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Review

Alteration of consciousness in focal epilepsy: The global workspace alteration theory

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ABSTRACT

Alteration of consciousness (AOC) is an important clinical manifestation of partial seizures that greatly impacts the quality of life of patients with epilepsy. Several theories have been proposed in the last fifty years. An emerging concept in neurology is the global workspace (GW) theory that postulates that access to consciousness (from several sensorial modalities) requires transient coordinated activity from associative cortices, in particular the prefrontal cortex and the posterior parietal associative cortex. Several lines of evidence support the view that partial seizures alter consciousness through disturbance of the GW. In particular, a nonlinear relation has been shown between excess of synchronization in the GW regions and the degree of AOC. Changes in thalamocortical synchrony occurring during the spreading of the ictal activity seem particularly involved in the mechanism of altered consciousness. This link between abnormal synchrony and AOC offers new perspectives in the treatment of the AOC since means of decreasing consciousness alteration in seizures could improve patients' quality of life.

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1. Introduction

Alteration of consciousness (AOC) is a usual semiological feature in generalized seizures and frequently occurs in partial seizures [1,2]. In this review, we will focus on the mechanisms leading to AOC in partial seizures and, particularly, in the most frequent type of chronic drug-resistant partial epilepsies, the temporal lobe epilepsies (TLEs).

For many patients, AOC is one of the most dramatic clinical manifestations of TLE, often causing important handicap and potential source of injury. In line with this, the international classification of epileptic seizures has made impaired consciousness the cornerstone by which the main categories of partial seizures, simple and complex, are distinguished [3]. Although the question of how to define and categorize consciousness in the context of epileptic seizures remains the topic of debate [4], the central role of this entity in existing seizure classification emphasizes an essential characteristic that, in many cases, has significant repercussions on the quality of life of patients with epilepsy.

Whereas the structural and functional changes observed in the partial epilepsies, especially TLE, have been largely studied, the mechanisms leading to AOC remain rather poorly known [5]. We recently proposed that AOC in temporal lobe seizures could be explained by an alteration of “global workspace” functioning [6,7], a theory that we will develop in the next paragraphs.

2. The global workspace (GW) model of consciousness

As previously described [6], the GW model, initiated by Bernard Baars' theoretical work [8], proposes that at any given time, many modular cerebral networks are active in parallel and process information in an unconscious manner. In this context, consciousness would correspond to the broadcasting of information to a global workspace. Dehaene, Changeux, Naccache, and colleagues developed these principles and elaborated a plausible functional neural architecture to the GW [7,9,10]. In particular, they proposed that conscious access would be causally related to a mechanism of top-down attentional amplification into a self-sustained brain-scale state of coherent activity that involves many neurons distributed throughout the brain. The long-distance connectivity of these “workspace neurons” can, when they are active for a minimal duration, make the information available to a variety of processes including perceptual categorization, long-term memorization, evaluation, and intentional action. According to this model, global availability of information through the workspace is

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what we subjectively experience as a conscious state. Neurophysiological, anatomical, and brain-imaging data strongly argue for a major role of the prefrontal cortex (especially anterior cingulate region), the parietal cortex, and the areas that connect to them.

Most empirical tests of GW theory predictions have focused on the access to consciousness issue (see [11] for review), which refers to neural mechanisms enabling an initially nonconscious perceptual representation, encoded in specialized local cortical networks, to be "broadcast" to the GW network as a conscious percept. This issue of "conscious access" explores the transitions between nonconscious processing and conscious processing in a conscious subject, which, in practical terms, can be studied in a variety of sensory modalities, for example, the subject's reaction to visual or auditory stimuli. Several studies combining electrophysiological measures with subjective perceptual reports strengthen the hypothesis that conscious access is a late (~300 ms in the visual modality) neural event associated with brain-scale pattern coherent activity including frontal and parietal areas (for recent reviews, see [12–14]. It was recently shown that this late conscious access could even act on a nonconscious visual representation several hundreds of milliseconds after stimulus disappearance [15]. This finding highlights both the relatively long-lasting forms of nonconscious memories (visual short-term or iconic memories [16] and, therefore, the durable impact of top-down processes on them.

Similar evidence in the auditory modality can be provided using an auditory task enabling distinction of nonconscious processing of auditory novelty (as indexed by the mismatch negativity or MMN) from the conscious detection of auditory rule violation (P3b event, [17]). To do so, we presented subjects with violations of temporal regularities that were either local in time or global across several seconds. Local violations led to an early response in the auditory cortex, independent of attention, or the presence of a concurrent visual task, whereas global violations led to a late and spatially distributed response that was only present when subjects were attentive and aware of the violations. This late marker of conscious access to auditory information is similar to that reported in the visual modality, suggesting that we may tap into a similar signature indexing GW activity whatever the perceptive modality is. Building on this work, we have also shown that patients with impaired consciousness (e.g., patients in the vegetative state) usually lack this signature, whereas they can show cortical responses to sounds and to local violations (e.g., MMN) [18,19].

