Seizure Semiology: An Overview of the ‘Inverse Problem’

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The inverse problem is commonly referred to as the process of identifying the brain source of the discharges recorded on the scalp surface. Furthermore, in correlating the ictal source with the clinical expression or presentation of epilepsy, the description of focal seizure manifestations is commonly made with reference to an involved side or lobe. Usually, however, the anatomic origin of particular seizure signs or symptoms is often not known at initial presentation. Therefore, one may also postulate an inverse problem for the issue of anatomoclinical correlation, i.e., how to infer the epileptogenic (or, in a less favorable case, the symptomatogenic) focus from the analysis of seizure semiology.

A seizure classification based exclusively on semiology (i.e., independently from other ancillary information, such as EEG or neuroimaging) is believed to improve and complement the clinical information data needed for presurgical evaluation, as it has been pointed out by the ‘Cleveland School’ \cite{1, 2}. Indeed, four spheres have been identified: sensorial (auras), motor, consciousness, and autonomic; special categories may be added if none of the preceding sphere applies. Seizures affecting consciousness may be labeled as ‘dialectic’ in order to avoid confusion with syndromes (e.g., absence). Motor seizures are divided into simple and complex (hyper- and automotor). Finally, atonic, astatic, hypomotor (when consciousness is not testable), akinetic, negative myoclonic and aphasic

\textbf{Key Words}
ictal manifestations / Postictal manifestations / Focal seizures / Lateralization / Localization / Epilepsy

\textbf{Abstract}
In clinical practice, a classification of seizures based on clinical signs and symptoms leads to an improved understanding of epilepsy-related issues and therefore strongly contributes to a better patient care. The inverse problem involves inferring the anatomical brain localization of a seizure from the scalp surface EEG, a concept we apply here to correlate seizure origin with seizure semiology. The spheres of sensorium, motor features, consciousness changes and autonomic alterations during ictal and post-ictal manifestations are reviewed, including several subdivisions used to better categorize particular features. Particular attention is given to behavioral features, as well as to features occurring in idiopathic generalized epileptic syndromes and psychogenic nonepileptic spells.

This paper is dedicated to the memory of Edward B. Bromfield, MD (1951–2009).
manifestations may also occur as special manifestations [1].

Here we review current knowledge regarding ictal and postictal manifestations of focal seizures, focusing first on symptoms and signs, and then inferring seizure origin. While several items reflect the reviews by the Cleveland group, to which we refer for further reading [1, 2], we add some recently analyzed features, such as gustatory sensations, multiple auras, several psychic and behavioral manifestations, hyperkinetic and gyratory seizures, nonclonic ictal hand motions, and changes in cardiac rhythm. We conclude by reviewing data regarding idiopathic generalized epilepsy (IGE) and psychogenic nonepileptic seizures. A systematic description of the differential diagnosis towards nonepileptic disorders and nonepileptic seizures. A systematic description of the differential diagnosis towards nonepileptic disorders and the phenomenology of peri-ictal psychosis are beyond the scope of this paper.

**Sensory Phenomena**

Auras are ictal sensory phenomena occurring at the beginning of a focal seizure and with preserved consciousness, and are reported by 22–83% of the patients [3]; the longer the subsequent seizure, the higher the likelihood of forgetting the aura. Furthermore, auras seem to be less prevalent after seizures arising from the dominant temporal lobe as compared to the nondominant, and in seizures occurring during sleep [4]. An aura is the result of the first involved symptomatic region, and needs to be differentiated from nonspecific prodromes. The latter, characterized mainly by headache, vague nonascending and long-lasting abdominal sensations or dysphoria, may precede (focal) seizures by many minutes (usually >5) [5]; up to 17% of the patients with epilepsy may report them [5]. In contrast, auras are generally experienced immediately prior to the loss of consciousness. Interestingly, sensory auras are invariably recognized as pseudohallucinations by patients [3], meaning that their unreal character is readily identified.

