Very slow EEG responses lateralize temporal lobe seizures

An evaluation of non-invasive DC-EEG

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Abstract—Background: This study tested the idea that very slow EEG responses (direct current [DC] potential shifts) could be detected noninvasively during temporal lobe (TL) seizures, and that these shifts give lateralizing information consistent with that obtained by other methods. Methods: Seven patients with TL epilepsy (TLE) were recorded with scalp DC-EEG technique at bedside. All recordings were performed simultaneously with conventional EEG (scalp in five, and intracranially in two; two patients with scalp recordings were recorded intracranially later). Seizures in five patients originated in the mesial TL. Ictal DC shifts were evaluated by comparing them to the temporal evolution of ictal discharges, and by comparing the laterality of these shifts to the side of seizure onset defined by routine EEG and other presurgical diagnostic tests. Results: All seizures (35/35) were associated with negative DC shifts at temporal derivations (30 to 150 μV relative to vertex), beginning at the electrical seizure onset, and lasting for the whole seizure. In eight seizures (five patients) with documented mesial TL onset, the polarity of the DC shift was initially positive followed by a negative one after lateral spread of seizure activity. In all cases, the side of the EEG shift agreed with other diagnostic tests, and, at times, was more clearly lateralized than the conventional scalp EEG. Conclusions: DC-EEG recordings are practical and achievable at the bedside. Ictal DC shifts are consistently observed in scalp recordings in TL seizures, and reliably lateralize them. This method may hold promise in reducing the need for invasive monitoring in patients with TLE where other noninvasive tests are equivocal.

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Neurosurgical treatment of medically intractable seizures requires determination of the site of origin (epileptogenic zone)—this is initially attempted by ictal video EEG recordings with scalp electrodes, correlated with other noninvasive studies, particularly neuroimaging.1 However, ictal EEG often gives equivocal information about the localization or laterality of seizure origin,2–5 or it is incongruent with other tests, leading to the requirement for further, invasive ictal recordings with intracranial electrodes. A potentially straightforward way to enhance the utility of scalp recorded EEG in seizure localization, and to reduce the need for invasive recordings, would be to detect electric signals that are associated with seizures but reflect mechanisms that differ from those giving rise to the fast ictal activity detected by conventional EEG techniques. It is well established by a large number of animal experiments,6–8 and by early invasive recordings on humans,9,10 that seizures are associated with very slow EEG responses called direct current (DC) potential shifts. They are, however, not detected by conventional clinical EEG techniques owing to high pass (i.e., low cut) filtering. Recording of these low frequencies requires a genuine DC-EEG amplifier and nonpolarizable (i.e., Ag/AgCl) electrodes.11

There are no published noninvasive DC-EEG recordings of human focal epilepsy. Some articles from the last 10 years have studied low-frequency fluctuations with conventional EEG amplifiers and arrays of polarizable subdural electrodes. One study12 used stainless steel electrodes and found baseline shifts in only some seizures, whereas another group13,14 used platinum electrodes (which have somewhat better low frequency recording properties15) and observed highly localized ictal shifts that were congruent with but more localized than the AC-EEG. The latter study14 also re-
Table 1 Summary of the patient data including the other clinical findings used for lateralization of the seizure focus

