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Review

Lateralizing signs during seizures in focal epilepsy

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Abstract

This article reviews lateralizing semiological signs during epileptic seizures with respect to prediction of the side of the epileptogenic zone and, therefore, presurgical diagnostic value. The lateralizing significance of semiological signs and symptoms can frequently be concluded from knowledge of the cortical representation. Visual, auditory, painful, and autonomic auras, as well as ictal motor manifestations, e.g., version, clonic and tonic activity, unilateral epileptic spasms, dystonic posturing and unilateral automatisms, automatisms with preserved responsiveness, ictal spitting and vomiting, emotional facial asymmetry, unilateral eye blinking, ictal nystagmus, and akinesia, have been shown to have lateralizing value. Furthermore, ictal language manifestations and postictal features, such as Todd's palsy, postictal aphasia, postictal nosewiping, postictal memory dysfunction, as well as peri-ictal water drinking, peri-ictal headache, and ipsilateral tongue biting, are reviewed. Knowledge and recognition of semiological lateralizing signs during seizures is an important component of the presurgical evaluation of epilepsy surgery candidates and adds further information to video/EEG monitoring, neuroimaging, functional mapping, and neuropsychological evaluation.

Keywords: Focal epilepsy; Lateralizing signs; Epilepsy surgery; Seizure semiology

1. Introduction

Resective epilepsy surgery aims at the complete resection of the epileptogenic zone, i.e., the area of cortex that is necessary to produce clinical seizures, while sparing eloquent cortical areas [1]. Diagnostic elements that help in the presurgical estimation of the epileptogenic zone and tailoring of surgical intervention are seizure semiology, electrophysiological recordings, neuroimaging, functional testing, and neuropsychological assessment. Ictal semiology improves lateralization and localization of the epileptogenic zone and adds additional information to the ictal EEG [2]. Additionally, patients with lateralizing auras during seizures have a significantly better outcome after epilepsy surgery than those without lateralizing features [3].

Lateralizing semiological signs during seizures, however, cannot lateralize a seizure focus with absolute certainty, and always have to be considered in the context of a complete presurgical diagnostic epilepsy evaluation, including video/EEG monitoring, imaging studies, language lateralization, and neuropsychological assessment, if clinically indicated. Semiology can reflect only the symptomatogenic zone and, therefore, can give only indirect information about the seizure onset zone or the epileptogenic zone, as the epileptic activity may have spread from a "silent" cortical area into a different cortical area that actually produces symptoms.

Determination of the lateralizing significance of semiological manifestations remains difficult and frequently has to rely on case series and retrospective analysis. Findings are usually descriptive and statistics are frequently not calculated or difficult to calculate because of the small numbers of patients. Only a few series confirmed the laterizing sign by several observers, and

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interobserver agreement (κ) is available only in some studies [4]. Furthermore, the group from which the patients were selected is often not well described, and therefore, numbers of patients that did not have the lateralizing sign are unknown, making statistical analysis difficult. Only few studies also included the patients in whom the auras did not occur in their statistical analysis [5]. Additionally, the gold standard in the detection of the epileptogenic zone, seizure freedom after surgery, is often not available, making the description of the lateralizing sign less valid, because the lateralization of the epilepsy focus could not be determined with absolute certainty.

The increasing importance of seizure semiology and clinical lateralizing information has recently also been recognized by the ILAE. Terminology based on the semiological seizure classification [6] has been introduced to better describe clinical semiological patterns which may be of localizing or lateralizing significance [7]. This has also been incorporated into recent proposals for epilepsy classification [8,9].

The following sections provide a brief overview of selected semiological signs and symptoms during seizures, including lateralizing auras, motor and language manifestations, and lateralizing postictal signs.

2. Lateralizing auras and prodromes

2.1. Sensory auras

The frequency of somatosensory auras ranges between 1 and 60% of patients [10]. Maugiere and Courjon described 127 patients with somatosensory auras selected among an epilepsy population of 8938 [11]. All except one patient had unilateral sensory symptoms. In 92 patients a structural lesion could be identified, and in 32, EEG seizures were recorded. Upper limb, hand, and face were most frequently involved [11]. All patients with a known lesion and unilateral auras had symptoms contralateral to the suspected epileptogenic zone [11]. However, these authors reviewed the literature and pointed out that ipsilateral sensory auras have been reported. Tuxhorn et al. reviewed 600 patients and found 72 patients (12%) with sensory auras [10]: in 46% the suspected epileptogenic zone was contralateral to the aura, in 6% it was ipsilateral, in 24% there was no identifiable unilateral lesion, and in 25% the aura was not lateralized. Tuxhorn et al. noted that sensory auras are more reliable if they are well localized, in a distal extremity, and associated with a ''sensory march'' [10].

2.1.1. Mechanism

Somatosensory auras result from activation of the contralateral primary somatosensory area (Brodmann areas 1–3) in the postcentral gyrus. Contralateral sensory symptoms have been demonstrated by cortical stimulation in these areas [12]. Additionally, stimulation of the supplementary sensory motor area in the mesial superior frontal gyrus can produce somatotopically organized sensations [13]. Furthermore, second sensory area activation in the upper bank of the sylvian fissure can lead to bilateral sensory symptoms [14].

2.2. Painful auras

Contralateral localization of the epileptogenic zone in patients with unilateral painful auras had already been suggested by Gowers in 1901 [15]. Young and Blume found 24 patients with painful auras among 856 patients with epilepsy, and 10 of these 24 had unilateral pain [16] (1.2%). Patients with unilateral pain had a suspected symptomatogenic zone in the postcentral gyrus and parietal lobe contralateral to the painful aura as evidenced by clinical and EEG data [16]. Localized contralateral pain associated with parietal seizures has also been described by Siegel et al. [17]. Nair et al. reviewed 604 consecutive cases and found 25 patients with painful auras; 5 of these 25 patients had unilateral painful auras [18]. Interestingly, painful somatosensory auras were contralateral in 3 patients with presumed perirolandic epilepsy, but 1 of the 2 patients with unilateral pain and temporal lobe epilepsy had ipsilateral representation of the aura [18].

2.2.1. Mechanism

The ictal localization of painful epileptic seizures in patients with perirolandic epilepsy is usually within the primary somatosensory cortex. However, in patients with temporal lobe epilepsy, activation of the secondary somatosensory area may lead to ipsilateral representation. Furthermore, involvement of the thalamus cannot be ruled out [19]. Nair et al. suggested that pain is related to a more intense stimulation of the somatosensory area, and this may be supported by the finding that painful auras can be preceded by a tingling feeling that slowly increases to pain [18]. Similar findings have also been described during cortical stimulation [20].