Somatosensory phenomena most often arise from the parietal lobe (primary somatosensory cortex, S1) [6], or more rarely from the posterior insula-parietal operculum (supplementary somatosensory area, S2) [7, 8]; they may also occur during supplementary motor area (SMA) seizures [3]. Localization can be inferred according to the following features: auras related to S1 are well localized, discriminatory, and spread relatively slowly (like a sort of ‘jacksonian march’), whereas symptoms arising from S2 are ill-defined, often accompanied by pain, spread within seconds, and may be contra- or ipsilateral [7]. SMA involvement elicits diffuse contralateral or bilateral tingling, and a sensation of movement [3, 9], the semiology is thus very similar to S2 involvement.

A lateralized ictal headache is usually ipsilateral to a temporal or occipital focus [3], whereas preictal headache has been reported in up to 11% of pharmaco-refractory patients with localization-related epilepsy; it may result from increased blood perfusion, or release of neuropeptides [10]. Postictal headache, conversely, is relatively frequent, and of no localizing value, apart from the idio- pathic focal epilep-sies of childhood, where, again, it points to a posterior focus.

Gustatory auras are also related to the insular region [7, 11]; they often display a metallic-rubbery character, and occur with other sensory changes related to S2 involvement, or unpleasant sensations of the pharynx: the early combination of visceral, somatosensory and motor signs, especially if involving the buccopharyngeal region, has recently been described to suggest an insular focus [12]. Visual phenomena of elementary colorful character, but also including amaurosis, arise from the contralateral occipital lobe, and present a more formed character if involving the associative cortex located more rostrally [3, 13]. Elementary auditory manifestations are produced in the primary auditory cortex [14]; if unilateral, these phenomena point to the contralateral hemisphere [3, 15], since most auditory fibers cross within the brainstem. Complex auditory auras arise from the temporoparietal junction. Musicogenic seizures may have an acoustic aura: two types of events have been described. One arising from the laterotemporal regions (auditory cortex), the other from the mesiotemporal structures (emotional component) [16]. The delay between the auditory trigger and the seizure onset suggest that these events are due to involvement of auditory association areas, rather than being simple reflex seizures occurring from the primary auditory cortex [17]. Olfactory sensations are the result of activation of the anterior mesiotemporal lobe (‘uncinate fits’), and are nearly always unpleasant, consisting of smells of burning or rotten nature [3]. Vertigo might be elicited by the insular-parietal-temporal junction [6, 18]; it appears to be a very rare symptom and needs to be differentiated from the much more frequently reported, unspecific prodromal ‘dizziness’. Viscerosensory manifestations are often characterized by stereotypical feelings of nausea, ascending sensations, and occasionally pain, and occur shortly before the rest of the seizure. Although these are most often encountered in mesiotemporal seizures, especially at the onset, similar manifestations may
be elicited after stimulation of the insula, SMA, and the thalamus [3].

Although patients reporting several different experiences preceding a loss of consciousness may raise concerns about possible nonepileptic seizures, the pattern of multiple auras was recently observed in 0.4% of subjects undergoing long-term EEG monitoring [19]. Interestingly, a strong predominance of nondominant hemispheric lateralization was found, mostly involving the temporal or posterior regions, probably leading to more accurate reporting following the relative preservation of language in these cases.

Psychic Manifestations

This group of symptoms has also been defined rather as being part of ‘complex internal’ sensory manifestations, since ‘psychic’ may be perceived as an ambiguous term [20]. These manifestations are dominated by experience of déjà-vu, which points to a mesiotemporal origin without lateralizing value [21]; this is however not specific of epilepsy. Another interesting symptom is forced thinking, which has been reported to be related to frontal (more verbal character) or mesiotemporal (more emotional features) regions of the dominant hemisphere [22]. Ictal fear has been related to involvement of the amygdala and is a relatively frequent reported symptom; rarer phenomena are ecstatic auras, which are also related to the amygdala [23, 24]. None of these phenomena have clear lateralizing values. These have to be differentiated from an orgasmic aura, also an uncommon feature arising for the nondominant mesiotemporal, or more rarely parasagittal parietal regions, and possibly with female predominance [25, 26]. Ictal autoscopy, an exceptional phenomenon characterized by the sight of the patient’s body from outside it, has been linked to the nondominant parietal lobe [27, 28].