<table>
<thead>
<tr>
<th>Patient no./sex/age, y/handedness</th>
<th>Seizure type</th>
<th>Ictal semiology</th>
<th>Neuropsychological deficits</th>
<th>Neuroradiology</th>
<th>Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/M/36/R</td>
<td>SPS (also GTC)</td>
<td>Mostly subclinical</td>
<td>L &gt; R</td>
<td>MRI normal</td>
<td>NO</td>
</tr>
<tr>
<td>2/F/41/R</td>
<td>CPS, B</td>
<td>Loss of speech, chewing</td>
<td>NL</td>
<td>MRI normal</td>
<td>Mild gliosis, no MTS</td>
</tr>
<tr>
<td>3/F/32/R</td>
<td>CPS, B</td>
<td>Unresponsiveness, chewing</td>
<td>NL</td>
<td>MRI normal</td>
<td>NO</td>
</tr>
<tr>
<td>4/F/35/R</td>
<td>CPS</td>
<td>Staring, unresponsiveness, moaning</td>
<td>L &gt; R</td>
<td>MRI focal signal enhancement on R temp</td>
<td>Ganglioglioma in lateral cortex</td>
</tr>
<tr>
<td>5/M/35/R (post-traumatic)</td>
<td>CPS and GTC</td>
<td>Unresponsiveness, chewing, shifting in bed</td>
<td>L &gt; R</td>
<td>MRI cystic encephalomalacia in L temp</td>
<td>Mild gliosis, no MTS</td>
</tr>
<tr>
<td>6/M/21/R</td>
<td>CPS (some B)</td>
<td>Staring, confusion</td>
<td>L &gt; R</td>
<td>MRI normal, FDG-PET L temp hypometabolism</td>
<td>Mild gliosis, no MTS</td>
</tr>
<tr>
<td>7/F/45/R</td>
<td>CPS</td>
<td>Staring, chewing, eye blinking</td>
<td>L &gt; R</td>
<td>MRI L, MTS, interictal SPECT normal, ictal SPECT L temp hyperperfusion</td>
<td>MTS</td>
</tr>
</tbody>
</table>

SPS = simple partial seizure; GTC = generalized tonic-clonic; NO = not operated; CPS = complex partial seizure; B = bilateral spread; NL = not lateralizing; MTS = mesial temporal sclerosis; temp = temporal.

We recently developed DC-EEG techniques capable of stable, long-term bedside recordings from human scalp (see also reference 17). This is a relatively easy and inexpensive method, which makes it an ideal candidate as a clinical tool. In this study we examined a series of patients with temporal lobe epilepsy (TLE) undergoing presurgical evaluation. The main objective of this study was to find out whether ictal DC shifts are measurable from human scalp, and, if so, whether these DC shifts could be used to determine the side of seizure origin in TLE.

**Methods.** Seven patients (table 1) with TLE were studied. DC-EEG was performed at bedside in the epilepsy monitoring unit, simultaneously with long-term EEG-videotelemetry monitoring (LTM) for presurgical evaluation. No restrictions of patients daily activities were needed other than those required by the LTM. This study was approved by the Human Subjects Committee of the University of Washington. Informed consent was obtained from all subjects according to the Declaration of Helsinki.

**DC-EEG method.** Scalp DC-EEG was recorded using a custom-designed 16-channel DC-EEG amplifier (bandwidth DC, 160 Hz; high input impedance differential preamplifiers equipped with circuits for automatic electrode offset voltage compensation and testing of electrode-skin contact impedance) and sintered Ag/AgCl electrodes with 12 mm² of active area (type E220N-LP; In Vivo Metric, Ukiah, CA). We used custom-made electrode holders to lift the electrodes 6 mm above the skin, and thereby to form a closed space that was filled with electrode gel (Sigma Gel, Parker Laboratories, NJ). The relatively large volume of the gel together with the airtight contact between the holder and the skin minimized drying of gel, which would cause marked baseline drifts due to changes in electrode potentials. The electrode holders were attached to the skin with collodion, and the skin beneath was sintered with circuits for automatic offset voltage compensation 160 Hz; high input impedance differential preamplifiers equipped with the custom-designed 16-channel DC-EEG amplifier (bandwidth DC, short-circuit skin-generated potentials). After allowing 10 to 15 minutes for stabilization, baseline drift was always unidirectional and less than 500 µV per hour. DC-EEG electrodes were always placed symmetrically and their locations conformed to the international 10:10 system. Most of the electrodes were placed around the temporal lobes, two to three electrodes were in the midline, and in some cases frontal, central, and parietal locations were added. Reference electrode was at vertex. In addition, one or two channels for recording eye movement (disposable Ag/AgCl disk electrodes; Nicolet, WI) were included to confirm that the DC shifts during seizures were not due to electric fields caused by eye movements. EEG signals were sampled at 500 Hz by a 12-bit data acquisition board with an amplitude resolution of 2.4 µV. The software for data recording and analysis was programmed under Labview (National Instruments, Austin, TX).

