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REVIEW

## Hyperreligiosity in malignant brain tumors: a case report and accompanying bibliographic review

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### ABSTRACT

Religion is a complex cognitive process with biopsychosocial and cultural dimensions, product of the activation of different circuits of the neocortex. In some cases, religiosity can appear as a pathological correlate in patients with brain lesions in the areas involved. We present the clinical case of a patient with an astrocytoma in the right prefrontal region, with apparent inflammatory involvement of the right temporal lobe. This tumor debuted almost exclusively as an alteration of personality consisting of hyperreligiosity, logorrhea, and mystical experiences. A review of the literature has been conducted and possible pathophysiological mechanisms are proposed.

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### KEYWORDS

Hyperreligiosity; astrocytoma; limbic encephalitis; hallucinations; ecstatic seizures

### Introduction

In his novel *Lying Awake* (Salzman, 2000), Mark Salzman describes the case of a Carmelite nun who wrote an abundance of poetry and essays and who called herself Sister John of the Cross, in remembrance of the XVI century Spanish mystic poet. While writing her texts, she had exquisite visions and mystical experiences. Her writings are an inspiration for many people both inside and outside the congregation. One day, those profound spiritual experiences were found to be due to right temporal lobe (RTL) epilepsy, caused by a brain tumor, thereby providing a rational explanation for her headache, her numinous visions, and for her passion for writing. This constellation of symptoms consisting of hyperreligiosity, mystical experiences, hypergraphia, and hyposexuality has been reported in patients with RTL epilepsy and is known as Gastaut–Geschwind syndrome (Trimble & Freeman, 2006). The novel revolves around a person endowed with delicate poetic sensitivity, who must confront the rational explanation for a medical disorder more than mystical or supernatural causes and, in so doing, must undergo surgical treatment that will end up by removing the source of experiences that, for years, have validated her religious vocation.

Fictional literature has managed to imaginatively recreate physicians' and patients' hopes, doubts, fears, and inner conflicts that are normally inaccessible for direct scrutiny, hereby enabling us to reflect on existential aspects of neurological diseases or the human condition. However, fiction inevitably entails prototypical descriptions that often do not correspond to how these diseases manifest in the real world. In medical literature (as opposed to fiction), there is not an abundance of pure cases of hyperreligiosity associated with neurological diseases.

The following is the case report and overview of a patient in care at our hospital for several months, who had assimilated the product of a diseased state of mind into her *self* or *her ego*.

In this case, there was also a medical procedure that could alleviate her symptoms, albeit at the expense of eradicating precious religious, intimate experiences that, in the short term, provided her with tremendous emotional well-being.

### Result

The patient was a 60-year-old female at the time of diagnosis who was happy and positive by nature. In the previous two months, her neurobehavior had changed, exhibiting apathy, sadness, abulia, withdrawal, subtle changes in personality noticed by her family, slowness, awkwardness, and exacerbation of her religious behavior. The people around her attributed these symptoms to a reactive depressive disorder due to the cancer a relative had recently suffered and for whom she was still caring at the time.

The patient had no history of neurological diseases, psychotic disorders, anxiety, or mood disorders, except for a self-limiting adjustment disorder years earlier that had resolved without requiring medication. Insofar as her personality traits were concerned, she was not a woman given to exaltation, suggestion, or repeated obsessions. These characteristics were in stark contrast to the fact that in the space of a very short time, she had developed a growing interest in the Bible and other sacred writings and spent the hours of the day reciting endless religious litanies.

The patient had not displayed strong faith up until that time, despite the fact that she lived in one of the communities having the highest percentage of practicing Catholics in the world. However, she did consider herself to be a believer; hence, it was not a case of religious conversion as previously reported in the literature (Waxman & Geschwind, 1974).

