This is the third in a series of featured controversial articles, on medical, psychological, or related issues. I hope to stimulate discussion, letters, and interaction in Telicom and also possibly on outside forums, such as ISPE-net. I focus on the areas where the mythology may need to be broken and where limitations may not necessarily be recognized. This article has several parts, each interrelated yet independent and some co-authored by Dr. Dietrich Blumer. As with all publications, information such as this must be considered only after consultation with physicians and any medical information recorded here should not substitute for such consultations.

The Paroxysmal Disorders: Insights into the controversy of medical diagnosis and terminologies.

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With Dietrich Blumer MD, DFAPA.

Abstract

Recurrent, episodic conditions in medicine (paroxysmal disorders) have been seriously neglected in many ways. They require more adequate terminology, delineation of diagnostic criteria, appreciations of the conditions in all the different ethicobiopsychofamiliosociocultural contexts, and awareness of the need for management after adequate evaluation. This has led by necessity to the development of various historical measures that can be administered in a standard way—the Inventory of Neppe of Symptoms of Epilepsy and the Temporal Lobe (INSET) and Soft Organic Brain Inventory of Neppe (SOBIN) particularly as well as specialized investigations such as Home Ambulatory Electroencephalography (AEEG).

The new condition of Paroxysmal Neurobehavioral Disorder is presented for the first time in publication. The difficulties of differentiating between atypical epileptic seizures and non-epileptic events are tabulated in detail. The name, Paroxysmal Somatoform Disorder, is revived as far the most appropriate though largely synonymous with the preceding labels of Hysteroepilepsy, Hysteroseizures, Pseudoseizures and Nonepileptic Seizures. A controversial condition, Paroxysmal Startle Disorder, one major manifestation of this Paroxysmal Somatoform Disorder is postulated not only to exist, but argued to demonstrate an important biological mechanism for Paroxysmal Somatoform Disorder. Finally, a new name is suggested, namely Paroxysmal Photosensitive Disorder. The criteria for this condition are broadened as it not only may manifest in frank seizure phenomena, but alternatively in behavioral, cognitive and affective phenomena that may be subtle, or in significant headaches, like migraines. These new categorizations of paroxysmal disorders create a better way of conceiving of these episodic conditions but remain controversial because they involve new ways of seeing old phenomena.

Keywords

Affective, Anticonvulsants, Antipsychotic Medication, Atypical Spells, Behavioral, Carbamazepine, Chindling, Cognitive, Consciousness, Controversial PTLSs (CPTLSs), Controversy, Déjà Vu, Diagnostic Criteria, Disintegrative PTLSs (DPTLSs), Electroencephalogram (EEG), Epilepsy, Epileptic Seizures, Episodic, Episodic Phenomena, Ethicobiopsychofamiliosociocultural, Ethicospirituobiopsychopharamacofamiliosocioculturaloeconimopoliticomilitarality, Evaluation, Faints, Hallucinogen, Headaches, Historical Measures, Home Ambulatory Electroencephalography (AEEG), Hysteroepilepsy, Hysteroseizures, Inventory Of Neppe Of Symptoms Of Epilepsy And The Temporal Lobe (INSET), Irritability, Kindling, Medicine, Mesial Temporal Lobe, Migraines, Neppe Temporal Lobe Questionnaire, Non-Epileptic Seizures (NES), Non-Epileptic Temporal Lobe Dysfunction, Nonresponsive Psychosis, Not Necessarily Disintegrative PTLSs (NPTLSs), Olfactory Hallucinations, Paroxysmal Disorder, Paroxysmal Neurobehavioral Disorder, Paroxysmal Photosensitive Disorder, Paroxysmal Somatoform Disorder, Paroxysmal Startle Disorder, Paroxysms, Partial Seizures, Photosensitive Epilepsy, Photosensitive Seizures, Possible Temporal Lobe Symptoms (PTLSs), Post-Ictal, Pseudoseizures, Rage Attacks, Recurrent, Refractory, Seizures, Soft Organic Brain Inventory Of Neppe (SOBIN), Somatization, Spells, Standardization, Syncope, Temporal Lobe, Temporal Lobe Dysfunction, Terminology.

Paroxysmal disorders: A Historical and Terminological Perspective (Part 1).
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The History

It was 1977. I saw a patient who had a refractory psychotic condition. The patient had a history of hallucinogenic abuse and did not respond to conventional antipsychotic agents. He was at times auditorily hallucinated, agitated, somewhat irritable, and would fluctuate in mood within seconds. He was severely sedated, had other side-effects, and did not improve when he had been given even the average doses of antipsychotic agent most psychotic patients would improve on.

I carefully considered my options. Could it be that in addition to the only low doses of antipsychotic agent that the patient could tolerate without side-effects, but was not responding to, we should also give him low doses of an anticonvulsant? I chose phenytoin. The patient responded dramatically.

I saw a second patient, this time with no history of hallucinogen abuse, but again with similar kinds of symptoms. I wondered whether or not the same pathology—some (not yet defined) kind of abnormal electrical firing, possibly in the temporal lobe—was going on in the brain. Again, the patient responded to anticonvulsant agents in addition to the low dose of antipsychotic medication.

A third patient with similar symptoms clinched the deal: I needed to do a double blind study, I realized I needed to put these "abnormal firings" out and that medication for seizures should do that. I hypothesized the main area of abnormal firing could be the temporal lobe of the brain, as the temporal lobe is conventionally the great integrator of higher brain function.[1]

First, I had to choose an appropriate anticonvulsant. Ironically, this time, I did not choose phenytoin, possibly the most commonly used standard anticonvulsant of the 1970s, because in high doses it could easily produce toxicity and did not improve patient's cognitive function.

And so, I set up a double blind study on carbamazepine (Tegretol) on all ostensibly non-epileptic chronic patients with electroencephalographic (EEG) temporal lobe foci in a mental hospital. I chose Tegretol because this anticonvulsant historically, based on the data we had at the time, had the least amount of cognitive side effects. There was very little disturbance of thinking, and in fact, on the appropriate doses, patients improved profoundly clinically. This randomized, crossover design, placebo controlled study became a landmark for research in the area[2], and I presented it at the Epilepsy International Congress in Japan in 1981[3]. It was the first (and remains the only) double blind study of Carbamazepine as adjunctive medication in patients with temporal lobe abnormalities on EEG[4]. I did not realize how important that study was at that point in time, but subsequently this study and my follow-up work, plus the studies by Okuma in Japan[5] and also Robert Post at the National Institute for Mental Health in the United States[6], totally changed the face of psychiatry such that millions of patients were being treated with anticonvulsants[7, 8] for conditions such as Bipolar Disorder and Nonresponsive Psychosis with irritability and agitation.[5, 6, 9, 10]

The controversy

This was a condition without a name. I had labeled it "temporal lobe dysfunction"[11], but that could manifest in too many different ways. I realized we were likely dealing with a "paroxysmal" phenomenon.

"Paroxysmal" is a fancy word for episodic phenomena, as opposed to chronic phenomena. Many paroxysms are epileptic seizures coming in bursts in abnormal brain waves and correlated with clinically obvious seizure manifestations. Many patients with seizures that are "generalized from the start" (so-called primary generalized seizures such as in "grand mal") or with "partial seizures" (seizures that have a specific origin in the higher brain, like in the temporal lobe so they are "focal" and may or may not generalize) would manifest such seizure phenomena on brain wave measures, as in the electroencephalogram (EEG). They would often have spiking or sharp waves, or mixtures of spiking and very slow wave manifestations (e.g. <4 cycles per second). But not all paroxysms are epileptic seizures: We talk of paroxysms of sneezing, or of coughing, and these don't manifest with epileptic seizures! Also potentially such paroxysms could be non-epileptic episodic phenomena maybe even hysterical.

We also began to realize that some would regard these patients with these refractory conditions without overt obvious full-blown epileptic manifestations but with the hypothesized abnormal firings within the brain, not as a kind of epilepsy. Indeed, for many years (a quarter of a century so far) neurologists would argue that this was indeed not epilepsy because we were not seeing so-called "paroxysmal episodes of spiking and sharp waves". And, indeed, the EEG would sometimes be quite normal as we would use surface, scalp electrode placements, and deep firing may not manifest on the surface or alternatively because firing was episodic we would not see any abnormalities during our short EEG measure.[12, 13]

Instead, we might have seen some slowing in some focus of the brain, such as the temporal lobe[14]. We would debate what these were. They were not seizures, but what

were they? Could we call them "spells"? But some "spells" were linked with seizures, others with syncope (faints), still others had links with cardiac arrhythmias, and still others were hysterical. "Spells" was too non-specific. So we tried "atypical spells". But what did this "atypicality" imply?

