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Epilepsy and the Sensory Systems

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The relations of epilepsy and the sensory systems are bidirectional. Epilepsy may act on sensory systems by producing sensory seizure symptoms, by altering sensory performance, and by epilepsy treatment causing sensory side effects. Sensory system activity may have an important role in both generation and inhibition of seizures.

When epileptic seizures are concerned, motor signs predominantly come to mind, and an important question is whether consciousness is affected (1). The involvement of the sensory systems is often forgotten, although it should be equally important. Sensory systems can be involved in two ways as epilepsy and its treatment can affect sensory performance, whereas sensory input can have an important role in ictogenesis.

Actions of Epilepsy on Sensory Systems

Three types of action on sensory systems should be considered: 1) depending on anatomy, seizures may affect sensory systems and produce sensory symptoms as auras; 2) altered sensory performance may occur for unknown reasons; and 3) epilepsy treatments may alter sensory functions.

Sensory Symptoms as Auras

Auras of the visual cortex mostly appear in the contralateral hemifield. They are mobile more often than stationary, appearing in colors, including black and white, and as dots, stars, or shapes. Some patients report concentric narrowing of vision and even blindness. Visual illusions (metamorphopsias, dyschromatopsias, macropsy, and micropsy) indicate involvement of the parietal cortex, whereas complex hallucinations are produced in the temporal and sometimes frontal lobe. EEG-fMRI of a complex visual hallucination in a photosensitive patient revealed bilateral activation of the anterior colliculi, lateral geniculate bodies, and thalamus along with photosensitive responses of the occipital, frontal, and parietal cortex (2). The most important differential diagnosis is visual aura of migraine, which may have similar characteristics but usually last >5 minutes, whereas epileptic auras rarely last more than 2 minutes. The existence of a borderline condition, "migralepsy," combining elements of both diagnoses remains under discussion (3).

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Auditory auras are less frequent and appear as simple noises, rarely clear tones. They may be rhythmic and are often directed, indicating a focus in the contralateral Heschl gyrus. Musical hallucinations are very rare.

Somatosensory auras occur frequently together with focal motor seizures as paresthesias of local onset often with a centripetal Jacksonian march. A rare variant consists of intense pain accompanying a focal tonic or dystonic seizure. Such patients may try to react to the pain by voluntary movements of the affected limb, which often leads to a misdiagnosis as psychogenic nonepileptic seizures. Transient postictal reduction of the somatosensory evoked potential can support the diagnosis (4).

Proprioceptive auras such as illusions of movement, alien limb, or hemineglect often remain undiagnosed as they are not sufficiently known.

Olfactory and the rarer gustatory auras have been described by Gowers (5) and related to the temporal lobe by Jackson (6). In a systematic investigation of 217 medically intractable temporal lobe epilepsies (7), 12 patients (5.5%) reported olfactory auras that were unpleasant in all cases but one and were usually combined with epigastric sensations, nausea, or fear, but only once with a gustatory perception.

An important but often ignored possibility is the development of aura continua, a particular type of sensory status epilepticus where fragments of the patient's habitual focal seizures are repeated in a sequence that may be so dense that the patient perceives them as continuous. If there is no history of previous seizures, the condition may be very difficult to identify as epileptic. Aura continua is the sensory equivalent to epilepsia partialis continua (EPC) (8) and is also referred to as sensory EPC.

Altered Performance of a Sensory System

It is little known that, apart from the just-mentioned and potentially long-lasting sensory changes by EPC, altered sensory performance for largely unknown reasons may be found in epilepsy (9). This has been systematically investigated for olfactory performance in temporal lobe epilepsy (TLE), where it was correlated with reduced olfactory bulb volumes (10).

Epilepsy Treatments May Alter Sensory Functions

The sensory systems may be affected by treatment with antiepileptic drugs (AEDs). Best known of these adverse effects are the visual field defects that are observed in up to one-third of patients treated with vigabatrin (11). Polyneuropathies have been described as side effects of several drugs, but these are rare, and the causative attribution is not always convincing. Reduced hearing, ageusia, and dysosmia have been reported in solitary cases, whereas reduced smell is difficult to distinguish from the just-mentioned epilepsy-related hyposmia.

