# The Neural Substrates of Religious Experience

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*Religious experience is brain-based, like all human experience. Clues to the neural substrates of religious-numinous experience may be gleaned from temporolimbic epilepsy, near-death experiences, and hallucinogen ingestion. These brain disorders and conditions may produce depersonalization, derealization, ecstasy, a sense of timelessness and spacelessness, and other experiences that foster religious-numinous interpretation. Religious delusions are an important subtype of delusional experience in schizophrenia, and mood-congruent religious delusions are a feature of mania and depression. The authors suggest a limbic marker hypothesis for religious-mystical experience. The temporolimbic system tags certain encounters with external or internal stimuli as depersonalized, derealized, crucially important, harmonious, and/or joyous, prompting comprehension of these experiences within a religious framework.*

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Religious experience is brain-based. This should be taken as an unexceptional claim. All human experience is brain-based, including scientific reasoning, mathematical deduction, moral judgment, and artistic creation, as well as religious states of mind. Determining the neural substrates of any of these states does not automatically lessen or demean their spiritual significance.[1] The external reality of religious percepts is neither confirmed nor disconfirmed by establishing brain correlates of religious experience. Indeed, it has been argued that demonstrating the existence of a neural apparatus sustaining religious experience can reinforce belief because it provides evidence that a higher power has so constructed humans as to possess the capacity to experience the divine.[2] For the behavioral neurologist and neuropsychiatrist, the challenge is to delineate the distinctive neural substrates of religious experience and their alteration in brain disorders.

Investigation of the neural ground of religious experience is hampered by the absence of a widely accepted animal correlate that would allow laboratory experimentation. Evidence with neuroanatomic import is largely derived from clinical observations in patients with focal brain lesions, especially epileptic disorders, and much of this is anecdotal. We will review data that have been collected on religious experience in normal individuals and in different neurologic and neuropsychiatric syndromes. From this scattered literature, a pre-

liminary unifying model of the brain basis of religious experience may be constructed.

## CIRCUMSCRIPTION OF THE TOPIC

Most religious experience parallels ordinary experience. The religious sentiments include religious joy, religious love, religious fear, and religious awe. These religious emotions are analogues of ordinary emotions of joy, love, fear, and awe, differing not in their emotional tone, but only in being directed to a religious object. Their neural substrate is likely to contain nothing of a specifically religious nature, but instead to rest upon the same limbic and subcortical networks that support non-religious joy, love, fear, and awe, directed by dorsolateral and orbital frontal cortices to religious rather than nonreligious targets. The neural substrates of human emotionality have been extensively delineated.[3,4]

Similarly, religious language depends upon the customary dominant-hemisphere perisylvian language cortices for its production, differing only in taking sacred rather than nonsacred topics as linguistic themes. Focal left-hemisphere lesions produce aphasia for religious discourse that parallels aphasia for nonreligious discourse, as common clinical experience attests. Prosody and other emotional contributions to discourse of the right hemisphere apply to both religious and non-religious themes, and nondominant-hemisphere lesions have been reported to produce parallel impairments of religious and nonreligious emotional processing.[5] Similarly, scholastic/talmudic reasoning is ordinary reasoning applied to religious problems and is undoubtedly mediated by the same neural networks in frontal and parietal multimodal association areas.

A first general observation, then, is that the neural substrate for the preponderance of religious affect and cognition is the whole human brain, employing processing that is parallel, distributed, affective, and symbolic, with contributions of large-scale neurocognitive networks subspecialized for linguistic, prosodic, logical, and affective processing.

What might be peculiarly distinctive to religious experience would appear, on first inspection, to reside not in the domains of affect, language, or cognition, but in perception. It is the direct sensory awareness of God or the divine that is a quintessential mark of specifically religious experience. There is, however, no identifiable separate organ of religious perception.[6–8] Accordingly, sensory apprehension of the divine is likely to be mediated, at least in part, by the neural systems for ordinary tactile, visual, auditory, and olfactory perception. William James and others have suggested, and we concur, that perception of the divine occurs not through the operation of a distinctive sensory faculty, but through the superimposition upon ordinary sensations of a unique numinous-mystical feeling, a feeling of direct awareness of a sacred or divine presence.[8,9] Studies of healthy individuals and neuropsychiatric populations support this hypothesis and suggest a distinctive neurolimbic substrate.

## RELIGIOUS EXPERIENCE IN NORMAL INDIVIDUALS

Surveys suggest that religious-numinous experiences are common in both children and adults, across different historical eras, and across all cultures.[10–15] In national surveys in the United States, Britain, and Australia, 20% to 49% of individuals report having personally had numinous experiences, and this figure rises to more than 60% when in-depth interviews of randomly selected individuals are conducted.[8] Hardy and his colleagues[8,16] identified eight major types of numinous experience in British individuals, encompassing, in descending order of frequency, 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." Studies in identical and fraternal twin pairs raised apart suggest that genetic factors account for 50% of interindividual variance in religious interests and attitudes.[17] The cross-cultural ubiquity of numinous experiences and the heritability of religious dispositions argue strongly for a biologic basis, but fail to indicate the specific neural mechanisms involved. Clues to neural substrate must be gleaned from the sites of brain disorders that provoke qualitatively similar experiences.

## EPILEPSY AND RELIGIOUS EXPERIENCE

Humanity has long recognized a direct link between epilepsy and the divine. The early Greeks viewed epilepsy as a "sacred disease," a visitation from the gods, until the notion of divine genesis of seizures was dispelled by Hippocrates.[18] In the Medieval and early Renaissance periods, wide currency was given the biblical view that epileptic seizures are manifestations of de-

monic possession (Mark 9:14–29).[19] Esquirol[20] in 1838 and Morel[21] in 1860 recognized a heightened "religiosity" of epileptics, which they attributed to disability, social isolation, and greater need for religious consolation. The first reported conversion experience directly related to a seizure was noted by Howden,[22] whose patient experienced being transported to Heaven during a fit. Spratling[23] in 1904 reported a religious aura in 52 of 1,325 patients with epilepsy (4%). In the early 20th century, Turner[24] and others suggested that epileptics develop a distinctive interictal character, among the features of which is religious fervor. A substantial number of founders of major religions, prophets, and leading religious figures have been documented as having or suggested to have epilepsy (Table 1).

Modern investigations of epilepsy-related religious experience have been marked by contradiction and conflict. This confusion in part reflects failure to distinguish among epilepsy-related religious experiences of ictal, subacute postictal, and chronic interictal occurrence. The phenomenology and neurobiology of each differ in important aspects.

### Ictal Events

Ictal events of any type may be the subject of religious or cosmological explanation. Seizures are paroxysmal, riveting, and unexpected—sudden intrusions of unanticipated and often extraordinary experience into the ordinary daily flow of consciousness. Patients who have culturally acquired explanatory systems of a religious character naturally tend to interpret any ictal experience as possessing religious significance. Studies have demonstrated that experiences that are personal, important, negative, and medical, like most seizures, are particularly likely to be interpreted in a religious framework.[25]

Some psychologists of religion have attempted to explain religious experience by employing classical attribution theory. Experiments demonstrate that individuals not only interpret, but also inwardly experience, the same physiologic stimuli in strikingly different ways according to the cognitive expectations they carry. In laboratory studies, identical, pharmacologically induced sympathetic arousals are variably labeled and are experienced across the spectrum of valence, from rewarding to distressful, according to the individual's cognitive set at onset.[26] Attribution theory predicts that religious individuals with epilepsy will often experience intrinsically neutral ictal physiologic events as having a religious-numinous character. This mechanism may indeed mediate some ictal religious experiences.

