

Ambulatory Electroencephalograms in Neuropsychiatric Practice: Opening Pandora's Jar

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Abstract

Since the advent of imaging studies such as magnetic resonance imaging (MRI), the role of electroencephalograms (EEGs) has diminished. Simultaneously, computerized scanning and miniaturization of the EEG and its components have allowed us to obtain lengthier recordings in an ambulatory setting. We report on 261 ambulatory electroencephalograms performed consecutively in the two year period of 2011 and 2012 in a busy neurology and neuropsychiatry practice with predominantly geriatric patient population. 23% of these patients had abnormal AEEGs demonstrating clear-cut epileptogenic discharges. The role of these findings in clinical practice, especially in geriatric and psychiatric populations is discussed.

Keywords

Ambulatory Electroencephalogram, Geriatric, Psychiatric

1. Introduction

The dramatic and sudden change in personalities and thrashing associated with fits in an epileptic attack led to the obvious conclusion by Babylonian and Indian civilizations, and these attacks were supernatural in origin. They also believed that the epileptics were souls bridging the gap between human being and deity, either of

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good or evil nature. Hippocrates was the one to suggest seizures as a disease of the brain.

Medieval physicians were aware of more subtle presentations of epileptic seizures. Abulquasim, a physician to the Caliph at Cordova described hallucinatory phenomenon as a symptom of a brain seizure. He described a patient who saw a black woman with leather garment before falling down [1]. Lennox reported a case by a fifteenth century physician Antonicus Guainerius where a choreic youth in his paroxysms saw wonderful things [1]. Hughlings Jackson wrote that it is not very uncommon for epileptics to have vague and exceedingly elaborate mental states at the onset of epileptic seizures. He called these elaborate mental states “intellectual auras” [2] [3]. Wilder Penfield and Phanor Perot in their seminal work clearly demonstrated that electrical stimulation of the brain produced very complex “experiential hallucinations” [1].

In the 20th century, we were able to correlate distinct clinical manifestations of seizures with EEG findings. EEGs also opened the doors to the diagnosis of less spectacular syndromes of petit mal seizures. Video EEG recordings from comprehensive epilepsy centers are replete with instances of bizarre behavior, which previously would have been considered as psychiatric in origin, but are really seizures originating in the frontal lobes of the brain. Recently, once again, the recognition of nonconvulsive status epilepticus (NCSE) has forced us to accept that the ictal manifestations are not always as clear-cut as we previously thought. In one study, emergency department patients with persistent, unexplained, altered consciousness were referred for EEGs. In those patients, who had an emergency EEG, 37 percent had NCSE [4]. That article was published in 1994 and it has taken non-epileptologists almost 20 years to recognize NCSE as a clinically significant entity.

We are now able to record EEGs for a considerable length of time in an outpatient setting, resulting in the availability of a large amount of data. Our data will show that longer EEG recordings significantly increase the likelihood of detecting epileptogenic abnormalities in neuropsychiatric patients who had episodic intrusive neuropsychiatric dysfunctions (EINDS). Our study opens Pandora’s jar, and it is a challenge to correlate our EEG findings with clinical symptoms.

2. Methods

In an outpatient setting, careful neuropsychiatric histories were taken, and an added emphasis was placed on asking questions geared to elicit information from patients, caregivers, and family members about EIND symptoms. The questions asked were designed to gather information about unexpected and intrusive symptoms the patient experienced, which occurred and departed suddenly without precipitating environmental stimuli, and met the criteria of being atypical or unusual. The symptoms involved the following neurocognitive domains: 1) Awareness; 2) Perception; 3) Affective/Mood states; 4) Psychosis; 5) Illusions, or hallucinations; 6) Motor symptoms; 7) Speech symptoms; 8) Any other unusual symptoms. These events were fairly stereotypic and recurrent. While some patients had easy to diagnose epileptic symptoms such as motor manifestations, and olfactory hallucinations, most patients’ symptoms were elicited only after direct questioning. Each cognitive domain described above was thoroughly explored for EINDS. These EINDS lasted mostly for seconds to minutes but at times patients were symptomatic for hours.

30 minute EEGs were performed on 613 patients. EEGs were performed using Cadwell equipment, and were recorded using international 10:20 system of electrode placement. Some of the diagnoses in these patients include encephalopathy, TIA like symptoms, stroke, various epilepsies, dementia, memory problems, altered mental status, syncope, atypical headache, atypical mood disorder, atypical psychosis, confusional episodes, musical ear syndrome, peduncular hallucinosis of L’Hermitte, hydrocephalus, concussion, and traumatic brain injury.