In terms of neural network synchronization, several studies point to the importance of "slow" oscillations including theta, alpha, and beta bands in the coordination of distant brain areas, whereas local synchronization would mostly rely on fast gamma-band activities [13,20–23,25].

Taken together, these results strongly suggest that long-distance corticocortical synchronization plays a fundamental and causal role in conscious processing and top-down control [23,24–26]. Seizures characterized by AOC provide a unique model for studying reversible changes of conscious level in vivo, particularly in the context of intracerebral EEG data. The exploration of AOC contemporary to seizure activity can provide precious specifications of the dynamics and range of neural coherence associated with conscious processing. In particular, we have previously shown that an excess of synchronization, within corticocortical and corticothalamic networks, was associated with conscious impairment in temporal and parietal seizures [27,28].

3. Alteration of consciousness in epilepsy: a summary of putative mechanisms

Temporal lobe epilepsy (TLE) is the most frequent cause of partial seizures with AOC and, to date, the most studied in this context with intracranial EEG data [29,30]. Seizures in TLE are characterized by epileptic discharges originating from one or several regions of the temporal lobe (often from the mesial temporal regions) and propagating through an interconnected network within both cortical and subcortical structures [31]. Video-EEG recordings have shown that ~60%–80% of patients suffering from TLE have AOC during their seizures [32]. The most frequent criterion for defining AOC is the absence of interaction with the examiner during a seizure (loss of contact). One of the major limits of any clinical study looking at consciousness during seizures is indeed the lack of an accepted tool to measure AOC, since the clinical appreciation of AOC is a quite elusive concept in epileptology due to its subjective nature [1]. A description by an external observer cannot directly represent the subjective experience of the patient during his seizure. In general, clinical studies rely on indirect criteria for the measure of consciousness, that is, objective signs of impaired contact with the environment and the examiner. Recent studies have proposed 2 to 4 criteria to estimate consciousness during seizures [33–36]. We have suggested an 8-criterion scale, the Consciousness Seizure Scale (CSS), which has good inter- and intra-observer reliability [27] and is clinically practicable. A validated 20-point scale detailing subjective features of level and content of consciousness has been described [37].

Another group has recently evaluated a standardized 3-level procedure for ictal examination, modified from an existing coma recovery scale [38]. Different hypotheses have been proposed to explain how temporal lobe seizures could impair consciousness [39]. Intracerebral EEG recording studies have suggested that alteration of consciousness is related to the spread of epileptic discharge to cortical structures contralateral to the origin of the seizures and that AOC could be more frequent in seizures affecting the dominant hemisphere [33]. Bilateral involvement of the temporal lobe is a classical factor explaining loss of memory, but it has been shown that AOC may occur during apparently unilateral TLE seizures [29,30]. Munari and colleagues studied this question using SEEG, reporting a large series of 100 patients with TLE and a total of 388 seizures, of which 178 showed altered ictal consciousness [29]. Given the large size of the patient group, comparison was possible not only of individual seizures but also groups of patients (those who lost consciousness at the onset of every seizure versus those who never lost consciousness). The authors observed that patients with altered consciousness were also more likely to present complex semiology (such as dyspraxic automatisms) as well as extratemporal semiology, with, overall, a longer duration of ictal discharge (average seizure duration of 90 s when altered consciousness occurred, in contrast to 47 s for seizures with no loss of consciousness). The presence of extratemporal ictal signs (such as lateralized tonic posturing or clonic jerks and subsequent generalization) was also associated with a longer duration of ictal discharge. Over half of the cases with AOC showed propagation to the contralateral hemisphere, especially contralateral temporal lobe. In contrast, patients who never lost consciousness were more likely to present subjective epigastric sensation at seizure onset in the context of a shorter discharge limited to unilateral temporal structures. Munari's team found a higher occurrence of loss of consciousness in seizures involving bilateral temporal structures. This was in agreement with the observations by Gloor [30] and by Bancaud and Talairach [40] that bilateral temporal ictal involvement is frequently associated with loss of consciousness (complex partial seizures), but that bitemporal seizure discharge is not obligatory for loss of consciousness to occur.

Metabolic neuroimaging studies using ictal SPECT in order to study the increase of cerebral blood flow (CBF) in regions affected by seizures have suggested that secondary involvement of the thalamus and/or subcortical structures during seizures plays a determinant role in the impairment of consciousness [34,35]. In comparison with seizures not associated with AOC (simple partial seizures), seizures with AOC (complex partial seizures) are associated with a significant bilateral increase in CBF in the thalamic nuclei. Thalamic involvement during TLE seizures has previously been shown by direct intracerebral EEG recording [31,41]. In one study, the degree of thalamic involvement was correlated to the presence of AOC during seizures [31].

According to SPECT and EEG approaches, Blumenfeld and colleagues also suggested that AOC occurs when the associative cortices are secondarily impaired [35,36] and proposed the "network inhibition"