I linked up these conditions to a phenomenon called kindling, which Dr. Graham Goddard had characterized as the lighting of an abnormal fire in the brain, a small stimulus that previously was sub threshold which suddenly became threshold and caused a response. It seemed this was what we were dealing with.[15] The model fitted, but it took many years for colleagues to appreciate its diagnostic relevance. In my 1989 book, *Innovative Psychopharmacotherapy*, I discussed the concept of kindling in this context, but I submitted a new additional condition namely "chindling".[16, 17] "Chindling" was effectively a chemical kindling phenomenon. Instead of electrical stimulation experimentally inducing the abnormalities as in kindling, chindling involved mobilization by chemical manifestations, producing some complex and slightly different biochemical changes to those found in kindling, and mobilizing a variety of abnormal behavioral and psychological underlying brain conditions. Possibly because of lack of publicity, the term "chindling" has never taken off, though I still regard it as possibly the critical mechanism for these anticonvulsant responsive conditions.[18]

But we were still looking for a name for my condition I was labelling "temporal lobe dysfunction". I was using the term, "non-epileptic temporal lobe dysfunction'' to differentiate it from "epileptic temporal lobe dysfunction" so that some of my more staid neurological colleagues would not have a non-epileptic seizure![19] But already I had delineated out symptoms that seemed to arise from firing in the temporal lobe, but which were not conventionally being called epilepsy or seizure disorders, and may indeed not have been.

These were associated with abnormalities on electroencephalograms at times, but at other times because of the depth of the firing of the focus in the brain the surface electroencephalogram was normal. Consequently, it was necessary to develop a series of questionnaires. The first such questionnaire was the Neppe Temporal Lobe Questionnaire, and it was the subject of intensive analysis in my early work (Masters and Doctoral theses) on the temporal lobe and subjective experience in the mid- and late-1970s.[20], and later on in my studies on déjà vu[21]. It was embraced by another doctoral student and thereafter in other research. Subsequently, it was developed by Dr. Michael Persinger in Canada in his research[22], and by Dr. Richard Roberts in Iowa[22], as well as by Dr. Marty Stein in Washington D. C.[23] All modified it, though the latest version the *INSET* (Inventory of Neppe of Symptoms of Epilepsy and the Temporal Lobe) possibly is the most useful clinically, based on my experience in the area over three decades. And was this adequate? Or should we have another measure, too, to help us? I developed the *SOBIN* (Soft Organic Brain Inventory of Neppe) to look at impairments of higher brain function.

Dr Dietrich Blumer and I first met at one of the epilepsy congresses in the 1980s. We were of like mind. We were a very rare breed. We were studying something that was not usual. We were two neuropsychiatrists trying to understand the science of epilepsy—epileptology. We realized there was an application of anticonvulsants in a variety of ostensibly different, as yet unclassified, psychiatric disorders where we could impinge on behavior[24].

We needed a name for our "non-epileptic temporal lobe dysfunction" which responded to anticonvulsants. In about 1988, Dr. Dietrich Blumer and I named the condition *"Paroxysmal Neurobehavioral Disorder"*, although we never formally published using this topic title, but we would use it diagnostically, and I would lecture on it.

The other paroxysmal disorders

But Dr. Blumer and I realized there was a need to clarify such related terminologies. We needed to discuss the various paroxysmal disorders. What about patients who were being labeled as having "hysterical seizures", but which were not epileptic? Does *"paroxysmal somatoform disorder"* and individual *"paroxysmal somatoform spells"* fit[25]? What about that subpopulation of these "hysterical seizures" who were apparently using a "startle" mechanism—so-called *"paroxysmal startle disorder"*[26] ?

And what about the underlying symptoms that we needed to analyze to find suitable patients? And could we better improve our yield by using the technology of *Home Ambulatory EEG*? And was there even a situation in the environment such as flashing lights that were invidious to some patients and producing its own paroxysmal manifestations? Would *"paroxysmal photosensitive disorder"* meet the need for a label for this condition?

Paroxysmal neurobehavioral disorder—a new syndrome (Part 2).
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Paroxysmal neurobehavioral disorder is the name we have given for a disorder that was without a name, but which appeared common and was important to delineate. The paroxsymal element implied episodic brain components producing changes in mental state and manifesting in changes in behavior.

Once we had recognized that certain conditions were episodic and, based on both logic and empirical observation of response to anticonvulsants, appeared to relate to some kind of pathophysiological firing within the brain, we were able to realize that we had actually delineated a new condition. Although, Dr. Blumer and I have described this condition in lectures and in diagnoses, this actual label of Paroxysmal Neurobehavioral Disorders is being used here for the first time. (We had written a chapter on this condition in 1992 for a book but the book was never published.)

We realized that the anticonvulsants were often adjunctive to other medications depending on symptomatology. This ostensible firing within the brain should theoretically respond to appropriate anticonvulsant medication, with or without such other medications, such as antipsychotics, antidepressants or antianxiety medications depending on specific symptom circumstances. The choices were complex, dose dependent, required careful assessment and indicative of the close links of chemical alterations (neurotransmission) with the electrical corrections (anticonvulsants acting on ionic interchanges), or linking with specific firing type neurotransmitters like glutamine and gamma-amino-butyric acid.[16, 17]

Initially we called these conditions spells. We did not want to call them seizures. Later on we called them atypical spells, but the question came up again whether or not

one was dealing with a particular phenomenon, whether this was hysterical, psychological, or actually physically based with some kind of firing abnormality going on in the brain.[24]

Paroxysmal Neurobehavioral Disorder (PND) was our attempt at indicating this broad spectrum of conditions that was not associated with seizures, but responded to anticonvulsant medication, had episodic quality about them, and had a variety of different features. We hypothesized that this was linked up with the temporal lobe in general because it is the great integrator of the brain, and dysfunction produces disintegration. This may manifest with abnormal brain firing, or potentially it may manifest as a nonepileptic malfunction. All the same, we find certain anticonvulsant medications on their own, or sometimes with other medications, help.

In 1989, we attempted a classification of these various paroxysmal disorders. (Table 1) We realized there were many possible symptoms, most frequently occurring in combination.

- First, we regarded this as associated with a mood disturbance at times, where the mood could be elated or dysphoric or there could be major fluctuations even over seconds or minutes, which would be a very rapid kind of cyclothymia. These patients may be misdiagnosed as bipolar because of periods of elevated mood. However, the mood elevations were not over days, but over seconds and minutes with profound fluctuations of mood and switching on and off of symptoms.
- Secondly, there was the irritability and the impulsive component, where these patients literally had explosive outbursts which they could not fully control. These outbursts may or may not have been fully precipitated and were linked up at times with some amnesia. These episodes were often short-lived lasting just seconds. During the 1990s, terminology changed and some of these patients were regarded as having the entity of intermittent explosive disorder (IED). This was associated with episodes of loss of control, disproportionate aggression, no impulsiveness between, and would occur in the absence of psychosis, personality disorder, conduct disorder, and intoxication, and also in the absence of the agitation and irritability linked with simple frustration. The rage symptoms in IED involved the dyscontrol, and the likelihood is that these features like many other PND features are linked with the medial temporal lobe. This firing may have occurred without manifesting on surface electrodes.
- Thirdly, another variant would be the schizophreniform or other psychotic presentations of features where these patients were exhibiting paranoid delusional or cognitive distortions with bizarre transient thoughts that could later become entrenched. They may also have been exhibiting perceptual distortions which may have been visual hallucinatory, olfactory hallucinatory in terms of smell distortions, or auditory distortions, such as buzzes or hums.
- Another possible manifestation was the anxiety component where many of these people exhibited any or several agitation related features: ruminations—thoughts which were repetitive and went on and on, with mulling behaviors, panic with acute anxiety—so-called fear of a fear, phobias directed towards avoiding specific events, thoughts or actions, or they may have exhibited generalized anxiety phenomena.

- These patients may also have reported fluctuating difficulties with focusing and with this attention deficit would also be reports of losing time, or of blanking out, or of difficulties with memory.
- Then there were those patients who had real confusional episodes with real memory impairments almost like they were not registering information because of clouded consciousness.
- There were also those whose families or loved ones reported personality changes where there was increased rigidity, misinterpretations of information and difficulties conceptualizing.

