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REVIEW ARTICLE

Neurology of ecstatic religious and similar experiences: ecstatic, orgasmic, and musicogenic seizures. Stendhal syndrome and autoscopic phenomena☆

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Abstract All human experiences, including mystical and religious ones, are the result of brain functional activity. Thanks to the study of cases of ecstatic epilepsy with structural (MRI) and functional neuroimaging (fMRI, PET, SPECT) and neurophysiological technologies (recording and stimulation with intracranial electrodes), we now have a better knowledge of certain mental states which involve pleasant and affective symptoms and clarity of mind. These ecstatic experiences are thought to be caused by the activation of the anterior insular cortex and some neuronal networks (basically related to mirror neurons and salience) participating in introspection, social cognition, memory, and emotional processes. Thus, neuroscience could explain in a retrospective way some facts surrounding the situations of such relevant figures as Paul the Apostle, Teresa de Cepeda y Ahumada, and Dostoevsky, whose origin was previously considered paranormal or supernatural. Ecstatic epilepsy shares symptoms and mechanisms with orgasmic epilepsy (spontaneous orgasms in the course of epileptic seizures), musicogenic epilepsy (epileptic seizures triggered by listening to a certain musical piece), and also with Stendhal syndrome (neuropsychiatric disturbances caused when an individual is exposed to large amounts of art) and some autoscopic phenomena (out-of-body experiences that occasionally take place in imminent death situations). In all these events, there are pleasant and affective symptoms which have a great impact on patients.

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PALABRAS CLAVE
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Neurología del éxtasis y fenómenos aledaños: epilepsia extática, orgásmica y musicogénica. Síndrome de Stendhal. Fenómenos autoscópicos

Resumen Todas las vivencias del ser humano, incluidas las experiencias místicas y religiosas, tienen que ver en último término con la actividad funcional de su cerebro. El estudio, mediante técnicas de neuroimagen estructural (RM) y funcional (RMf, PET, SPECT) y técnicas neurofisiológicas con registros y estimulación mediante electrodos intracraneales, de casos de epilepsia extática nos ha proporcionado un mejor conocimiento de ciertos estados mentales, en los que hay síntomas con especiales connotaciones placenteras-afectivas y de clarividencia. Se postula que tales estados de éxtasis se producen por activación de la corteza insular anterior, conexionada con redes neuronales (por defecto, saliencia y neuronas en espejo), que intervienen en la introspección, cognición social, el procesado emocional y la memoria. De este modo, la neurociencia puede aportar una explicación científica, incluso de un modo retrospectivo, a algunos hechos y situaciones relacionados con personajes relevantes (Pablo de Tarso, Teresa de Cepeda y Ahumada, Dostoievski), que, en ámbitos extracientíficos, se consideran de origen paranormal o hasta sobrenatural. Con la epilepsia extática comparten síntomas y mecanismos fisiopatológicos la epilepsia orgásmica (excitación sexual que puede desembocar en orgasmos espontáneos en el transcurso de crisis comiciales), la epilepsia musicogénica (crisis comiciales desencadenadas por particulares emociones generadas al escuchar un determinado fragmento musical), así como en el síndrome de Stendhal (cuadros neuropsiquiátricos precipitados por una contemplación masiva de obras de arte) y algunos fenómenos autoscópicos (sobre todos las experiencias extracorporales, que ocasionalmente tienen lugar en situaciones de muerte inminente): en todos ellos existe sintomatología placentera-afectiva de alto impacto para los sujetos afectados.

Introduction

According to the dictionary of the Royal Spanish Academy, the term ecstasy, from the Ancient Greek ἔκστασιζ, has 3 different meanings: (1) a pleasant state of emotional exaltation and admiration; (2) a state of the soul characterised by a mystical union with God through meditation and love, and through suspension of the exercise of the senses; and (3) a synthetic drug with hallucinogenic and aphrodisiac effects.