Human experience, however, is clearly not simply the product of an interaction of nonspecific physiologic arousal with set cognitive schemata. Epileptic auras themselves are the most convincing evidence of the insufficiency of attribution theory, instead demonstrating the existence of distinct physiologic neural substrates for several specific emotional states. Several "psychic" auras, including depersonalization, derealization, dreamy states, autoscopy, and ecstasy, are particularly likely to engender religious interpretation and experience, and merit detailed review.

Among individuals with partial complex seizures, the frequency of auras ranges from 23% to 83%, and up to one-quarter of auras are psychic in content.[27–29] The most common psychic or experiential ictal manifestations of temporal lobe epilepsy are fear, déjà vu, jamais vu, memory recall, and visual and auditory hallucinations.

Hughlings Jackson[30] was among the first to identify and characterize less common ictal "intellectual auras" ("dreamy states," "cognitive auras") in which the experience of the immediacy and liveliness of one's own or external reality is altered.[31] The intellectual auras include depersonalization, derealization, and double consciousness. Depersonalization auras produce an alteration or loss of the sense of one's own reality, often accompanied by a sense of detachment from others and the environment, and of acting like an automaton. Derealization auras generate an alteration or loss of the sense of the reality of the external environment—for example, the feeling that the external surround is just a dream—and also are often associated with a sense of detachment. Double consciousness ("mental diplopia") auras create a simultaneous experience of persisting remnants of one's normal consciousness and of a new quasi-parasitical consciousness with a different perception of reality. Auras of depersonalization, derealization, and dreamy state account for approximately one-quarter of psychic auras.[32]

Well-documented localizations of spontaneous discharges or electrical stimulations producing intellectual auras are extremely rare. Available evidence, however, suggests that mesolimbic structures, the hippocampus and especially the amygdala, are likely the critical generators of a feeling of unreality about the self or external reality.[33,34] The experience of unreality occurred in 9% of patients with temporal lobe epilepsy in one series, often accompanied by a sensation of fear.[35] One patient in Penfield's series[36] had a sense of "not being in this world" each time the first temporal gyrus was stimulated, reflecting either direct lateral temporal cortical excitation or rapid spread of afterdischarge to mesolimbic structures. One patient in Gloor and colleagues' more recent series[37] repeatedly experienced a faraway feeling during stimulation of temporal mesolimbic structures.

TABLE 1. Historical-religious figures suggested in the medical literature to have had epilepsy

| Person | Description of Spells | Frequency | Likelihood of Epilepsy | Differential Diagnosis[a] | Religious Aspects |
|---|---|---|---|---|---|
| Saint Paul (?–65 C.E.) | Conversion on road to Damascus: sudden bright light, falling to the ground, hearing the voice of Jesus, blindness for 3 days with inability to eat or drink Ecstatic visions | Unknown | + | CPS with generalization[52,133,134] Psychogenic blindness Burns of cornea/retina Vertebrobasilar ischemia Occipital contusion Lightning-stroke Digitalis poisoning Vitreous hemorrhage Migraine equivalent | Father of Catholic Church Possible ecstatic aura, interictal hypermoralism, hyperreligiosity, hypergraphia |
| Muhammad (570–632) | Pallor, appearance of intoxication, falling, profuse sweating, visual and auditory hallucinations | At least several | + | Complex partial seizures[135,136] | Islamic prophet |
| Margery Kempe (ca. 1373–1438) | A cry, falling with convulsive movements, turning blue, nausea, psychotic behavior | Recurrent | + | Epilepsy[137] Hysteria Postpartum psychosis Migraine | 14th-century Christian mystic and autobiographer |
| Joan of Arc (1412–1431) | "I heard this Voice [of an angel] . . . accompanied also by a . . . great light. . . . there is never a day when I do not hear this Voice; and I have much need of it." | At least daily by the time of her execution in 1431 | + | Ecstatic partial seizure and musciogenic epilepsy[138] Intracranial tuberculoma | Extraordinary, deeply held, idiosyncratic religious beliefs motivating martial prowess in the defense of Orléans |
| St. Catherine of Genoa (1447–1510) | Extreme sense of heat or cold, whole-body tremor, transient aphasia, automatisms, sense of passivity, hyperesthesia, regression to childhood, dissociation, sleepwalking, transient weakness, transient suggestibility, inability to open eyes | Unknown | + | Complex partial seizure[52] Hysteria | Christian mystic |
| St. Teresa of Ávila (1515–1582) | Visions, chronic headaches, transient LOC, tongue-biting | 1 major LOC spell; frequent headaches | + + | Complex partial seizure[52] Hysteria | Catholic saint |
| St. Catherine dei Ricci (1522–1590) | LOC, visual hallucinations, mystical states | Every Thursday at noon with recovery by Friday at 4:00 P.M. | + | Complex partial seizure[52] | Catholic saint |
| Emanuel Swedenborg (1688–1772) | Acute psychosis, foaming at the mouth, olfactory, gustatory, and somatic hallucinations; ecstatic aura, falling, LOC, convulsions, hallucinations, postictal trance states | Recurrent | + + | Complex partial seizure[139,140] Mania Schizophrenia | Founder of the New Jerusalem Church |
| Ann Lee (1736–1784) | Visual, auditory hallucinations | From childhood until at least 1774 | + | Epilepsy[22] | Founder of the Shaker movement |

(continued)

**TABLE 1.** Historical-religious figures suggested in the medical literature to have had epilepsy (*continued*)

| Person | Description of Spells | Frequency | Likelihood of Epilepsy | Differential Diagnosis[a] | Religious Aspects |
|---|---|---|---|---|---|
| Joseph Smith (1805–1844) | Speech arrest, fear, "pillar of light," hearing voices, "When I came to . . . I found myself lying on my back looking up at heaven." | One clear conversion event (1820) | + | Complex partial seizure[53] | Founder of Mormonism |
| Fyodor Mikhailovitch Dostoievsky (1821–1881) | Sense of bliss, then a cry, a fall, generalized tonic-clonic seizure with frothing at the mouth and injuries. Postictal intense depression and guilt, lasting several days | Every few days to every few months | +++ | Complex partial seizure with generalization[41,43] Primary generalized seizures[41] Hysteria | Influential Russian novelist. Ecstatic auras: "I have really touched God. He came into me myself; yes, God exists, I cried, and I don't remember anything else." Interictal religiosity, increasing with age |
| Hieronymous Jaegen (1841–1919) | Mystical experiences, visual hallucinations, headaches | Unknown | + | Complex partial seizure[53] Migraine | German mystic |
| Dr. Z (Arthur Thomas Myers; 1851–1894) | Pallor, vacant look, perseveration of "yes" to any remark, tongue smacking, *déjà vu*, right-sided motor signs, postictal passivity | Multiple episodes 1871–1894 | +++ | Complex partial seizures[141] Left temporal lobe lesion on autopsy | Late-life interest in afterlife, reincarnation; prominent in the Society for Psychical Research |
| Vincent Van Gogh (1853–1890) | Sense of vertigo, tinnitus, hyperacusis, xanthopsia, restlessness, delirium | About 1 dozen spells between the ages of 35 and 37 | + | Complex partial seizure with postictal psychosis[42] Ménière's disease[142] Digitalis intoxication Meningoencephalitis luetica Schizophrenia | Renowned painter Hyperreligiosity |
| St. Thérèse of Lisieux (1873–1897) | Violent trembling, visual hallucinations, wounding by a "shaft of fire," mystical conversions | Several spells after age 9 | ++ | Complex partial seizure[53] | Catholic saint |

*Note:*   CPS=complex partial seizures; LOC = loss of consciousness.
[a]All diagnoses listed in this column have been advanced in the medical literature.

