Case Report

Nonconvulsive status epilepticus with an unusual EEG: A fresh look at lateralities of motor control and awareness

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Abstract

This article is an account of a patient with nonconvulsive status epilepticus associated with an unusual EEG. The importance of recording speed in lateralizing the hemisphere of onset of epilepsy is emphasized, on the basis of one-way callosal traffic theory. From this vantage point, the following were deemed responsible for the currently divergent views on the lateralizing significance of various signs and symptoms in epilepsy: (1) the dichotomous nature of laterality of motor control, which is the same as that of seizure onset; (2) the probabilistic nature of the availability of the callosal channel for transfer of epileptiform discharges from the major to the minor hemisphere (i.e., the random variability of synaptic transfer); (3) the dynamic (varying) expanse of the epileptic region within the major hemisphere. Other data reviewed indicated that measuring the reaction time of two symmetrically located effectors is the most robust way of determining the laterality of the major hemisphere, with the side of shorter reaction time being opposite to the major hemisphere. Clinical presentations of seizures reflect the probabilistic involvement of different regions of the major hemisphere by the epileptic process and the spread of the epilepsy to the minor hemisphere via the callosum. Termination of seizure activity with diazepam was associated with simultaneous recovery of awareness and speech in this case.

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1. Introduction

How do we assess the awareness of a person who cannot communicate or obey orders? This article explores the issues surrounding that question. The inquiry was occasioned by an awake but noncommunicative patient, who became communicative following intravenous injection of diazepam. She was first seen as the EEG was being recorded. Because of the role of this mode of investigation in similar circumstances, this inquiry is biased toward those electroclinical aspects that are germane to the relationship between lateralities of motor control, seizure onset, and awareness. Using insights from a new understanding in callosal traffic, that is, that motor and sensory communications between the hemispheres are one-directional (from the major to the minor in motor domains, and from the minor to the major hemisphere in somatosensory domains) [1–3] additional data are reviewed supporting the concept of speech as a marker of the major hemisphere, wherein all commands are initiated and to which all signals from the nondominant side of the body must enter for conscious apprehension. Evidence is reviewed indicating that as a result of directionality in callosal traffic, and the excitatory nature of signals traversing the callosum from the major to the minor hemisphere, it is not possible for seizures to start in the minor hemisphere; and that the symptomatology of seizures is related to the extent of intra- and interhemispheric spread of the epileptic process, rather than being engendered by a specific “lobe” in the major hemisphere.
2. Case report

B.G. was a 77-year-old right-handed woman admitted to a hospital with the chief complaint of “confusion and being unresponsive.” She was normotensive with a regular heartbeat. A few weeks earlier she had been hospitalized at a teaching facility in Charlottesville, VA, USA, for a similar reason. During the current hospitalization, she was periodically incoherent, regaining her vivaciousness within an hour or so without remembering the event. At times she was quietly holding food in her mouth as she looked incoherent and unresponsive. There was no history of convulsions in the past or of head trauma. There were two distant cousins who had seizures, but she knew of no details regarding them. Her past history was neurologically unremarkable. She was not taking any anticonvulsants.

When seen for the first time she was sitting calmly in a wheelchair. She appeared oblivious to her surroundings and was unable to carry out simple commands such as closing the eyes, speaking, and moving her tongue. There was no blinking in response to visual threats. When asked to squeeze the hands of the examiner, she feebly made an attempt with each hand. A grasping response was noted when the examiner withdrew his hand from the patient’s right hand. According to the technician, the patient had been bubbly and alert the day before, when she underwent an EEG (with normal results). She had experienced difficulty removing the chart from the patient’s hands in preparation for the second EEG. The patient did not respond to a request to walk to the EEG table, necessitating the recording for the second EEG. The patient did not respond to a teaching facility in Charlottesville, VA, USA, for a similar reason.