2.3. Peri-ictal headache

Bernasconi et al. reported peri-ictal headache in 47 of 100 patients. The headache was more likely to be ipsilateral to the seizure onset focus in temporal lobe epilepsy (90% of cases) [21], whereas headache in non-temporal lobe epilepsy was not lateralizing. The epileptogenic zone was determined by MRI and video/EEG and, in 68% of these patients, by ''response to surgical treatment'' [21].

2.3.1. Mechanism

The mechanism of peri-ictal headache remains unclear. Bernasconi et al. suggested vasodilation and postictal hyperemia with subsequent activation of the trigeminal nervous system as a potential underlying mechanism [21].

2.4. Auditory auras

The literature on auditory auras has been reviewed by Foldvary et al. In this review, frequency of auditory auras ranged between 2 and 16% of patients, depending on the type of auditory aura included (complex vs simple) and depending on the reviewed population. The Cleveland Clinic series included 18 patients with auditory auras. Fifteen heard bilateral sounds and three located the aura to the contralateral ear [22]. The epileptogenic zone was determined by seizure freedom after epilepsy surgery in 10 and by presurgical evaluation in 8 [22]. Recently, unilateral ear plugging has been reported in three cases to lateralize seizure onset to the contralateral temporal lobe auditory cortex [23]. The epileptogenic zone has been confirmed by seizure freedom after surgery in two and by presurgical epilepsy evaluation in one case [23].

2.4.1. Mechanism

Auditory auras indicate activation of the superior temporal gyrus. Although this area receives input from both sides, stimulation can produce sounds, e.g., buzzing, chirping or ringing, that are perceived contralateral to the stimulated side [24]. Bilateral sound perception has also been described after unilateral stimulation [24].

2.5. Visual auras

Homonymous hemifield defects and auras can lateralize the seizure focus to the contralateral hemisphere. Williamson et al. reported unilateral visual auras in the contralateral visual field in 6 of 25 patients with occipital lobe epilepsy determined by semiology, EEG, and imaging features [25]. Salanova et al. described 12 of 42 patients with visual manifestations in the contralateral hemifield. The epileptogenic zone was determined by clinical, EEG, and imaging findings, and seizure freedom after resection was confirmed in 46% of patients [26]. Interestingly, all patients with complex visual auras (e.g., Rembrandt's self-portrait or characters from a comic book) had right hemispheric epilepsy. This finding has been confirmed by Boesebeck et al., who described 5 patients with complex visual auras and right hemispheric epilepsy among 42 patients [3]. The epileptogenic zone was determined by video/EEG, imaging, and seizure freedom after resection in 19 of 42 patients [3]. Interestingly, complex visual auras were seen only when the lesion involved the temporal lobe [3,27].

2.5.1. Mechanism

Simple visual auras with limited movement within the contralateral visual field are thought to arise from stimulation of area 17 [28]. Prominent movement of the object suggests localization in the contralateral Brodmann areas 18 and 19. More complex visual auras may arise from the temporo-parieto-occipital junction [28].

2.6. Ipsilateral ictal piloerection

Ictal piloerection (''goose bumps'') has been described in 0.15% of patients undergoing video/EEG monitoring [29]. Previous case reports of unilateral piloerection hypothesized occurrence of piloerection ipsilateral to the seizure focus [30,31]. In a recent series, ictal piloerection was observed in 14 of 3500 patients who underwent video/EEG monitoring, and 5 of these 14 patients presented with unilateral or initially unilateral piloerection. Four of five patients in this series and an additional 12 of 14 patients in the literature review demonstrated unilateral or initially unilateral piloerection that was ipsilateral to the seizure focus (84%) [29].

2.6.1. Mechanism

Unilateral piloerection is most likely generated by the central autonomic network, which includes the insula with its viscerotopical organization, the amygdala, the hypothalamus, the midbrain reticular core, and the midbrain periaqueductal gray. Stimulation of the anterior cingulate gyrus [32], the amygdala [33], and the parahippocampal gyrus [29] has been shown to produce piloerection, and, therefore, these areas may be involved in the generation. However, most of these studies were not controlled for afterdischarges after stimulation, and therefore, conduction to a different area cannot be excluded [29].

2.7. Ictal urinary urge

Although urinary urge was described half a century ago by Feindel and Penfield [34], its lateralizing significance has only recently been pointed out by Baumgartner et al. [35]. In this study, 6 of 227 patients with temporal lobe epilepsy confirmed by video/EEG and neuroimaging were found to have nondominant temporal lobe epilepsy [35]. Results were confirmed in a second study that found urinary urge in 6 additional patients with nondominant hemisphere epilepsy among 3446 patients undergoing video/EEG monitoring [36].

2.7.1. Mechanism

Lesional studies and functional imaging studies indicate localization of the symptomatogenic zone in the mesial frontal region or in the medial temporal gyrus and the operculum [37–39].

2.8. Orgasmic auras

Janszky et al. reported a case of orgasmic auras and reviewed the literature on orgasmic auras [40]. A total of 22 cases were reviewed. Fifteen of these 22 cases had unilateral EEG findings, and 13 of these 15 patients had right hemispheric epilepsy. In a second evaluation step, only 9 patients with seizure freedom after surgery or confirmed epileptogenic lesion on neuroimaging were included. All 9 patients who fulfilled these stricter definition criteria of the epilepsy focus had right hemispheric epilepsy [40]. In another study, Janszky et al. report seven patients with orgasmic auras and localization of the epileptogenic zone, by clinical means, EEG, and MRI, to the right temporal lobe in six patients and to the left in one patient [41]. Others have also reported cases of orgasmic auras with seizures, as determined by EEG, arising from the left hemisphere [42].

2.8.1. Mechanism

The symptomatogenic zone is usually located in the right (nondominant) mesiotemporal and right frontal areas, possibly involving the amygdala [41]. This is also supported by an increase in right-sided perfusion as recorded during orgasms in men [43].