Deep similarities are readily apparent between these intellectual auras and alterations in the experience of reality that are a common feature of intense, nonepileptic religious experience. Individuals undergoing sudden religious awakening or conversion often report abruptly perceiving their ordinary, unenlightened selves as hollow, empty, and unreal (depersonalization) as a prelude to finding a truer, more authentic, religiously grounded self. Similarly, a sense of suddenly seeing through a veil of appearances previously taken for real (derealization) to a deeper, supernatural, genuine reality is a frequent aspect of mystical-numinous experience. Also, doubling of consciousness—a simultaneous perception of a higher, purer, religiously oriented self and a baser, irreligious self contesting for control of one's actions and spirit—is a recurrent leitmotif of religious experience. Although many individuals do not associate their intellectual auras with religious experience, it seems likely that repeated, intense, visceral experiences of the self or the external world as unreal would tend to foster a belief in a supranatural ground of reality and a religious outlook.

Another experiential ictal phenomenon that may become affiliated with religious experience is autoscopy, the experience of seeing oneself. Autoscopic experiences may be divided into two categories: 1) seeing one's double, a hallucinatory percept of one's own body visualized in external space, and 2) out-of-body experience, a feeling of leaving one's body and viewing it from another perspective, often from above. Autoscopic phenomena occur in healthy individuals, especially in settings of extreme stress and anxiety, and in a variety of neurologic and psychiatric disorders.[38,39] In the series of Devinsky et al.,[40] 6% of consecutive patients with epilepsy reported autoscopy as an ictal or postictal experience. Among patients with identifiable seizure foci, 88% had temporal lobe involvement. No preponderant trend in laterality of seizure focus was evident. Illustrating the potential for this type of epileptic experience to evolve a religious character, one patient with out-of-body transport experienced passage from a department store floor to a celestial realm (Hécaen,[38] case 7).

Ecstatic seizure experiences, ictal and peri-ictal, have been especially closely linked to religious experience. Dostoyevsky provided riveting and influential descriptions of his own ecstatic-religious epileptic experiences in letters, in other autobiographical writings, and in his fiction:[41–43]

> The air was filled with a big noise, and I thought it had engulfed me. I have really touched God. He came into me myself; yes, God exists, I cried, and I don't remember anything else. You all, healthy people, he said, can't imagine the happiness which we epileptics feel during the second before our attack. I don't know if this felicity lasts for seconds, hours, or months, but believe me, for all the joys that life may bring, I would not exchange this one. Such instants were characterized by a fulguration of the consciousness and by a supreme exaltation of emotional subjectivity. (Dostoyevsky, The Idiot)

The term ecstatic seizure has been applied to two types of experience, often coexisting. The first is primarily an emotional experience of deep pleasure, the cognitive content of which may vary. The second is primarily a cognitive experience of insight into the unity, harmony, joy, and/or divinity of all reality, usually with pleasurable accompanying affect. Ecstatic seizures of either type are rare. Pleasure as an ictal emotion is reported by less than 0.5% of epileptics.[44,45]

The available evidence suggests a temporolimbic origin for ecstatic seizures. Pleasurable emotions may be induced in humans by depth electrode stimulation of the amygdala, albeit rarely,[46,47] and has been associated with hippocampal-septal hypersynchrony.[48] The few well-studied modern clinical cases of ecstatic seizures all appear to have had a temporolimbic substrate. All 7 of Williams's patients with ictal pleasure had temporal or peritemporal foci.[49] Morgan[50] described a patient whose seizures consisted of feelings of detachment, ineffable contentment, and fulfillment; visualizing a bright light recognized as the source of knowledge; and sometimes visualizing a bearded young man resembling Jesus Christ. Computed tomography disclosed a right anterior temporal astrocytoma. Following anterior temporal lobectomy, ecstatic seizures resolved. Cirignotta et al.[51] described a patient whose seizures were characterized by estrangement from the immediate environment, ineffable joy, and total bliss (without a religious content). Continuous EEG monitoring capturing such a seizure demonstrated a right temporolimbic discharge. Naito and Matsui[52] described an older woman whose seizures were characterized by joyous visions of God and the sun: "My mind, my whole being was pervaded by a feeling of delight." Interictal EEG demonstrated spike discharges in the left anterior and middle temporal region during sleep.

### Postictal Experiences

In an influential paper, Dewhurst and Beard[53] described 6 patients who experienced dramatic and often lasting religious conversions in the postictal period. The conversions occurred during the first hours or days following episodes of increased seizure activity, usually bouts of complex partial seizures of temporal origin. More recently, several groups have demonstrated that post-

ictal psychoses, in contrast to acute or chronic interictal psychoses, are particularly likely to have a religious character.[54-56] Postictal psychoses generally emerge after an exacerbation in seizure activity. Contrary to classical teaching, they usually appear in patients with a clear, not clouded, consciousness, after a lucid interval of hours or days since the last seizure (average 1.2 days). Grandiosity and elevated mood are common accompaniments. In a study of 91 patients with epilepsy-related psychosis, Kanemoto et al.[56] found that 23% of postictal psychoses had a religious content, versus only 3% of acute interictal psychoses and 0% of chronic interictal psychoses. Illusion of familiarity, mental diplopia, and feeling of impending death occurred almost exclusively in the postictal psychosis group. Complex partial seizures of temporal origin predominated in all three groups and accounted for 80% of the patients with postictal psychoses.

Interictal Experiences

Since Esquirol in the early 19th century, religious preoccupation has been suggested to be a common feature of the interictal character of individuals with epilepsy. Waxman and Geschwind[57] reawakened interest in this topic when they suggested that hyperreligiosity and intense philosophical and cosmological concerns were leading features of a distinctive interictal personality syndrome of temporal lobe epilepsy. Additional features of this putative syndrome are hypermoralism, deepened affects, circumstantiality, humorlessness, interpersonal viscosity, aggressive irritability, and hypergraphia.

Quantitative support for this syndrome was provided by Bear and Fedio,[58] among whose findings was that religiosity trait scores were significantly higher in patients with temporal lobe epilepsy than in normal or neuromuscular patient control subjects. In a subsequent study, Bear and colleagues[59] found that religiosity trait scores distinguished temporal lobe epileptics from aggressive character disorder patients, affective disorder patients, and generalized or extratemporal focal epilepsy patients. Religiosity scores were similar between patients with temporal lobe epilepsy and patients with schizophrenia, but these groups differed in viscosity, hypergraphia, and other features.