**Analysis.** Exact timing of electrical seizure onset, electrical generalization of the seizure, and clinical seizure onset (for seizure semiology, see table 1) were determined from the LTM recording by two board-certified experienced electroencephalographers (J.W.M. and M.D.H.). The occurrence and possible temporal difference of DC shifts between left and right side were analyzed by reformulating the derivations to midline references, either to Pz alone or to calculated average of midline electrodes (e.g., AFp2 + Cz + Pz). Average reference was used to mitigate the effect of midline signal on the trace. For all our analyses, DC shifts were defined as a clear baseline deviation with duration of longer than 5 seconds, and in close temporal proximity to ictal electrographic discharge. Both board-certified electroencephalographers (J.W.M. and M.D.H.) independently agreed upon the timing and location of the DC shifts for each seizure.

**Results.** We recorded 35 seizures, all of which had a focal origin. In one patient (no. 7) all the seizures were subclinical (all over 4 seconds, mean duration 20 seconds) and confined to one side only, but he had normal results on MRI scan and did not undergo subsequent surgery. In the other patients the seizures (n = 9) spread bilaterally and they showed clear clinical manifestations. Owing to equivocal laterality of seizure onset, arrays of intracranial subdural electrodes were utilized in four patients. Two (nos. 5 and 6) had intracranial electrodes during the DC-EEG recording, and two (nos. 2 and 4) had intracranial recording done at a later session. Intracranial recording of all these four patients demonstrated that the onset of the seizures took place in the mesial TL (table 2). In addition, one more patient (no. 7) with bilateral seizure onset at scalp recording was considered to have probable
mesial TL origin of seizures, because of her MRI (left mesial temporal sclerosis) and ictal SPECT (left mesial temporal hyperperfusion) findings (see table 1). As to potential problems caused by artifacts, gross movements after generalization of the seizures did not obscure the onset of DC shifts in the beginning of seizures. Some problems were, however, caused by chewing, persistent ictal gaze shifts (not by blinking), and possible gross movements before seizure onset. Although we were able to distinguish DC shifts during every seizure, we recognize the possibility that DC shifts may be missed occasionally because of these types of artifacts.

General observations of DC shifts during seizures. All 35 seizures were associated with DC shifts of considerable amplitude (30 to 150 μV) in temporal derivations relative to midline reference. Polarity of the shift in the temporal derivations was either positive or negative (relative to vertex) in the beginning of the seizure, whereas it was always negative during the later, bilateral seizure activity. The overall pattern (polarity and form) of DC shift was consistent for each seizure of a given patient. DC shift was consistently observed first on the side of seizure onset, and it commenced within few seconds after the beginning of the high voltage spiking. Every unilaterally persisting seizure was associated with a clear unilateral DC shift (figure 1), which lasted until the end of electrographic discharge. During seizures with bilateral spread the DC shifts were always confined to the area with high voltage fast spiking discharge (figure 2); i.e., DC shift became bilateral only after the spread of seizure activity. In seizures with a very rapid (within seconds) bilateral spread, lateralization was possible by an initially more pronounced DC shift on the side of onset.

Comparison of DC-EEG and invasive recordings: Mesial vs lateral temporal lobe. Four patients underwent intracranial recording, which enabled comparing of DC shifts during seizure activity in mesial temporal regions (usually recorded from electrodes over the parahippocampal gyrus) vs lateral temporal regions (electrodes over neocortical regions). Activity from mesial TL is typically not seen at scalp with conventional EEG techniques, or it may even be detected bilaterally. Interestingly, we observed an initial positive DC shift in all seizures (n = 7) with mesial TL onset (figures 2 and 3). The DC shift in these cases was seen in the temporal and mastoid derivations. When the seizures spread to the lateral temporal subdural electrodes, negative DC shifts developed (see figures 2 and 3). Likewise, in some seizures the highest amplitude of spiking fluctuated between mesial and lateral TL derivations, and was also reflected in the polarity of the