3. Lateralizing ictal features

3.1. Version

Wyllie et al. reviewed 74 seizures in 37 patients with lateral head and eye movements during seizures. As compared with previous studies that did not report the lateralizing significance of head turning, which included also mild and less forced cases of head turning [44,45], version was defined in this study as a forced and involuntary movement resulting in sustained unnatural positioning. Seizure focus was determined by EEG recordings. Only versive movements were found to be of lateralizing significance and were always contralateral to the side of seizure onset [46]. Kernan et al. found that forced head deviation was contralateral in more than 90% of seizures, when the seizure developed into a generalized tonic–clonic seizure or occurred within 10 s prior to generalization. These findings have been confirmed by others [47]. Chee et al. reviewed the lateralizing significance of version in 38 selected patients with frontal and temporal lobe epilepsy and found version in 45% of patients with a positive predictive value of 94% [4]. These authors found it to be particularly reliable (100%) if the version is seen immediately prior to the tonic–clonic phase of a seizure, if version is associated with neck extension, and if version is associated with late ipsiversion after the end of a generalized tonic–clonic seizure [4].

3.1.1. Mechanism

The mechanism of contraversion is most likely activation of frontal eye and motor areas anterior to the precentral gyrus (Brodmann areas 6 and 8). Similar movement could also be reproduced by electrical stimulation of these areas [12,48].

3.2. Late ipsiverson at the end of a generalized seizure

The lateralizing value of ipsilateral forced head and eye version at the end of a generalized tonic–clonic seizure has been highlighted by Wyllie et al. [49]. In a study of 61 seizures in 27 epileptic patients with version, 9 patients presented with a late versive movement at the end of a generalized tonic–clonic seizure [49]. When initial contraversion persisted during the generalized phase, late head deviation was contralateral (3 patients). When initial contraversion ended during the generalized phase, late version was ipsilateral (6 patients) [49]. Seizure focus was lateralized by EEG in this series. Chee et al. found late ipsiversion after an initial contraversive movement prior to generalization in 6 of 38 selected patients always ipsilateral to the epilepsy focus as determined by ictal EEG [4].

3.2.1. Mechanism

Mechanisms of late ipsiversion may be similar to those of version and related to predominant activation of one hemisphere after the other during a generalized tonic–clonic seizure phase. Initially, ictal activation of Brodmann area 6 leads to contralateral version prior to secondary generalization, possibly followed by exhaustion or inhibition in this hemisphere. Later, predominance of the ictal discharge with activation of the frontal area in the hemisphere contralateral to seizure onset leads to late ipsiversion [49].

3.3. Unilateral clonic activity

Unilateral clonic activity is one of the oldest known lateralizing features during seizures and was first systematically analyzed by Bravais in 1827 [50]. It has been defined as "myoclonic jerks that recur at regular intervals of less than 1 to 2 seconds" [6]. Unilateral clonic activity is one of the most frequent (56%) lateralizing signs during epileptic seizures [51]. The hand and face are most frequently involved [52]. Janszky et al. found unilateral clonic activity in 33% of patients with frontal lobe epilepsy rendered seizure free after epilepsy surgery. Clonic activity was ipsilateral to the seizure focus in 2 and contralateral in 10 patients [53]. Similar results have been obtained in infants seizure free after epilepsy surgery [54]. Ipsilateral clonic jerking may in part be explained by the phenomenon of the last clonic jerk (see below).

3.3.1. Mechanism

Clonic seizures are most likely the clinical correlate of activation of the primary motor area. Electrical stimulation of the primary motor area (Brodmann area 4) was shown to reproduce clonic activity [55], and a polyspike-and-wave pattern in the primary motor area was seen on subdural grid studies during clonic seizures [55]. The epileptic clonus presented with synchronous contractions of agonistic and antagonistic muscles on EMG, and the period of contraction correlated with spikes on subdural recordings [55]. Clonic activity has also been described with stimulation of the prefrontal area (Brodmann area 6) [56].

3.4. Significance of last clonic jerk

Leutmezer et al. [57] investigated 70 patients with mesial temporal lobe epilepsy due to hippocampal sclerosis and Engel class I or II seizure outcome after 1 year. Asymmetric ending was seen in 30 (interobserver reliability, 96.7%) of 43 patients with secondary generalized tonic–clonic seizures [57]. The last clonic jerk occurred ipsilateral to the hemisphere of seizure onset in 25 of 30 patients [57]. The positive predictive value of this sign was estimated at 83.3%. Trinka et al. [58] analyzed the significance of an asymmetric clonic ending of generalized tonic–clonic seizures in 57 patients with temporal lobe epilepsy. Twenty-nine patients were seizure free for at least 1 year after epilepsy surgery, and of 28 patients with temporal lobe epilepsy diagnosed by presurgical evaluation, including video/EEG and MRI, 23 had an asymmetric ending to a generalized tonic–clonic seizure. The last clonic jerk was seen ipsilateral to the seizure onset zone in 17 of the 23 patients ($P < 0.001$). Interobserver agreement was excellent ($\kappa = 1.0$).

3.4.1. Mechanism

Possible suspected mechanisms include metabolic or ischemic exhaustion and lack of transmitters due to repeated firing versus postictal inhibitory depression, e.g., with GABA overshoot [57]. This mechanism may terminate a seizure more frequently in the hemisphere of seizure onset because this hemisphere was affected for a longer period at the end of the seizure.

3.5. Unilateral tonic activity

The lateralizing value of tonic seizures was analyzed by Werhahn et al. [59]. One hundred twenty-three patients with 170 tonic seizures were selected from 481 consecutive patients with focal epilepsy as determined by presurgical evaluation with video/EEG and neuroimaging (MRI or CT) [59]. Among 24 patients with a known epileptogenic zone and unilateral tonic seizures, the epileptogenic zone was always classified correctly by a blinded observer. However, not all authors found unilateral tonic activity predictive of the epilepsy focus. In a study by Bleasel et al., tonic limb posturing was seen in 17.7% of temporal lobe epilepsy cases and 15% of extratemporal lobe epilepsy cases [60]; tonic seizures correctly predicted the side of onset in 40% of temporal lobe epilepsy cases and in 67% of extratemporal lobe epilepsy cases [61]. In a series by Janszky et al., unilateral tonic posturing in patients with frontal lobe epilepsy was contralateral in 89% of cases [53].

3.5.1. Mechanism

The mechanism of unilateral tonic seizures is most likely activation of the supplementary motor area (SMA) [61]. This has been demonstrated by cortical stimulation [24] and intracranial stereoelectroencephalography [62]. Convexity premotor areas, e.g., Brodmann area 6, the anterior cingulate gyrus, and subcortical structures, e.g., the basal ganglia, cannot be ruled out in the generation of tonic seizures [61–63]. Interestingly, tonic activity can, in exceptional cases, also be elicited during electrical stimulation of the primary motor area [6].