Head and Limb Movements

Head version is probably the most frequently encountered sign in focal seizures [15, 29], occurring in 35–40%. Forced and sustained (>5 s) head and eyes deviation has a positive predictive value (PPV) of 94% for contralateral localization, mostly in the temporal or frontal lobes, rising to 100% if accompanied by neck extension and immediately followed by generalization [15, 29]. It is thought to arise from the involvement of the frontal eye field [30]. Mouth deviation also shows a high PPV of 92% (contralateral), especially if accompanying forced head version [29].

Nonversive head turning (seemingly purposeful) is less common, occurring in about 25%, and has an 80% PPV for ipsilateral lateralization mostly within the temporal lobe [29], often occurs at the beginning of mesiotemporal seizures, and is practically never followed by a generalization [31]; it is probably the consequence of the involvement of basal ganglia, and, if arising from the frontal lobe, has been described in orbitofrontal, frontopolar or dorsolateral seizures [31]. Ipsilateral version may also be observed at the end of a generalized convulsion [30]. Of note, one possible source of confusion are seizures originating form the SMA, where the head may turn in either direction as compared to the focus [9].

Focal clonic or tonic activities also have an excellent lateralizing value, since these are almost invariably contralateral to the triggering hemisphere; the movements arise after involvement of the motor cortex in the frontal lobe [29].

Hyperkinetic seizures arise from the orbital or mesial regions of the frontal lobe, where they tend to occur in brief and frequent attacks, often out of sleep [32]; however, they may be also observed in seizure arising from the temporal lobe, when the discharges reach the frontal lobe [33], as well as from the anterior insula [34]. In this context, seizures with violent behavioral manifestations and fear tend to arise from the ventromesial frontal regions, whereas relatively mild, horizontal movements coupled with dystonia are mostly seen when the mesial premotor cortex is involved [35]. Gyratory seizures have been reported to result from activation of the contralateral frontomesial region if heralded by forced head turning, and ipsilateral if presenting with an en bloc version of the body [36]; furthermore, rotations around the horizontal body axis seem to be predictive of a mesial frontal origin [37].

Asymmetric termination of the clonic phase has a predictive value of around 80%: the last cloni are ipsilateral to the seizure onset in both temporal and frontal lobe seizures [38]. Postictal paresis (Todd’s phenomenon) is another excellent lateralizing sign [39]: it is consistently contralateral to the seizure onset, with a median duration of only 3 min, and without a difference between temporal and frontal seizure origin [40]. It has been mainly associated with unilateral dystonia and ictal limb immobility. The latter is actually a rare phenomenon [41], suggesting an active inhibitory process, described in lesions of the primary somatosensory area [42], the temporal lobe [41],
or the prefrontal cortex [43]. Accordingly, the ipsilateral head turn and the resulting variant of gyraly seizure could possibly be interpreted as a consequence of a contralateral neglect.

**Eye and Eyelid Movements**

Unless accompanying a headturn (see above), isolated sustained eye movements are relatively uncommon. Isolated eye deviation per se does not seem to have a lateralizing value, especially in young children [39]. Unilateral blinking points to an ipsilateral, mostly temporal or frontal seizure focus [44], but might also be encountered in occipital seizures [45]. Ictal nystagmus is the consequence of a contralateral hemisphere seizure, either in the regions responsible for contralateral saccades, or in the locations inducing ipsilateral smooth pursuit [39, 46, 47].