Sensory Systems in Ictogenesis

Seizure precipitation by sensory stimuli in reflex epilepsies (12) has long been known, but it has only much more recently been understood what important contributions these relations offer to our understanding of natural ictogenesis in humans (13). Less well-known, in spite of an even longer tradition (5), is the opposite possibility that ictogenesis is counteracted by sensory stimuli (14). The following sensory systems are involved: vision, somatosensory, proprioception, auditory, and olfaction.

Vision

By far most reflex epileptic mechanisms are related to the visual system. They comprise photosensitivity, eye closure sensitivity, fixation-off sensitivity, and pattern sensitivity.

Photosensitivity (PhS)

PhS in its common form (15) consists of the precipitation of generalized spike and wave (SW) discharge on the EEG, often with an occipital accentuation, or seizures by intermittent light stimulation (ILS). The EEG discharge is called the photoparoxysmal response (PPR). The evoked seizures are bilateral myoclonic, absence, generalized tonic-clonic (GTC), or visual auras (2). The response is dependent upon the flicker frequency, where the most sensitive range usually is from 14 to 30 Hz. Considering epilepsy syndromes, PhS is closely related to juvenile myoclonic epilepsy (JME) (16), where it occurs in up to 90% of cases (17). Recent research has contributed much to the understanding of why visual stimuli in the brains of these patients are processed in a way that produces epileptic seizures. A MEG study of gamma oscillations revealed increased γ synchrony in response to ILS if the stimulation resulted in a PPR, whereas γ oscillations in the same patients did not differ from controls when no PPR was produced. Increased synchrony was predominantly fronto-central in patients with myoclonic seizures, and parietal with absences (18). In addition, an investigation of the phosphene threshold to transcortical magnetic stimulation demonstrated visual cortex hyperexcitability in photosensitive patients with idiopathic generalized epilepsy (IGE) (19). An EEG-fMRI study showed activation of the premotor and parietal cortex 3 seconds before the PPR (i.e., at the time of increased γ synchrony), whereas the same areas were deactivated at PPR onset. Unlike spontaneous SW discharge, the thalamus was not involved, and the PPR appeared as the result of a transcortical cascade of events (20). To sum up, PhS at present seems to be related to hyperexcitability of the visual cortex, resulting in an upregulation of occipito-frontal and occipito-parietal pathways with the consequence of a transcortical cascade of events producing the PPR. Considering the frequency of PhS in JME, this may represent a basic mechanism of ictogenesis in this syndrome.

A variant of PhS exists in some progressive myoclonus epilepsies, where SW occur at low-frequency (1–4 Hz) ILS and single light flashes (12). Two animal models of PhS exist in the Senegalese baboon *Papio papio* and the Fayoumi chicken and have both similarities and dissimilarities with human PhS (21). No recent research seems to have been done with any of these.

Eye Closure Sensitivity (ECS)

ECS refers to the precipitation of generalized SW discharge, often with occipital accentuation, within 2 seconds of eye closure. The clinical response consists of eyelid myoclonia, and this is the presenting symptom in eyelid myoclonia with absences (Jeavons syndrome) (22), but they also occur in 15 to 20 percent of patients with JME (23). ECS often overlaps with PhS, but the two traits are not identical (12). Occasionally, eyelid myoclonia in the same patients may occur without concomitant SW (24). From an EEG-fMRI study in Jeavons syndrome, it was concluded that the eyelid myoclonia are generated in the occipital cortex (25), but all patients studied were also photosensitive, so the relation to ECS was not unequivocal. An important role for the supplementary motor area in the ictogenesis of reflex eyelid myoclonia was also proposed (13).

Fixation-Off Sensitivity (FOS)

FOS is characterized by the appearance of epileptiform discharge occurring after eye closure and lasting as long as the eyes remain closed (26). The same effect can be produced when Frenzel goggles are placed before the open eyes (27). FOS is most commonly encountered in patients with idiopathic childhood occipital lobe epilepsies but may also be observed in cases of symptomatic or cryptogenic focal and generalized epilepsies, as well as in asymptomatic nonepileptic individuals (26, 27). The ictogenic mechanisms of FOS are not yet known.