Table 1 PAROXYSMAL NEUROBEHAVIORAL DISORDER
(Neppe, Blumer 1989, modified 2008)
1. MOOD (elated, dysphoric, cyclothymic, bipolar)
2. IRRITABLE, IMPULSIVE (e.g. intermittent organic explosive disorder)
3. SCHIZOPHRENIFORM (e.g. paranoid, perceptual, delusional, cognitive distortions)
4. ANXIETY (e.g. ruminative, panic, phobic, generalized)
5. SOMATIZATION
6. AMNESTIC or CONFUSIONAL phenomena (e.g. attentional, paramnesic, clouding, blank outs)
7. PERSONALITY (e.g. changes in tolerance, skill set, interactions)
8. COMPLEX (>3categories)
9. Not otherwise specified

The above features were possibly the most common: However, in some patients with Paroxysmal Neurobehavioral Disorders, there were the translations into somatization and pain—in this context it is important to recognize the difference from Paroxysmal Somatoform Disorder, which could be a form of nonepileptic seizure.

We realized that these were not single entities, and these could be complex and manifest with at least two or three different categories. As with all the prevailing psychiatric nomenclatures at the time, we realized there was a "not otherwise specified" component.

The recognition of this disorder is critical.
These patients were not being treated. There was no known treatment. There were no marketed drugs for these kinds of indications, yet these patients invariably appear to respond to anticonvulsant medications.
We do not have double blind studies on this, but have seen this empirically happen consistently and repetitively hundreds of times. At this stage, I would question the ethicality of a placebo controlled study because the manifestations do not require statistical analyses but appear obvious for all to see.

There is most frequently a need for appropriate adjunctive medications:
At times when there is a depressive component, patients need antidepressant adjunct: One of us (DB) has significant experience with the tricyclic antidepressants
Secondly, in that regard; there are frequently tinges of psychotic thinking with disordered thought, associations, illogicality, and paranoid overlay: These patients need antipsychotic medication but in very low dosage.
Thirdly, one of us (VN) has been using the only marketed azapirone medications, namely buspirone. This compound is a "normalizer" of serotonin regulating the serotonin 1A receptor at both autoreceptor levels as well as post-synaptically.

However, again as a caution: This entity does not officially exist. There are no known officially approved marketed drug treatments worldwide for these indications: The necessary first stage is always a diagnostic label; only after that comes official treatment sanction. This makes PND controversial. We believe, however, that this cluster of symptoms responds to appropriate pharmacotherapy, almost invariably including anticonvulsants.

Paroxysmal disorders: Home ambulatory EEG as objective screening (Part 3)

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When one does an electroencephalogram (EEG) measuring brain waves, the object is to find abnormal functioning. This abnormal functioning may be in paroxysms (discrete episodes) running for seconds or longer, manifesting as episodes of abnormal waves which are not expected at that time. In conventional neurological conditions where people manifest full-blown seizure phenomena, this often involves some sort of spiking or combination sharp waves and spiking. However, in psychiatric disorders this very often involves a certain slowing. A second component may be abnormalities despite the absence of any paroxysmal episodes, there are focal areas of difference, for example in the temporal lobe of the brain.

Conventionally, when one does electroencephalograms, one may do a 20 to 60 minute recording during wakefulness. The degree of yield from a neurological perspective in patients with a full-blown seizure disorder is reasonably high. However, in patients with atypical paroxysmal conditions, the yield appears to be far, far lower. Indeed, one has to be lucky, to find abnormalities. Consequently an increased yield is aimed at: Many of these patients receive in addition, "sleep EEGs". However, frequently, they are not even lucky enough to fall asleep, in the extra 20 or 40 minutes that may be allocated. However, the yield remains low. Consequently, special electrodes placements, sometimes up the nose (nasopharyngeal) or alternatively lower down near the temples or even inferior to them (below there—sphenoidal electrodes sometimes even under the skin) try to obtain a higher yield of temporal lobe pathology.[27] In our lab, we use what is called a T1-T2 lateral temporal montage array and add to it monitoring with an electrocardiogram to ensure abnormalities are not deriving from the heart.

Again, the success rate has been small—possibly only a few percent higher yield, questioning whether such uncomfortable procedures are ethical and worth the trouble.[7] Depth electrode placements deep into the brain considerably increase the yield by picking up previously "silent" areas close to the abnormalities but currently are limited to candidates for epilepsy surgery or particularly intractable individuals as the morbidity, costs and inconvenience are considerable.[28-30]

Whereas experimental and research models of diagnosing epilepsy certainly can include functional magnetic resonance imaging (fMRI), positron emission tomography (PET) and single photon emission computerized tomography (SPECT), and there is accumulating literature for the use of these modalities in that regard, there are still significant diagnostic difficulties for them not to become routine: For example, during actual paroxysmal epileptic events, there may be hyperperfusion vs the hypoperfusion during ostensible interictal phases. EEG monitoring is still the standard.[31-33]

However, the major advance that has occurred has been the opportunity to monitor these patients for several days in their normal environment at home. This is called Computerized Ambulatory Electroencephalographic Monitoring (AEEG).[34-36] Patients go home after they are hooked up via a complex very expensive, battery operated recording device looking rather like a Sony Walkman recorder. A computer records the brain waves in 16-21 channels.

If patients have any kind of episode, they press a push button, so as to analyze what happened at that time in the brain. These "pushbuttons" mark the brain waves at the time and expert readers can go backward in time two minutes to delineate whether the events actually began earlier.

AEEGs also measure all depths of sleep (not just the Stage 1/ 2 sleep we mainly see in regular Sleep EEGs). This increases the potential yield of positive results—a normal record does not mean that it would not have been abnormal at another time. Because of this, we monitor patients with atypical paroxysmal conditions for a prolonged period of time, such as 3 days. The yield is reasonably high particularly with sophisticated apparatuses such as 21 electrode placements using the Sleep-Med Digitrace AEEG machine.[37]

Whereas the use of video-cameras is particularly valuable in a hospital setting where patients are sometimes off their anticonvulsant medications and resting in bed, such extra monitors may be restrictive in a home environment, where ultimately interpretations are based on the actual EEG tracing, not on the associated videotape.[38-40]

At times, we monitor numbers of episodes over time, repeating this test. However, patients may still only have episodes infrequently, like every three weeks or every three months. Consequently, even a three day period of time, may not always pick up abnormalities. But there is fortunately an up side: Even when patients are having overt epileptic episodes only every three or six months or even every two years, we may still note silent episodes of abnormal firing in the brain during the AEEG. Sometimes this may be 20 or 30 times in a night and this may explain previously undiagnosed reasons for fatigue or other kinds of symptoms such as chronic irritability.

The population is specialized. AEEG is not a panacea test for all. The need for it is often based on the detailed history and evaluation including the listings of possible temporal lobe symptoms and of suspicious possible paroxysmal events occurring on the standardized screen for such events (the INSET, The Inventory of Neppe of Symptoms of Epilepsy and the Temporal Lobe). Usually, regular sleep and wake EEGs don't fully delineate the exact focal abnormalities in difficult to diagnose cases. Moreover, these usual regular (one hour) EEGs don't supply the data for the number of and frequency of daily paroxysmal events; nor does it delineate markers of actual relevant pushbutton symptoms; and these short office EEGs also cannot adequately demonstrate the extent of control of seizures or atypical spell or abnormal electrical events on a current specific medication regimen, let alone elicit them.

The technique is specialized. For example, recordings are done at a sampling rate of 200 samples per second, per channel, allowing for a relatively high frequency response of 70 cycles/second (Hz). Playbacks are done with digital high frequency filters noted at the top of each page. EEG is marked both by the patient pressing pushbuttons and by an automatic seizure computer designed to detect and record EEG abnormalities including seizure and spike discharges.[41, 42] The seizure computer stores all automated seizure detection files—we humans still have a job, because for the next five years anyway we may be better at reading what is artifact and what is not!

The advent of Ambulatory Electroencephalogram has been a major boon allowing epileptologists to measure objective change of certain patients. At times, we are able to dispense with this, as they are able to detect every episode of EEG.

The realization that there could be electrical and chemical abnormalities going on in the brain was a kind of epiphany for me. It was the theme of *Innovative Psychopharmacotherapy*[16, 17] where the realization that some of these episodic kinds of conditions were treatable by appropriate anticonvulsants allowed me, and later on many of my colleagues, to help a large population of people who otherwise would have suffered. The key element is that treatment is available either for epileptic seizures or for such conditions as paroxysmal neurobehavioral disorder. Evaluations of these underdiagnosed atypical spells can be helped by monitoring electrographically events while the spells are happening in reality and this is the value of this AEEG technology that began in earnest in the early 1990s.

Paroxysmal disorders: The INSET as a subjective screen: (Part 4)
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To evaluate paroxysmal phenomena in the brain—symptomatic of episodic brain firing—one needs to be able to screen for symptoms. Traditionally, in Medical Practice, a history is taken. It is useful to have a series of structured questions that can be routinely completed. For this purpose, I developed a new questionnaire, which I called the INSET, or Inventory of Neppe of Symptoms of Epilepsy and the Temporal Lobe. This is a historical probe, just as one will attend a physician and fill in forms pertaining to gastrointestinal symptoms, such as nausea, vomiting, diarrhea, and abdominal pains.