3.6. Asymmetric tonic limb posturing (“figure-of-4 sign”)

Asymmetric tonic limb posturing (ATLP) has been defined “as a striking asymmetry of limb posture during the tonic phase of a GTC [generalized tonic–clonic seizure]. One arm is rigidly extended at the elbow, often with the fist clenched tightly and flexed at the wrist, whereas the opposite extremity is flexed at the elbow” [64]. This precedes bilateral tonic arm posturing at the beginning of the secondary generalized phase and has also been termed the “figure-of-4sign” in the literature because the position of the arms represents a 4 [60,64]. Kotagal et al. retrospectively reviewed 59 secondary generalized tonic–clonic seizures in 31 patients seizure free after epilepsy surgery, and prospectively analyzed 64 secondary generalized tonic–clonic seizures in 26 patients and found the extended elbow contralateral to the side of seizure onset in 35 of 39 cases [64]. ATLP was also noted by Trinka et al. in 23 of 57 retrospectively and prospectively reviewed patients. ATLP was contralateral in 70%, ipsilateral in 17%, and bilateral in 13% of patients ($P < 0.001$) [58]. Jobst et al. described asymmetric tonic arm extension combined with opposite arm flexion and found it to be contralateral in 94% of patients with temporal lobe epilepsy and documented seizure freedom 12 months after surgery [65].

3.6.1. Mechanism

Asymmetric tonic limb posturing may be seen after electrical stimulation and epileptic activation of the SMA [13,66]. SPECT during frontal lobe seizures indicated increased perfusion of the basal ganglia, the SMA, and the prefrontal motor cortex. ATLP may

therefore be related to asymmetrical activation of the SMA or prefrontal areas [61–63].

3.7. Predominantly unilateral spasms

Predominantly unilateral spasms are helpful in lateralizing the epileptogenic zone to the contralateral hemisphere. Asymmetry of infantile spasms was previously reported in 12 of 60 patients (20%) under the age of 12 months [67]. Although no follow-up after epilepsy surgery was reported, the EEG, MRI, PET, and neurological examinations also indicated an epileptogenic zone in the contralateral hemisphere. In a more recent study, the same authors assessed the treatment response of vigabatrin in infantile spasms and reported that 3 of 44 patients (6.8%) had asymmetric spasms [68]. Others have also reported clinical asymmetry of infantile spasms in patients with agenesis of the corpus callosum [69] or following corpus callosotomy [70]. Additional evidence for focal, cortical involvement in infantile spasms derives from lateralized hypsarrhythmia on the EEG [71] and focal lesions on neuroimaging [72]. These results were confirmed in 4 of 19 infants who became seizure free after epilepsy surgery. However, one additional infant had bilateral asymmetric spasms that were either contralateral or ipsilateral to the side of the epileptogenic zone (80% reliability) [73].

3.7.1. Mechanism

The mechanism of predominantly unilateral spasms may be explained by interruption of interhemispheric connections by an underlying lesion. A spontaneous decrease in interhemispheric fibers has been noted in the normal development of cats [74]. Asymmetry of clinical spasms may be a reflection of the incomplete seizure spread pattern across the immature corpus callosum.

3.8. Unilateral dystonic posturing

The lateralizing value of unilateral dystonic posturing was first described in the English literature by Kotagal et al. [75]. A total of 118 seizures in 31 consecutive patients who became seizure free after temporal lobectomy and in 10 patients who underwent video/EEG evaluation were reviewed. Unilateral dystonic posturing was observed in 41 seizures in 18 patients and the dystonic posturing was always (100%) contralateral to the side of seizure onset [75]. These findings have frequently been confirmed since then [4,60,76,77]. Yen et al. reviewed 83 patients who became seizure free after temporal lobectomy and found 29 patients with dystonic posturing. In only one of these patients was dystonic posturing ipsilateral to the epileptogenic zone (96%) [78].

3.8.1. Mechanism

The mechanism of unilateral dystonic posturing is most likely spread to the ipsilateral basal ganglia, as proposed by ictal SPECT studies [79]. Furthermore, interictal PET studies demonstrated hypometabolism in the contralateral striatal and orbitofrontal regions in 16 of 18 patients with ictal dystonic posturing [80]. These findings are compatible with the initial hypothesis of Kotagal et al. suggesting involvement of the ventral striatum, pallidum, sensory motor area, and anterior cingulate gyrus, as direct spread from the hippocampus and amygdala via the fornix. Although Bennett et al. reported dystonic posturing in a patient with seizures arising from the sensory motor area, the posturing appeared to have been qualitatively different (and tonic) from the more dystonic posturing seen in temporal lobe epilepsy [81].

3.9. Unilateral automatisms and dystonic posturing

In association with unilateral dystonic limb posturing, Kotagal et al. described automatisms in the side opposite the dystonic limb [75]. In the Dupont et al. study, 26 of 60 patients with temporal lobe epilepsy had unilateral motor automatisms [82]. Interestingly, the automatisms were predominantly ipsilateral in patients with mesial temporal lobe epilepsy and exclusively contralateral to the epileptogenic zone in patients with neocortical temporal lobe epilepsy. Additionally, the combination of contralateral dystonic posturing and ipsilateral automatisms was observed only in mesial temporal lobe epilepsy.

3.9.1. Mechanism

A partial release phenomenon and activation of a specific brain region are discussed as underlying mechanisms. Stimulation of mesiotemporal structures causes automatisms with loss of consciousness [83]. Stimulation of the anterior part of the cingulate gyrus leads to automatisms with preserved responsiveness. Interestingly, this could be observed after stimulation of the right and left sides [84]. Unilateral automatisms are thought to be bilateral automatisms, but contralateral automatisms are overridden by dystonic posturing in the contralateral hand [75].

3.10. Automatisms with preserved responsiveness

Automatisms with preserved responsiveness were first described by Ebner et al., who evaluated 123 patients with temporal lobe epilepsy diagnosed by video/EEG and MRI, 7 of whom had automatisms and preserved consciousness (5.7%). Automatisms with preserved responsiveness were observed exclusively during seizures arising from the right nondominant temporal lobe and occurred in 10% of these patients. They were not

observed during seizures arising from the left temporal region [85]. Automatisms and preserved consciousness have also been described in an additional case of right temporal lobe epilepsy [86] and have been confirmed in a patient with left hemispheric epilepsy and right-sided language dominance [87]. However, language lateralization was not confirmed in this case. Janszky et al. described a 25-year-old woman with automatisms and preserved responsiveness in the setting of right temporal lobe epilepsy diagnosed by seizure freedom after right-sided amygdalohippocampectomy and with right-sided language dominance diagnosed by transcranial Doppler ultrasound and ictal dysphasia [88]. This is the first reported exemption from the otherwise reliable lateralization of the seizure focus based on automatisms and preserved responsiveness to the nondominant hemisphere.