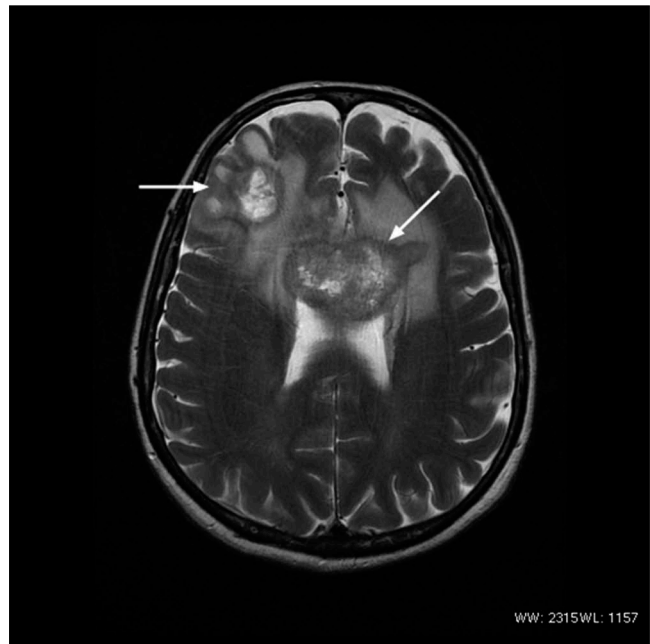
The religious logorrhea surprised the people around her, although she perceived it to be valuable and positive, instilling in her a sense of tremendous well-being. There was no sign of

psychomotor agitation, nor could any fear, commotion, mania, obsession, or worry be inferred from her behavior. The patient usually recorded the audio of her mystical sessions in which she stated that she was seeing, feeling, and conversing with the Virgin Mary. The patient's mystical experiences presented in the form of visual, auditory, and other sensory hallucinations, all of which were religious and had to do with the Virgin Mary. These episodes could last for hours or even days, displaying no associated seizures, neurological deficits, loss of consciousness, or amnesia of what had happened once the episode had passed. Timewise, they did not appear to be episodic and followed no preestablished time pattern. Her mind interpreted and re-elaborated these episodes in line with her way of thinking. Days after these experiences, she was less ecstatic, although she maintained her faith and continued to think that the experiences had been both valid and real.

Our patient did not have the same cultural baggage that Salzman attributes to the nun in his book. Even so, she changed the essays for audio recordings that she felt compelled to make with exceptional diligence. In these recordings, she spoke with great emotion about how the Virgin Mary was everyone's "beloved mother" and, hence, was therefore her mother, too. She also talked to her about how to soothe and save the world.

The patient underwent a brain magnetic resonance imaging (MRI) in an MRI LX 1.5T, GE Medical Systems, Milwaukee (WI), equipment. The imaging protocol included T1-weighted image (T1WI) and T2-weighted image (T2WI), fluid attenuation inversion recovery sequence, univoxel proton magnetic resonance spectroscopy, diffusion-weighted imaging (DWI), and a T1WI with intravenous contrast (gadolinium).

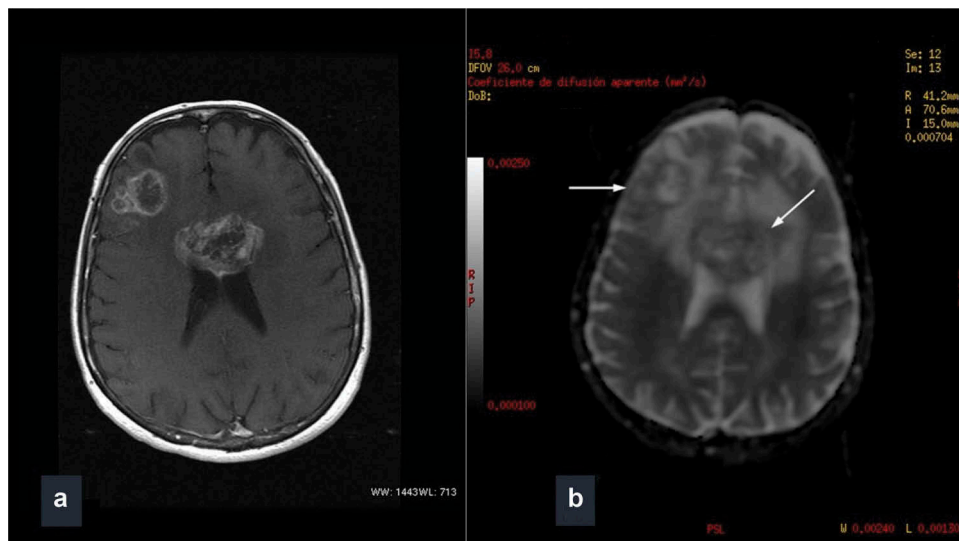
Conventional images showed a lesion located in the cortex and subcortical white matter in the middle frontal gyrus (prefrontal region) and a deeper bulky mass centered in the genu of the corpus callosum. These lesions had a heterogeneous signal intensity on T2WI and fluid attenuation inversion recovery with internal areas of necrosis and hemorrhage and were surrounded by white matter involvement compatible with