The INSET is valuable because we cannot routinely do expensive tests like ambulatory EEGs on all patients, and in any event we are able to elicit historical lifetime information not just information for three days of recording. This implies a far higher yield. On the other hand, the objectivity of an outside and very confirmatory EEG recording cannot be denied.

Why is the temporal lobe specifically delineated out here? Simply because this anatomico-physiological area of the higher brain has a particularly high yield for eliciting the symptoms of such conditions as Paroxsymal Neurobehavioral Disorder (PND) and of other paroxysmal brain conditions. The temporal lobe of the brain is the great integrator. This means that when the patient exhibits impairments in the temporal lobe, he/she manifests *disintegrative* symptoms. Many of these symptoms are paroxysmal in nature, which means that this questionnaire can be a probe for paroxsymal seizure like symptoms. Moreover, there are very few findings on physical examination that can point to the temporal lobe of the brain unless the patient has a tumor or large obstructing structural lesion. Consequently, we rely on history.

Symptoms have been attributed to the temporal lobe via two main methods: stimulation during neurosurgery and through the clinical features of temporal lobe epilepsy. Non-specific symptoms (e.g. depersonalization) and apparently more specific symptoms (e.g. olfactory hallucinations), which apparently rarely occur without temporal lobe dysfunction, can be so differentiated. Nevertheless, symptom specificity is debatable. Consequently, I have called such apparently pathognomonic symptoms "possible temporal lobe symptoms" (PTLSs).[20]

The INSET has been a mainstay of my neuropsychiatric examinations for the last two decades and is administered in general to all patients with neuropsychiatric or behavioral neurological disorders. We use a shortened version of this INSET with a series of fifty-five questions, probing to establish if there is any evidence for seizure disorders or temporal lobe symptoms. By these means, one is able to amplify further positive symptoms. As importantly, one is able to also monitor change over time. What was the patient at their worst in terms of frequency? What is the patient currently? How is the patient once they have received appropriate anticonvulsant medication?

Such a historical instrument is particularly useful in monitoring change, and the change that occurs can, at times, can be quite profound with appropriate medications. Detailed questions can be used to probe for positive responses on the Short INSET that is used. This is the Long INSET. Realistically, however, given a background training in epileptology, we need not use this second historical probe except for research.

The earliest origins of looking at temporal lobe symptoms were in 1977.[43] At that time, I did a detailed review of the literature of all reported symptoms, published on both epileptic and non-epileptic symptoms of temporal lobe disease, and then developed an initial classification, probing for several different levels of symptoms of temporal lobe dysfunction.[44] I followed this through with further research.[45, 21] The INSET is, in my opinion, the best historical screen following on my initial Neppe Temporal Lobe Questionnaire, and with respect, far more clinically relevant and usable than others that have derived from this NTLQ (Persinger, Roberts, Stein).

These are reflected in Table A.

Table A. POSSIBLE TEMPORAL LOBE SYMPTOMS (PTLSs)
Disintegrative PTLSs (DPTLSs)
Symptoms Requiring Treatment: Paroxysmal (Recurrent) Episodes of:
1. Epileptic amnesia;
2. Lapses in consciousness;
3. Conscious "confusion" ("clear" consciousness but abnormal orientation, attention and behavior);
4. Epileptic automatisms;

5. Masticatory-salivatory episodes;
6. Speech automatisms;
7. "Fear which comes of itself" linked to other disorders (hallucinatory or unusual autonomic);
8. Uncontrolled, unprecipitated, undirected, amnesic aggressive episodes;
9. Superior quadrantic homonymous hemianopia;
10. Receptive (Wernicke's) aphasia;
11. Any CPTLSs or NPTLSs with ictal EEG correlates.

Seizure related features (SZs)

Any typical absence, tonic or clonic or tonic-clonic or bilateral myoclonic seizures in the absence of metabolic, intoxication or withdrawal related phenomena.

Not Necessarily Disintegrative PTLSs (NPTLSs)

Symptoms Not Necessarily Requiring Treatment Paroxysmal (Recurrent) Episodes of:
1. Complex visual hallucinations linked to other qualities of perception such as voices, emotions, or time
Any form of:
1. Auditory perceptual abnormality;
2. Olfactory hallucinations;
3. Gustatory hallucinations;
4. Rotation or disequilibrium feelings linked to other perceptual qualities;
5. Unexplained "sinking," "rising," or "gripping" epigastric sensations;
6. Flashbacks;
7. Illusions of distance, size (micropsia, macropsia), loudness, tempo, strangeness, unreality, fear, sorrow;
8. Hallucinations of indescribable modality;
9. Temporal lobe epileptic déjà vu (has associated ictal or postictal features (headache, sleepiness, confusion) linked to the experience in clear or altered consciousness);
10. Any CPTLSs which appear to improve after administration of an anticonvulsant agent such as carbamazepine.

Controversial PTLSs (CPTLSs)

1. Severe hypergraphia;
2. Severe hyperreligiosity;
3. Polymodal hallucinatory experience paroxysmal (recurrent) episodes of:
4. Profound mood changes within hours;
5. Frequent subjective paranormal experiences e.g. Telepathy, mediumistic trance, writing automatisms, visualization of presences or of lights/colors round people, dream extrasensory perception, out-of body experiences, alleged healing abilities;
6. Intense libidinal change;
7. Uncontrolled, lowly precipitated, directed, non-amnesic aggressive episodes;
8. Recurrent nightmares of stereotyped kind;
9. Episodes of blurred vision or diplopia.

I called the most specific symptoms *Possible Temporal Lobe Symptoms* (PTLSs). These were symptoms that appeared to derive from the temporal lobe of the brain. Common examples are:

- burning, rubbery smells lasting seconds (episodic olfactory hallucinations)
- short-lived, staring blanking out episodes;
- profound disturbances of mood, switching on and off in seconds;
- symptoms of a rising sensation in the epigastrium, moving upwards towards the chest, and unrelated to meals.

I distinguished between disintegrative temporal lobe symptoms and not necessarily disintegrative ones, for example, the olfactory (smell) phenomena above may be unpleasant but not cause definite difficulties; on the other hand, uncontrolled profound explosions of anger with some amnesia reflect disintegrative PTLSs.

There were also frank symptoms of Epilepsy itself such as generalized tonic-clonic seizures (grand mal) and also post-ictal (after the seizure) events such as severe headache, confusion—clouded consciousness and also disorientation.

Then there were controversial possible temporal lobe symptoms (CPTLSs) These implied further research was needed as to their status as their origins or impingements on the temporal lobe were uncertain but the evidence was relevant linking the two. Amongst these CPTLSs that my research has demonstrated as having a link are subjective paranormal experiences—so-called psychic experiences like reports of subjective extra-sensory perception, and out of body experiences. We have been able to show that these features correlate with temporal lobe symptomatology in both a state and a trait manner, but also occur independently.[20]

Then there are non-specific kinds of symptoms.

These all come together as symptoms that one would probe in an instrument such as the INSET. A longer version of the INSET also existed, and this longer version went into greater detail, I generally use the short version because I am able to assess the historical probe, always looking at linking of various kinds of symptoms and their relevance to other kind of symptomatology, such as analyzing the déjà vu phenomenon and seeing whether or not this fits that fabric. Essentially, therefore, temporal lobe screens and screens for brain dysfunction are very useful in assessing episodic paroxysmal kinds of conditions.

Major difficulties exist in interpreting the pathophysiological origins of PTLSs. What makes olfactory hallucinations, déjà vu or rage attacks relevant for the diagnosis of temporal lobe epilepsy? Is it necessary to analyze the exact phenomenological context of these experiences to interpret such PTLSs with any value? It is. Three of my major research projects have supported this hypothesis.[20, 21, 46] We interpret the presence of "possible temporal lobe symptoms" in the context of paroxysmal disorders by considering the company they keep: Are they linked to definite epileptic features such as tonic-clonic seizures or automatisms or is there coexistence of headache, sleepiness and clouded consciousness after PTLSs implying post-ictal features. However, the "company they keep" may imply the independent co-existence (i.e. not linked in time as part of the same event) of other epileptic features. Thus it would be reasonable (but only of provisional certainty) to interpret recurrent, episodic PTLSs as partial seizures when the patient has other, separate, proven epileptic features (e.g. tonic-clonic seizures). We also need to analyze each symptom in detail as otherwise we may not equate like with like. This was demonstrated in my detailed déjà vu research.[21] Finally, we correlate these findings with the EEG and anticonvulsant response.