Bear,[60] enlarging upon Gastaut and colleagues' original hypothesis,[61] suggested that interictal spiking and kindling in temporal lobe epileptics leads to intensified sensory-limbic connections. Neutral stimuli are endowed with exaggerated affective tone and significance. Religious and cosmological beliefs are natural responses of patients continually encountering objects and events of heightened meaningfulness and rele-

vance. Animal models of interictal behavioral change have been created, and several additional plausible neurobiological mechanisms for seizure-induced alterations in interictal behavior have been described.[62-64]

Several groups, however, have failed to confirm findings of heightened interictal religiosity among temporal lobe epileptics.[65-67] Differences in religiosity measures and in control group selection account for some of the conflict among studies. An attractive unifying hypothesis is that religiosity is not a universal interictal personality trait among individuals with temporal lobe epilepsy, but emerges in a subgroup, especially those with more active seizure disorders. Several mechanisms may singly or in combination drive the development of religiosity. These may include a desire for religious solace; a need to explain abrupt, sometimes bizarre seizure experiences (attribution theory); a response to ictal numinous experiences; lesional disruptions of the temporal lobe, giving rise to seizures and hyperreligiosity as independent outcomes; abnormal religious interests arising as products of interictal psychopathology;[68] and seizure-induced alterations and intensification of sensory-limbic integration.

NEAR-DEATH EXPERIENCES

Individuals in severe, life-threatening circumstances often experience a variety of unusual mental phenomena. Anecdotal autobiographical and literary descriptions of near-death experiences date back centuries. The first systematic study was performed by Heim[69] in 1892, collecting the accounts of over 30 survivors of falls in the Alps, and subsequent investigators have surveyed patients surviving cardiac arrest, near drowning, and a variety of other conditions.[70-72] Although some near-death experiences are distressing or hellish,[73] most are serene and joyful and may produce profound and long-lasting changes in beliefs and values. The most common features of near-death experience reports are a sensation of peace; a lack of emotion and a feeling of detachment; a sense of being out of the body viewing the self; a sensation of traveling in a darkness or void at the end of which is an encounter with light; a life review;[74] altered passage of time, usually slowed; and a sense of harmony or unity. Thus, depersonalization, derealization, autoscopy, and time distortion are frequent features.

The brain basis of near-death experiences is conjectural. Sociocultural factors and expectations clearly influence the content of near-death experiences,[75] but an underlying driving biologic mechanism appears likely.

One speculation supported by scattered available evi-

dence is endorphin-induced limbic system activity.[76,77] The limbic system is richly endowed with opiate receptors.[78] In an animal model, beta-endorphin administration into the cerebrospinal fluid produces marked increases in limbic neuronal activity at the same time that the animals become outwardly immobile.[79,80] A sudden increase in beta-endorphin in brain tissue, cerebrospinal fluid, and serum occurs in dogs conscious at the moment of cardiac arrest, but not in anesthetized animals.[77]

A second intriguing hypothesis relates near-death experiences to N-methyl-D-aspartate (NMDA) receptor blockade by putative endogenous neuroprotective molecules that dampen glutamate excitotoxicity in hypoxic-ischemic settings.[81] Exogenously administered ketamine, phencyclidine, and other NMDA blockers have been reported to induce several aspects of the near-death experience in normal individuals, including depersonalization, hallucination, sensory deprivation, and elated mood.

Several authors have suggested that depersonalization phenomena may be hard-wired, predetermined responses of the nervous system to extreme stress, and that they may have adaptive benefit.[40,70] For prey trapped by a predator, passive immobilization, feigning death, may promote survival. More generally, the clarity of perception and insight associated with dissociation might allow individuals to identify and carry out previously unrecognized strategies to escape desperate, life-threatening circumstances.

## HALLUCINOGENS

The classic hallucinogenic agents include lysergic acid diethylamide (LSD), psilocybin, and mescaline.[82] Prototypical experiences after hallucinogen ingestion include visual illusions and hallucinations, often vividly colored; depersonalization and autoscopy; euphoria; and awareness of a larger intelligence or presence.[83] These experiences closely parallel religious numinous and mystical experience. Mescaline-containing peyote has been employed to foster religious reveries in the Native American Church, and psilocybin has been demonstrated to prompt mystical religious experiences during Protestant church services.[84-86] In one series of 206 observed hallucinogen ingestion sessions, chiefly of LSD and peyote, 96% of subjects experienced religious imagery of some kind, 91% saw religious buildings, and 58% encountered religious figures.[87]

Although the hallucinogenic drugs share dopaminergic and noradrenergic properties, current views affiliate their psychedelic properties with serotonergic agonist activity, particularly at $5-HT_2$, $5-HT_{1A}$, and $5-HT_{1C}$ receptors, widely distributed in basal ganglia, cortex, and temporolimbic structures.[82,88] The precise anatomic substrates for various features of hallucinogen-induced experience have not been elucidated, but the temporal lobe plays an important role. Patients given LSD before and after temporal lobectomy showed reduced richness of induced perceptual experience after temporal lobe resection.[89] The cognitive expectation set of the user strongly influences the quality and interpretation of the experience induced by hallucinogens.

## DELUSIONAL DISORDERS

Religious delusions are a feature of schizophrenia and other psychotic illnesses. Distinguishing culturally accepted religious-mystical beliefs from bizarre psychotic delusions poses both a practical challenge to clinicians and an epistemologic-theoretical challenge to the foundations of psychiatric nosology.[90-94]

Mystical states and psychotic states are both characterized by apparent delusions, hallucinations, strange behavior, and social withdrawal. Ultimately, no diagnostic system can irrefutably characterize certain beliefs as delusional, as having no correspondence to objective reality. Several features, however, do tend to differentiate culturally idiosyncratic psychotic states from culturally validated mystical states (Table 2). In general, religious hallucinations and delusions of psychotic origin are more likely to be auditory, to focus on illness and deviance, to involve personal grandiosity, to produce affectual distress or indifference, to lead to progressive social isolation, to involve thought blocking, and to be recognized as bizarre and invalid by members of the patient's own subculture.

Delusions occur at some stage of the course of illness in 90% of schizophrenic patients.[95] Delusions of reference, of persecution, of self-depreciation, and of being controlled are the most typical aberrant beliefs in schizophrenia; they are present respectively in 12%, 10%, 8%, and 4% of unselected patients. But religious delusions are common, being present in 3.2% of unselected patients.[96] Religious delusions are one of the 13 categories of delusional belief in the Present State Examination.[97]

The specific content of religious delusions in schizophrenia is shaped by an individual's culture.[98] These effects vary not only across contemporary cultures, but also across historical time. In Britain, the frequency of preoccupations and delusions of a religious character among individuals with schizophrenia declined from 65% in the mid–19th century to 23% in the mid–20th

TABLE 2. Features tending to distinguish mystical and psychotic states

| Feature | Mystical State | Psychotic State |
|---|---|---|
| Hallucinations | Often visual; typically elderly, wise counselors | Predominantly auditory; often accusatory |
| Vocabulary | Religiously imbued word choice, generally harmonious connotations: God, Christ, soul, peace, spirit | Frequent themes of illness and deviance |
| Personal role | Individual as self-negating vessel for higher power | Personal grandiosity and omnipotence |
| Affect | Ecstatic, joyful | Indifferent or terrified |
| Duration of state | Transient, usually hours, resolves completely | May persist for months or years and leave residual delusions, reduced social function |
| Withdrawal | Facultative: eventual return to share experience with others | Obligatory: progressive isolation |
| Disordered speech output | Glossolalia (speaking in tongues): output language is unknown and incomprehensible to speaker; fluency retained | Thought disorder: output may contain neologisms and bizarre associations, but is predominantly in known language; thought blocking may occur |
| Cultural compatibility | Beliefs are recognized as valid by others in the patient's culture or subculture | Beliefs are rejected by others in the patient's culture or subculture |

Note: Based, in part, on references 91, 143–145.

century, while those of a sexual character increased.[99]

Theories of the neurobiological genesis of delusions in schizophrenia have emphasized several distinct mechanisms. The process of belief formation can be divided into several component operations: initial perception of the surround, logical and probabilistic reasoning about initial perceptions, generation of beliefs, and information search to corroborate or refute such beliefs. Defects in each of these operations have been identified in schizophrenic populations,[100,101] including the occurrence of anomalous perceptual experiences,[102] defects in formal logical reasoning[103] and Bayesian inference,[104] and bias in search for confirmatory or disconfirmatory evidence. Some authors have emphasized the role of "delusional mood"—an affectual change that precedes the appearance of overt cognitive delusions.[105] The patient is anxious, restless, and suspicious and feels that some important event is about to happen. The world feels strange, transformed, unreal. Attention and concentration may be impaired. This altered mood state drives the development of delusional thinking.