Table 2 Summary of the electrophysiologic findings from conventional EEG (intracranial and scalp) and DC-EEG recordings

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>scalp EEG</th>
<th>Intracranial EEG</th>
<th>DC-EEG recording</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ictal onset</td>
<td>Duration, h</td>
<td>No. sz</td>
</tr>
<tr>
<td>1</td>
<td>L anterior temporal</td>
<td>L temporal</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>L anterior temporal</td>
<td>L temporal</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>L and R anterior temporal</td>
<td>R temporal</td>
<td>21.5</td>
</tr>
<tr>
<td>4</td>
<td>L and R anterior temporal</td>
<td>R temporal</td>
<td>16</td>
</tr>
<tr>
<td>5</td>
<td>L and R anterior temporal</td>
<td>L frontotemporal</td>
<td>11</td>
</tr>
<tr>
<td>6</td>
<td>L and R anterior temporal</td>
<td>L temporal</td>
<td>24</td>
</tr>
<tr>
<td>7</td>
<td>L anterior temporal</td>
<td>Bilateral temporal</td>
<td>1.5</td>
</tr>
</tbody>
</table>

All grids were placed over fronto-temporo-parietal convexity.
DC = direct current; SZ = seizures; OF = orbitofrontal.
The potential shifts during focal seizures in humans.\textsuperscript{10,12-14} The origin of TL seizures.\textsuperscript{10} Additional clinically useful information on the side of lateralization of the DC shifts agrees with the prospect that noninvasive DC-EEG could reduce the need of invasive monitoring. In our study, all DC shifts were evaluated retrospectively when the time of seizure onset was known. Validation of the clinical accuracy of our findings will require a prospective, blind analysis of DC shifts without knowledge of exact electrical seizure onset times. Also, all our patients had TLE, and hence further studies are needed to test the value of DC-EEG in seizure localization in patients whose seizures originate in other cortical (e.g., frontal or parietal) areas.

Discussion. In current clinical practice lateralization of seizures is based on pieces of evidence gathered from multiple diagnostic techniques. Often an intracranial recording is required because of equivocal information obtained by other methods. Any additional noninvasive method of lateralization, such as the DC-EEG technique used in the current study, might reduce the need of invasive monitoring. In our study, lateralization of the DC shifts agrees with that obtained from conventional presurgical evaluation. Hence this approach holds promise to provide additional clinically useful information on the side of origin of TL seizures.

There have been a number of prior studies of slow potential shifts during focal seizures in humans.\textsuperscript{10,12-14} However, except for the early intraoperative recordings,\textsuperscript{10} true DC recording techniques were not used, unlike the current study. Recordings of focal seizures using arrays of polarizable subdural electrodes demonstrated localized shifts in some patients.\textsuperscript{12-14} Recordings with scalp Ag/AgCl electrodes have been reported in three patients with extratemporal lobe seizures with conventional amplifiers with a long time constant,\textsuperscript{14} revealing baseline fluctuation with some seizures. Because of the technical differences and because these patients did not have TL seizures, the results cannot be meaningfully compared to the current study.

Previous animal studies\textsuperscript{6-8} and some invasive recordings on humans\textsuperscript{9,10} have established the idea that seizure activity is always associated with a negative DC shift at the cortical surface. The current study demonstrates DC shifts at human scalp. We also show that the distribution of ictal DC shifts is limited to seizure activity; i.e., the DC shifts are unilateral until the electrographic discharge spreads bilaterally. Compared to conventional EEG, DC-EEG may thus give more information about the laterality of ictal discharge. It is notable that in the current study all DC shifts were evaluated retrospectively when the time of seizure onset was known. Validation of the clinical accuracy of our findings will require a prospective, blind analysis of DC shifts without knowledge of exact electrical seizure onset times. Also, all our patients had TLE, and hence further studies are needed to test the value of DC-EEG in seizure localization in patients whose seizures originate in other cortical (e.g., frontal or parietal) areas.