Ecstasy is a special mental state involving a disconnection from reality and focus on the inner world, where one experiences a vivid feeling of lucidity and plenitude, accompanied by great satisfaction. The ecstatic individual feels transported by an indescribable "supernatural force" to an ineffable "higher dimension." Other terms for this phenomenon include rapture, euphoria, and exultation. Ecstasy may be spontaneous or triggered by a number of stimuli or situations, including music, light, emotion, drugs, fasting/hunger, meditation, litanies (repetition of words or phrases), and certain brain disorders. Ecstasy is not always pathological; rather, it may be regarded as a hyperfunction that not all individuals are able to experience. Ecstasy is not always religious; it may also be secular, and both types may boost intellectual and artistic activity.[1,2] Several authors have interpreted these mystical feelings of union with God as temporal lobe epileptic seizures. Some recent studies with functional MRI (fMRI), single photon emission CT (SPECT), positron emission tomography (PET), electroencephalography, and magnetoencephalography have shown activation of multiple interconnected brain regions (neural networks).[3–5]

Ecstasy may be regarded as a state of supreme joy; however, a similarly intense pleasure may also be obtained from sex,[6] music,[7] or art,[8] and may be associated with autoscopic phenomena. This study provides a neuroscientific review of certain pathological situations (ecstatic epilepsy and similar experiences) producing extremely pleasurable emotions. We conducted a literature search on PubMed and Science Direct using the keywords mentioned above.

Development

Ecstatic epilepsy

Ecstatic epilepsy is characterised by recurrence of a special type of epileptic seizure that modifies the patient's mood and affect; patients experience intense feelings of pleasure, wellness, peace, beauty, and plenitude, occasionally with religious connotations. These symptoms, which vary in intensity and duration, may present alone or combined with other types of symptoms. People initially began to become aware of ecstatic epilepsy after Gastaut's dissertation (William G. Lennox Lecture, 1977)[9] on the epileptic seizures experienced by the Russian writer Dostoevsky (1821-1881).

Dostoevsky made some of his characters suffer, or rather enjoy, the seizures he himself had experienced. An example of this is the description of the paroxysms experienced by Dostoevsky's character Mishkin in *The idiot*: ''*I experience a feeling of happiness such as it is quite impossible to imagine in a normal state and which other people have no idea of. I feel entirely in harmony with myself and the whole world, and this feeling is so strong and so delightful that for a few seconds of such bliss one would gladly give up ten years of one's life, if not one's whole life.*'' Dostoevsky's condition had been discussed previously to Gastaut's dissertation.[10] Ecstatic seizures had also been described in patients with Urbach-Wiethe disease, a condition associated with calcifications in the amygdalae.[11] Other historical cases with a retrospective diagnosis of ecstatic epilepsy, which have also been studied in the literature, include those of Saint Paul and Saint Teresa of Ávila.

In 1987, Landsborough[12] hypothesised that Saint Paul (5-64 AD) had ecstatic seizures based on an episode he experienced on the road to Damascus. Saint Paul describes the episode in the third person (II Corinthians 12:1-4): ''*It is not expedient for me doubtless to glory. I will come to visions and revelations of the Lord. I knew a man in Christ above fourteen years ago, (whether in the body, I cannot tell;or whether out of the body, I cannot tell: God knoweth;) such an one caught up to the third heaven. And I knew such a man, (whether in the body, or out of the body, I cannot tell: God knoweth;) how that he was caught up into paradise, and heard unspeakable words, which it is not lawful for a man to utter.*'' The cause of this episode is unclear and no evidence of further episodes is available. The subsequent blindness, which lasted around 3 days, would seem to be too long-lasting to be considered a postictal symptom. The case of Saint Paul is similar in a sense to a case marvellously described by Sacks[13]: Dr Cicoria, an American physician, was hit by a lightning, which changed his life; he left traumatology and began devoting his time to music. Similarly, Saint Paul stopped persecuting Christians and spent the rest of his days spreading Christianity across the Roman Empire. Dr Cicoria could never fully forgive the nurse who saved his life for stealing a few seconds of immense joy from him.

The case of Saint Teresa of Ávila is undoubtedly the best documented historical case of ecstatic epilepsy. In 2003, García-Albea[14] published a comprehensive study of this character, reviewing the treacherous life and illness of the Carmelite nun and proposing a diagnosis of ecstatic epilepsy. In her autobiography, Saint Teresa narrates how at the age of 43, she began to experience unpredictable episodes of ecstasy of varying duration (''in as short time as it takes to recite a Hail Mary''): ''*In sum, the imagination, however keen it may be, cannot paint or sketch what this light is like, or any of the things the Lord gave me knowledge of. He bestows along with this knowledge a delight so sublime as to be indescribable, for all the senses rejoice to such a high degree and in such sweetness that the delight cannot be exaggerated—so it's better not to say any more.*'' At the age of 17, Saint Teresa had experienced severe encephalopathy with generalised motor seizures; when she was 24, she fell into a postictal coma, even receiving her last rites. Based on these episodes and the subsequent development of ecstatic seizures, García-Albea suggests that cerebral cysticercosis, which was endemic in the Iberian Peninsula at that time, may be responsible for Saint Teresa's seizures.

