, sensory deprivation, or sleep—the activity of medial DA systems is unleashed from its external anchor, which can lead to incorrect attributions of self-initiated or internally generated activity (e.g., hallucinations) (see [Bentall, 1990](#), for a review) and/or empirically unsubstantiated associations of external events (e.g., superstitions). It is notable in this regard that religious explanations are most widely accepted when empirical (scientific) feedback is not readily available or is considered unsatisfactory—e.g., in the origins of the cosmos and the origins of life, in cases of miraculous healing, or in reference to eerie coincidences. When reduced 5-HT activity is accompanied by a reduction in the inhibition and updating provided by the “executive” (purposeful) intellect housed in the prefrontal cortex (e.g., [Ruchow, Grothe, Spitzer, & Kiefer, 2002](#)), activity of the mesolimbic dopaminergic system becomes even more random.<sup>15</sup> (see Fig. 3). In a mild form, the enhanced medial DA output may serve to loosen associations, inspire paranormal (schizotypal) beliefs in the “relatedness” of random events while at the same time reducing the propensity to test those beliefs ([Brugger, 2001](#)), and may even be associated with expanded creativity. In an extreme form, this activity results in bizarre attributions of causality and relatedness and other manifestations (including religious and other delusions) characteristic of actual schizophrenic thought ([Brugger et al., 1994; Rotenberg, 1994](#)).

<sup>15</sup> The role of prefrontal “intellectual” activity in inhibiting chaotic DA activity is illustrated by the effects of performing mental arithmetic tasks on the inhibition of hallucinations caused by sensory isolation ([Zuckerman, 1969](#)).

That the gap between intellectual genius and pre-occupation with religious themes and even religious delusions is a subtle one is illustrated by the following conversation with John Nash, one of many great minds to have bridged that gap:

“‘How could you’, began [Harvard professor George] Mackey, ‘how could you, a mathematician, a man devoted to reason and logical proof . . . how could you believe that extraterrestrials are sending you messages? How could you believe that you are being recruited by aliens from outer space to save the world? How could you . . .?’ . . .

‘Because’ said Nash said slowly in his soft, reasonable southern drawl, as if talking to himself, ‘the ideas I had about supernatural beings came to me the same way that my mathematical ideas did.’ ” (Nasar, 1998, p. 11).

## 6. General conclusions

The theory put forth in this paper proposes that religious behavior—and especially those experiences that have occurred and continue to occur in the most spiritually oriented individuals—are largely a product of the extrapersonal brain systems that predominate in the ventromedial cortex and rely heavily on dopaminergic transmission. By contrast, systems dealing more with body-oriented space in parietal and other dorsal brain areas and predominantly utilizing serotonergic and noradrenergic circuits appear to be less activated during religious behavior. Like the extrapersonal systems and other phenomena mediated by them such as dreams and hallucinations, religion appears to be biased toward distant (upper) space and time, although the left-hemispheric predominance shown for dreams and hallucinations has yet to be proven for religious behavior. Mild elevations of DA or ventromedial cortical activity can shift the balance toward extrapersonal space and promote a belief in paranormal and spiritual phenomena, whereas more extreme imbalances can lead to the religious delusions and obsessions found in various clinical disorders.

*There is no evidence, however, that specific brain regions or mechanisms are devoted to religious activity per se.* Rather, religion appears to have co-evolved with other DA-mediated phenomena such as abstract reasoning. The same extrapersonal phenomena (e.g., out-of-body experiences, delusions of grandiosity, and obsessiveness) may have different interpretations and themes in individuals and societies of a religious versus nonreligious persuasion.

Although the neuropsychology of religion has become a topic of greater interest in recent years, religion is arguably still under-researched as a brain phenomenon relative to language, visual perception, music, and even mathematics. Nevertheless, religious and paranormal beliefs, experiences and practices can be readily explored by means of attention and bisection paradigms (to measure spatial biases), probabilistic tasks such as those used by Brugger and colleagues and Woldford et al. (2000) (to assess quasi-superstitious behavior), trait scales such as religiosity, magical ideation, and schizotypy, animal models (e.g., superstitious behavior), and numerous neuroscientific measurement techniques. The theoretical model provided in this paper will hopefully provide an impetus for future studies of religious activity using the above paradigms.

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