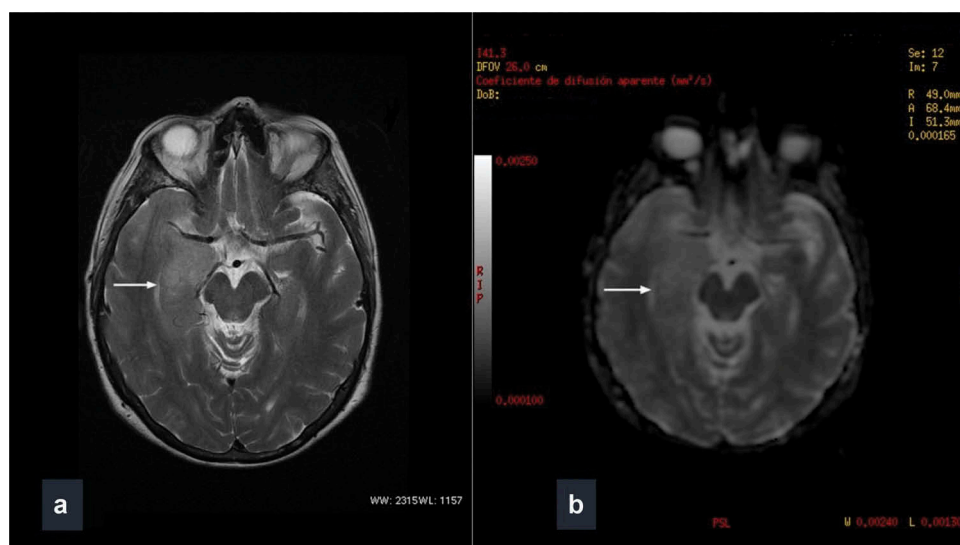
**Figure 1.** Axial T2WI shows the cortical and subcortical lesion in the right frontal lobe and the bulky mass centered in the genu of the corpus callosum (arrows).

vasogenic edema, although microscopic infiltration interconnecting the lesions was probably present (Figure 1). On DWI and apparent diffusion coefficient (ADC) maps, a restricted diffusion in the periphery of the lesions could be seen, which correlated with the pattern observed on T1WI after intravenous gadolinium administration consisting of a predominant peripheral enhancement (Figure 2). The magnetic resonance spectroscopy centered within the lesion of the corpus callosum identified increased choline and lipids and decreased *N*-acetylaspartate.

MRI also showed thickening and homogeneously increased signal intensity on T2WI in the right medial temporal lobe (MTL) where DWI and ADC maps revealed slightly increased



**Figure 2.** (a): Axial T1WI with gadolinium shows peripheral heterogeneous enhancement of the lesions. (b): On ADC map a facilitated central diffusion and restriction in the peripheral component of the tumors is seen (arrows).

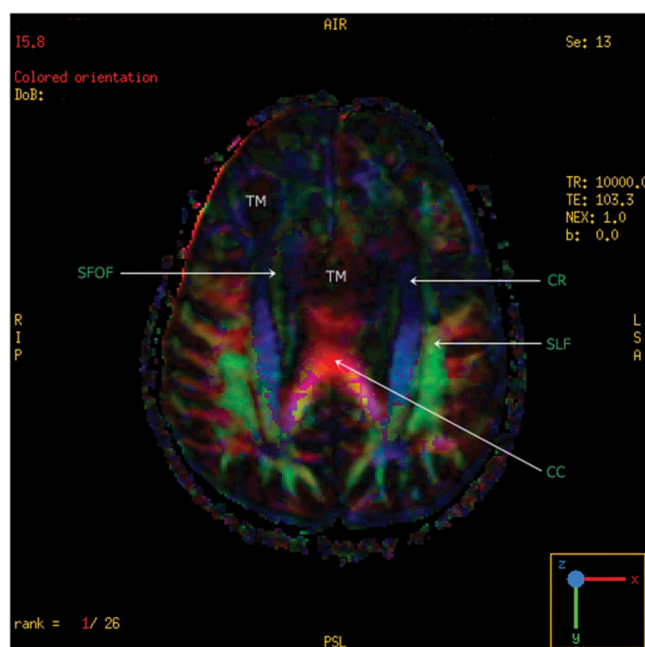


**Figure 3.** (a): Axial T2WI in which the involvement of the medial region of the RTL can be seen (arrow). (b): ADC map shows slightly increased signal intensity in relation with facilitated diffusion (arrow).

diffusion and no enhancement on the study with intravenous contrast (Figure 3). This right medial temporal involvement behaved differently from the other lesions and was distinctly separate from them, which led to the initial, imaging-based suspicion that it could be a high-grade, multicentric glial tumor with peritumoral edema.

