The value of auras in epilepsy surgery evaluation

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Abstract

The aura symptomatology, such as the seizure, is the result of the activation of specific brain areas, the location and extension of which represents the symptomatogenic zone. However, the symptomatogenic zone may not correspond to the epileptogenic zone, the complete removal or disconnection of which is necessary to achieve the “seizure free” condition (1). It is well known that the localization of the EZ and the determination of its extension still represent a major challenge for several reasons (2-4): 1) no diagnostic method exists to directly localize the EZ; 2) to obtain a favorable surgical outcome, five cortical zones [symptomatogenic zone (SZ), irritative zone, ictal onset zone, epileptogenic lesion, and functional deficit zone] should overlap significantly; 3) most of the cortex is silent; 4) the symptomatology often emerges only when the epileptic activity spreads from the epileptogenic zone to the symptomatogenic zone; 5) multiple symptomatogenic zones may be activated concurrently, producing misleading findings; 6) seizures may arise from different areas and evolve in the same symptomatogenic zone, producing similar clinical symptoms; 7) age, cognitive and mental status, and mood of the patient and observers and their ability to describe ictal symptoms may influence the correct EZ localization. However, seizures tend to follow preferential pathways and even if the analyzed symptoms have no useful localizing or lateralizing value, they may indicate which network has been activated. At the seizure onset, the aura can provide important localizing and lateralizing information, for example a simple visual aura may be arising from the occipital lobe, where as an elementary auditory aura may originate from the lateral temporal lobe (5-9). Nevertheless, the localization and lateralization role of the auras must be analyzed with extreme caution during the epilepsy surgery evaluation because of the aforementioned reasons (5).

Auras: localization and lateralization

Visual and auditory auras include simple and complex manifestations. In general, simple visual and auditory auras typically result from the activation of the respective primary cortices (10), while complex auras suggest the activation of the temporo-occipital junction (11, 12). Complex visual auras could be also elicited by the activation of the basal temporal cortex (13). Specifically, when the simple visual symptom is lateralized to one hemifield the EZ is usually in the contralateral occipital lobe, while when they are restricted to the upper or lower quadrant the EZ is in the contralateral infra- or supracalcarine fissure, respectively (8, 14). Instead, visual distortion is generally the result of activation near the optic radiation (14). Major lateralizing issues are associated with auditory auras because usually the patients have difficulty lat-

Introduction

The goal of the epilepsy presurgical evaluation is to identify the epileptogenic zone (EZ), the complete remo-
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eralizing the sound and even when the sound is perceived as lateralized, it does not have a reliable localizing and lateralizing value (15). Close to visual and auditory association areas, in the temporo-parietal junction there is the EZ of vertiginous auras that in fact are usually associated with visual or auditory symptoms (14). Studies with cortical stimulation showed the extension of the vertiginous auras EZ above and below the Sylvian fissure, including the parietal operculum and the middle and posterior part of the superior and middle temporal gyri (16).

Olfactory auras show a low localizing value because they could be observed in seizures arising from the mesial temporal lobe and the occipital lobes (17-19). Furthermore, several studies showed olfactory sensations after the stimulation of the olfactory bulb, the insular cortex, the posterior part of the orbitofrontal region (olfactory illusion), and the amygdala (attention to olfactory auras in case of amygdala neoplasm) (14, 20). Since the olfactory auras are often associated with gustatory phenomena, the main issue for many patients is to differentiate the gustatory auras from olfactory disturbances (21). For the aforementioned reasons the olfactory auras must be analyzed with extreme caution (17).

Gustatory auras alone have no lateralizing value even though it has been shown that the stimulation of the parietal operculum, insular cortex and medio-basal temporal regions generate gustatory hallucinations (21). The somatosensory auras are localizing and lateralizing enough and they affect somatosensory regions of the body. When the symptomatology is distributed distally and unilaterally, the EZ is usually localized in the primary sensory cortex, while bilateral and more widespread symptoms may be produced from the second somatosensory area and from the supplementary sensorimotor area, even if the latter produces poorly localizing somatosensory symptoms (22). The second somatosensory area can also produce ipsilateral symptoms and a sensation of pain or warmth (23).