**Dystonic Posturing**

Unilateral limb dystonia occurs in about 20–37% of focal seizures, and has a PPV of 93% for a contralateral focus [15, 29]; it is more often encountered in temporal than frontal lobe seizures, probably after involvement of the basal ganglia. A variant is the sign of four [48], in which the extended arm is contralateral to the seizure onset. Tonic limb posturing is not exclusively seen in temporal lobe epilepsy, but is also a feature of frontal lobe and SMA seizures. In the latter case, the lateralizing value is very poor, according to the tight interhemispheric connections at this level [49]. A fencing posture has been described by Penfield and Welch [50], although in its classical form it is not frequently encountered [9]; more often, one observes a head turn with asymmetric posturing of the upper limbs: the most extended limb suggests a focus in the contralateral hemisphere, especially if accompanied by unilateral clonic activity.

**Automatisms**

Unilateral automatisms occur in about 25% of focal seizures, showing a 100% PPV for ipsilateral focality, mostly in the temporal lobe, or the limbic structures and the orbital regions of the frontal lobe [29, 45]. Interestingly, ictal automatisms with preserved consciousness, a rare phenomenon, point to the nondominant, mesiotemporal lobe [51]. This might be explained by a preferential involvement of the midbrain reticular formation during dominant temporal lobe seizures as compared to nondominant [52]. Postictal nose wiping has an excellent lateralization value (>90%) to the ipsilateral side (temporal lobe more than frontal lobe) [15]; it could be the consequence of a contralateral postictal paresis. Different from automatisms are rhythmic ictal, nonclonic hand motions, in the form of low-amplitude milking, grasping, or pill-rolling movements [53]; they have been described as an early contralateral sign in temporal lobe epilepsy, preceding dystonic posturing, and occurring in about 10% of them.

**Behavioral and Phasic Manifestations**

Ictal speech has been described in up to 10–20% of complex-partial seizures, and shows a PPV of about 80% pointing to the nondominant temporal lobe [29], whereas postictal dysnomia, encountered in roughly the same percentage, has a 100% PPV for the dominant hemisphere [29]. Ictal vocalizations are mostly seen during frontal lobe seizures, especially from the orbitofrontal and parasagittal regions [45], but may also present as a loud scream at the beginning of generalized seizures.

Behavioral arrest and consciousness impairment are characteristic for seizures arising from the temporal lobe, the cingulum or the orbitofrontal region [45]; when the temporal lobe is involved, this semiology suggests a lateralization towards the dominant side [54]. Late loss of contact (>40 s into the seizure) is observed in mesiotemporal seizures as opposed to laterotemporal seizures, having an early onset of consciousness impairment [18]. In this context, seizure duration may also help to differentiate mesio- from laterotemporal onset, the former often having longer seizures with rare generalizations (up to 2/year) [18]. If the SMA is primarily involved, consciousness may be preserved. The same, despite bilateral motor manifestations, also occurs in insular seizures, [7] or as an exceptional phenomenon in laterotemporal lobe seizures [55].

Rarely, ictal humming or singing may be observed; they are reported in about 1% of patients admitted to an epilepsy unit [56]; anatomically, temporal lobe and prefrontal cortex have been implicated, as part of the network underlying musical processing and without clear lateralization.
Autonomic Manifestations

A very rare but intriguing sign is represented by pilo-motor phenomena. If unilateral, they point to an isplateral focus with temporal lobe involvement, probably following activation of the amygdala, the insula, or the posterior hypothalamus [57].

Ictal tachycardia is very frequent and has no localizing value, conversely, ictal bradycardia or asystole are very rare phenomena [58]. They are related to temporal lobe foci, with no localizing value, as they are probably induced by bilateral activation of mesiotemporal and insular regions [59, 60]. Dyspnea is also linked to the insula [7].

Ictal spitting has been related to the nondominant temporal lobe [61]. Although the same region has been implicated in cases of vomiting [62], ictal nausea and vomiting probably occur following activation of the anterior insula [63].