We have used other instruments to assist us as well. For example, the SOBIN (Soft Organic Brain Inventory of Neppe) was developed in 2002 and we have significant experience with it. But it does not evaluate the paroxysmal itself, although picking up soft brain damage. It is valuable in screening for photosensitive seizures, however, and this result may prove to correlate strongly with ambulatory EEG. It also details laterality (e.g. handedness and footedness).

We have used the Short INSET on many hundreds of patients over the past fifteen years and correlated this data with more than a thousand other pieces of information in each instance including Ambulatory EEG and monitoring clinical response over time. Therefore, we have a well tried and tested instrument but we have no gold standard to compare it to, because it is the gold standard in its class!

Paroxysmal disorders: A summary differential diagnosis of epileptic seizures, non-epileptic seizures and syncope. (Part 5)

Vernon M Neppe MD, PhD, FRSSAf, DFAPA, BN&NP, MMed.

We need to understand the difference between difficult to diagnose epileptic seizures and those that are conventionally regarded as having psychological associations, so-called non-epileptic seizures and the condition of fainting, due to low blood pressure or slowed pulse or vagal stimulation or circulatory collapse.

Abnormal electrical paroxysmal epileptic firing during an attack is the only real way of demonstrating a genuine epileptic seizure. Clearly if such events occur in sleep it is most likely to reflect genuine epilepsy.

Also, the diagnosis of NES is a positive one: It is not simply not finding active epileptic seizures during EEG monitoring. It should be borne in mind that even when strange events occur without EEG correlates, these may derive from deep within the brain, e.g. in the mesial temporal lobe. It is a difficult, uncomfortable inpatient procedure to drop electrodes through boring a hole in the skull: These depth electrodes down the middle of the brain certainly may yield a great deal picking up deep firing that is sometimes missed, but, ironically, even then the electrodes need to be precisely placed as very local firing may not spread.[47, 48]

NES is a positive diagnosis because there are invariably good psychological reasons why the events are occurring at those times and these have good predisposing pathology like sexual or physical abuse or major needs for attention.

Table I reflects the differentiating features of NES from regular epileptic seizures and from syncope (faints). The features listed reflect general rules and are not specific but some features like the variability of NES compared with the stereotypical (specific march of the same symptoms and signs every time) features of epileptic seizures are more specific than others: "Normal" in this table implies statistically no different from the general population. I have incorporated as much of the literature as possible to produce as extensive information as possible for Table I.

Table I: Differentiation of Epileptic Seizures, Pseudoseizures (Nonepileptic Seizures) and Syncope

Quality	Epileptic seizure	PSD (NES)	Syncope
During the event			
Consistency between events	Stereotypical	Variable in quality and sequencing	Consistent but does not have a march of several symptoms.
Eyes[49]	Open deviated	Close	Open deviated
Rouse during episode	Not usually	Yes	No but very quick
duration	10–180 seconds usually	Variable, longer	Brief

afterwards	Perplexed, disorientated	Surprised Sometimes crying or emotional	
Color skin[49]	Normal or blue	Normal	Pale
Breathing[49]	Normal	Increased or normal	Shallow
Pain[25]	Classically, post-ictal (after event) headache	Preceding pain or headache; may also follow events	
Autonomic symptoms	Nausea or vomiting at times	Less likely nausea	Nausea may relate to the orthostatic (low blood pressure) changes.
Event	No specific pelvic thrusting;	May have pelvic thrusting	
Kind of attack	Consistent attack	Variable description	Falling; consistent
Incontinence	Sometimes	Can occur	
Self-injury	Sometimes inadvertent	Can occur	
In sleep	Yes	Not	Not
Audience	Yes or no	No	Yes or no
Rouse during episode	No. Unless partial (focal)	At times	No but short-lived
Management			
Response to anticonvulsants	Good	May be poor	None
Saline infusion[40, 50]	No different	May yield event	No different
Hypnotizability[51-54]	"Normal" suggestibility	Very suggestible	Unstudied; normal?
Pathology			
Pathophysiology of neurological condition.	Anatomically and physiologically consistent	May be inconsistent	Consistent with underlying pathology
EEG	Abnormal usually can be normal	Normal usually can be abnormal	Normal
Biological basis	Abnormal firing in the brain with possible march of symptoms	Likely basis biologically. May resemble startle pathways.	Relates to blood pressure, pulse, vagus nerve
Psychopathology			
Past psychiatric history	Minority	Almost invariable	Like normal population
Previous dynamics	No reason	Sexual / physical abuse	
Current triggers	Often aggravates	Often aggravates	
Dynamics appropriate	No	Yes	Not usually
Specific triggers	Frequent, same	Variable, stress	Sometimes
Stress	Aggravates	Aggravates markedly	Sometimes
Psychological gains	None. Distressing to the patient and family.	Frequent. Others controlled by it.	None. Distressing to the patient and family.
Kind of patient[7, 8]	Usually normal individual (epilepsy standard); small proportion associated brain damage/ pathology (epilepsy plus)	Majority may have an underlying brain organic basis (e.g. Epilepsy, mental retardation, severe psychopathology)	Normal
Interface	Can occur with NES usually separately	Occurs in about a sixth with true epilepsy	No relationships
Monitoring time	May or may not show any events depending on seizures	Events frequently occur in first 48 hours.[55]	No epileptic events; usually normal as lying down.

Monitoring by video	Video events appear to be epileptic seizures on EEG	Video not correlated with epileptic seizures on EEG.[55]	No epileptic events on EEG or video
Post traumatic stress disorder	Rare	Common	Normal

A "normal" EEG tracing particularly in the absence of deep intracranial electrodes, even when associated with characteristic bizarre movements does not make a positive diagnosis of pseudoseizures: Unfortunately, such labels made by negation are inappropriate, but all too prevalent. There remains no substitute for appropriate psychodynamics.[47, 48, 56]

Paroxysmal somatoform disorder Pseudoseizures—the misdiagnosed label; a new terminology: Paroxysmal somatoform disorder (Part 6).
Vernon M Neppe MD, PhD, FRSSAf, DFAPA, BN&NP, MMed.
Dietrich Blumer MD, DFAPA.

The term "seizure", although not regarded as synonymous with epilepsy by specialists, is often is perceived as synonymous with epilepsy. Technically, epilepsy is a condition in which the patient has two or more events separated in time, without obvious precipitator, such as high fevers. The manifestations of epilepsy are variable, involving some impairment of consciousness (we refer to these as complex seizures) all the way through to total impairments (as in tonic clonic seizures and other usually generalized manifestations). Epilepsy may also manifest variably with alterations in perception, awareness, emotionality or behavior and the diagnostic feature commonly relates to manifestations on electroencephalogram confirming such a diagnosis.

When one encounters acute episodes of "spells", where patients have shaking attacks, or strange behaviors, but are not having true epileptic seizures, neurologists, psychiatrists and epileptologists have used a variety of different terms.

The problem is some patients have episodes which are not as clear cut and this is, where labels come in such as "Nonepileptic Seizure" (NES).[57, 58] What would be an appropriate but descriptive non-prejudicial term for patients who have phenomena that resemble epileptic seizures but which are in reality psychogenically induced? This is an active area of debate in neuropsychiatry and epileptology. The number of terms suggested for such a phenomenon is indicative of the difficult status of such events in conventional medical terminology. Unlike the entity of paroxysmal neurobehavioral disorder, a name exists for the condition: It's just the name is controversial.

Three decades ago, clinicians were calling these events hysterical epilepsy, hysteroepilepsy or hysterical seizures.[59] The term hysteria then went out of favor in psychiatry and with it, thankfully, the entity of "hysterical seizures".

One common term today is pseudoseizures.[60, 61] This raises a new area of debate as to its appropriateness. The events are not epileptic seizures hence the "pseudo" component. However, they are not pseudo in that they are extremely real episodes and pseudo implies a disparaging element to the events. We dislike the pejorative inference on the nature of these episodes. Patients feel badly, guilty, distressed, or resentful that their condition is perceived in a pseudo-artificially -sense and that they are being

actively accused of causing it. Whereas this may or may not be true, this perception is unhealthy and inappropriate.

Moreover, Slavney emphasizes the active role of the experient in the pseudoseizure—they are doing it to themselves, it's not happening to them—in this way, it is pseudo, but it has implications in primary and secondary gains, such as sick role and attention.[62] Such events are generally not consciously motivated: The patient is not malingering his illness, nor is it consciously performed. The condition does not appear to have direct environmental gain—it is not consciously factitious.

A second common term, possibly the most common today, is the term above, namely, "Nonepileptic Seizure" (NES). This followed pseudoseizure, but this attempt was neutral in connotation and acceptable in denotation[61]. However, it fails because of the inherent paradox in the terms. A seizure has an inherent component of being paroxysmal (episodic event lasting seconds), and indeed, NES and pseudoseizures are therefore paroxysmal. Moreover, the recognition of the biological basis of this event is negated by such terminology despite it being very real.