The case of Joan of Arc (1412-1431) was studied by d'Orsi and Tinuper[15] in 2006. According to these researchers, Joan of Arc had partial temporal lobe epilepsy with auditory features: from the age of 13, she claimed to hear divine voices, which first commanded her to live a devout life, then instructed her to fight for the coronation of Charles VII and lead the French army against the English during the Hundred Years' War. Based on Joan of Arc's auditory symptoms, the researchers suggest that the condition was autoimmune, caused by antibodies attacking epitempin (or leucine-rich glioma-inactivated protein 1), or genetic, resulting from mutations in the gene encoding the protein.

After Gastaut's studies, several cases of ecstatic epilepsy and some reviews of the topic were published.[16–19] The temporal lobe was regarded as the brain region most likely to be responsible for ecstatic epilepsy. Dostoevsky is a superb example of a ''temporal lobe personality,'' as described by Geshwind[20]: he had mania/depression, disexuality, aggressiveness, religiosity, paranoia, viscosity, and hypergraphia. The exacerbated religiosity and hypergraphia of Saint Teresa and Saint Paul are also noteworthy.[21,22] Iniesta[23] analyses the potential influence of epilepsy on Dostoevsky's literary work.

Since time immemorial, epilepsy has been thought to be divine or demonic in origin. Since the time of Hippocrates, it has been suggested that seizures originate in the brain and are not divine in nature; however the idea has survived until very recently. Numerous saints and religious leaders are thought to have experienced seizures. Devinsky and Lai[21] list up to 20 religious figures who had epilepsy, including pharaoh Amenhotep IV, the Jewish prophet Ezekiel, the Buddha, Julius Caesar, the prophet Muhammad, several Christian saints and mystics, and Kierkegaard, the father of existentialism.

Stereo-EEG findings and functional neuroimaging data gathered during seizures suggest that ecstatic seizures originate in the anterior insular cortex.[24–26] The insula integrates data from the body and the external world with emotions and memories, transforming these data in global perceptions.[27,28] The insula is part of the salience network, which is involved in attention and executive processes. Proprioception involves the default mode network[29] and the mirror neuron network (perception of emotions, empathy, aesthetic appreciation, moral behaviour, theory of mind),[30] both of which are connected with the precuneus and anterior insula. A recent study with volumetric MRI found greater grey matter volume in the precuneus of individuals with higher subjective happiness scores.[31] The brain does not passively process information; rather, it actively generates inferences and hypotheses about the nature and cause of the information perceived. Ecstasy is a dysfunction in error prediction, resulting in a feeling of peace, well-being, and clarity, due to impaired integration of multisensory and interoceptive stimuli.[32]

Stendhal syndrome

The Basilica di Santa Croce, in Florence, houses the tombs of such renowned scholars, writers, and artists as Galileo

Galilei, Vittorio Alfieri, Machiavelli, and Michelangelo. A statue of Dante Alighieri stands on a pinnacle on the church's façade, and an empty tomb awaits the author's remains. In 1817, French writer Henri-Marie Beyle (1783-1842), better known by his pseudonym Stendhal, experienced intense emotions (''celestial feelings that only the beauties of art and sentiments of passion can offer'') and psychosomatic manifestations (tachycardia, fainting) after visiting the monument; he describes these in his book *Rome, Naples, Florence*.[33]