Ictal laughing (gelastic seizures) classically occurs in children with hypothalamic hamartoma, but may be observed in temporal or, more rarely, frontal (cingulus) seizures in adults [64], no lateralization value is recognized. As a rule, it is not accompanied by emotional perception of happiness, but temporal foci may rarely induce laughter with mirth; furthermore, hypothalamic gelastic seizures are generally brief. Ictal smiling (without laughing) is probably more frequent, having been reported in 6–11% of patients undergoing long-term monitoring [65, 66]. It is most often encountered in nondominant, posterior (temporo-parieto-occipital) localizations. Ictal weeping (dacrystic seizures), again with no particular accompanying feelings, has been rarely described in mesiotemporal seizures without a clear lateralization [67, 68].

Other autonomic manifestations, such as mydriasis and flushing, have no specific localizing value, as they may be associated with mesiotemporal, insular and frontal (parasagittal, orbitofrontal) lobe involvement [45]. The same applies for urinary incontinence [69], which seems more common after convulsions (probably following a sudden rise in intra-abdominal pressure). Incontinence is also encountered in seizures arising from the parasagittal portion of the frontal lobe [45].

It is important to underscore that an age-dependent occurrence of localizing manifestations seems to occur, paralleling brain maturation. Seizure in pre-school subjects tend to be shorter and to show fewer localizing signs than those occurring in older children [70]; furthermore, as compared to children, adults more often show automatisms and lateralizing signs, especially in temporal lobe epilepsy [71]. This likely reflects dynamic brain maturation across different ages.

Focal Signs in Generalized Epilepsies

It is important to bear in mind that the discussed signs are not specific for focal seizures: focal phenomena may occur in IGE, and thus represent potentially misleading features. In a retrospective study, focal EEG signs were reported to occur in 35% (7/20) of mostly medically refractory IGE patients, and clinical signs pointing to a focal origin also occurred in 35% (7/20, 2 patients had both EEG and clinical focal features), including the figure of four, nose wiping, unilateral dystonia, head version, and postictal hemiparesis [72]. In another observation, forced ictal head version was found in 5/20 subjects with IGE, and 2 of them had version to the other side in other seizures [37]. Even gyratory seizures have been described [37, 73]; again, the rotation sense may change from one seizure to the other. Recently, asymmetric termination of the tonic phase has also been described in about 20% of primarily generalized seizures [38]. It has also been reported that patients with IGE may mention auras in the seconds or minutes before a seizure, with a prevalence (up to 70%) similar to that of subjects suffering from localization-related epilepsy [74]; as compared with the latter, patients with IGE tend to perceive their warnings in the midline of the body and to have a less discriminatory (precise) anatomical character. Visual auras are also described, and they tend to occur as very brief flashing sensations [75]. All these falsely localizing signs might reflect the occurrence of – mostly nonspecific – structural brain abnormalities, which have been described in up to 1 in 4 patients with IGE and, again, seem to correlate with the degree of EEG focal features [76], a not uncommon occurrence in this diagnostic group [72, 77].