Psychogenic seizure was another popular alternative term, but again the word seizure is controversial, although the psychogenic nature of the event is emphasized. This may not be pleasant for the patient to hear as the term psychogenic in psychiatry has become almost as unfashionable as hysterical.

Camouflage terms reflecting more non-prejudicial frameworks, yet emphasizing the connection with the body, have led to the whole area of Somatoform disorders being studied. Several other alternatives exist[63]: the conversion nature of the events suggests "conversion fits". The problem is, it is inaccurate: whereas conversion phenomena do occur, dissociative elements exist as well. Moreover, we often refer to conversion in the context of negative events - paralysis, mutism, and these are classically positive activities. A different term, Doxogenic Seizures introduces the esoteric term "doxogenic", implying the patient's own mental conceptions and, in fact, Merskey has also used the term in the multiple personality disorder implying a common theme which is unproven and probably unlikely - the two conditions do not appear to markedly co-exist.[63]

Can terms like "epilepsy" and "seizures" be linked with "pseudo" or "hysterical" or "somatoform" or "conversion" or some other equivalent? Not appropriately: These events are not epileptic seizures so that broadening the term "seizure" would create a new ballgame[62]. It would mean other paroxysmal events would compromise the essential character of epileptic firing in the brain. If we did so such events as syncope and pain which also involve non-epileptic short-lived episodes of impaired consciousness, as well as sensory perception discomfort, or motor movements would all be incorporated under "seizure"!

This then restarts the debate on the nature of seizures - whether we ought to be limiting the term to epileptic firing. Alternatively there is the term "pseudo-attacks". This brings the debate on pseudo back to the forefront and introduces a new source of prejudice, namely the "attack". Is a pseudoseizure an attack - if it's psychologically induced is the patient the victim of the attack or the cause of the action? Attack seems as prejudicial as seizure.

What terms can be used? We feel badly about adding to this debate new terms, but clearly the old ones are unacceptable.

There is a need for a term describing short-lived episodic phenomena of concern to patients or those around them—the term "spell" accurately describes this. But this is non-specific. We don't know what kind of spell. Is it syncope (faint)? Is it epilepsy itself? Is it vascular such as a transient ischemic attack? Is it psychological as in NES?

We feel the term ought to be non-prejudicial for the patient, not reflect episodic organic firing in the brain, yet allow for the fact that numerous patients labeled with NES, actually turn out to have real though atypical seizures on depth telemetry, and that real seizures commonly co-exist in patients with NES (maybe as high as 50% to 80% or as low as 12%-18%). We want to emphasize the essential episodic nature of the events which are usually sudden and have onsets over seconds and usually last short time - generally seconds or minutes occasionally hours or days.

Consequently they are paroxysmal. We and others have used the term spell for a nonprejudicial way to describe such paroxysmal attacks of altered or impaired consciousness, behavior, emotions, perceptions or motoric movements. We need to replace seizure with something and spell seems more logical than somatoform seizure for example but only until the diagnosis is made because it is too non-specific.

There is a major advantage to using the term spell. Clusters of events can easily be combined into a disorder or syndrome encompassing the paroxysmal disorders. Spell as defined is paroxysmal and delineates the episodic nature of the illness and is particularly valuable considering our other suggested related classification of Paroxysmal Neurobehavioral Disorder. It would even include PND. Spells imply that these are happening as single discrete episodes in time, and moreover, a series of spells of may ultimately lead to a diagnosis of a syndrome or disorder cluster. It is at this point that we use the label Paroxysmal Somatoform Disorder. These may include also bodily episodes, such as faints or episodic pain or headache. Spells are non-prejudicial. They do not imply seizure phenomena, and yet do not connote conversion, dissociation, hypochondriasis or hysteroid behavior either. But they are too non-specific for NES.

We also do not believe rare and idiosyncratic terms like Conversion fits, Pseudo-attacks and Doxogenic seizures have a place.[63]

Moreover, we want to link with conventional DSM and ICD nomenclature, now and in the future. We need to reflect conscious or unconscious behavior of episodic bodily or mental kind non-prejudicially, and it would be worth having a term such as somatoform—resembling bodily symptoms.[64, 65] This has been introduced into psychiatric classifications since about the 1990s as in the Diagnostic and Statistical Manual-IV (DSM-IV).

The Somatoform element we believe to be useful because it emphasizes the bodily symptoms elements, and as many as two thirds of these patients have pain syndromes, such as headaches, preceding the NES or as part of it[25]. Hence, Somatoform Spells would allow differentiation from syncopal or pain episodes. But we want to be more specific: What of people who have repetitive somatoform spells—they would have PSD or Paroxysmal Somatoform Disorder (PSD).[25, 66] We respectfully, therefore, add to the tumult of terms this one.

Another comment is apposite: There is increasing support for the biological origins in the brain of PSD. In fact, the mechanism of the "startle" response may account for a considerable number of these events and the startle reflex is a well-demonstrated phenomenon. In man, the eyes close, the mouth grimaces, and the muscles assume a defensive posture. A complex neuronal pathway involving auditory and/or visual

connections to the lemnisci and pontomedullary reticular formation reticulospinal pathways may be involved.[25, 26] Exaggerated startle reflexes are well-demonstrated in classic post-traumatic stress disorder patients who have experienced sexual abuse or traumatized in war.[25] Certainly, therefore a subpopulation of PSD may be startle episodes (paroxsymal startle disorder) as well as the various pain related phenomena or other atypical spells.[67, 68]

The aphorism "the number of medications used for this condition attests to nothing working" may be applied at times to terminology and this has been so here. We therefore reject the two most commonly used today, Nonepileptic seizure (NES) and Pseudoseizure. We respect but reject the older terms, such as Psychogenic seizure, Hysterical seizure, Hysterical epilepsy, Hysteroepilepsy, Hysterical seizures. We believe the term to use should be Paroxysmal Somatoform Disorder (PSD) for this controversial entity and that individual episodes would then be called somatoform spells.[66] This eliminates previously involved prejudicial or inaccurate labeling and diagnostic features.

Paroxysmal Photosensitive Syndrome: Photic stimulation, the EEG and environmental ethics (Part 7)
Vernon M Neppe MD, PhD, FRSSAf, DFAPA, BN&NP

We recognize the Americans for Disabilities Act (ADA) and provide wheelchairs and onramps for those who are physically disabled. We also provide in the United States special education for those who are at need, but there is a subpopulation of patients who appear to have been entirely neglected. I call these patients Paroxysmal Photosensitivity Disorder (PPD). Many of these patients have an underlying seizure disorder. But some of them manifest with headaches, such as migraines, or irritability and agitation. The commonality is an intense dislike of flashing lights, such as discothèque lights or strobe lights.

A special kind of light sensitivity, namely paroxysmal photosensitivity is a condition detected on the electroencephalography (EEG). This paroxysmal reaction is to Intermittent Photic Stimulation (IPS)—the phenomenon of light fluctuations is episodic and repeated. This EEG response, elicited by IPS or by other visual stimuli of daily life, is called Photo Paroxysmal Response (PPR). PPRs are well documented in epileptic and non-epileptic subjects.

Photosensitive synchronization at certain frequencies is almost invariable in everyone. However, rarely in normal individuals does this stimulus evoke epilepsy. Even in epileptics, full blown photosensitive epilepsy is a rare reflex kind of epilepsy (possibly 2% in its full form though in those with generalized epilepsy it may occur in up to a third)[69]. It is characterized by seizures in photosensitive individuals.

However, modern technology has increased the exposure to these potential seizure precipitants in people of all ages—and possibly children and adolescents are the most at risk. Video-games, computers, photocopying machines, discothèques and televisions are very common triggers in the daily life of susceptible individuals. The mechanisms of generation of PPR are poorly understood, but genetic factors play an important role.[70]

As background to this, we examine briefly the different brain rhythms.

When one performs an electroencephalogram (EEG) on a patient, we test using Intermittent Photic Stimulation (IPS). We find that virtually everyone will synchronize at a certain point with the frequency of flashing lights. This is the nature of the brain as it is so basic. Various names are given for the different rhythms (See Table a)

Table a

EEG Brainwave Sample	Brainwave Frequency	State of Consciousness
Beta	13 - 40 cps	Fully awake and alert; clear consciousness
Alpha	8 - 13 cps	Relaxed, daydreaming "relaxation"
Theta	4 - 7 cps	Deeply relaxed, light sleep,
Delta	0.5 – 4 cps	Dreamless. Deep sleep or unconscious.