In 1989, the Florentine psychiatrist Graziella Magherini[34] published the results of a study including 106 tourists who consulted her over a period of 10 years with a wide range of psychiatric and somatic alterations after visiting the artistic treasures of her magnificent hometown; manifestations were acute and of short duration (lasting from a few hours to one week). Magherini coined the eponym ''Stendhal syndrome'' to describe these symptoms. Over half of her patients had ideational and perceptive alterations (delusion, hallucinations, depersonalisation), nearly one-third displayed emotional alterations (depression, anxiety, euphoria), and a small percentage (5%) showed psychosomatic alterations (dizziness, sweating, tachycardia, precordial oppression, epigastric pain, fainting). Half of the patients had a history of psychiatric disorders; patients mainly came from Western countries and many either regarded themselves as artists or had a keen interest in art.[34] Dario Argento's film *The Stendhal syndrome*, released in 1996, popularised the controversial disorder, which some authors have referred to as hyperkulturemia.[35]

Few cases of Stendhal syndrome have been reported in the scientific literature. A group of Spanish neurologists, including the author of this review, participated in a prospective study: we completed a questionnaire after taking a guided tour of Florence and attending a lecture by Margherini. According to the results, 25% of survey respondents had experienced minor symptoms of the syndrome, mainly in the form of intense, pleasant emotions.[36] Upon viewing Holbein's *The body of the dead Christ in the tomb*, in Basel, Dostoevsky himself experienced an episode of immobility, disconnection, and an abnormal facial expression (not followed by motor seizures), lasting several minutes, which some authors have identified as Stendhal syndrome but which may also be interpreted as an ecstatic seizure.[37] Jerusalem syndrome shares some of the symptoms of Stendhal syndrome, but is triggered by religious rather than aesthetic excitement.[38]

Orgasmic epilepsy

The human sexual response cycle is mediated by the brain; this complex process comprises the following stages: (1) increased sexual desire accompanied by a state of emotional tension; (2) sexual arousal accompanied by swelling and/or lubrication of the external genitalia due to different stimuli (sensory, psychological); (3) masturbation or copulation (plateau phase of sustained sexual arousal); (4) ejaculation in men and vaginal and anal muscle contraction in women, accompanied by orgasm (extremely pleasurable mental state occurring during and after ejaculation/spasms); and (5) resolution and refractory period. Numerous researchers have studied the human sexual response cycle, using mainly visual stimuli and fMRI and PET imaging, and report the involvement of multiple brain areas: the orbitofrontal cortex (deactivation during orgasm), anterior cingulate gyrus, insula (mainly during the stage of sexual arousal, especially in women), temporal lobe (anterior pole, hippocampus, parahippocampus, and amygdala), and subcortical regions (cerebellum, pons, periaqueductal grey matter, hypothalamus, thalamus, caudate nucleus, claustrum). The left amygdala is activated during arousal and deactivated during orgasm; the opposite occurs with the right amygdala. The sexual response cycle usually involves a balance between hemispheres; lesions to the right hemisphere cause more symptoms of hypersexuality.[39–42]

''Orgasmic epilepsy'' and, more broadly, epilepsy with sexual ictal manifestations, are a type of epilepsy in which seizures are associated with a state of arousal similar to that experienced during sexual activity and, in some cases, orgasms identical to those occurring during sexual intercourse. This rare type of epilepsy has distinct characteristics: the seizure focus is frequently located in the medial region of the non-dominant temporal lobe; neuroimaging studies may or may not reveal structural lesions; women are more frequently affected; amygdalohippocampectomy is usually an effective treatment, although some patients undergoing the procedure complained of losing the pleasant sensations experienced during sexual aura.[43–50] Reflex seizures triggered by orgasm during sexual intercourse[51] and seizures associated with pelvic motions similar to those occurring during intercourse (seizure focus normally located in the anterior cingulate gyrus) are not considered orgasmic epilepsy per se.[52,53]

Musicogenic epilepsy

At first glance, and from an evolutionary perspective, music (unlike such other pleasant activities as sexual activity and eating) seems to provide few advantages for human survival; however, there are several arguments in support of the opposite hypothesis. Music can evoke or reinforce emotional experiences in humans (pleasure, happiness, sadness, amazement, rage, melancholy, love, hate, patriotism, etc.). Music probably developed before language as a means of expressing feelings and promoting social relationships (which also produce pleasure and promote human survival). Gooseflesh, piloerection, and ''shivers down the spine'' are vegetative manifestations associated with a strong emotional response upon hearing or performing music. As occurs with any other type of language, the processing of music in the brain involves specific mechanisms. The emotional response to music is independent of such factors as pitch, timbre, rhythm, melody, and harmony. This has been demonstrated in functional neuroimaging studies and case reports of patients with brain lesions resulting in alterations in the emotional response to music. The superior temporal gyrus and the frontal lobe activate during melody analysis, whereas timbre and pitch are processed by the auditory cortex. The hippocampus, amygdala, and insula are involved in emotional processing.[54–59]