Neuroanatomically, these psychologic mechanisms implicate frontal systems (deductive and Bayesian reasoning),[106] parietal systems (perceptual distortion),[107] and temporolimbic systems (altered mood and affective charging of stimuli)[107] in the genesis of schizophrenic delusions.

Mood congruence is the distinctive feature of hallucinations and delusions with a religious content in mood disorders. As many as 75% of patients with mania exhibit delusions, and these are typically grandiose.[108,109] Grandiose delusions have been classified into delusions of 1) special abilities (inventor, athlete, spiritual healer),

2) grandiose identity (descendant of a famous historical figure, incarnation of God), 3) wealth, and 4) special mission (fated to solve the problem of war, selected by God to carry a message to world).[110] Conversely, delusions in depressed patients are often guilt-ridden or accusatory and may include reproachful voices or visions perceived as divine in origin.

Both manic and depressive delusions illustrate the vulnerability of perceptual and cognitive systems to affective influence. Overwhelming positive or negative moods generated in ascending aminergic and serotonergic neurotransmitter systems lead to 1) misinterpretation of chance anomalous perceptual experiences and 2) cognitive bias—acceptance only of mood-congruent outcomes of logical and probabilistic reasoning.

## CORTICAL DEGENERATIVE DEMENTIAS

The religious experience of patients with dementing disorders has been little studied, and extensive empirical data are lacking. Relevant preliminary observations from our experience and recent literature are of interest for two disorders: Alzheimer's disease and frontotemporal dementia.

Patients with Alzheimer's disease typically demonstrate a progressive loss of religious interest and behaviors, illustrating that the neurobiologic substrates of religious experience can be revealed by conditions that produce hyporeligiosity as well as hyperreligiosity. Passivity and decreased spontaneity are common in moderate to advanced Alzheimer's disease.[111] In one study of 80 Alzheimer's patients, the most frequent personality changes were diminished initiative with growing

apathy in more than 60% and relinquishment of hobbies in more than 50%.[112] In our experience, this decreased pursuit of lifelong interests commonly extends to and compromises religious concerns. The likely mechanisms are diminution of temporolimbic-cortical connections, leading to decreased affective charging of cognitions and stimuli, and disrupted cortical association area connections, producing impaired intellectual ability to construct religious cognitions. In addition, pathologic experiences in Alzheimer's disease are not usually of a religious character. Delusions in Alzheimer's disease are typically of the simple persecutory type, without religious content.[113] Memory impairments foster suspiciousness, and cortical association area loss precludes the elaboration of more complex delusional themes.

In contrast, a subset of patients with frontotemporal dementias exhibit hyperreligiosity. In the index family for chromosome 17–linked frontal dementias, 3 of 12 affected individuals showed hyperreligious behavior.[114] Among patients with asymmetric atrophy, increased religiosity appears to occur more frequently with right rather than left frontotemporal atrophy (Bruce Miller, M.D., personal communication, January 1997). We speculate that two neurobehavioral processes heighten religious experience and interests in these patients. First, daily experiences receive increased positive valuation as a result of predominance of left hemisphere (positive) over right hemisphere (negative) valence systems.[115] Second, orbitofrontal atrophy promotes impulsivity, leading to greater willingness to accept and proclaim religious explanations for frequently encountered positive, harmonious phenomena.

## A UNIFYING HYPOTHESIS: LIMBIC MARKERS AND RELIGIOUS EXPERIENCE

The core qualities of religious and mystical experience, assented to by a wide variety of psychologists of religion, are the noetic and the ineffable—the sense of having touched the ultimate ground of reality and the sense of the unutterability or incommunicability of the experience.[13,14,116–121] Frequent additional features are an experience of unity, an experience of timelessness and spacelessness, and a feeling of positive affect, of peace and joy. We suggest that the primary substrate for this experience is the limbic system. Temporolimbic epileptic discharges can produce each of these components in fragmentary or complete form: distancing from apparent reality (depersonalization, derealization), timelessness and spacelessness (autoscopy, time distortion), or positive affect (ecstatic auras).[122]

The limbic system integrates external stimuli with internal drives and is part of a distributed neural network that marks stimuli and events with positive or negative value.[123–125] This role of the limbic system is of great evolutionary value, marking the valence and the importance of a novel stimulus or experience for accurate memory encoding and automatic future retrieval. Moreover, in addition to simple positive or negative valence, limbic discharges can produce experiences that are intermediate between customary divisions between affects and cognitions. For example, a sense of "familiarity" arises in the limbic system as a quasi-emotional marker of experience. Usually the limbic familiarity jibes with explicit recall, but it can appear discordantly, producing déjà vu or jamais vu experiences. We suggest that, similarly, limbic charges may mark experiences as 1) depersonalized or derealized, 2) crucially important and self-referent, 3) harmonious—indicative of a connection or unity between disparate elements, and 4) ecstatic—profoundly joyous. This limbic activity underlies certain psychic seizure auras, near-death experiences, and the religious and mystical experiences of normal individuals.

An attractive feature of this hypothesis is that it offers a new account of the brain basis of the ineffability of religious experience. Several theorists in the past have advanced an explanation of ineffability that was based on hemispheric specialization.[126–131] In a variety of guises, the hypothesis was advanced that numinous religious experience is a right hemisphere event and consequently holistic and nonverbal. When transferred to the left hemisphere, the experience is translated into an analytic and verbal version that is inherently incomplete, and consequently the experience is reported as ineffable. These theories have several fundamental defects, chiefly that they rest upon metaphorical rather than process-specific accounts of dominant and nondominant hemisphere functions and that they do not clearly apply to individuals with an intact corpus callosum and unitary conscious experience.

The limbic-marker hypothesis provides an entirely different explanation for the ineffability of religious experience. The perceptual and cognitive contents of numinous experience are seen as similar to those of ordinary experience, except that they are tagged by the limbic system as of profound importance, as detached, as united into a whole, and/or as joyous. Consequently, descriptions of the contents of the numinous experience resemble descriptions of the contents of ordinary experience, and the distinctive feelings appended to them cannot be captured fully in words. Like strong emotions, these limbic markers can be named but cannot be communicated in their full visceral intensity, resulting in a report of ineffability.

The limbic marker theory is testable in several respects. It predicts that functional neuroimaging during numinous experiences in individuals who have repeated religious transports would reveal alterations in limbic system activity. It predicts that loss of the ability to have numinous experiences will occur in individuals with bilateral limbic pathology (Klüver-Bucy syndrome) but not other focal lesions. It predicts that more detailed depth electrode studies will map numinous experience to stimulations at limbic and not other sites.