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At other times, she behaved as if she were not present. There was no drooling. She remained continent throughout. No myoclonic jerking was noted anywhere. During this time the electroencephalograph was recording high- and medium-voltage polymorphic spike–slow waves or slow wave potentials at 3–4 cycles/second. These were at times generalized and at other times local with variable focality. The recordings were made employing the 10–20 system of electrode placement, with the standard speed and montages as indicated in Figs. 1 and 2. The aforementioned polymorphism was frequently interrupted by unusual short-lasting bursts of nonlateralized high-voltage, (often) nonfusiform fast activity within the alpha range, often ending with a slow wave. They occurred with the eyes held closed as well as open. Nose wiping was observed on a few occasions. Intravenous injection of 5 mg diazepam resulted in quick restoration of the EEG to a normal pattern, together with resumption of responsiveness for the first time (evidenced by return of speech), with the abnormal spike–slow wave activity becoming intermittent after the first injection. The EEG became normal in appearance after the injection of a second 5 mg of diazepam. The sequence of events, as documented, leaves no doubt as to the relationship between diazepam-induced suppression of seizures and the reappearance of consciousness and speech in this case. She soon fell asleep and was taken back to her room. On awakening, she could not recall any of the events that had occurred earlier in the laboratory.

She was prescribed topiramate 200 mg twice per day with the diagnosis of new-onset seizure disorder and discharged home. She has experienced no further attacks since. Two EEGs after discharge have been normal. A CT scan of the brain revealed mild atrophy, and ultrasound of the carotids was unremarkable. Her neurological examination on follow-up remains within normal limits for her age. The brain MRI scan performed after the EEG, with and without contrast, was unremarkable.

3. Discussion

The return of normal speech and awareness seconds after intravenous injection of diazepam as the EEG returned to normal is a feature that must be considered in arriving at a diagnosis in this case. In a recent review, cases similar to B.G.’s have been described under a variety of titles, such as: unclassifiable silent status epilepticus; nonconvulsive status epilepticus; epileptic aphasia; complex partial or psychomotor status; nontonic-clonic status with altered consciousness; de novo absence status of late onset; and monosymptomatic dysphasic status epilepticus [4]. Accordingly, absence of a definitive focality or laterality, as seen in B.G.’s case, has been construed as evidence against the diagnosis of complex partial seizures. However, it has also been argued that the focal nature of the epileptogenic process may not be captured at the time the EEG is recorded. Even if that argument is accepted, there remains the methodological problem of false lateralization of “temporal lobe epilepsy” by electroencephalography (in about a third of tumor cases) [5] and the fact that resorting to invasive techniques is associated with an increased rate of surgical failures in treating recurrent seizures [2]. Thus, in B.G.’s case, we are left with the noncommittal designation of absence/nonconvulsive status epilepticus in an elderly woman without a history of seizures.

Although B.G.’s clinical presentation was not unique, her EEG was highly unusual, characterized by occurrences of periodic high-voltage nonlateralized epileptiform discharges within the alpha range. To my knowledge, this pattern has not been reported before.

In a review of the grand mal pattern of Gibbs, Gibbs, and Lennox, Rodin et al. briefly mention the occurrence of an 8–10 cycle/second rhythm occurring in the tonic phase of seizures “when an artifact free record could be obtained,” resembling configurations seen in the present case [6]. However, B.G. never suffered from grand mal seizures in the past, nor was she using any anticonvulsant medications. Rodin et al. reviewed their records for occurrences of 15–25 cycle/second beta activity associated with altered level of awareness (e.g., staring), a situation entirely
different from that prevailing in the present case in terms of the EEG finding. Bauer et al. has reported episodic occurrences of 10 cycle/second high-voltage activity lasting 10 seconds or longer associated with incoherence, in a case with history of seizure disorder [7]. We are therefore left with the de novo presentation of fluctuating level of awareness associated with a previously undescribed EEG pattern in a patient with a normal MRI scan of the brain who regained her faculties immediately after the seizure was terminated with intravenous diazepam, remaining amnesic of the event.

4. Resolution of some of the controversies surrounding similar cases

The following comments provide a background for resolving some of the controversies surrounding the laterality of conscious awareness and the onset hemisphere in seizures associated with speech arrest and fluctuating level of awareness as witnessed in B.G.: According to the anatomical understanding under review, (neural) handedness bespeaks of proximity of the dominant side of the body to the command center (the major hemisphere, hemisphere

Fig. 1. Epileptiform activity detected with the patient out of contact. Periodic, nonlateralized, high-voltage epileptiform activity (within the alpha range) continued until disrupted by intravenous injection of 5 mg diazepam in two consecutive doses. Calibration signal applies to both figures; sensitivity = 7 μV/mm. Double banana electrode placement.
of speech) by a callosal width. This callosal proximity is reflected in the shorter reaction time of all the effectors on the dominant side compared with the same effectors on the nondominant side [1–3]. As the (neurally) nondominant side of the body is connected to the command center indirectly, that is, via the callosum, there is a delay in the reaction time for the effectors located on that side; this amounts to the interhemispheric transfer time (IHTT). Stated differently, evidence indicates that the minor hemisphere has no motor initiative of its own and there are no motor communications from the minor to the major hemisphere (see below for further explanation) [1–3]. Rather, the minor hemisphere implements the biddings of the command center, where all actions are planned and executed (including speech).