Post-processing techniques were performed and mean diffusivity and fractional anisotropy maps were obtained. Overall, an increased mean diffusivity in the involved areas and a decreased fractional anisotropy were seen. In addition, colored orientation fractional anisotropy maps were obtained making it possible to assess the involved fasciculus that included association fibers such as the superior longitudinal fasciculus and the superior fronto-occipital fasciculus, projection fibers such as the corona radiata, and commissural fibers such as the commissure of the corpus callosum (Figure 4).

A right frontal biopsy was taken, and the tumor was seen to correspond histologically to a glioblastoma multiforme. No electroencephalographic evaluation was undertaken at that time given the patient's evolution and decline. The neoplasm was beyond the limits of neurosurgery and was therefore treated with radiotherapy and chemotherapy (temozolomide), as per the standard protocol for this type of tumor (Stupp's schedule) (Stupp et al., 2009). Antipsychotic treatment (haloperidol 15 mg per day) was also prescribed, as these cases sometimes respond to drugs of this type. No anticonvulsant treatment was prescribed. The patient completed the radio-chemotherapy protocol in October 2012. Over the course of the five weeks that treatment lasted, the rapture and evangelical visions gradually disappeared, although she continued to believe that they were valid and true. We did not see any changes in behavior. Two months after completing radiotherapy, the patient suffered an ischemic stroke of the left middle cerebral artery and was unable to continue her cancer treatment with temozolomide. At that time, the patient underwent non-enhanced cerebral computed tomography (CT) that showed full resolution of the changes in the right MTL

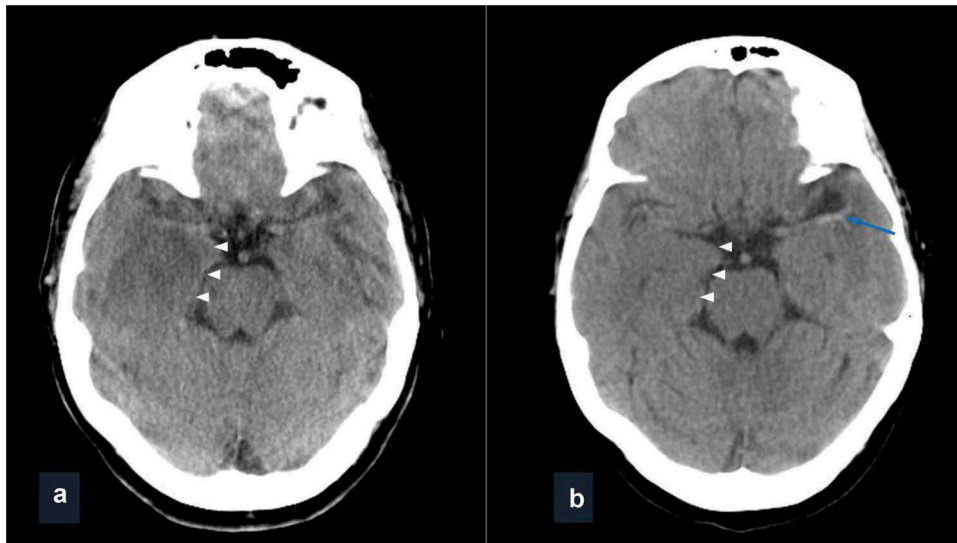


**Figure 4.** Colored orientation FA map where the right frontal and corpus callosum tumors (TM), as well as the tracts of white matter of the superior fronto-occipital fasciculus (SFOF), superior longitudinal fasciculus (SLF), corona radiata (CR), and corpus callosum (CC) can be identified. To view this figure in color, please see the online version of this journal.

(Figure 5 and section on "Discussion"). Eight months after the diagnosis of her brain tumor, in April 2013, the patient passed away due to tumor progression. During the months following her stroke, she was highly impaired in general, with severe cognitive dysfunction, and was cared for by a palliative homecare unit.

## Discussion

We must begin by pointing out that neurobehavioral disorders can be the first symptom of intracranial lesions (Blustein &



**Figure 5.** (a): Initial nonenhancement brain CT exhibits slight thickening and hypodensity of the right MTL (arrowheads). (b): Two months later, morphology and density of the right MTL (arrowheads) are normal. Hyperdense middle cerebral artery sign associated with thrombosis (blue arrow). To view this figure in color, please see the online version of this journal.