We note in conclusion that although the psychology of religion has a long and honorable history,[132] investigations of the neural substrates of religious experience are in their infancy. Humanity has been called *homo religio*—the religious animal. Behavioral neuroscience must encompass a fully realized account of the neural substrates of religious experience if it is to achieve a systematic understanding of the brain basis of all human behavior. The task before neuropsychiatrists and behavioral neurologists is to fully understand brain disorders that promote, intensify, or alter religious experience—unique clues to the neural basis of the spiritual nature of humanity.

### References

1. James W: Religion and neurology, in The Varieties of Religious Experience. New York, Longmans, Green and Co, 1902
2. Mackay DM: International biologists' attitudes toward science and religion project (oral interview archive). Los Angeles, CA, UCLA-Reed Neurologic Research Center, October 1981
3. Ross ED, Homan RW, Buck R. Differential hemispheric specialization of primary and social emotions. Neuropsychiatry, Neuropsychology, and Behavioral Neurology 1994; 7:1–19
4. Heilman KM, Bowers D, Valenstein E: Emotional disorders associated with neurological diseases, in Clinical Neuropsychology, 3rd edition, edited by Heilman KM, Valenstein E. New York, Oxford University Press, 1993, pp 461–498
5. Miller DA: Neuropsychology and the emotional component of religion. Pastoral Psychology 1995; 33:267–272
6. Feuerbach L: Lectures on the Essence of Religion (1851), translated by Mannheim R. New York, Harper and Row, 1967
7. James W: The reality of the unseen, in The Varieties of Religious Experience. New York, Longmans, Green and Co, 1902
8. Hay D: "The biology of god": What is the current status of Hardy's hypothesis? International Journal for the Psychology of Religion 1994; 4:1–23
9. Gendlin E: Experiencing and the Creation of Meaning. Glencoe, IL, Free Press, 1962
10. Hardy A: The Biology of God. New York, Taplinger, 1975
11. Hay D: Religious Experience Today: Studying the Facts. London, Mowbray, 1990
12. Tamminen K: Religious experiences in childhood and adolescence: a viewpoint of religious development between the ages of 7 and 20. International Journal for the Psychology of Religion 1994; 4:61–85
13. Wach J: Types of Religious Experience. Chicago, University of Chicago Press, 1951, pp 30–47
14. Stace WT: Mysticism and Philosophy. New York, Macmillan, 1960
15. Carmody DL, Carmody JY: Mysticism. New York, Oxford University Press, 1996
16. Hardy A: The Spiritual Nature of Man. Oxford, Clarendon Press, 1979
17. Waller NG, Kojetin BA, Bouchard TJ, et al: Genetic and environmental influences on religious interests, attitudes, and values: a study of twins reared apart and together. Psychol Sci 1990; 1:138–142
18. Hippocrates: The Genuine Works of Hippocrates. London, Sydenham Society, 1846, pp 843–858
19. Taxil J: Traicté de l'épilepsie [Treatise on epilepsy]. Tournon, 1602
20. Esquirol JED: Des maladies mentales [On mental illness]. Paris, Balliere, 1838
21. Morel BA: Traité des maladies mentales [Treatise on mental illness]. Paris, Masson, 1860

22. Howden JC: The religious sentiments in epileptics. J Ment Sci 1872/1873; 18:491–497
23. Spratling WP: Epilepsy and Its Treatment. Philadelphia, WB Saunders, 1904
24. Turner WA: Epilepsy. London, Macmillan, 1907
25. Spilka B, Schmidt G: General attribution theory for the psychology of religion: the influence of event-character on attributions to God. Journal for the Scientific Study of Religion 1983; 22:326–339
26. Schachter S, Singer JE: Cognitive, social, and physiological determinants of emotional states. Psychol Rev 1962; 69:379–399
27. Palmini A, Gloor P: The localizing value of auras in partial seizures: a prospective and retrospective study. Neurology 1992; 42:801–806
28. So NK: Epileptic auras, in The Treatment of Epilepsy: Principles and Practice, edited by Wyllie E. Philadelphia, Lea and Febiger, 1993, pp 369–377
29. Mendez MF, Cherrier MM, Perryman KM: Epileptic forced thinking from left frontal lesions. Neurology 1996; 47:79–83
30. Jackson JH, Stewart JP: Epileptic attacks with a warning of a crude sensation of smell and with the intellectual aura (dreamy state) in a patient who had symptoms pointing to a gross organic disease of the right temporo-sphenoidal lobe. Brain 1899; 22:534–549
31. Devinsky O, Luciano D: Psychic phenomena in partial seizures. Semin Neurol 1991; 11:100–109
32. Mendez MF, Engebrit B, Doss R, et al: The relationship of epileptic auras and psychological attributes. J Neuropsychiatry Clin Neurosci 1996; 8:287–292
33. Gloor P: Experiential phenomena of temporal lobe epilepsy. Brain 1990; 113:1673–1694
34. Fish DR, Gloor P, Quesney FL, et al: Clinical responses to electrical brain stimulation of the temporal and frontal lobes in patients with epilepsy. Brain 1993; 116:397–414
35. Weil AA: Ictal emotions occurring in temporal lobe dysfunction. Arch Neurol 1959; 1:87–97
36. Penfield W, Jasper H: Epilepsy and the Functional Anatomy of the Human Brain. Boston, Little, Brown, 1954
37. Gloor P, Olivier A, Quesney LF, et al: The role of the limbic system in experiential phenomena of temporal lobe epilepsy. Ann Neurol 1982; 23:129–144
38. Hécaen H, de Ajuriaguerra J: Méconnaissances et hallucinations corporelles [Somatic delusions and hallucinations]. Paris, Masson, 1952
39. Dening TR, Berrios GE: Autoscopic phenomena. Br J Psychiatry 1994; 165:808–817
40. Devinsky O, Feldmann E, Burrowes K, et al: Autoscopic phenomena with seizures. Arch Neurol 1989; 46:1080–1088
41. Voskuil PHA: The epilepsy of Fyodor Mikhailovitch Dostoevsky

(1821–1881). Epilepsia 1983; 24:658–667

42. Gastaut H: New comments on the epilepsy of Fyodor Dostoevsky. Epilepsia 1984; 25:408–411

43. Geschwind N: Dostoievsky's epilepsy, in Psychiatric Aspects of Epilepsy, edited by Blumer D. Washington, DC, American Psychiatric Press, 1984, pp 325–334

44. Williams D: The structure of emotions reflecting in epileptic experiences. Brain 1956; 79:29–67

45. Devinsky O, Feldmann E, Bromfield E, et al: Structured interview for simple partial seizures: clinical phenomenology and diagnosis. Journal of Epilepsy 1991; 4:107–116

46. Stevens JR, Mark VH, Ervin F, et al: Deep temporal stimulation in man. Arch Neurol 1969; 21:157–169

47. Obrador S, Delgado JMR, Martin-Rodriguez JG: Emotion areas of the human brain and their therapeutic stimulation, in Cerebral Localization, edited by Zulch KJ. Berlin, Springer, 1973, pp 171–183

48. Mandell AJ: Toward a psychobiology of transcendence: God in the brain, in The Psychobiology of Consciousness, edited by Davidson JM, Davidson RJ. New York, Plenum, 1980, pp 379–464

49. Williams D: The structure of emotions reflected in epileptic experience. Brain 1956; 79:29–67

50. Morgan H: Dostoyevsky's epilepsy: a case report and comparison. Surg Neurol 1990; 33:413–416

51. Cirignotta F, Todesco CV, Lugaresi E: Temporal epilepsy with ecstatic seizures (so-called Dostoyevsky epilepsy). Epilepsia 1980; 21:705–710