- For example, when strobe lights are flashed in the beta range, at 13 Hz (cycles per second), the patient synchronizes rather remarkably in their brain even when their eyes appear shut. We see a 13 cycles per second synchrony occurring.
- For many patients, there is also a synchrony occurring around 8 cycles per second, which is the lower level of the alpha rhythm. This raises possible questions of links with earth events as an 8 Hz rhythm (or more specifically on average 7. 83 Hz although this varies enormously), is the earth's own rhythmic ionospheric cycle, the so-called Schumann Resonance[37 p.85]. Could this possibly explain why some may be sensitive to certain natural disasters like earthquakes?
- Thirdly, there are those who synchronize at much lower levels, for example 3 cycles per second, in the delta range and there are those who synchronize at much higher levels, over 20 cycles per second.

There are many techniques, meditative, biofeedback, entrainment and others, that use the different brain wave rhythms therapeutically. Ultimately individuals learn to entrain themselves and the improvements may relate to diminished headaches, pains, improved mood, less fatigue and being able to experience realities that are not generally accessible. These various potential therapeutic modalities in skilled hands may be valuable.

Just as there is good, there are also sometimes problems. This is where the Americans for Disabilities Act (ADA) may want to re-examine criteria.
The practical significance of this is the pathology that may occur.
Certain symptoms may be induced.

Society is at times aware of these problems: One goes to the theater, and occasionally one sees signs saying "flashing lights" or "strobe lights".
However, most often we see nothing. This can be fatal.

A patient with a seizure disorder that is well-controlled is driving his or her motor vehicle and encounters a flashing light at a store or from a police car driving by may have an epileptic seizure, lose consciousness and be killed or kill others. Such visual phenomena, and possibly also auditory phenomena, may induce this synchronization of brain waves, and this mobilization, and this may produce a variety of different symptoms.

Impaired consciousness in situations requiring full attention are the most extreme example, but migraineurs[71, 72] and others who may be nauseated autonomically or become acutely irritable or depressed as part of their paroxsymal neurobehavioral disorder may suffer.

Whereas many of these are simply called Photosensitive Seizures or Photosensitive Epilepsy. This entity has not been named before in its syndrome (cluster of features form). I hypothesize here controversially that this is a far broader spectrum. These patients will often respond to anticonvulsants, and in my experience, drugs such as Topiramate (Topamax) are particularly useful under these circumstances. It is difficult to find appropriate sunglasses or shading of the eyes that help, although that may. The problem may still be that synchronization can occur ostensibly even with eyes closed. Nevertheless, the easiest prevention is simply to control the visual stimulus and avoid obvious sources. Stimulus modifications may be very important and useful to seizure prevention, and almost invariably antiepileptic drugs are needed.[70] This may be so, but is not adequately studied in non-epileptic conditions of paroxysmal photosensitivity such as migraines and irritability.

I see this as one trigger of what I have called "paroxysmal neurobehavioral disorder".

This disorder is quite different from people who complain of being light sensitive—any light, where the frequency is unimportant.

I submit the name Paroxysmal Photosensitive Disorder. The paroxysmal implies the recurrent, episodic phenomena that trigger the event, and the photosensitivity implies the specific frequency producing pathological synchronization with brain waves. A subpopulation of these patients would have seizures, migraines, and emotional symptoms, such as lability of affect, depression, irritability may be alternative manifestations. We as a society should be taking note and improving life for those with this specific disability.

Paroxysmal disorders; a brain firing perspective to terminology and diagnosis
The ethicobiopsychofamiliosociocultural approach. (Part 8)
Vernon M Neppe MD, PhD, FRSSAf, DFAPA, BN&NP, MMed.

There is an ethics to the practice of medicine, an attempt to try to improve the patient at every kind of level. We often use biological treatments, such as medications, for underlying biological conditions. The manifestation of Paroxysmal Somatoform Disorder is a typical example, however, of psychological triggers producing conditions which may appear to manifest physically but have an underlying psychological component, most likely predisposed by an underlying biological basis. The role of the family within all these conditions is enormously important, and education is highly relevant in that regard. Our society is both accepting and rejecting of such conditions—accepting by recognizing aspects of illness, and rejecting by not being aware of the manifestations that patients cannot fully control.

Cultures are so variable. In some cultures, epilepsy is regarded as "the Sacred Disease" as Hippocrates put it. In others, there is the awareness of the potential heightened level of reality of patients with seizure disorders.

Putting these different system levels together, we have the ethicobiopsychofamiliosociocultural framework for paroxysmal conditions, as well as any other medical condition. Indeed, we can make this a basis for the various different systems approaches.

As an aside, the term, ethicobiopsychofamiliosociocultural appears first in my book, *Cry the Beloved Mind.*[37] It is technically the longest word in the English language, 35 letters with ethicobiopsychofamiliosocioculturality beating out supercalifragilisticexpialidocious (34 letters), which Webster's Dictionary still lists as the longest, other than some complex combination suffixes given to chemicals or generally non-existent medical conditions. It also far beats out an early pretender, floccinaucinihilipilification (29 letters) meaning estimating worthlessness, which was the same length as an earlier term of mine, biopsychofamiliosociocultural which originally appeared in 1989 in the first edition of *Innovative Psychopharmacotherapy*.[17]

Ultimately, one may find a time where one is applying more systems and it would then not be inappropriate to talk about the ethicospirituobiopsychofamiliosocioculturaloeconimopoliticomilitaral approach. Clearly such words have adverbs, ethicospirituobiopsychofamiliosocioculturaloeconimopoliticomilitarally and nouns such as ethicospirituobiopsychopharamacofamiliosocioculturaloeconimopoliticomilitarality (80 letters). Lengthy terms such as these must be meaningful in context and the broadest approach in a military communist dictatorship may allow appropriate use of such terms! But not here… All of these are not just a variety of different terms put together, but reflect our various systems approaches and the unity not only of medicine, but of all our thinking.

The approach to these paroxysmal conditions has, indeed, required this ethicobiopsychofamiliosocioculturality and more. The ethics relates to our need to act to assist individuals who are photosensitive from becoming ill, initially at least as a society, putting up appropriate warnings and realizing that the cultural fabric of flashing lights for fun may be harmful. All paroxysmal conditions, be they epileptic seizures, paroxysmal somatoform disorder or paroxysmal neurobehavioral disorder all have biological bases, require pharmacotherapy in approach and appropriate psychological management and understanding.

The concept of paroxysmal in medicine has been neglected: It is far easier to delineate the physical signs and objectively demonstrate conditions that are either acute but persist, such as eliciting acute inflammation of the throat based on a red, swollen pharynx and mild pyrexia with a history of sore throat, and chronic conditions such as an underlying heart valve lesion that persists whenever one sees the patient. Contrast this with episodic conditions: These are far more difficult to appreciate as the patient may be normal most of the time, but manifest acute, profound, severe and at times overwhelming anger.

This totally changes their relationship with their environment, with their families, with their culture, with their society, with their occupational interactions. Patients may manifest confusion at times, with clouding of consciousness or disorientation or may manifest subtle impairments of affect, emotionality, and of drive, of volition. All of these mental status features may produce a combination in relation to their environment which can impact their lives and impact others. We are dealing with an ethicobiopsychofamiliosociocultural world, and the world of the episodic, of the paroxysmal, be it a paroxysmal sneeze or cough or several paroxysmal disorders. Examples of these disorders are Paroxysmal Neurobehavioral Disorders with its various sub-manifestations in different aspects of mental status; Paroxysmal Somatoform Disorder, largely synonymous with the conditions that were previously called Hysteroepilepsy, Hysteroseizures, Pseudoseizures and Nonepileptic Seizures; Paroxysmal Startle Disorder, which may be one major manifestation of this Paroxysmal Somatoform Disorder; and Paroxysmal Photosensitive Disorder, which rarely manifests in frank seizure phenomena, but possibly more commonly involves flashing lights at a specific frequency inducing subtle behavioral, cognitive and affective phenomena or significant headaches. Recognition of these disorders is critical so that appropriate management can take place. Moreover, the categorization of paroxysmal disorders creates a better way of conceiving of these episodic conditions.

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References:

1. Neppe, VM. The electrical-chemical dichotomy: A journey of two continents, in *The History of Psychopharmacology Autographical Accounts. Volume 4*, 4 Edited by Ban T. Budapest, Hungary, Animula, 2004, 455-461.

2. Neppe, VM. Carbamazepine as adjunctive treatment in nonepileptic chronic inpatients with EEG temporal lobe abnormalities. *J Clin Psychiatry*. 1983, 44:9, 326-331.

3. Neppe, VM. Carbamazepine as adjunct treatment in the chronic psychiatric patient with electroencephalographic temporal lobe foci, in *Abstracts: Epilepsy International Congress, Kyoto, Japan*, 1981, 149.