Seeman, 1972); any patient over the age of 40 years with altered mental, emotional, or cognitive status should therefore be evaluated by a physician and, if other causes (e.g., medications, substance abuse, etc.) are ruled out, neuroimaging should be ordered. Primary psychiatric diseases tend to debut earlier, in adolescence or young adulthood.

Briefly, this patient's pathology is compatible with complex partial seizures originating in the right MTL, with religious phenomenology in spite of being unable to perform an electroencephalogram due to the poor clinical course. On imaging, the findings suggest a multifocal glioblastoma with right frontal and corpus callosum involvement, adjacent vasogenic edema, as well as an area where the signal is altered in the temporal lobe, probably related to postictal changes, without ruling out other inflammatory (limbic encephalitis) or tumor-related (gliomatosis cerebri) disturbances. In fact, the glioblastoma multiforme is a tumor having generally diffuse margins, resulting from the invasion of adjacent tissues. Furthermore, it is typically surrounded by cerebral edema and multifocal in 10–20% of the cases, although it is less frequently multicentric (Kyritsis, Levin, Yung, & Leeds, 1993). As illustrated by this case, the heterogeneous presentation pattern comprises a diagnostic challenge, not uncommonly confused with a tumor accompanied by inflammation (Deramecourt et al., 2009; Nagata et al., 2010; Nam, Choi, Kim, & Cho, 2011; Riela, Sires, & Penry, 1991; Sun et al., 2014). Nonetheless, the CT displaying apparent normalization of the right temporal involvement flies in the face of a multicentric tumor, though this technique is less sensitive than MRI in capturing subtle alterations. Moreover, an infarct was detected in the territory of the left medial cerebral artery. On the other hand, in order to impute this lesion to limbic encephalitis, it would have to be confirmed by cerebrospinal fluid analysis, since imaging is not so specific as to be able to guarantee it without this datum. However, the patient's general status precluded further complementary testing.

All these lead us to believe that finding reversible brain changes on the margin of the main mass is suggestive of postictal encephalitis (with transient seizure-induced brain changes) following nonconvulsive seizures. In fact, epilepsy is the symptom that is more common with gliomas, occurring in approximately half of all patients (van Breemen et al., 2009). However, this clinical suspicion cannot be confirmed without performing an electroencephalogram. In the case of our patient, the reason for not expanding the study with this test and not administering anticonvulsants was threefold: (1) the clinical course appeared to be psychotic in its timeline and time pattern and improved with neuroleptic treatment; (2) the changes on the MRI were temporary and were interpreted as possibly inflammatory; and (3) the aggressiveness of the glioblastoma multiforme made it difficult to carry out further examinations. Nevertheless, we consider that occult epilepsy could be a plausible diagnosis.

In fact, the most widely studied cases of hyperreligiosity are those that occur in individuals with epilepsy, principally of the RTL. A highly conspicuous trait of these patients is that they may associate especially rich, upsetting, or intense spiritual experiences (Devinsky & Lai, 2008). For example, in 1970, Kenneth Dewhurst and A. W. Beard reported the case of a bus conductor from London who suffered an epileptic seizure (ecstatic) of the RTL while collecting tickets from the passengers and, at that precise instant, he felt that he had suddenly found himself in Heaven, telling the surprised passengers about his elation. The patient went through various phases, from mystical rapture, serene religious feeling, and the loss of faith several years afterward (Dewhurst & Beard, 1970). Most reports coincide in that the subjects perceive light and being transported to a luminous, expansive, highly meaningful reality with peace, harmony, hope, peace, and ecstasy in which the spirit is freed from earthly and bodily constraints (Devinsky & Lai, 2008). These spiritual experiences may be deistic, depending on the subject's personal elaboration or cultural substrate. It has been estimated that approximately 1% of

temporal lobe epilepsy sufferers experience ictal religious episodes (Kanemoto & Kawai, 1994). These patients have reported diverse experiences, from very intense emotions about the close presence or vision of the Divine to auditory hallucinations of the voice of God, apparitions of divine figures, messages to be obeyed, or divine mandates to be fulfilled that, on rare occasions, are criminal or repetitions of religious discourses. In these cases, the mystical experiences are frequently emotionally intense, with theological ruminations, flashbacks, numinous auras, states of deep religious conviction, feeling the presence of or becoming one with the Universe or with the eternal (Landtblom, 2006). Often, the religious personality in these cases is unorthodox and exuberant, not uncommonly having paranormal content and multiple deviations from standard religions (Waxman & Geschwind, 1974). Moreover, electroencephalographic studies have been conducted in Carmelite nuns who have demonstrated that mystical experiences are measured by striking changes in the power or coherence of their brain waves (Beauregard & Paquette, 2008).