Out of these 613 patients, 265 patients had EINDS. On 30 minutes EEGs four patients had temporal Interictal Epileptogenic Abnormalities (IEAs), and one patient had a clinical seizure. The remaining 261 patients underwent 16 channels, 72 hours ambulatory electroencephalograms (AEEGs) utilizing a Cadwell EEG recorder with a 10:20 system of electrode placement. Electroencephalograms were read using the PERSYST REVEAL, and MAGIC MARKER computerized spike detection system followed by a single neurologist’s confirmation of or rejection of detections by the REVEAL, and/or MAGIC MARKER system. The epileptogenic abnormalities were classified as:

1. Interictal Epileptogenic Abnormality (IEA)
2. Clinical Seizure
3. Electrographic Seizure

IEA was defined using strict “Gloor Criteria” [5]

1. Epileptiform discharges (spikes, sharp waves, and spike wave complexes) are unarguably discrete events, not just accentuation of part of an ongoing sequence of waves.
2. Most epilepticform discharges have a more complex morphology than background rhythms.
3. The epilepticform events appear asymmetric in contour.
4. Most spikes and sharp waves are followed by a slow wave.
5. They have a physiological potential field involving many electrodes.

3. Results

Out of 261 patients, 60 (23%) had clear-cut epileptogenic abnormalities with most IEAs emanating from temporal head regions. Fourteen patients had extratemporal or generalized IEAs. None had an electrographic or clinical seizure. This is in contrast to asymptomatic adults, without a history of migraine or a family history of epilepsy, where only 0.7% IEAs were found during overnight AEEGs, however the duration of recordings in that study was only for twenty-four hours [6].

The following list summarizes IED EEG findings by cerebral locations and their EIND correlates

3.1. Left Temporal Head Region (Electrodes T-3, T-5)

- Non-responsive to verbal commands
- Loss of consciousness
- Generalized jerking
- Visual illusions
- Jerking of right upper extremity
- Amnesia for purposeful behavior
- Depersonalization
- Confusional episodes
- Aimless wandering
- Lip smacking
- Loss of balance
- Olfactory hallucinations
- Gustatory hallucinations
- Somatic delusions
- Unprovoked episodic rage
- Left upper and lower extremity jerking
- Loss of consciousness
- Tonic clonic seizure
- Jamais vu
- unusual head sensations
- “not feeling quite right”
- Ipsiversive eye deviation
- Right upper extremity jerking
- Visual hallucinations
- Dazed facial expression
- Episodes of collapse
- Tunnel vision

3.2. Right Temporal Head Region (Electrodes T-3, T-5)

- Depersonalization
- Prolonged sleep
- Lengthy verbal delays responding to questions
- Vacant stare
- Extreme emotional lability
- Somatic delusions
- Loss of time

- Vertigo
- Cognitive “fog”
- Disorientation
- Visual illusions
- Sensation of suffocation
- Déjà vu
- Visual hallucinations
- High pitched frightening musical sounds
- Sudden loss and recovery of speech
- Auditory hallucinations
- Unusual colors in the visual field
- Olfactory hallucinations
- Sudden speech arrest
- Mood swings from irritability to anger to laughing to giddiness
- Eyes rolling up
- Confusion
- Dizziness
- Emotional lability
- Disorientation
- Jamaisvu
- Olfactory hallucinations
- Prolonged loss of consciousness followed by fatigue and exhaustion
- Loss of time
- Amnesia for purposeful behavior

3.3. Bitemporal Head Region (Electrodes T-3, T-5, T-4, T-6)

- Eye deviation
- Right upper extremity jerking
- Episodic explosive behavior with amnesia
- Loss of consciousness
- Jerking movements of upper extremities
- Feeling hot
- Eyes rolling-up

3.4. Right Frontal Head Region (Electrodes F-4, F-8)

- Confusion
- Execution of complex irrelevant activities
- Déjà vu
- Olfactory hallucinations
- Vacant stare
- Generalized tonic-clonic seizure
- Speech arrest
- Jamaisvu
- Vacant stare

3.5. Right Frontotemporal Head Region (Electrodes F-8, T-4)

- Episodic confusion
- Non-responsive to verbal commands
- Loss of awareness of surroundings

3.6. Bifrontal Head Region (Electrodes F-4, F-8, F-3, F-7)

- Generalized tonic clonic seizures without aura

- Brief staring episodes

3.7. Right Central Head Region (Electrode C-4)

- Inappropriate behavior, e.g. disrobing in public
- Generalized tonic clonic seizure

3.8. Bicentral Head Region (Electrodes C-3, C-4)

- Loss of consciousness

3.9. Left Parietal Head Region (Electrode P-3)

- Reduction in field of vision and loss of color vision
- Visual illusions
- Visual hallucinations
- Feelings of electric current throughout the body
- Slurred speech
- Confusion
- Vertigo
- Expressive aphasia