3.10.1. Mechanism

The mechanism of automatisms and preserved responsiveness remains unclear. Automatisms may be a partial release or activation phenomenon as discussed above. Although loss of consciousness is usually seen when both hemispheres are affected by the ictal discharge [83], it can also be observed during unilateral seizures [89]. However, no specific single site is associated with loss of consciousness. Lux et al. analyzed the localizing value of ictal loss of consciousness and found it frequently impaired in patients with left temporal or bitemporal seizure activity [90]. Bilateral automatisms with preserved consciousness could be elicited during right- or left-sided unilateral stimulation of the anterior part of the cingulate [84]. Therefore, loss of consciousness does not appear to be a precondition for the presence of automatisms.

Another hypothesis suggests that simultaneous receptive and expressive aphasia during seizures arising from the dominant hemisphere associated with limited testing could mimic loss of consciousness and, therefore, mask the actual number of patients with automatisms and preserved consciousness in dominant temporal lobe epilepsy [88].

3.11. Emotional facial asymmetry

Facial asymmetry in patients with temporal lobe epilepsy was first described by Remillard et al. [91]. This asymmetry was more pronounced on emotional movements. Fifty patients were prospectively examined for facial asymmetry. Seizure onset zone was determined by EEG. Contralateral lower facial weakness was present in 27 of 37 patients with a unilateral temporal focus (73%), whereas 13% had ipsilateral facial asymmetry. This was compared with a control group of 25 patients without epilepsy who had only 33% facial asymmetry [91]. These findings have been confirmed in a selected case series of 13 patients with facial asymmetry [92]. Twelve of these patients underwent surgery; pathology revealed mesial temporal sclerosis in all patients and 10 of 12 became seizure free [92]. Another more recent study prospectively investigated 50 patients with hippocampal atrophy on MRI and seizure freedom or 90% seizure reduction after surgery and reported almost identical numbers [93]. Thirty-six of 50 patients (72%) had unilateral facial asymmetry, and in 31 patients (86%) this was contralateral to the side of the MRI findings [93]. Interestingly, these authors noted a relationship between duration of epilepsy and presence of facial asymmetry.

3.11.1. Mechanism

Remillard et al. suspected that motor neurons in the suprasylvian areas, in addition to mesial temporal areas, may be affected by the pathology [91], but also indicated that emotional facial movements may be mediated through a pathway different than voluntary facial movement. This has been confirmed by lesional studies that report isolated emotional and volitional facial paresis [94]. Emotional facial paresis has been described in patients with lesions in the frontal lobe, the striatum and internal capsule, the anterolateral and posterior thalamus, and the insula and the operculum [94]. Interestingly, impaired facial emotion recognition, especially fear, is also impaired in right mesial temporal lobe epilepsy [95] and may not require an intact visual cortex but only a functioning amygdala [96].

3.12. Ictal spitting

Ictal spitting is a rare epileptic event occurring in approximately 0.3% of the epilepsy monitoring unit population [97]. Voss et al. reviewed 2500 patients and found 5 with ictal spitting and right temporal lobe epilepsy. The epileptogenic zone was determined by seizure freedom or greater than 90% seizure reduction after epilepsy surgery [98]. An additional case of left temporal, nondominant temporal lobe epilepsy has also been reported [99]. Kellinghaus et al. described 12 patients with ictal spitting and 9 of these had right temporal, nondominant hemisphere seizure onset [97]. In this series the epileptogenic zone was confirmed in 3 of 12 by resection and seizure freedom, and in the remaining 9 patients, by EEG and imaging data. Also reviewed were 20 cases of ictal spitting in the literature, 14 of whom were found to have seizure onset in the right, nondominant hemisphere.

3.12.1. Mechanism

Pathophysiological mechanisms of ictal spitting may be similar to those for the generation of oroalimentary automatisms, which are related to either a release phenomenon or a cortical activation phenomenon. A statistical seizure component analysis of mesial temporal lobe

epilepsy found oroalimentary automatisms relatively earlier in the course of seizures than nonspecific behavioral movements, suggesting spread from one area to another [100]. Devinsky et al. suggested an asymmetry for oroalimentary and autonomic mechanisms with the central autonomic network favoring the right hemisphere, as seen in ictal vomiting [101] or ictal urinary urge [35].

3.13. Ictal vomiting

Kramer et al. reported 9 patients with ictal vomiting among 450 patients (2%) undergoing video/EEG monitoring and found EEG seizures lateralized to the right hemisphere in all of them [102]. These results were confirmed by Kotagal et al. [100,103]. Devinsky et al. described two additional cases of left temporal lobe epilepsy and ictal vomiting [101]. These authors also reviewed 16 previously reported cases of ictal emesis, including the cases of Kramer et al.; 14 of these 16 cases were lateralized to the right. In one case, ictal vomiting occurred as the seizure spread from the left to the right temporal lobe, and the other patient had right-sided language dominance as evidenced by intracarotid amobarbital testing. Devinsky et al. therefore suggested that ictal vomiting is associated with nondominant temporal lobe epilepsy [101]. Chen et al. reported 3 additional cases of ictal emesis among 156 consecutive patients on the monitoring unit, and 2 of the 3 became seizure free after epilepsy surgery [104]. Two of these patients (one with seizure freedom after surgery) had a left temporal seizure focus and left hemisphere-dominant language. However, review of the EEG samples provided in these two cases shows that vomiting is correlated with seizure propagation from the left to the right in both cases, with bitemporal discharges during the episode of ictal emesis [104]. Nevertheless, ictal vomiting may not be confined exclusively to the nondominant hemisphere. Schäuble et al. reviewed the Mayo Clinic experience and found 2 of 11 cases with ictal vomiting and left hemispheric seizures. In one of these cases left temporal discharges were documented with bilateral temporal depth electrodes in a left hemisphere language-dominant patient [103,105].

3.13.1. Mechanism

Nausea and vomiting have been reproduced during stimulation of the insula in animal studies [106] and humans [107]. Decrease in gastric motility has been observed after resection of the insular cortex [108]. Interestingly, stimulation of the mesial temporal structures also leads to nausea and vomiting [107]. These results have been confirmed by ictal SPECT during seizures with ictal vomiting in two patients. Baumgartner et al. reported activation of the medial, lateral superior, and inferior structures of the nondominant temporal lobe [109]. In addition to temporal structures, mesial frontal region and parts of the limbic circuit of Papez have been associated with the generation of nausea and vomiting [103,110].