Anatomically, therefore, the executive hemisphere sits ipsilateral to the nondominant side of the body and controls the events occurring below it, via the corpus callosum. It is in this respect that the similarity of the ratio of epileptiform discharges associated with speech disturbance...
A similar left hemisphere/right hemisphere ratio was documented in another report, in which a statistically significant predominance of epileptiform discharges in the left hemisphere was observed in 1254 EEGs (left/right hemisphere ratio = 79%/21%) [8]. Furthermore, the same asymmetry (in brainedness) has been observed by Penfield and Roberts [9] (left/right hemisphere ratio = 90/20) and Roux et al. [10, p. 1797] left/right hemisphere ratio = 44/10) in two other large series of patients with epilepsy undergoing surgery.

If one-way callosal traffic theory accurately describes the wiring that governs laterality of motor control (as sketched above), a reversal of the above ratio would be expected in neural handedness (brainedness) as delineated earlier; that is, the ratio of the hand with faster reaction time to the hand with slower reaction time must be the reverse of the above-mentioned ratios. This prediction has been verified numerous times in experiments on manual reaction times above-mentioned ratios. This prediction has been verified numerous times in experiments on manual reaction times [1–3]. The broader meaning of these time-resolved experiments is as follows: Behavioral handedness is a statistical reflection of neural handedness, and their difference (dissociation) reflects the absence of a choice as to laterality of the hemisphere with which we speak (i.e., brainedness, the executive hemisphere) and the obvious choice we have as to the hand we adopt as our favorite (as they both are normally under our full control). With this insight, we have now arrived at the resolution of an age-old controversy surrounding lateralities of handedness and brainedness, exemplified in the following observations.

As reviewed elsewhere [1–3], the dichotomy of the command structure is revealed in: (1) our inability to strike two notes simultaneously on a keyboard (even though written for simultaneous delivery, the so-called melody lead of the right hand in piano players); (2) our inability to move the bowing and the fingering hand simultaneously when playing the violin (the bowing hand precedes the fingering hand by an average of 60 ms even though simultaneity is intended); and (3) the faster response of the right hand when we type with a typewriter. In this respect, earlier plunging into action of the right hand with direct connection to the major hemisphere (the left hand, in neural right-handers) has been documented as an earlier onset of readiness potentials over the major hemisphere in high-resolution EEG studies in self-paced exercises. Cui et al. provided an estimate of ~600 ms for the earlier onset of activity of the left/major hemisphere in their recent study (Fig. 5 and p. 56) [11]. It will be recalled that the faster responsiveness of the right hand is the basis for the asymmetry of crossed–uncrossed differentials in the Poffenberger paradigm. The absence of such differentials when using the dominant hand, compared with their presence when employing the nondominant hand, was recently confirmed by Fendrich et al. [12].

The dissociability of brainedness (neural handedness) and dexterity (behavioral handedness) has been the basis for distinction between motor dominance and hand preference. For example, for a left handed woman who sustained ischemic infarction of the entire callosum and who displayed laterality indexed findings similar to those of right-handers after similar injury, Lausberg et al. arrived at the above-mentioned solution [13]. Mismatching of neural and behavioral handedness also occurred in a right-handed woman reported by McNabb et al. [14]. She developed a right-sided alien hand after an infarct of the left superior and medial frontal and parietal cortex, as well as the genu and body of the corpus callosum. Contrary to expectations in movement-related cortical potential studies, however, moving the right finger was associated with bilateral cortical activity in her case (not the left, as is the case in neural and behavioral right-handers) [1–3, 11].