In the case of postictal encephalitis, the physiopathological substrate of the MRI alterations would be related to the vascular and metabolic response and would correspond to vasogenic and cytotoxic edema, respectively. There are also indications that would suggest the coexistence of common genetic mechanisms and pathways for the gliomatogenesis and the epilepsy associated with these tumors (Berntsson, Malmer, Bondy, Qu, & Smits, 2009; Sontheimer, 2008). Peritumor adenosine kinase deregulation would play a role in the cancer-related epileptogenesis (de Groot et al., 2012).

Of course, there is another credible explanation that has been contemplated previously in the medical literature. It postulates that the patient had a psychotic syndrome, perictal, or not, for which she ended up being treated (Kanemoto, Oshima, Tadokoro, & Kanemoto, 2006). In fact, other authors consider that the experiences associated with epileptic seizures are, more often than not, due to accompanying psychiatric co-morbidity (Connell, Keaveney, & Paul, 2013). On the other hand, during interictal periods, a personality pattern is commonly found, characterized by greater concern for highly abstract philosophical issues, feelings of personal destiny, very strong moral tendencies, or religious beliefs that frequently contrast with the type of education received or the person's cultural context (Trimble & Freeman, 2006).

Pathological religious experiences have been reported in relation to various diseases, such as autism, Parkinson's disease, neurosyphilis, dementia, sleep deprivation, sensorial isolation, hallucinogenic drug use, obsessive-compulsive disorder, manic-depressive disorder, schizophrenia, often as part of dissociative states with altered self-identity (Giaquinto, Bruti, Dall'Armi, Palma, & Spiridigliozzi, 2011). Cases of hyperreligiosity have been reported in individuals with atrophy of the RTL (Everhart, Watson, Bickel, & Stephenson, 2015). However, none of these conditions appear to play a role in this patient's clinical manifestations. There is also a field of research that postulates that the interindividual differences in religious behavior may be founded in neurobiochemical variations such as the density of serotonin receptors (Borg, Andree, Soderstrom, & Farde, 2014).

The severity of the disease presented here, in comparison to the, a priori, less aggressive diagnosis of Sister John of the Cross' tumor (Salzman, 2000), did not expunge the moral issue in the consultation that had been raised in the book; that is, whether or not it is advisable to reverse all of the clinical symptoms, with no regard for their nature or for the fact that they had become an unarguable source of serenity and well-being (Glannon, 2005). In fact, patients who undergo mystical experiences speak of similar accompanying feelings of pleasure or ecstasy (Stefan et al., 2004). The medical literature contains several examples of how effective treatment of the underlying organic pathology is capable of mitigating the episodes of abnormal behavior or psychiatric disturbance associated with them (Filley & Kleinschmidt-DeMasters, 1995). Certainly, it is true that medication exerted a similar effect in this case. As the neuroleptics and cancer treatment started to have their effect, we saw how the symptoms began to remit.

From this clinical observation, two main ideas have stood out. First of all, there is the fact that religion is a phenomenon that emerges from the brain and that depends on a complex neural network, the effective functioning of which has been in the process of fine-tuning since the dawn of human civilization (Schmidt, 2010). The subtle neuronal equilibria that generate the spiritual phenomenon are susceptible to becoming disarranged in different ways due to the altering of any of the brain circuit *hubs* (Paloutzian & Park, 2014). Second is the issue of the constitution of the true *self*, which should at the very least be fruit of the individual's conscious legitimation of themselves, of their interests, and of their place in the world (Frankfurt, 1988). In the case of our patient, it is clear that the religious experience represented a fracture that did not form part of the prior argumentarium of her life; that it was not preceded by a gradual change in her thinking and acting, nor was there any kind of trigger or reason except for the disease, and hence, it can be considered a clearly pathological experience.

It is worth asking oneself how often the behavioral alterations and, specifically, hyperreligiosity as an isolated symptom of debut, occur in brain tumors. For years, it has been known that some central nervous system diseases, including tumors, make their clinical debut in the form of personality changes (Partlow, del Carpio-O'Donovan, Melanson, & Peters, 1992), hallucinations, psychosis (Shah, Gordon, Bregy, Shah, & Komotar, 2014), and other complex disturbances in perception.