Poorly localized or lateralized sensations affecting the whole body do not have any localizing and lateralizing value (22, 23). Brain stimulation studies showed various types of somatosensory auras by stimulation of the insular cortex and false interpretations of somatosensory auras due to imperceptible muscle contractions, after motor area stimulation (23). More complex is the definition of the symptomatogenic zone of the autonomic auras, which are produced mainly by activation of the insular cortex, but also by the anterior cingulum, supplementary sensorimotor area, or amygdala (24). The most common type of autonomic aura is the abdominal aura, which is mainly elicited from temporal lobe epilepsies, but it may also be triggered by extratemporal seizures (e.g., from the frontal lobe and insula) (25). When abdominal auras are associated with vomiting the EZ may be in the non-dominant temporal lobe (26). Also orgasmic auras, occasionally accompanied by viscerosensory symptoms, have been mainly observed in right temporal lobe epilepsy (in women) (27). Instead, the EZ of genital auras, characterized by unpleasant mixed sensations of pain and fear, is usually located in the postcentral parasagittal region, but when such auras are bilateral the origin is most commonly in the second sensory area (28).

The temporal lobe (neocortex and mesial structures) is also involved in psychic auras, with the exception of forced thoughts and fear, which are generally observed in frontal lobe epilepsy and in a more extensive area including amygdala, hippocampus, mesial frontal region and temporal neocortex, respectively (24, 29). In addition, multiple auras can occur with different seizures or during the same seizure, either simultaneously or sequentially. However, multiple aura scan originate in a single EZ, usually located in the temporal or posterior quadrant foci, which appear to be caused by the sequential or simultaneous activation of multiple symptomatogenic zones (30). In multiple auras it is possible that different single auras reflect different propagation pathways from the same focus (30).

An example of a likely pitfall

Recently Russo et al. described the interesting case of a 16-year-old female with seizure onset characterized by olfactory auras arising from the occipital lobe, although the brain MRI revealed hippocampal sclerosis (19). By considering that olfactory auras should indicate an EZ much likely localized in the mesial temporal lobe, the presence of hippocampal sclerosis has easily suggested the EZ location. The EEG showed an ictal onset over the ipsilateral occipital region, which was confirmed by 3D-EEG source imaging. FDG-PET and ictal-SPECT findings did not provide useful information for the localization. After invasive evaluation, a limited resection was performed over the occipital lobe with long-term seizures freedom.

This case showed that the mesial temporal region, although affected by hippocampal sclerosis, was likely secondarily activated by ictal discharges propagated from the primary hub of the network localized in the occipital lobe. The concept of hub is very important for the surgical treatment because it is common opinion that some brain regions are more responsible for seizure onset and propagation (hub), while others (nodes) are only remotely involved (31, 32). Therefore, from a practical standpoint, in our case the hippocampus was most likely only a non-pacemaker propagating node of the network, while the occipital region was the primary epileptogenic zone.

In conclusion, this case emphasized the importance of exercising caution when using the auras as localization tool and analyzing the aura typology in association with the other seizure features, EEG and neuroimaging findings, because pitfalls are around the corner.

How we can limit the pitfalls

It is well known that to establish the consistency of the semiological features it is essential to observe multiple
seizures through a careful review of the video-EEG recordings, searching for a significant degree of concordance of data by remembering the main rule that the ictal EEG seizure onset should precede or be simultaneous with the clinical seizure onset.

Even when the video-EEG concordance is clear enough the data should be assessed in parallel with information from non-invasive structural and functional neuroimaging and neuropsychological studies to limit as much as possible the pitfalls in EZ localization. Finally, when the non-invasive presurgical evaluation is not sufficient to localize the EZ it is necessary to proceed with the invasive presurgical evaluation.

Conclusions

Epilepsy surgery has become an important treatment option in patients with medically refractory epilepsy. The ability to precisely localize the epileptogenic zone is crucial for surgical success. Auras could be an important localizing and lateralizing tool, but they should be taken into consideration with extreme caution for the main reason that seizure semiology is determined by the pathway of seizure propagation into complex networks with an elevated risk of obtaining a false localization. Therefore, to optimize the surgical outcome, the careful interpretation of ictal semiology in conjunction with other components of the presurgical evaluation should be mandatory.

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