3.14. Unilateral ictal eye blinking

Wada described five patients with unilateral eye blinking ipsilateral to the ictal discharge in 1980 [111]. Benbadis et al. identified 14 patients with unilateral blinking unassociated with facial clonic activity among 914 patients (1.5%) undergoing video/EEG monitoring during a 30-month period [112]. Unilateral blinking was ipsilateral to the epileptogenic zone in 10 of 12 patients with a unilateral EEG focus (83%). The epileptogenic zone was identified by resection and seizure freedom or greater than 90% reduction in seizures in 5 and by EEG and imaging in the remaining 9 patients [112]. Another series reviewed 239 patients and found 2 patients (0.8%) with ipsilateral ictal blinking [113]. The epileptogenic zone was determined by video/EEG and MRI [113].

3.14.1. Mechanism

The symptomatogenic zone for ipsilateral ictal eye blinking is unknown. Ipsilateral blinking has been described during stimulation of subdural cortical electrodes [114] and, also, after cortical stimulation in the cat [115]. Blink reflex studies suggest involvement of the inferior postcentral area [116].

3.15. Nystagmus

Epileptic nystagmus has been described previously as a lateralizing sign in adults [117,118] and children [119,120]. Some authors consider epileptic nystagmus as a form of versive seizures [121]. Ictal nystagmus is often associated with seizures arising from the posterior head regions [117,118,120–129]. In all of these cases the EEG changes were contralateral to the fast phase of the nystagmus. In our series, we observed nine cases of epileptic nystagmus among 1838 epilepsy patients. The epileptogenic zone was determined by seizure freedom after surgery in three and by neuroimaging and EEG data in six. The fast phase of the nystagmus was always contralateral to the epileptogenic zone [130]. Anecdotal reports of unilateral epileptic nystagmus lack good documentation at this point [131].

3.15.1. Mechanism

Several underlying mechanisms of epileptic nystagmus have been suggested [117,118]. One hypothesis postulates that the activation of cortical saccade areas induces clonic contralateral conjugate fast eye movements combined with a defect in the gaze-holding system possibly due to rhythmic seizure discharges, which

allows the eyes to drift back. Contraversive saccades have been described in primates after stimulation of frontal [132] and parietal [133] regions, and these regions could possibly generate similar eye movements in humans. Eye version has also been observed after stimulation of Brodmann area 19 [134]. Another mechanism could be the activation of slow ipsiversive smooth pursuit regions. Slow ipsiversive eye movements have been described after stimulation of smooth pursuit regions in monkeys in the most inferior portion of the frontal eye field [135] and a region in the superior temporal sulcus within the temporo-occipital cortex [136]. The fast corrective contralateral phases of the nystagmus are most likely generated as a reflective correction mechanism of the brain stem because of an eccentric orbital eye position or very fast smooth pursuit eye movements [118,137]. A third mechanism could involve activation of cortical optokinetic regions and subsequently subcortical structures including the nucleus of the optic tract, which can also cause ipsiversive slow eye deviation according to stimulation studies in the monkey [138].

3.16. Unilateral ictal akinesia

Negative motor phenomena have already been described by Gowers [15]. Unilateral ictal limb immobility was observed in 5–24% of patients with focal epilepsy [51,139]. It was contralateral in 5 of 94 consecutive patients with focal epilepsy determined by presurgical evaluation [139]. Bleasel et al. observed contralateral ictal limb immobility in 4 of 54 patients with focal epilepsy and seizure freedom after surgery (34 temporal) [60]. The interobserver reliability κ was high in this series [60]. Noachtar and Lüders report 6 cases with lesions in the contralateral hemisphere as determined by EEG or neuroimaging and 3 additional cases. In all cases, the ictal akinesia was contralateral to the suspected epileptogenic zone [140,141]. Also, ictal limb immobility was always contralateral to the epileptogenic zone as determined by MRI and EEG in 24.6% of 328 patients [51].

3.16.1. Mechanism

Mechanisms of ictal akinesia most likely involve activation of negative motor areas [141]. Stimulation of prefrontal areas, particularly of the inferior frontal gyrus, and stimulation anterior to the SMA have been shown to inhibit voluntary movements in humans [141].

4. Lateralizing language features

4.1. Ictal speech

Early reports indicated a predominance of ictal speech in right temporal lobe epilepsy [142,143]. Koerner and Laxer reviewed 84 patients with focal seizures, of whom 13 had ictal speech. Twelve of the thirteen had left-sided seizures, and Wada testing revealed left-sided language dominance in 10 and bilateral language dominance in 3. Seizure outcome after epilepsy surgery was "good" [144]. Gabr et al. observed normal speech in 12.5% of cases, and 83% of these had seizures arising from the nondominant hemisphere [145]. These findings were confirmed by others [4,146,147].

4.1.1. Mechanism

The mechanism of ictal speech is unclear. Penfield and Rasmussen noted inappropriate speech after stimulation of the temporal lobe, but did not comment on lateralization [148]. Serafetinides and Falconer suspected either the dominant hemisphere from inhibition through the nondominant hemisphere or, alternatively, overexcitement of the nondominant hemisphere [142].

4.2. Ictal aphasia and dysphasia

Ictal aphasia presents with either receptive, expressive, or mixed aphasia [6]. Milder forms of ictal aphasia may include ictal dysphasia [145]. Ictal aphasia can be elicited only in the conscious patient. Serafetinides and Falconer described 34 patients with ictal dysphasia and temporal lobe epilepsy as determined by interictal EEG. The epileptogenic zone was confirmed in 17 patients (16 left) by seizure freedom after epilepsy surgery [142]. Almost all additional cases with ictal speech had seizures or status epilepticus arising from the dominant hemisphere [146,149]. Only one patient with a nondominant hemisphere seizure and "speech arrest" has been described [145]. To our knowledge, no cases of ictal aphasia with seizure freedom after nondominant hemisphere epilepsy surgery and language dominance determined by Wada testing have been observed to date.

4.2.1. Mechanism

Ictal aphasia is related to electrical activity in the language-dominant hemisphere [150]. Subdural cortical stimulation of three distinct areas while the patient is reading aloud demonstrated language representation in the inferior frontal gyrus (Broca), the supramarginal and superior temporal gyrus (Wernicke), and the basal temporal area (Lüders) [151,152]. It can be speculated that patients with bilateral language representation or crossed language representation may have aphasia after right and left hemispheric seizures.

