

What You See Is Not What You Get

Believing Patient-Reported Seizure Counts

THE PHILOSOPHER FRIEDRICH WAISMANN motivated the existence of his subject as a human intellectual endeavor arising from unexpected bewilderment, akin to boarding a train, spending a few hours traveling in a single direction, and suddenly arriving at the station of original departure. “We all have our moments when something quite ordinary strikes us as queer . . . facts . . . stare at us with a puzzling expression, and we begin to wonder whether they can possibly be the things we have known all our lives. . . .”¹

In their article in this issue of the *Archives*, Hoppe et al² perform such a rug-pulling maneuver from under the feet of any doctor who has ever staffed an epilepsy clinic, inquired about the patient’s seizure frequency in the usual manner, made appropriate changes to prescription anticonvulsants, patted the patient on the back, arranged a review appointment, and sat back to savor a job well done. The authors’ data starkly prove that, on average, patients report fewer than half of all of their seizures. Further, exhorting patients to keep an accurate tally with seizure diaries and reminders is fruitless. The implications

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for an individual patient are disturbing: the “seizure-free” individual may not be so; the medically controlled patient may in fact be intractable; the Engel class II surgical outcome may actually be Engel class III or worse. Equally unsettling are the authors’ observations extrapolated to patient populations. For instance, how believable are comparative data from clinical drug trials that report 40% fewer seizures with drug X than with placebo?

Hoppe and colleagues studied 582 seizures of partial onset in 91 patients undergoing continuous inpatient video-electroencephalographic (VEEG) monitoring. Monitoring with VEEG is the accepted objective gold standard for both seizure characterization and the syndromic classification of epilepsy.^{3,4} Its disadvantages are high cost and labor intensiveness. However, as a technique for the diagnosis, classification, and management of epilepsy, it is difficult to do better. Monitoring with VEEG is mandatory for the evaluation of potential surgical candidates, including those who formed the authors’ study cohort. All of the patients were asked to document their seizures. Comparison was made of patient-documented seizures with those objectively found by analysis of VEEG monitoring data. The results were

startling. Fifty-five percent (323 of 582) of all of the seizures went unreported. Eighty-six percent of seizures occurring out of sleep were undocumented; the corresponding figure for seizures arising in wakefulness was 32%. Seizure type significantly influenced patient reporting: simple partial seizures were reported 74% of the time; complex partial seizures, 27%. There was a tendency for seizures arising from the language-dominant hemisphere to be reported less often than seizures from the opposite side. In an ingenious design, the authors randomized their patients to either receive a daily reminder to document their seizures or not; all of the patients were told this once, at the beginning of the evaluation. The results were contrary to our expectation—there was no significant difference in seizure reporting between the 2 groups. The authors concluded the following: (1) underreporting of seizures in patients with epilepsy is significant and common, and (2) it cannot be fixed by physician encouragement to do otherwise.

The message was perhaps implicit in other literature. In an outpatient setting without VEEG monitoring, a systematic approach was sufficiently revealing to Heo et al⁵: of their 134 subjects, only 67% were always aware of their seizures when compared with observers’ accounts. In the ambulatory EEG study by Tatum et al,⁶ 38.8% of records with seizures had at least a few seizures not signaled by button presses. Two previous VEEG monitoring studies^{7,8} hinted that seizures were unreported because of ictal amnesia. Errors in counting were thus not due to poor “bookkeeping”; patients were unaware of seizures even when questioned immediately after individual events. The contributions by Hoppe and colleagues are in the size of their data set (easily the largest VEEG monitoring study to date addressing this question), their clever experimental design, and their robust conclusions, intelligible to even the nonspecialist.

Does all of this demolish the epileptologist’s main interrogative tool, the question, “How many seizures have you had over these past few weeks?” No, we maintain. The authors’ data themselves suggest how the question may be resurrected. They state that 44% of all of the seizures arose in sleep, 86% of which went unreported. We thus compute that $44\% \times 86\% = 38\%$ of all of the seizures were unreported nocturnal ones and $55\% - 38\% = 17\%$ of all of the seizures were daytime unreported ones. The latter, and more respectable, figure probably constitutes the dropout fraction of seizures that patients can reasonably be expected to report. One resolution, therefore, is to regard the frequency of nocturnal seizures as an unknown and assess patients suspected of

any nocturnal seizures via the objectivity of ambulatory EEG or VEEG monitoring. For daytime seizures, the rate of underreporting is just less than 1 in 3; acknowledge and factor this into clinical decision making, particularly in patients with complex partial seizures. Another observation by Hoppe and colleagues can be valuably turned into a "practice parameter": their patients only activated the push-button alarm in 51 of 582 seizures (9%). If this implies that only an equivalent number of seizures had an identifiable aura, a reasonable though not infallible assumption,⁹ then most seizures (approximately 90%) were not prefaced by auras. Recognizing that patient memory of a seizure is usually that of the aura, we suggest that if patients do not report preictal auras, their physicians should not believe their reported seizure frequency. Conversely, do patients with auras report their seizures more consistently? This is a question not settled in the work by Hoppe and colleagues but clearly worthy of further study.

In summary, Hoppe and colleagues convey important lessons regarding the objectivity of seizure reporting by patients. The implications of this valuable work for large-scale clinical trials, population-based questionnaires, and other epidemiologic studies are immediate. For the individual practitioner, the main lesson is acknowledging the pitfalls of routine clinical questioning of patients with seizures, especially those with complex partial seizures. However, the lack of accuracy of patient self-reporting can be ameliorated, we observe from the authors' own data, by disambiguating nocturnal and daytime seizures on the one hand and seizures with and without aura on the other. Finally, what about patients with generalized epilepsies, patients unable to self-report seizures for other reasons, children, etc? Finding out will be interesting and important.

On a different point, we can only advocate the wider use of VEEG monitoring in the clinical practice of treating epilepsy. An alternative to VEEG monitoring is the development of better ambulatory technology; current methods of prolonged outpatient multichannel EEG recording are difficult to perform and to interpret for a host

of reasons. We suggest that future developments in this area be directed to robustly answering (whether through EEG, electromyography, or autonomic function monitoring) just the single question, how many seizures?

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