Psychogenic Nonepileptic Seizures

Patients with psychogenic nonepileptic seizures (PNES) account for about 20% of admissions in a long-term monitoring EEG unit [78], and about 10% have concurrent epileptic seizures [79]. Characteristic clinical features suggesting PNES are a very gradual onset or termination of the events, often not followed by a postictal state; discontinuous, irregular, asynchronous motor activity with a waxing and waning intensity, side-to-side...
head movement, pelvic thrusting, opisthotonic posturing, and preserved awareness during bilateral motor activity [80] (table 1). It should be noted that bilateral arm movement with preserved consciousness can occur with myoclonic seizures in juvenile myoclonic epilepsy, and with SMA seizures, and exceptionally in temporal lobe seizures [55]. Ictal eye closure [81], resistance to eye opening and to the passive release of one arm onto the face are also frequently encountered in PNES and are rather specific, as is ictal stuttering, although this occurred in only 9% of PNES patients in a one series [82]. However, cataplepsy (such as when the elevated arm does not fall when released) can occur with complex partial status epilepticus [83]. The postictal breathing pattern is deep, slow and loud after epileptic seizures, and superficial and fast after nonepileptic spells [84]. In our experience, it is not rare to observe concomitant hyperventilation with a positive Chvostek sign on gentle percussion of the facial nerve during the spell; furthermore, generally there is no intervening cyanosis even after prolonged convulsions of non-epileptic origin. While oral lacerations (including tongue bites), and, to a lesser extent, urinary incontinence have been shown to be highly suggestive of epileptic seizures, or less frequently of syncope, since these signs are only rarely seen after PNES [69], at times patients with PNES may be hurt during their spells. It is therefore strongly advisable not to rely solely on these features in diagnosing nonepileptic seizures: in this context, ictal semiology alone shows a rather low inter-rater agreement even among experienced epileptologists [85]. PNES diagnosis should always be formulated based on video-EEG analysis of typical events integrated with clinical history, neurological and psychiatric examinations. Table 1 gives an overview of the most important described features.

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>Anatomical origin</th>
<th>Lateralization</th>
<th>Reliability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well-defined somatosensory symptoms</td>
<td>parietal (primary sensory cortex)</td>
<td>contralateral</td>
<td>high</td>
</tr>
<tr>
<td>Unilateral elementary visual phenomena</td>
<td>occipital</td>
<td>contralateral</td>
<td>high</td>
</tr>
<tr>
<td>Ascending visceral feelings</td>
<td>mesiotemporal, insula, supplementary motor area</td>
<td>none</td>
<td>moderate</td>
</tr>
<tr>
<td>Forced thinking</td>
<td>frontal or mesiotemporal</td>
<td>dominant hemisphere</td>
<td>moderate</td>
</tr>
<tr>
<td>Ictal fear</td>
<td>amygdala, hippocampus</td>
<td>none</td>
<td>high</td>
</tr>
<tr>
<td>Forced head version</td>
<td>frontal, temporal</td>
<td>contralateral</td>
<td>high</td>
</tr>
<tr>
<td>Nonversive head turning</td>
<td>temporal</td>
<td>ipsilateral</td>
<td>moderate</td>
</tr>
<tr>
<td>Focal clonic activity</td>
<td>frontal (primary motor cortex)</td>
<td>contralateral</td>
<td>high</td>
</tr>
<tr>
<td>Unilateral dystonia</td>
<td>temporal or frontal (basal ganglia)</td>
<td>contralateral</td>
<td>high</td>
</tr>
<tr>
<td>Nystagmus</td>
<td>frontal eye field or parieto-temporal junction</td>
<td>contralateral to fast component</td>
<td>high</td>
</tr>
<tr>
<td>Ictal laughing</td>
<td>hypothalamus, temporal, mesiofrontal</td>
<td>none</td>
<td>moderate</td>
</tr>
<tr>
<td>Ictal eye closure</td>
<td>nonepileptic seizure</td>
<td>none</td>
<td>high</td>
</tr>
<tr>
<td>Asymmetric termination of cloni</td>
<td>temporal, frontal</td>
<td>ipsilateral (to the last cloni)</td>
<td>high</td>
</tr>
<tr>
<td>Postictal paresis</td>
<td>frontal, temporal</td>
<td>contralateral</td>
<td>high</td>
</tr>
<tr>
<td>Postictal nose wiping</td>
<td>temporal, frontal</td>
<td>ipsilateral</td>
<td>high</td>
</tr>
<tr>
<td>Postictal aphasia/dysnomia</td>
<td>frontal, temporal, parietal</td>
<td>dominant hemisphere</td>
<td>high</td>
</tr>
</tbody>
</table>

Table 1. Overview of some ictal or postictal clinical features with regard to anatomical origin and their reliability

References
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