52. Naito H, Matsui N: Temporal lobe epilepsy with ictal ecstatic state and interictal behavior of hypergraphia. J Nerv Ment Dis 1988; 176:123–124

53. Dewhurst K, Beard AW: Sudden religious conversions in temporal lobe epilepsy. Br J Psychiatry 1970; 117:497–507

54. Logsdail SJ, Toone BK: Post-ictal psychoses. Br J Psychiatry 1988; 152:246–252

55. Savard G, Andermann F, Olivier A, et al: Postictal psychosis after complex partial seizures: a multiple case study. Epilepsia 1991; 32:225–231

56. Kanemoto K, Kawasaki J, Kawai I: Postictal psychosis: a comparison with acute interictal and chronic psychoses. Epilepsia 1996; 37:551–556

57. Waxman SG, Geschwind N: The interictal behavior syndrome of temporal lobe epilepsy. Arch Gen Psychiatry 1975; 32:1580–1586

58. Bear DM, Fedio P: Quantitative analysis of interictal behavior in temporal lobe epilepsy. Arch Neurol 1977; 34:454–467

59. Bear D, Levin K, Blumer D, et al: Interictal behaviour in hospitalised temporal lobe epileptics: relationship to idiopathic psychiatric syndromes. J Neurol Neurosurg Psychiatry 1982; 45:481–488

60. Bear DM: Temporal lobe epilepsy: a syndrome of sensory-limbic hyperconnection. Cortex 1979; 15:357–384

61. Gastaut H, Morin G, Leserve N: Étude du comportement des épileptiques psychomoteurs dans l'intervalle de leurs crises [Study of the interictal behavior of psychomotor epileptics]. Annales Medico-Psychologiques 1955; 113:1–27

62. Adamec RE: Partial kindling of the ventral hippocampus: identification of changes in limbic physiology which accompany changes in feline aggression and defense. Physiol Behav 1991; 49:443–453

63. Griffith N, Engel J, Bandler R: Ictal and enduring interictal disturbances in emotional behaviour in an animal model of temporal lobe epilepsy. Brain Res 1987; 400:360–364

64. Engel J, Bandler R, Griffith NC, et al: Neurobiological evidence for epilepsy-induced interictal disturbances. Adv Neurol 1991; 55:97–111

65. Willmore LJ, Heilman KM, Fennell E: Effect of chronic seizures on religiosity. Transactions of the American Neurological Association 1980; 105:85–87

66. Sensky T, Wilson A, Petty R, et al: The interictal personality traits of temporal lobe epileptics: religious belief and its association with

67. Tucker DM, Novelly RA, Walker PJ: Hyperreligiosity in temporal lobe epilepsy: redefining the relationship. J Nerv Ment Dis 1987; 175:181–184

68. Roberts JKA, Guberman A: Religion and epilepsy. Psychiatric Journal of the University of Ottawa 1989; 14:282–286

69. Heim A: Remarks on fatal falls. Yearbook of the Swiss Alpine Club 1892; 27:327–337

70. Noyes R, Kletti R: Depersonalization in the face of life-threatening danger: a description. Psychiatry 1976; 39:19–27

71. Rodin E: The reality of death experience: a personal perspective. J Nerv Ment Dis 1980; 168:259–263

72. Owens JE, Cook EW, Stevenson I: Features of "near-death experience" in relation to whether or not patients were near death. Lancet 1990; 336:1175–1177

73. Greyson B, Bush NE: Distressing near-death experiences. Psychiatry 1992; 55:95–110

74. Stevenson I, Cook EW: Involuntary memories during severe physical illness or injury. J Nerv Ment Dis 1995; 183:452–458

75. Kellehear A: Culture, biology, and the near-death experience. J Nerv Ment Dis 1993; 181:148–156

76. Carr DB: Endorphins at the approach of death (letter). Lancet 1981; 1:390

77. Sotelo J, Perez R, Guevara P, et al: Changes in brain, plasma, and cerebrospinal fluid contents of beta-endorphin in dogs at the moment of death. Neurol Res 1995; 17:223–225

78. Kuhar MJ, Pert CB, Snyder SH: Regional distribution of opiate receptor binding in monkey and human brain. Nature 1973; 245:447–450

79. Henriksen S, Bloom F, McCoy F, et al: Beta-endorphin induces nonconvulsive limbic seizures. Proc Natl Acad Sci USA 1978; 75:5221–5225

80. Ableitner A, Schulz R: Neuroanatomical sites mediating the central actions of beta-endorphin as mapped by changes in glucose utilization: involvement of mu opioid receptors. J Pharmacol Exp Ther 1992; 262:415–423

81. Jansen K: Neuroscience, ketamine, and the near-death experience, in The Near-Death Experience Reader, edited by Bailey LW, Yates J. New York, Routledge, 1996, pp 265–282

82. Strassman RJ: Hallucinogenic drugs in psychiatric research and treatment. J Nerv Ment Dis 1995; 183:127–138

83. Strassman RJ, Qualls CR, Uhlenhuth EH, et al: Dose-response study of N,N-dimethyltryptamine in humans. Arch Gen Psychiatry 1994; 41:98–108

84. LaBarre W: The Peyote Cult, 5th edition. Norman, OK, University of Oklahoma Press, 1989

85. Pahnke WN: An analysis of the relationship between psychedelic drugs and the mystical consciousness. Doctoral dissertation, Harvard University, 1963

86. Doblin R: Pahnke's "Good Friday Experiment": a long-term follow-up and methodological critique. J Transpers Psychol 1991; 23:1–28

87. Masters REL, Houston J: The Varieties of Psychedelic Experience. New York, Holt, Rinehart, and Winston, 1966

88. Joyce JN, Share A, Lexow N, et al: Serotonin uptake sites and serotonin receptors are altered in the limbic system of schizophrenics. Neuropsychopharmacology 1993; 8:315–336

89. Serafetinides EA: The significance of the temporal lobes and of hemisphere dominance in the production of the LSD-25 symptomatology in man. Neuropsychologia 1965; 95:53–63

90. Heise DR: Delusions and the construction of reality, in Delusional Beliefs, edited by Oltmanns TF, Maher BA. New York, Wiley, 1988, pp 259–272

91. Greenberg D, Witzum E, Buchbinder JT: Mysticism and psychosis: the fate of Ben Zoma. Br J Med Psychol 1992; 65:223–235

92. Barnhouse RT: How to evaluate patients' religious ideation, in Psy-

chiatry and Religion: Overlapping Concerns, edited by Robinson LH. Washington, DC, American Psychiatric Press, 1986, pp 89–106

93. Gaines A: Delusions: culture, psychosis, and the problem of meaning, in Delusional Beliefs, edited by Oltmanns TF, Maher BA. New York, Wiley, 1988, pp 230–258

94. Winters KC, Neale JM: Delusions and delusional thinking in psychotics: a review of the literature. Clin Psychol Rev 1983; 3:227–253

95. Cutting J: Descriptive psychopathology, in Schizophrenia, edited by Hirsch SR, Weinberger DR. Cambridge, MA, Blackwell Science, 1995, pp 15–27