3.10. Right Parietal Head Region (Electrode P-4)

- Loss of consciousness

3.11. Generalized

- Generalized tonic-clonic seizure
- Absence seizures

4. Discussion

The strength of our study is in the large number of cohorts, EEGs done with the same equipment, EEGs performed by a single technologist, and EEGs read by a single neurologist, using well accepted criteria for IEAs. The obvious weakness of our study is that it is a retrospective study, and a uniform questionnaire was not used to elicit symptoms of EINDS. Our study shows that Ambulatory EEGs increase the likelihood of detecting epileptogenic IEDs in neuropsychiatric, predominantly geriatric, patients. There was a considerable overlap between EINDS and cerebral locations of IEAs. It was difficult to predict location of IEAs based on EIND symptoms. While these are the only findings our study suggests, our data may have relevant clinical utility. It would be worthwhile to review possible implications our findings in some common clinical settings.

4.1. Implications in NCSE

NCSE has become a more recognized clinical entity which has caused us to rethink our understanding of the etiology of clinical seizures. It stands to reason that NCSE may not occur *de novo*, but at least some patients, if not in all of them, would have presented as nonconvulsive seizures (NCS) prior the development of NCSE. The presentation, described in the literature of NCSE, includes impairment of cognition, speech arrest, subtle twitches of the muscles, head or eye deviation, dilated pupil, increased blood pressure or arrhythmias, automatism, bizarre behaviors that include hallucinations and wandering. In some patients, a state of fear or ecstasy, lethargy, crying, perseveration, nausea/vomiting, laughter, anorexia, mutism, amnesia, catatonia and coma may also occur [4] [7]-[9]. The presentation in NCSE is so variable and wide ranging in its reach of cognitive domains that just a few years ago epileptologists would not have considered these presentations as “epileptic seizures”. The subtle EINDS found in our study may represent precursor of an eventual development of NCSE in some patients.

4.2. Implications in Psychiatric, and Elderly Patients

The presence of abnormal EEGs and widespread use of anticonvulsants in psychiatric practice also leads one to

think that epileptic phenomena may be at the root of some “purely psychiatric phenomena”. It is interesting to see the evolution of the specialties of psychiatry and neurology in the USA. Insular and distinct practices of psychiatry, and neurology, at least in the USA, are based on each specialty’s approach to patients. It is intriguing to note that this approach follows duality of mind and body by Rene Descartes, despite the fact that Cartesian duality views have long been discarded by later philosophers such, Spinoza, Leibniz and others. In modern medicine, specialties of psychiatry and neurology have gone on their own paths with an unhelpful attitude of “thou shall not speak to one another”. In this setting, it is difficult to reconcile the research that spans across these two specialties. Psychiatrists have focused on phenomenology and syndromic classifications of mental symptoms. This has resulted in development of a very complex diagnostic system, the latest being the Diagnostic and Statistical Manual-5 (DSM-5). They rely on getting a cluster of patients together in a specific diagnostic classification based on the phenomenology of mental symptoms. Any atypical presentation is called “other specified, or unspecified”, but a careful clinical history of EINDS is not generally obtained as part of the routine psychiatric interview. Psychiatrists rely very little on testing such as EEGs or MRIs. Nonetheless, a vast number of psychiatric patients have abnormal EEGs. Shelley and Trimble have reviewed these data demonstrating a recurring theme of significant EEG abnormalities in psychiatric populations [10]. One of the major problems in these studies is that there are no uniform criteria for IEAs, and many studies include, normal variants, such as 14 - 6 psychomotor variants, small sharp spikes, phantom spikes, wicket rhythms, mid temporal discharges (RMTD), phantom spike waves, as EEG abnormalities [11]. Even when numerous so called abnormalities are excluded from this body of literature, one is left with a significant number of psychiatric patients who have abnormal epileptogenic electroencephalograms.

In older individuals, and patients with dementia there is a five to ten-fold increase risk of seizures compared to the general population [12]. Many psychiatric conditions, including agitation in patients with dementia are successfully treated with anticonvulsant medications [13] [14]. This raises the possibility that epileptogenic activity may be a contributing factor in agitation in elderly patients.

It is important to tease out the semiology and phenomenology of their psychiatric presentation, specifically presence of EINDS. Additional evidence is not scientific, but based on prevailing methods of treating psychiatric patients. Psychiatrists have used anticonvulsants extensively in the treatment of a variety of psychiatric conditions with considerable success [13] [14]. This may suggest that antiepileptic medications may indeed be treating underlying unrecognized seizure disorders. Valproate, carbamazepine and lamotrigine appear to have the strongest evidence based support for use in psychiatric disorders [13].