Pattern Sensitivity

This reflex epileptic trait is defined by the provocation of absences with generalized SW of mostly occipital accentuation by strongly contrasting patterns, vertical stripes being most provocative (12). This sensitivity is mostly seen in IGE, and the majority of patients are also photosensitive (28). Patients with both pattern sensitivity and PhS seem to be most likely to have seizures provoked by television (12).

Somatosensory System

Seizures Precipitated by Touch

A seizure precipitated by touch is a rare type of reflex seizure. There is typically a trigger zone that is touch-sensitive and relates to some postcentral lesion. The provoked seizures typically are simple motor or sensorimotor (12).

Hot Water Epilepsy

Two varieties exist of seizures precipitated by hot water (12). In infants (onset before 1 year of age), there are no spontaneous seizures, and the reflex seizures stop spontaneously

after age 3. Complex partial seizures are precipitated when the child is placed into water of a temperature above 37.5°C. The precipitating mechanism seems to comprise somatosensory stimulation and a systemic rise of body temperature at an age when thermoregulation is not fully developed. No treatment is required, since bathing in lukewarm water is sufficient to prevent seizures.

The adult variant is most often seen in South India. Complex partial seizures are provoked by pouring hot water over the head. Some patients also have spontaneous seizures. This trait is often genetic, with autosomal dominant inheritance, and defective thermoregulation with a rise of systemic body temperature has been demonstrated. These patients can be treated by prophylactic benzodiazepine administration before a head bath (29).

Proprioception

Movement-induced seizures seem to form a continuum with touch-sensitive seizures and are like those caused by perirolandic lesions. The precipitating movements are individually specific, and the resulting seizures are focal motor, often with a somatosensory component. Precipitation by mere imagination of the triggering movement may occur (30).

Seizures precipitated by tooth brushing have been reported in several publications (12). The cases demonstrate some individual variability, and ictogenesis may comprise somatosensory, proprioceptive, and motor components in a complex programmed task (12).

Auditory

Startle seizures (31) are most often precipitated by sudden, loud, unexpected noises, and therefore are sometimes believed to be audiogenic seizures. However, startle seizures in the same patients can be equally precipitated by unexpected touch or visual stimuli, and there must always be an element of surprise. The trigger really is the motor start provoked by the sudden sensory stimuli, so startle seizures could be considered a variant of proprioceptive reflex seizures.

Audiogenic seizure precipitation by noises is common in rodents (32) but extremely rare in humans. Complex audiogenic seizure triggers include music (12, 33) and answering the phone in familial TLE with aphasic seizures (34), where a chromosome locus has been identified on 10q22-q24. Anecdotal reports exist of seizures precipitated by the voices of specific radio hosts (12).

Olfaction

Arrest of seizures by a strong olfactory impression was reported by Gowers (5), who found this method especially effective in patients who had an olfactory aura, while Efron (35, 36) described in detail a patient with TLE who became seizure free without drugs by systematic application of a precisely timed arresting olfactory stimulus. More recently, good effects of aromatherapy in intractable epilepsy have been reported (37).

Reports of seizure precipitation by olfactory stimuli are likewise rare (38, 39), and an entity of olfactory reflex epilepsy has never been described. However, a recent systematic investigation of the effect of olfactory stimuli on epileptiform EEG discharge revealed delayed responses in the minutes following exposure to an aromatic smell in about one-half of the patients. These responses were bi-directional (14): in IGE, they were inhibitory twice as often as excitatory, whereas in TLE, the relation was the reverse (40).

Conclusions

The relations of epilepsy and the sensory systems are numerous and deserve more attention than they have gotten so far. Epileptic seizures use sensory pathways causing not only momentary but also potentially long-lasting symptoms, and certain sensory functions such as olfaction may be affected in epilepsy by still insufficiently known mechanisms. However, altered sensory functions in patients with epilepsy may also be side effects of drug treatment. Nevertheless, several sensory systems may be strongly involved in seizure-generating mechanisms, with both excitatory and inhibitory effects. Recent research has made important contributions to the understanding of these processes.

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