96. World Health Organization: Schizophrenia: An International Follow-up Study. New York, Wiley, 1979

97. Wing JK, Cooper JE, Sartorius N: The Description and Classification of Psychiatric Symptoms: An Instruction Manual for the PSE and CATEGO system. Cambridge, England, Cambridge University Press, 1974

98. Westermeyer J: Some cross-cultural aspects of delusions, in Delusional Beliefs, edited by Oltmanns TF, Maher BA. New York, Wiley, 1988, pp 212–229

99. Klaf FS, Hamilton JG: Schizophrenia: a hundred years ago and today. Journal of Mental Science 1961; 107:819–827

100. Garety PA, Hemsley DR: Delusions: Investigations Into the Psychology of Delusional Reasoning. New York, Oxford University Press, 1994

101. Bentall RP: The syndromes and symptoms of psychosis, in Reconstructing Schizophrenia, edited by Bentall RP. London, Routledge, 1990, pp 23–60

102. Maher BA, Spitzer M: Delusions, in Comprehensive Handbook of Psychopathology, 2nd edition, edited by Sutker P, Adams H. New York, Plenum, 1993, pp 263–293

103. Von Damurus E: The specific laws of logic in schizophrenia, in Language and Thought in Schizophrenia, edited by Kasanin JS. Berkeley, CA, University of California Press, 1944, pp 30–44

104. Hemsley DR, Garety PA: The formation and maintenance of delusions: a Bayesian analysis. Br J Psychiatry 1986; 149:51–56

105. Wiggins OP, Schwartz MA, Northoff G: Toward a Husserlian phenomenology of the initial stages of schizophrenia, in Philosophy and Psychopathology, edited by Spitzer M, Maher BA. New York, Springer-Verlag, 1990, pp 21–34

106. Benson DF, Stuss DT: Frontal lobe influences on delusions: a clinical perspective. Schizophr Bull 1990; 16:403–411

107. Cutting J: The phenomenology of acute organic psychosis: comparison with acute schizophrenia. Br J Psychiatry 1987; 151:324–332

108. Carlson GA, Goodwin FK: The stages of mania: a longitudinal analysis of the manic episode. Arch Gen Psychiatry 1973; 28:221–228

109. World Health Organization: The International Pilot Study of Schizophrenia. Geneva, WHO, 1973

110. Leff JP, Fischer M, Bertelsen AC: A cross-national epidemiological study of mania. Br J Psychiatry 1976; 129:428–442

111. Petry S, Cummings JL, Hill MA, et al: Personality alterations in dementia of the Alzheimer type. Arch Neurol 1988; 45:1187–1190

112. Chatterjee A, Strauss ME, Smyth KA, et al: Personality changes in Alzheimer disease. Arch Neurol 1992; 49:486–491

113. Cummings JL: Organic delusions: phenomenology, anatomical correlations, and review. Br J Psychiatry 1985; 146:184–197

114. Lynch T, Sano M, Marder KS, et al: Clinical characteristics of a family with chromosome 17–linked disinhibition-dementia-parkinsonism-amyotrophy complex. Neurology 1994; 44:1878–1884

115. Davidson RJ: Anterior cerebral asymmetry and the nature of emotion. Brain Cogn 1992; 20:125–151

116. James W: The Varieties of Religious Experience. New York, Longmans, Green and Co, 1902

117. Otto R: The Idea of the Holy. New York, Oxford University Press, 1923

118. Byrnes JF: The Psychology of Religion. New York, The Free Press, 1984

119. Brown LB: The Psychology of Religious Belief. London, Academic Press, 1987

120. Clark WH: The phenomena of religious experience, in Religious Experience: Its Nature and Function in the Human Psyche, edited by Clark WH, Malony HN, Daane J, et al. Springfield, IL, Charles C Thomas, 1973, pp 21–40

121. Spika B, Hood RW, Gorsuch RL: The Psychology of Religion: An Empirical Approach. Engelwood Cliffs, NJ, Prentice-Hall, 1985

122. Joseph R: Neuropsychiatry, Neuropsychology, and Clinical Neuroscience, 2nd edition. Baltimore, Williams and Wilkins, 1996

123. Aggleton JP: The contribution of the amygdala to normal and abnormal emotional states. Trends Neurosci 1993; 16:328–333

124. Damasio AR, Tranel D, Damasio H: Somatic markers and the guidance of behavior, in Frontal Lobe Function and Dysfunction, edited by Levin H, Eisenberg H, Benton A. New York, Oxford University Press, 1991, pp 217–228

125. Saver JL, Damasio AR: Preserved access and processing of social knowledge in a patient with acquired sociopathy due to ventromedial frontal damage. Neuropsychologia 1991; 29:1241–1249

126. Jaynes J: The Origin of Consciousness in the Breakdown of the Bicameral Mind. Boston, Houghton Mifflin, 1976

127. Lex BW: The neurobiology of ritual trance, in The Spectrum of Ritual, edited by D'Aquili EG, Laughlin CD, Mcmanus J. New York, Columbia University Press, 1979, pp 117–151

128. Ashbrook JB: The Brain and Belief: Faith in the Light of Brain Research. Bristol, IN, Wyndham Hall Press, 1988

129. Persinger MA: Vectorial cerebral hemisphericity as differential sources for the sensed presence, mystical experiences, and religious conversions. Percept Mot Skills 1993; 76:915–930

130. D'Aquili E: The myth-ritual complex, a biogenetic structural analysis, in Brain, Culture, and the Human Spirit, edited by Asbrook JB. Lanham, MD, University Press of America, 1993, pp 45–75

131. Turner V: Body, brain, and culture, in Brain, Culture, and the Human Spirit, edited by Asbrook JB. Lanham, MD, University Press of America, 1993, pp 77–108

132. Wulff DM: Psychology of Religion, 2nd edition. New York, Wiley, 1996

133. Landsborough D: St. Paul and temporal lobe epilepsy. J Neurol Neurosurg Psychiatry 1987; 50:659–664

134. Vercelletto P: La maladie de Saint Paul. Rev Neurol 1994; 150:835–839

135. Trimble MR: The Psychoses of Epilepsy. New York, Raven, 1991

136. Temkin O: The Falling Sickness: A History of Epilepsy From the Greeks to the Beginning of Modern Neurology. Baltimore, Johns Hopkins University Press, 1971

137. Drucker T: Malaise of Margery Kempe. New York State Journal of Medicine 1972; 72:2911–2917

138. Foote-Smith E, Bayne L: Joan of Arc. Epilepsia 1991; 32:810–815

139. Johnson J: Henry Maudslay on Swedenborg's messianic psychosis. Br J Psychiatry 1994; 165:690–691

140. Foote-Smith E, Smith TJ: Emanuel Swedenborg. Epilepsia 1996; 37:211–218

141. Taylor DC, Marsh SM: Hughlings Jackson's Dr Z: the paradigm of temporal lobe epilepsy revealed. J Neurol Neurosurg Psychiatry 1980; 43:758–767

142. Arenberg IK, Countryman LLF, Bernstein LH, et al: Vincent's violent vertigo. Acta Otolaryngol 1991; 485:84–103

143. Buckley P: Mystical experience and schizophrenia. Schizophr Bull 1981; 7:516–521

144. Oxman TE, Rosenberg SD, Schnurr PP, et al: The language of altered states. J Nerv Ment Dis 1988; 176; 401–408

145. Group for the Advancement of Psychiatry: Mysticism: Spiritual Quest or Psychic Disorder? (Mental Health Materials Center, vol 9, publ no 97). New York, Mental Health Materials Center, 1976