Musicogenic epilepsy is a special type of reflex epilepsy, triggered in most cases by a specific piece of music, musical

style, instrument, or even composer; trigger factors vary between patients. First described by Critchley[60] in 1937, musicogenic epilepsy has been addressed by numerous studies, despite its low prevalence: a study by Pittau et al.[61] reviews 110 cases reported in the literature, summarising the patients' clinical, neuroimaging, and neurophysiological characteristics.

This type of seizure results in partial disconnection and is associated with a wide range of feelings (pleasant in many cases), changes in facial expression, oroalimentary automatisms, epigastric oppression, hand paraesthesia, blushing, tachycardia, and increased arterial blood pressure. The time lapse between the stimulus and seizure onset varies; on occasion, seizures occur in the absence of trigger factors. The pathogenesis of musicogenic epilepsy is thought to depend on the patient's cognitive and affective processing of music, rather than on pitch and melody. In most cases, neuroimaging studies reveal no structural brain lesions. The condition is more frequent in women and the seizure focus is usually located in the right temporal lobe. Studies with fMRI have shown that immediately before seizure onset, patients experience snowballing activation of different areas of the limbic system associated with emotional processing and control.[62–65]

Autoscopic phenomena

Autoscopic phenomena are complex hallucinatory experiences of seeing one's own body from an external perspective. They are classified, according to self-location, into 3 main groups: (1) out-of-body experiences: viewing one's body from above, with one's mind outside the body; these experiences have been reported by patients in situations of ''imminent death'' (some regard these experiences as a proof of body-soul separation before death and the idea of life after death), with psychiatric or neurological disorders, or experiencing religious ecstasy; (2) autoscopic hallucinations: viewing an exact mirror image of oneself with the mind remaining in the real body; and (3) heautoscopy: an intermediate state between out-of-body experiences and autoscopic hallucinations, with changes or fluctuations in the location of the mind, which leads patients to believe that there exists a double of themselves.[66–68]

Autoscopic phenomena are currently believed to be caused by impaired integration of spatial perception (afferences from the visual cortex) and somatic self-perception (proprioceptive and interoceptive sensory afferences from the parietal sensory cortex, and afferences from the vestibular cortex) at the level of the temporo-parieto-occipital junction. In 2002, Blanke et al.[67] induced autoscopic phenomena in epileptic patients by stimulating the temporo-parieto-occipital junction with intracranial electrodes. Temporal, insular, and parietal epilepsy[69–71] and migraine constitute the most frequent neurological causes of autoscopic phenomena, although some cases have also been associated with multiple sclerosis and hyperglycaemia.[72]

Patients experiencing ictal or postictal autoscopic phenomena of epileptic origin may have a wide range of sensations and perceptions: seeing lights, hearing voices, depersonalisation, a feeling of intense peace and joy, premonitions, regression in time, and panoramic life review. In a series of 100 patients with epilepsy, Greyson et al.[69] found 7 patients experiencing autoscopic phenomena; one of these patients reported extremely pleasant and beautiful experiences, such as a visit from an angel who showed him the woman whom he would marry but whom he had not yet met. Some patients believe these experiences have a religious or supernatural origin. Autoscopic phenomena have also been reported by patients in a situation of ''imminent death,''[73] extreme fear, or meditation.

Conclusions

Based on the assumption that all human experiences, including mystical and religious experiences, are ultimately linked to functional activity in the brain, neurophysiological and structural and functional neuroimaging studies of patients with ecstatic, orgasmic, and musicogenic epilepsy; autoscopic phenomena; and Stendhal syndrome may provide a deeper understanding of these patients' mental states. This result from the not necessarily pathological activation of neural networks associated with introspection, social cognition, emotional processing, and memory. Neuroscience may thereby provide a scientific explanation, even in retrospective cases, for some experiences of well-known figures which have traditionally been regarded as supernatural or paranormal.

Conflicts of interest

The author has no conflicts of interest to declare.

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