We did not observe DC shifts earlier than the ictal electrographic discharges, which is in line with the idea that ictal DC shifts reflect the ictal recruitment of cortical surface.\textsuperscript{8,10} and hence arise only after ictal discharges have begun. Many currently used functional imaging techniques (e.g., SPECT and PET) are based on the same rationale; i.e., detecting the volume of brain tissue primarily involved in seizure activity. Although lacking the spatial information of these imaging techniques, DC-EEG is able to show the changes in cortical seizure recruitment with a high temporal resolution, which is critical in cases with rapid bilateral spread.

Intracranial recordings are often required primarily because of the mesial TL origin of seizure activity, which may spread bilaterally before appearing in scalp electrodes.\textsuperscript{22-25} In this context it is intriguing that the ictal DC shifts in all five patients with mesial TL origin seizures suggested a side of seizure origin that was consistent with other clinical information (see tables 1 and 2). This observation raises the prospect that noninvasive DC-EEG could reduce the need for intracranial EEG in such cases. One may wonder why, in these cases, we saw initial positive DC shifts (relative to midline), which were followed by clear negative DC shifts only after the seizure activity spread to lateral TL or other areas in the neocortex (see figure 3). Previous studies have demonstrated that (epicortically) negative DC shifts are consistently seen with invasive foramen ovale electrodes in patients,\textsuperscript{9} whereas DC shifts with either positive or negative polarity may be observed.
using intracranial electrodes over lateral side of the TL during seizures with mesial TL or hippocampal origin in monkeys.\textsuperscript{6} Although the mechanisms that generate the characteristic shape of the DC responses seen in the current work during seizure onset remain to be worked out in future studies, the determination of the side of seizure origin with DC shifts can be based on observation of unilaterally pronounced DC shifts irrespective of their polarity.

Mechanisms of generation of slow EEG responses differ markedly from those giving rise to high frequency oscillations.\textsuperscript{11} Substantial evidence suggests that an important mechanism of slow EEG signals may be related to spatial potassium buffering by glial cells,\textsuperscript{26-30} especially during the slow unipolar DC shifts associated with seizure activity. Further, later in vitro studies with epileptic human hippocampal tissue have demonstrated that even glialic brain tissue (with Ammon horn sclerosis) is able to produce DC shifts (i.e., slow field potentials), which are to a large extent mediated by potassium ions.\textsuperscript{28} It is notable, however, that several studies have also provided evidence supporting the presence of intracranial, non-neural (i.e., other than neurons or glia) generation of slow DC shifts.\textsuperscript{31-34} The slowest EEG potentials may thus have marked non-neuronal components, especially epithelial potentials modified by pH or blood flow (the “blood brain barrier potential”).\textsuperscript{32-34} Although the question of the generator mechanisms is of considerable interest, the clinical utility of DC-EEG must be based on the empirical observations of the close correlation between DC shifts and seizure localization, such as was shown in the current study.

In pioneering work done in the 1960s, scalp DC-EEG recordings of generalized spike and wave discharges were consistently shown to be linked with negative DC shifts.\textsuperscript{35-37} These early DC-EEG recordings were performed with amplifiers that required frequent rebalancing to correct for baseline drift (Chatrian, personal communication). This technical shortcoming precluded the introduction of this technique into clinical practice, which explains why scalp recordings of focal seizures have not been previously performed. In our experience, DC-EEG is a reliable method that is readily applicable to bedside recordings once basic technical requirements are met. In short, one must use a genuine DC-EEG amplifier with sufficiently high input impedance and sufficient stability as well as a wide enough dynamic range combined with automatic offset compensation to avoid amplifier saturation due to possible artifactual changes or drift of the baseline. The electrodes must be reversible, because all polarizable electrode materials (such as gold, tin, platinum, or steel) are coupled in a mainly capacitative manner to their external environment, which leads to high-pass filtering at the electrode-gel interface.\textsuperscript{38} Among the currently available electrodes only those based on Ag/AgCl are adequate, and the sintered contact elements used in our study proved to be both maintenance-free and very stable. Our experience