Given that most reports are single clinical case reports, drawing conclusions as to incidence can be challenging, although one review concluded that some 22% of all brain tumors may debut with psychotic symptoms that are difficult to associate with concrete topographies (Madhusoodanan et al., 2010). Moreover, it is possible that these kinds of symptoms are underdiagnosed when they are mild and, in the case of brain tumors, because patients are not often asked in detail about their experiences or the spiritual aspects of their diseases.

With respect to associated symptomatology, neurobehavioral disorders can, in fact, comprise the presentation of a glioma (Blustein & Seeman, 1972) and can improve when treated (Filley & Kleinschmidt-DeMasters, 1995). Autoscopia (the individual sees themselves from outside of their own body) (Devinsky, Feldmann, Burrows, & Bromfield, 1989),

states of pleasure, ecstasy, or well-being (Stefan et al., 2004), numinous auras, which are those that are suggestive of phenomena having a spiritual intent or religious content, or metaphysical in nature (Dolgoff-Kaspar et al., 2011), as well as other premonitory or other kind of states, have been reported in relation to epileptic seizures and can even improve the decline in quality of life in certain pathologies (Giovagnoli, Meneses, & da Silva, 2006).

Religion is one of the most surprising biocultural adaptations of nature (Harris & McNamara, 2008). It is a complex cognitive process, product of the activation of several circuits of the neocortex, in which phenomena are often attributed to some kind of divinity, conceived of as being infinite and eternal, and by means of a causal chain, becomes the agent responsible for each religious experience (Proudfoot & Shaver, 1975). The neurobiochemical foundations of religion continue to be unknown, although the latest findings suggest that our brain might be programmed for religious experience (Fingelkurts & Fingelkurts, 2009). The presence of spiritual beliefs in all cultures, ages, civilizations, races, and geographies suggests the presence of neurological correlates (Devinsky & Lai, 2008). It is clear that all subjective human experience ultimately resides in the brain, the neural networks of which are responsible for all emotion and thought. Thus, neurological bases or patterns have been sought to shed light on this phenomenon, although they are never assumed to be a full description of it. In this regard, religiosity involves many facets of human cognitive and emotional activities, such as language, reasoning, joy, wonder, etc., and there may be areas or connections that are especially affected (Saver & Rabin, 1997).

In the case of our patient, the tentative search for possible topographic localizations or neurophysiological correlates is complex, despite how conspicuous the mass was and the possible epileptic etiology. Glioblastomas multiformes are highly invasive tumors that are not circumscribed to specific topographic zones; rather, they outgrow the territories in which they arise. These types of clinical symptoms, therefore, will rarely present as a purely psychiatric disorder and, in fact, will tend to associate with more comorbidity or with more complex polysyndromic situations as the disease progresses (Sokolski & Denson, 2003). From this perspective, the perfect correlation between the location of the lesion and behavior is not possible, since the inflammation, bleeding, and edema complicate even further the clinical-anatomic correlation. In contrast, for the paucity of data that exist, the neurophysiological substrate has been described fairly consistently in the literature for years.

More than 100 years ago, the American philosopher and psychologist William James outlined two varieties of religious experiences. On the one hand are those transmitted by family and society that generally materialize as complying with moral precepts, identification of group observance of dogmas, etc., whereas, on the other hand, there is another kind of spiritual experience, even more intense or more genuine in appearance if possible (James, 1985). In the words of James, they would be "not as a dull habit, but as an acute fever rather." Surely this is reductionistic, and religion has other components such as altruism, consolation, charity, hope, etc. Nevertheless, this approach could be valid, since tentatively, albeit consistently, neuroscience has

found that in the former case, the anatomic correlate appears to reside in the frontal lobes, whereas in the latter case, it would generally be temporal lesions. However, this may be a simplified approach. Thus, one study of functional MRI performed on Carmelite nuns to identify the neural correlates of religious experience detected multiple brain areas (e.g., right inferior and superior parietal lobules, right caudate, right medial orbitofrontal cortex, right middle temporal cortex, left medial prefrontal cortex, left anterior cingulate cortex, left inferior parietal lobule, left insula, left caudate, and left brainstem) involved in various aspects of religiosity (Beauregard & Paquette, 2006). The authors stated that this multiplicity of locations is not surprising given the fact that these experiences are complex and multidimensional.