The most remarkable example, however, remains the case of N.F. described in exquisite detail by Burklund and Smith, who included autopsy findings 18 months after left hemispherectomy [15]. The operation had left N.F. with no permanent linguistic consequences, indicating that the hemisphere removed was the minor hemisphere (see above). Five years earlier, N.F. had begun with focal right-sided seizures associated with “transient episodes of right hemiparesis and speechlessness.” In retrospect, it became known that the patient had harbored cystic astrocytoma of both frontal lobes. According to the anatomy under review, the transient right hemiparesis with focal seizures was a (false) lateralizing sign, caused by transcalsal transfer of epileptiform activity from the right (major) to the left (minor) hemisphere, affecting the neurally nondominant right hand (ipsilateral seizure). Gusmao et al. recently reviewed similar instances of seizures ipsilateral to the focus while describing a case of their own [16]. For demographic reasons, however, ipsilateral seizures resulting from transcalsal transmission of epileptic activity from the left to the right hemisphere are more common. An example with magnetic resonance images was published recently by Borges et al. [17].

This explains the conflicting data in the literature as to the lateralizing significance of head and eye turning—reflecting varying engagements of the two hemispheres at different times during a seizure, depending on stochastic availability of callosal transmission of epileptic discharges to the neighboring (minor) hemisphere. The same consideration applies to fluctuation of awareness in the course of a seizure, this time reflecting the extent of engagement of the major hemisphere by seizure activity [18]. To sum, because the minor hemisphere may not initiate movements of its own (see above), the possibility of it embarking on movements of any kind does not arise unless the lesion in that hemisphere raises the intracranial pressure, affecting the major hemisphere, or, when the case is one of erroneous designation of that hemisphere as the minor, based on the behavioral handedness of the subject. As a result, the subject matter of earlier debates on the lateralizing value
of different symptoms will change to the need for critical reappraisal of different modalities of investigation by epileptologists for lateralizing the major hemisphere.

At the same time, one-way callosal traffic circuitry expands the number of alternative presentations by doubling the varieties of handedness (neural and behavioral) and by recognizing the inherent randomness of availability of callosal transfer to motor signals destined for the minor hemisphere. Thus, although both hemispheres are capable of generating seizures at the population level, such a feat will remain impossible in an individual case because lesions affecting the minor hemisphere are associated with diminished excitability of both hemispheres. This is reflected in the increased reaction time of both sides of the body in lesions affecting the minor hemisphere [19].

Although, because of a conventionally slow recording speed (see below), the laterality of seizure onset in B.G. remained unknown, according to the time-resolved data reviewed, her fluctuating level of awareness was related to the extent of involvement of her major hemisphere at different times during the epileptic process (Fig. 1). Because she was right-handed there is an ~80% chance that the hemisphere involved with the epileptic process was the left hemisphere. The nose wiping displayed by the patient does not seem to have a lateralizing value [20]. She regained responsiveness to her surroundings and speech at the same time, immediately after the seizure was interrupted by intravenous injection of diazepam, indicating the close relationship between the neural representations of both faculties just mentioned (Fig. 2).

The literature, reviewed from the perspective of a one-way callosal traffic scheme, indicates that epilepsies vary in their manifestations according to the extent they engage neuronal aggregates subserving awareness within the major hemisphere, as well as the likelihood of invading the minor hemisphere via the callosus. In B.G.’s case, because both comprehension and motor abilities were affected by the epileptic process, the seizure must have involved the temporal as well as frontal lobes of the major hemisphere. Surprisingly, there has been no systematic treatment of the role of speed of recording in discerning the laterality of seizure onset since the issue was first raised by Bennett in 1953 [21]. (Currently, the speed of recording for routine EEG is set at 10 second per page.)

According to one-way callosal traffic circuitry, the role played by the callosus is one of connecting the two moieties of a bihemispherically distributed neuronal ensemble devoted to volition, with the controlling moiety residing in the major hemisphere [1–3]. In this respect, the recent report by Duane et al. [22] is a reminder of the importance of speed of recording in assigning the laterality of seizure onset/executive hemisphere. Increasing the recording speed from 4 to 10 pages per second revealed the laterality of the onset hemisphere (the right in that case) [22]. The other observation by Duane et al., that is, laterality indexed causation of sleep (amytal) or epilepsy (metrazol) in patients undergoing intracarotid studies, has been reported before, revealing bilateral suppression or activation of seizure activity by injection of the active substance into one (executive, major) hemisphere [23–25]. These observations and the preceding inquiry raise relevant issues that are not fully accounted for by concepts such as “kindling” and “secondary bilateral synchrony” [26].

References