![Figure 3. Comparison of direct current (DC)-EEG recordings (A–C) to an intracranial recording with subdural strip electrodes (D) during a complex partial seizure with left mesial temporal lobe (TL) onset (Patient 6). A through C are all in the same time scale (amplitude bar 200 \(\mu\)V for A and C, 30 \(\mu\)V for B). Traces in A show the seizure with DC-EEG recording. Traces in B show the slow component (subtraction of a high pass [as in C] signal from the DC-EEG) of the same EEG signal. Traces in C demonstrate the same EEG with conventional settings (i.e., high pass filtered at 0.5 Hz). Traces in the bottom (D) are selected channels from an intracranial recording, which has been stretched slightly to better illustrate the changes in fast activity. Seizure onset (mesial) and spread (to lateral) in the intracranial EEG are shown with respective arrows, and seizure spread to right mesial TL is shown with an asterisk. Note the prominent positive DC shift in the left temporal derivations after mesial TL activation, and the negative DC shift later after neocortical spread. All derivations in DC-EEG are referred to a linked \(C_z + P_z\), whereas traces in the intracranial recording are referred to a scalp electrode at vertex. Lateral eye movement artifacts before the seizure (marked with \(\$\) in trace A) have been removed offline in trace B before A – C subtraction in order to improve the visual clarity of the later occurring DC shift. RST = right mesial TL; RLT = right lateral temporal lobe; LST = left mesial TL; LLT = left lateral temporal lobe.](https://example.com/figure3)
with recordings lasting up to 24 hours indicates that it is possible to extend the duration to even several days as needed. An additional issue to be considered is the electrode-skin contact, where drying of electrode gel must be prevented, and scratching of skin must be performed to short-circuit skin potentials, such as galvanic skin responses (sweat artifacts). In practical terms, implementation of DC-EEG recording into routine clinical practice would be remarkably easy. DC-EEG amplifiers are not significantly more expensive than the current clinical amplifiers; suitable electrode material (Ag/AgCl) is sterilizable and has been in clinical use for decades; the specific holders used in our study can be integrated with the electrodes to make them easier to use; attachment of the electrodes on skin is practically as quick as with the conventional electrode types; and finally, sufficient scratching of the skin is so painless that we have successfully done that even with sleeping neonates.

The limitations of the DC-EEG technique are mostly similar to those of conventional EEG. Proper interpretation requires use of appropriate montages and familiarity with various sources of artifacts. When comparing DC-EEG and conventional EEG, the visual appearance of slow artifacts (e.g., eye and tongue movements; see online figure e1 at www.neurology.org) is somewhat different due to the lack of high-pass filtering in the former, and hence some experience is needed for their proper identification. Distinguishing between artifacts and seizure-related DC shifts, however, is easy because artifacts have their characteristic waveforms with a typically faster time course (only up to a few seconds) and usually a global distribution. Unlike in conventional EEG, skin potentials do not cause problems in DC-EEG recordings of the present kind because they have been excluded by puncturing the skin (see Methods). Movement artifacts just before and during seizure onset might occasionally make evaluation of DC shifts impossible. However, most of the movement artifacts can be avoided by firm attachment of the electrodes to the skin (e.g., with collodion), and by using appropriate placing of the reference electrode (e.g., vertex).

Our study shows that DC-EEG may be recorded bedside with easily achievable modifications of routine EEG techniques. Ictal DC shifts are consistently seen in scalp recordings, and the DC shifts give information that agrees with seizure localization as defined by the other established criteria. Our observation of DC shifts with mesial TL seizures also suggests that scalp-recorded DC-EEG might provide an invaluable tool in noninvasive determination of the side of seizure origin in these patients. Although in our study the number of patients was limited, and there is as yet no post-surgical follow-up to correlate the localizations of DC shift with a postoperative seizure-free outcome, our results are robust and consistent, and suggest a clinically useful role for DC-EEG. Further prospective studies are warranted, particularly in the subgroup of patients with TL seizures where ictal scalp EEG gives unclear lateralization.