The mechanism of action of anticonvulsant drugs in epilepsies are believed to be due to their GABAergic properties (e.g. Valproic acid, gabapentin, tiagabine, vigabatrin), action on voltage dependent calcium channels (e.g. gabapentin), inhibition of sodium currents (e.g. carbamazepine, phenytoin), inhibition of voltage dependent sodium channels (e.g. lamotrigine, and oxcarbazepine), targeting of glutaminergic receptors (e.g. felbamate, topiramate) [15].

Additional actions of anticonvulsants implicated in psychiatric conditions include increase in BDNF, increase in B-cell lymphoma-2 (Bcl-2), extracellular regulated kinase (ERK) cascade, inhibition of phospholipase A-2, inhibition of inositol biosynthesis, Akt signaling, and protein kinase C (PKC) inhibition. The inhibition of histone deacetylase may produce an antidepressant-like effect [16]. This complicates matters further and it is possible that these other actions and not the “antiepileptic” actions may be responsible for the effectiveness of anticonvulsants in psychiatric conditions.

4.3. Understanding Epileptogenic EEG Abnormalities and Mechanism of Action of Anticonvulsants

While an extensive discussion of the neurophysiology of epileptogenic abnormalities is beyond the scope of this paper, it is worthwhile, briefly, to review our current understanding of the neurophysiology of interictal spikes. An EEG is the summation of synchronized potential in the apical dendrites from a large ensemble of cortical neurons. An interictal spike is a brief morphologically defined event generated by synchronous discharges of a group of neurons from an epileptic focus [10] [17]. The relationship between interictal spikes and seizures that define acquired epilepsy has been controversial and has been debated for a number of years [18] [19]. Recent studies in rats in which Kainate-induced epilepsy suggests that spike-like wave forms precede the occurrence of spontaneous epileptic seizure [20] [21]. On the other hand, patients without seizures who have waveforms simi-

lar to what we call interictal spikes are rarely looked at to see whether they subsequently develop seizures or not [22]. What is generally ignored is what happens following an interictal spike. These spikes influence distributed cortical neuronal networks and interfere with cognition [23]-[25]. This surround inhibition concept was initially proposed by Prince, *et al.* suggesting that this zone of surround inhibition results in functional impairment perhaps producing psychiatric difficulties [26]. It is also possible to postulate that perhaps not the spike but the surround inhibition that occurs following spike may be responsible for psychiatric symptoms. The question is: are we able to suppress the spikes or should spikes even be suppressed at all? In that case, would the suppression of spikes lead to improved clinical conditions [27]?

In psychiatric and elderly patients, as in NCSE patients, a careful history of EIND could prompt the clinician to perform an EEG/AEEG. Abnormal EEG's or AEEG's could possibly guide psychiatrists to anticonvulsant treatment early on. Additionally, some of the other psychiatric medications that lower the seizure threshold would then be cautiously used. At least some percentage of patients who are "purely psychiatric" patients may have either concurrent neurological evidence of "psychic seizures", or their entire presentation could be as a result of these abnormalities.

4.4. Concluding Remarks

- The obvious weakness of our study is that it is a retrospective analysis, and a formal questionnaire for eliciting EIND was not utilized.
- In neuropsychiatric patients, and especially in the elderly, it is important to ask for EINDS that span the cognitive domains of awareness, perception, affective states, psychosis, illusion, hallucinations, motor and speech symptoms.
- Long recordings, which increase the sample size and reduce false negatives, increase the likelihood of detecting abnormal epileptogenic discharges.
- At least some patients with NCSE, possibly would be preceded by NCS. The patients in our study may reflect those patients. Are these the patients who would eventually go on to have NCSE when additional metabolic perturbations reduce the seizure threshold? Further research is needed in this direction.
- Are our patients, who have EINDS and epileptogenic EEG/AEEG, are the same patients that actually respond to anticonvulsant medications if they have a concurrent psychiatric illness, or is their psychiatric illness a result of ongoing epileptogenic activity and/or surround inhibition? Further studies are suggested in this area.
- Our study is in tandem with the observations of the great Hughlings Jackson, who said: "He who is faithfully analysing many different cases of epilepsy is doing far more than studying epilepsy. The highest centres ('organ of mind'), those concerned in such fits, represents all, literally all, parts of the body sensorially and motorially, in most complex ways, in most intricate combinations, etc. A careful study of many varieties of epileptic fits is one way of analysing this kind of representation by the 'organ of mind'." [2] [3]

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