4.3. Ictal vocalizations

Janszky et al. analyzed pure ictal vocalizations (excluding sounds related to clonus or respiration) in 27 patients with frontal lobe epilepsy and seizure freedom after surgery [153]. Pure ictal vocalizations

occurred in 11 patients, and 9 of these had left frontal lobe epilepsy. The authors suggested ictal vocalizations as a potential lateralizing sign in patients with frontal lobe epilepsy [153]. Wada testing was not available on all patients. Similar findings have also been observed by others [145,154].

4.3.1. Mechanism

The mechanism may be similar to lateralization of ictal speech with activation of Broca's area. However, ictal vocalizations have also been observed after stimulation of the contralateral non-language-dominant anatomical Broca equivalent [148]. Additionally, vocalizations have also been seen after stimulation of the SMA, but more frequently in the language-dominant hemisphere [155].

5. Lateralizing postical features

5.1. Postictal paresis (Todd's palsy)

Postictal paresis is one of the oldest described lateralizing signs [50,156]. Systematic analyses were recently performed by Kellinghaus and Kotagal [157] and Gallmetzer et al. [51]. Kellinghaus et al. reported 29 patients with postictal palsy among 4500 epilepsy patients undergoing video/EEG monitoring. In 27 patients, the suspected epileptogenic zone could be lateralized either by seizure freedom after epilepsy surgery or by EEG and neuroimaging data. Postical paresis was always contralateral to the side of seizure onset. Gallmetzer et al. observed 44 patients with postictal paresis among 328 patients (13.4%) [51]. The epileptogenic zone was determined by concordant findings between EEG and MRI in this population [51]. The postictal paresis was always contralateral to the suspected epilepsy focus. These findings were also noted in earlier series [158–160]. Bilateral postictal paresis has also been described [157,161].

5.1.1. Mechanism

Suspected mechanisms include neuronal exhaustion of the primary motor areas, e.g., due to increased lactic acid levels [162], and cerebrovascular dysfunction [163]. Alternatively, active inhibition, e.g., by endogenous endorphins, has also been proposed [157,164]. Additionally, basal ganglia involvement has been suspected in the postictal inhibition [51,157].

5.2. Postictal hemianopia

Only few cases of transient postictal hemianopia have been reported [165,166]. All of them were lateralized to the contralateral side of suspected seizure onset. The mechanisms may be similar to those of postictal paresis.

5.3. Postictal aphasia and dysphasia

Gabr et al. were the first to lateralize language dominance with Wada testing in all patients, and demonstrated that in 92% of patients with postictal dysphasia, the presumed epileptogenic zone was in the language-dominant hemisphere [145]. Others had similar results, with positive predictive values for postictal dysphasia and aphasia between 80 and 100% [144,146,167,168]. In particular, the time delay until language recovery after a seizure may be predictive [169]. Clinically, it may be difficult to differentiate between postictal confusion and aphasia. Language and speech testing for expressive, receptive, and global aphasia is therefore crucial.

5.3.1. Mechanism

The mechanism of postictal aphasia may be similar to that of postictal paresis. Aphasia may be related to either postictal exhaustion or active inhibition of the language areas and their connections in the dominant hemisphere. Lateralization may be misleading in cases with atypical language representation and after involvement of both hemispheres during seizures.

5.4. Postictal nosewiping

The lateralizing significance of postictal nose wiping was first systematically analyzed by Hirsch et al. and Leutmezer et al. in 1998 [170,171]. Hirsch et al. analyzed 87 patients with temporal lobe epilepsy (TLE) as defined by seizure freedom or greater than 90% seizure reduction after epilepsy surgery and extratemporal lobe epilepsy as confirmed by EEG and imaging. Postictal nosewiping within 60 seconds of the end of the seizure occurred in 53% of patients with TLE and was ipsilateral to the side of seizure onset in 92%. If it occurred more than once within 60 seconds of the seizure it was always ipsilateral to the seizure onset [170]. In the Leutmezer et al. study, ipsilateral nosewiping occurred in 86.5% of TLE patients. Conversely, nosewiping was ipsilateral in 54.5% of patients with extratemporal lobe epilepsy [171]. These results were confirmed by others [172,173].

5.4.1. Mechanism

The mechanism of postictal nosewiping remains unknown. Activation of the central autonomic network, in particular, the amygdala, has been suspected of causing nasal secretions. Wennberg reports one case in which depth electrodes showed ictal nosewiping only when ictal activity involved the amygdala, but not the hippocampus [173]. Use of the ipsilateral hand may be related to a mild contralateral postictal paresis or neglect [168,173].

5.5. Postictal disorientation

Prolonged spatial disorientation was more observed after right temporal seizures [167]. These authors analyzed 32 right hemispheric seizures and 33 left hemispheric seizures in 19 patients. The epileptogenic zone was estimated with neuroimaging and EEG. Disorientation for place was observed after 11 of 32 right hemispheric and 2 of 33 left hemispheric seizures [167].

5.5.1. Mechanism

Right hemispheric lesional studies confirmed representation of spatial and topographic orientation in the right nondominant parieto-occipital region [174].

5.6. Postictal flattened affect

In the above-mentioned study, Devinsky et al. also observed flattened or depressed affect in 40% of right hemispheric seizures and 12.5% of left hemispheric seizures [167].

5.6.1. Mechanism

Emotional specialization of the right hemisphere [175] and greater postictal disruption or suppression has been suggested as a possible explanation [95,167].

5.7. Ipsilateral tongue biting

Benbadis analyzed the significance of lateralized tongue biting in 106 patients [176]. Seven patients with a unilateral tongue bite had focal epilepsy and one had generalized epilepsy. The tongue bite was ipsilateral in five of seven patients with focal epilepsy (71%). The determination of the epileptogenic zone remains unclear but may have been based on video/EEG and MRI findings.

5.7.1. Mechanism

Benbadis suggested that the more frequent ipsilateral localization of tongue bite injuries may have been related to contralateral genioglossus muscle activation, causing deviation of the tongue to the opposite side [176].

5.8. Peri-ictal water drinking

The first large series of patients with peri-ictal water drinking was described by Remillard et al. in 1982 [177]. Trinka et al. described peri-ictal water drinking behavior during a seizure or up to 2 minutes after a seizure in patients with nondominant temporal lobe epilepsy [178]. The incidence of peri-ictal water drinking was 15.3% (10 patients among 68 consecutive patients). Three patients were excluded because of pending surgery or refusal to undergo epilepsy surgery. Seizure outcome after 1 year was Wieser I in all patients. Pathology consisted of hippocampal sclerosis in five, ganglioglioma in one, and astrocytoma in one patient [178].