References
Topiramate and word-finding difficulties in patients with epilepsy

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Abstract—Objective: To evaluate the prevalence of word-finding difficulties as a treatment-emergent adverse event in patients with epilepsy taking topiramate and to identify a clinical phenotype at risk. Methods: The authors investigated the relationship of word-finding difficulties to topiramate titration schedule, seizure frequency and pattern, and EEG and neuroradiologic findings in 431 consecutively and prospectively collected patients taking topiramate. Results: Thirty-one patients (7.2%) developed word-finding difficulties. Presence of simple partial seizures (OR = 6.7; p = 0.007) and a left temporal EEG epileptic focus (OR = 5.2; p = 0.021) were significantly associated with word-finding difficulties. Conclusions: The presence of word-finding difficulties seems to be a titration schedule independent phenomenon that occurs in a subgroup of patients with a specific biologic vulnerability.

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Topiramate (TPM) has reliably been shown to improve seizure control in children and adults with refractory partial epilepsy, and is also effective in the treatment of generalized tonic-clonic seizures.1,2 Generally, TPM has demonstrated a favorable adverse effect profile but adverse cognitive symptoms are also reported.3 Word-finding difficulties (WFD) occur in a minority of patients and are among the most intriguing treatment-emergent events. It remains unclear which patients may be susceptible to WFD and whether it is a dose-dependent phenomenon, linked to starting dose and titration time of the drug, or related to the patient’s epilepsy. We evaluated the prevalence of WFD as a treatment-emergent side event of TPM in patients with epilepsy; assessed the relationship with drug dose schedule, seizure frequency and pattern, and EEG and neuroradiologic findings; and identified a clinical phenotype at risk.

Methods. Study design and selection of subjects. TPM was registered in the United Kingdom in October 1995. Between October 1995 and December 2000, over 400 patients with epilepsy have been treated with TPM from the National Hospital for Neurology and Neurosurgery (Chalfont Center for Epilepsy and Queen Square sites). The data chosen represent the first consecutive 431, prospectively collected, patients, who carry through a period when prescribing habits for the drug were changed, and lower starting doses were given with slower titration schedule. Between 1995 and 1998, the starting dose was 50 mg a day with an escalation regimen of 50 mg every 2 weeks to maximum doses; from the second half of 1998, practice changed and the starting dose and increments were 25 mg. WFD (e.g., difficulty retrieving words and experiencing tip of the tongue phenomena or using wrong words) were identified by spontaneous patient reports and confirmed by clinical evaluation. A subgroup of patients underwent formal neuropsychological tests as a part of the routine neuropsychological assessment of our center and to explore the impact of TPM on cognitive function in a previous study.4 The following items were investigated: age when TPM was started; sex; handedness; epilepsy and seizure diagnosis (according to International League Against Epilepsy classification);5 age at onset and duration of epilepsy; family history of epilepsy and personal history of febrile convulsions; neuroradiologic features; localization and laterality of EEG epileptic abnormalities; seizure frequency before and after TPM therapy (classified as 1 to 10, 11 to 20, or >20 seizures/month); the antiepileptic regimen when TPM was started (classified as monotherapy, dual therapy, or polytherapy); antiepileptic drugs (AED) prescribed; type of associ-
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"Very slow EEG responses lateralize …"

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ONLINE DATA (Figure) for MS# 200201047

Online-Figure legend

Fig. (E)F-1 Chewing artefact in DC-EEG recording with comparison to high pass filtered (conventional EEG) waveform of the same trace. This trace is recorded during eating when the glossokinetic potentials are much stronger than during smacking associated with epileptic seizure. Many salient features make it easy to distinguish baseline fluctuations associated with chewing from the DC shifts caused by epileptic seizure (compare to Figs 1-3). Firstly, chewing responses in the temporal derivations are always symmetrical, ie. each bite causes similar glossokinetic potential in both temporal leads, and the associated baseline change is symmetrical. Secondly, looking with higher temporal resolution (3 sec epoch in the lower traces) reveals patterns that can not be accounted for by epileptic activity. Lateralization of seizure origin is based on the asymmetric of ictal DC shifts (as was the case in the present study). Hence chewing does not cause false lateralization, but, among other sources of EEG artifacts, it may occassionally make ictal recordings difficult to interpret.