In the woman whose case we report, there was extensive involvement of the limbic lobe and anterior pole of the RTL. In effect, the temporal lobes, particularly the RTLs (Devinsky & Lai, 2008), have been cited reiteratively in the development of ecstatic mystical experiences (Tucker, Novelly, & Walker, 1987; Willmore, Heilman, Fennell, & Pinnas, 1980), while other components of religious experience are related more with other topographical locations. In the case of Sister John of the Cross, it is possible that there was a disturbance at the level of the connection with the right angular gyrus that is partially responsible for identity and spatial orientation. A lesion at this level hinders the patient's ability to establish the limits between self and the rest of the universe (Spitoni et al., 2013). Thus, the RTL is critical for the perception of intense spiritual phenomena, similar to William James' description. Other regions reported in the literature as anatomic substrates of hyperreligiosity are the limbic system (Trimble & Freeman, 2006) and the hippocampus. The MRI volumetric studies reveal that patients with hyperreligious criteria have a significantly smaller right hippocampus, with no differences in the size of the amygdala (Wuerfel et al., 2004). The anterior rostral cingulate cortex has been linked to altruism.

In contrast, the frontal lobe is the phylogenetically youngest area of the central nervous system and plays a key role in the organization and integration of behavior (Mesulam, 1986). There are three types of frontal syndromes, depending on the precise location, and when involvement is bilateral, the syndrome is all the more dramatic (Filley & Kleinschmidt-DeMasters, 1995). It is well known that disturbances of more complex activities, such as conceptualization or personality, occur especially when there are prefrontal lesions (Campanella, Shallice, Lus, Fabbro, & Skrap, 2014). The frontal lobes have not been associated with such vivid religious experiences but are responsible for personality, including complex aspects such as politics, behavior, social relation, introspection (Brower & Price, 2001; Johnson et al., 2002), or greater religious interest as a personality trait (Floris et al., 2012). In our case, MRI abnormalities in the temporal lobe preclude the assumption that the frontal lobe lesion is the cause of the religious phenomena. However, the conspicuous abulia, apathy, and personality change observed in our patient are clear characteristics of frontal syndromes. Thus, in one series, 10% of the patients with fronto-temporal dementia underwent dramatic changes with respect to their previous political, social, or religious ideas. The majority of these

subjects presented involvement of the nondominant frontal lobe (Miller et al., 2001).

In general, we are dealing with scenarios in which the perception of self and of its limits is affected by reason a frontal lesion that provides the substrate of pathological religious experiences in which the individual will have the feeling of having coalesced with everything or with the Divine. Hence, the involvement of frontal medial cortex is necessary to be able to discern in the mind of others, which can be extended to include the ability to discern in the mind of God (Stuss, Gallup, & Alexander, 2001).

The areas of relation of the parietal lobes have also been implicated in the appearance of pathological religious experiences (Crescentini, Aglioti, Fabbro, & Urgesi, 2014). One brain perfusion study carried out in Tibetan monks while they meditated found that the substrate of some mystical experiences was the deafferentation of the postero-superior parietal lobe. This region has to do with spatial orientation and the perception of oneself in relation with the rest of the Universe (Newberg et al., 2001). In their pathological aspect, alterations in this area would give rise to a tremendous sense of uniting with Eternity and the Devine. Likewise, Azari et al. demonstrated the importance of a preestablished frontal-parietal circuit (Azari et al., 2001). The religious experience would occur when the products of this circuit are in consonance with the subject's previous religious belief system (Azari et al., 2001). According to this, religion would not only always be an emotional but also cognitive experience and, therefore, a truly human phenomenon.

When taken all together, we find that multiple structures are involved, including the limbic system (e.g., the amygdala), portions of the basal ganglia, the RTL, and the prefrontal cortex, particularly on the right side, which are the hubs in the circuit of religiosity. Key to these structures are the ascending serotonergic system and the dopaminergic system. All of these regions are highly interconnected. When it is stimulated in excess or affected by some kind of disease, religious ecstasy takes place. When cortical circuit activation prevails, religious ideations are the result. In contrast, when the limbic system or the basal ganglia are involved, we find obsessive ideations, changes in behavior rituals, and increased interest in stereotyped religious practices, such as prayer (Paloutzian & Park, 2014).

In short, several studies about exaggerated human behaviors, for instance, hyperreligiosity, time and again confirm their correlation with temporal and frontal lobe areas of the brain and with maladies such as epilepsy and cancer. However, we have yet to fully understand the neurological substrate of religiosity, taken to mean a more stable, daily, and permanent adhesion to a belief system that is positively associated with indicators of psychological and social well-being (satisfaction with life, positive affect, sense of family, and morality), and whether specific neuroanatomical variants might be hidden behind it.

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## Disclosure statement

No potential conflict of interest was reported by the authors.

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