5.8.1. Mechanism

Water-seeking behavior and drinking can be induced by stimulation of the lateral hypothalamus in rats [179]. Trinka et al. speculated that propagation of mesial temporal epileptiform discharges via pathways between the hypothalamus and the mesial temporal structures causes water drinking to quench the thirst caused by an epileptiform discharge [178]. The authors also indicate that this may be related to a general predominance of central autonomic network function in the right hemisphere [178].

5.9. Postictal verbal and visual memory impairment

Postictal memory impairment after temporal seizures has been suggested by Helmstaedter et al. [180]. Left-sided seizures have been associated with deterioration on verbal memory tasks, and right-sided seizures lead to deterioration on visual memory tasks in the immediate postictal period [180]. In a prospective study on 10 patients with unilateral TLE as demonstrated by video/EEG monitoring, patients with left temporal lobe seizures (but not right temporal lobe seizures) presented with impaired verbal memory function associated with left temporal seizures during the 24-hour retention interval [181]. Memory testing was significantly better on days without seizures in the same patients. No information on language dominance was available for this group.

5.9.1. Mechanism

Mechanisms of accelerated forgetting are most likely related to disturbance of memory consolidation in the mesial temporal region. Verbal memory testing may favor the left language-dominant hemisphere, and nonverbal memory may be affected predominantly by seizures arising from the non-language-dominant hemisphere.

6. Conclusion

Lateralizing signs in seizure semiology are an important facet in the complete presurgical evaluation of epilepsy patients. Seizure semiology and semiological lateralization constitute an important segment, but should never be the sole source of information as lateralizing signs may be occasionally misleading. Because of possible incongruence between the symptomatogenic zone, i.e., the cortical area that produces the symptoms during activation, and the epileptogenic zone, i.e., the area of cortex that is indispensable for the generation of seizures, no semiological lateralizing sign can lateralize the epilepsy focus with 100% certainty, and exceptions

to the rule may sooner or later be described in each of these signs due to variability in the anatomical organization of brain functions. Nevertheless, knowledge and recognition of semiological lateralizing signs during seizures are important in the presurgical evaluation of epilepsy surgery candidates and add further information to video/EEG monitoring, neuroimaging, functional mapping, and neuropsychological evaluation.

The list of lateralizing features increases steadily. The above-mentioned lateralizing signs are a subjective selection and not meant to be a complete list of possible lateralizing semiological features (Table 1). Other features, such as ictal autoscopy [182,183], ictal smile [184], ictal yawning [168], ictal lacrimation [168], ictal coughing [146,168], ictal panic attacks [185,186], and fear [187], have also been associated with possible right hemispheric lateralization, but these features are less well documented or are currently under investigation. Left hemispheric predominance of ictal cold has been suspected by Stefan et al. [188,189]. Furthermore, nonversive head deviation and turning during different stages of focal seizures [76] and combinations of asymmetric motor signs [53,65] may also have lateralizing value.

Lateralizing clinical features may not be limited to focal epilepsy and may also be seen in patients with generalized epilepsy [190]. Leutmezer et al. observed clinical signs pointing toward focal epilepsy in 7 of 20 patients with generalized epilepsy, including figure-of-4, version, unilateral tonic/dystonic posturing, postictal nosewiping and postictal hemiparesis [190]. Furthermore, all lateralizing features may be subject to plasticity and, therefore, may be misleading in patients with large intracranial lesions due to atypical functional cortical representation [54].

Combinations of two or more lateralizing signs in the same seizure or the same patient may have biased previ-

Table 1
Overview of selected lateralizing signs during seizures

Lateralizing sign	Frequency	Lateralizing value	Symptomatogenic zone
Aura			
Unilateral sensory aura [10]	6.1% epilepsy patients	89% contralateral	Brodmann areas 1, 2, and 3
Hemifield visual aura [26]	28.6% OLE[a]	100% contralateral	Brodmann areas 17–19 and adjacent areas
Motor			
Version [46,53]	22.2% FLE	100% contralateral	Brodmann areas 6 and 8
Clonic activity [53]	44.4% FLE	83% contralateral	Brodmann areas 4 and 6
Tonic activity [53]	48.1% FLE	89% contralateral	SMA, possibly also Brodmann area 6, the anterior cingulate gyrus, and subcortical structures
"Figure-of-4 sign" [60,64]	17.7% TLE; 15% ETLE	89% contralateral	SMA or prefrontal areas
Unilateral dystonic posturing [75,78]	43.9% TLE	100% contralateral; one exemption reported by Yen	Activation of basal ganglia
Automatisms and preserved consciousness [85,88]	5.7% TLE	100% non-dominant; one exemption reported by Janszky [88]	Unknown, possible impairment of consciousness with left or bilateral hippocampal impairment
Ictal spitting [97]	0.3% EMU patients	75% non-dominant	Possible asymmetry of the CAN
Ictal vomiting [102,105]	2% EMU patients	81% non-dominant	Medial, lateral superior and inferior structures of the nondominant temporal lobe and Papez circuit
Unilateral ictal eyeblinking [112]	1.5% EMU patients	83% ipsilateral	Unknown
Language			
Ictal speech [145]	34.2% EMU patients	83% non-dominant	Impairment of areas other than those involved in language production
Ictal dysphasia and aphasia [145]	34.2% EMU patients	100% dominant	Impairment of language areas
Postictal features			
Postictal palsy [157]	0.6% EMU patients	93% contralateral	Possible exhaustion or inhibition of Brodmann areas 4 and 6
Postictal nosewiping [170]	53.2% TLE	92% ipsilateral	Unknown

[a] CAN, central autonomic network; EMU, epilepsy monitoring unit; ETLE, extratemporal lobe epilepsy; FLE, frontal lobe epilepsy; OLE, occipital lobe epilepsy; SMA, supplementary motor area; TLE, temporal lobe epilepsy.

ous studies on lateralizing signs during seizures. A blinded observer may have been biased by the presence of another more reliable lateralizing sign during the same seizure. It is very difficult to control for this error, because many studies focus frequently only on selected lateralizing signs and do not mention other, possibly confounding signs and symptoms (see Table 1).

Recognition of the presence or absence of a lateralizing sign may be highly dependent on the level of training of the observer. Recent advances in digital quantification of lateralization and extent of movement may further validate the information gained from descriptive studies that are frequently confirmed only by interobserver agreement [191].

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