4. Neppe, VM. Carbamazepine in the psychiatric patient. *Lancet*. 1982, 2:8293, 33.

5. Okuma, T, Inanaga, K, Otsuki, S, Sarai, K, Takahashi, R, et al. Comparison of the antimanic efficacy of carbamazepine and chlorpromazine: a double-blind controlled study. *Psychopharmacology (Berl)*. 1979, 66:3, 211-217.

6. Post, RM. Use of the anticonvulsant carbamazepine in primary and secondary affective illness: clinical and theoretical implications. *Psychol Med*. 1982, 12:4, 701-704.

7. Neppe, VM, Tucker, GJ. Modern perspectives on epilepsy in relation to psychiatry: classification and evaluation. *Hosp Community Psychiatry*. 1988, 39:3, 263-271.

8. Neppe, VM, Tucker, GJ. Neuropsychiatric aspects of seizure disorders, in *Textbook of Neuropsychiatry* Edited by Yudofsky SC, Hales RE. Washington,D.C., American Psychiatric Press, 1992, 397-426.

9. Ballenger, JC, Post, RM. Carbamazepine in manic-depressive illness: a new treatment. *Am J Psychiatry*. 1980, 137:7, 782-790.

10. Okuma, T, Inanaga, K, Otsuki, S, Sarai, K, Takahashi, R, et al. A preliminary double-blind study on the efficacy of carbamazepine in prophylaxis of manic-depressive illness. *Psychopharmacology (Berl)*. 1981, 73:1, 95-96.

11. Neppe, VM. Non-epileptic symptoms of temporal lobe dysfunction. *S Afr Med J*. 1981, 60:26, 989-991.

12. Neppe, VM (eds). *Carbamazepine Use in Neuropsychiatry : J Clin Psychiatry Supplement 4*. 1988.

13. Neppe, VM, Bowman, BR, Sawchuk, KS. Carbamazepine for atypical psychosis with episodic hostility. *Journal of Nervous & Mental Disease*. 1991, 179:7, 439-441.

14. Neppe, VM. Review Article: symptomatology of temporal lobe epilepsy. *South African Medical J*. 1981, 60:27, 902-907.

15. Post, RM, Uhde, TW, Putnam, FW, Ballenger, JC, Berrettini, WH. Kindling and carbamazepine in affective illness. *J Nerv Ment Dis*. 1982, 170:12, 717-731.

16. Neppe, VM. *Innovative Psychopharmacotherapy*. New York: Raven Press. 1990.

17. Neppe, VM. *Innovative Psychopharmacotherapy*. New York: Raven Press. 1989.

18. Neppe, VM. Carbamazepine, limbic kindling and non-responsive psychosis, in *Innovative Psychopharmacotherapy* Edited by Neppe VM. New York, Raven Press, 1989, 123-151, Ch 125.

19. Neppe, VM. Differing perspectives to the concept of temporal lobe epilepsy. *The Leech*. 1982, 52:1, 6-10.

20. Neppe, VM. Temporal lobe symptomatology in subjective paranormal experients. *Journal of the American Society for Psychical Research*. 1983, 77:1, 1-29.

21. Neppe, VM. *The Psychology of Déjà Vu: Have I been Here Before?* Johannesburg: Witwatersrand University Press. 1983.

22. Persinger, MA. Seizure suggestibility may not be an exclusive differential indicator between psychogenic and partial complex seizures: the presence of a third factor. *Seizure*. 1994, 3:3, 215-219.

23. Stein, MB, Uhde, TW. Infrequent occurrence of EEG abnormalities in panic disorder. *Am J Psychiatry*. 1989, 146:4, 517-520.

24. Blumer, D, Neppe, V, Benson, DF. Diagnostic criteria for epilepsy-related mental changes. *Am J Psychiatry*. 1990, 147:5, 676-677.

25. Blumer, D. On the psychobiology of non-epileptic seizures, in *Non-epileptic seizures* Edited by Gates JR, Rowan AJ. Boston, Butterworth-Heineman, 2000, 305-310.

26. Blumer, D, Adamolekun, B. Treatment of patients with coexisting epileptic and nonepileptic seizures. *Epilepsy & Behavior*. 2008 (In press),

27. Ives, JR, Drislane, FW, Schachter, SC, Miles, DK, Coots, JF, et al. Comparison of coronal sphenoidal versus standard anteroposterior temporal montage in the EEG recording of temporal lobe seizures. *Electroencephalogr Clin Neurophysiol*. 1996, 98:5, 417-421.

28. Burneo, JG, Steven, DA, McLachlan, RS, Parrent, AG. Morbidity associated with the use of intracranial electrodes for epilepsy surgery. *Can J Neurol Sci*. 2006, 33:2, 223-227.

29. Diehl, B, Luders, HO. Temporal lobe epilepsy: when are invasive recordings needed? *Epilepsia*. 2000, 41 Suppl 3, S61-74.

30. Bechtereva, NP, Abdullaev, YG. Depth electrodes in clinical neurophysiology: neuronal activity and human cognitive function. *Int J Psychophysiol*. 2000, 37:1, 11-29.

31. Wieshmann, UC. Clinical application of neuroimaging in epilepsy. *J Neurol Neurosurg Psychiatry*. 2003, 74:4, 466-470.

32. Maehara, T. Neuroimaging of epilepsy. *Neuropathology*. 2007, 27:6, 585-593.

33. Duncan, JS. Neuroimaging methods to evaluate the etiology and consequences of epilepsy. *Epilepsy Res*. 2002, 50:1-2, 131-140.

34. Gonz Aacute Lez, J, Saiz, A, Mart Iacute, NH, Juntas, R, D, PER-MIN, et al. [The role of ambulatory electroencephalogram monitoring: experience and results in 264 records.]. *Neurologia*. 2008,

35. Chu, NS. Long-term ambulatory EEG evaluation of epileptic seizures and non-epileptic attacks: a study of 100 patients. *Zhonghua Yi Xue Za Zhi (Taipei)*. 1988, 42:5, 359-366.

36. Batho, KM, Leary, PM, Arens, L. The ambulatory electro-encephalogram as a diagnostic tool in a children's hospital. *S Afr Med J*. 1986, 70:7, 428-430.

37. Neppe, VM. *Cry the Beloved Mind: A Voyage of Hope.* Seattle: Brainquest Press (with Peanut Butter Publ. Publishing). 1999.

38. Marchetti, RL, Kurcgant, D, Neto, JG, von Bismark, MA, Marchetti, LB, et al. Psychiatric diagnoses of patients with psychogenic non-epileptic seizures. *Seizure*. 2008, 17:3, 247-253.

39. Varela, HL, Taylor, DS, Benbadis, SR. Short-term outpatient EEG-video monitoring with induction in a veterans administration population. *J Clin Neurophysiol*. 2007, 24:5, 390-391.

40. Ribai, P, Tugendhaft, P, Legros, B. Usefulness of prolonged video-EEG monitoring and provocative procedure with saline injection for the diagnosis of non epileptic seizures of psychogenic origin. *J Neurol*. 2006, 253:3, 328-332.

41. Schomer, DL. Ambulatory EEG telemetry: how good is it? *J Clin Neurophysiol*. 2006, 23:4, 294-305.

42. Schachter, SC, Ito, M, Wannamaker, BB, Rak, I, Ruggles, K, et al. Incidence of spikes and paroxysmal rhythmic events in overnight ambulatory computer-assisted EEGs of normal subjects: a multicenter study. *J Clin Neurophysiol*. 1998, 15:3, 251-255.

43. Neppe, VM. An investigation of the relationship between temporal lobe symptomatology and subjective paranormal experience - MMed Psych thesis. Johannesburg, University of the Witwatersrand, 1979, 1-178 &i-xv.

44. Neppe, VM, Ellegala, D, Baker, C. The Inventory of Neppe of Symptoms of Epilepsy and the Temporal Lobe (INSET) : A new rating scale. *Epilepsia*. 1991, 32:5, 4.

45. Neppe, VM. A study of déjà vu experience : thesis. Johannesburg, University of the Witwatersrand, 1981, 1-588, Vol 581-584.

46. Neppe, VM. Anomalies of smell in the subjective paranormal experient, in *Psychoenergetics - J of Psychophysical Systems*, 1983, 11-27.

47. Engel, J, Jr., Henry, TR, Risinger, MW, Mazziotta, JC, Sutherling, WW, et al. Presurgical evaluation for partial epilepsy: relative contributions of chronic depth-electrode recordings versus FDG-PET and scalp-sphenoidal ictal EEG. *Neurology*. 1990, 40:11, 1670-1677.

48. Staba, RJ, Wilson, CL, Bragin, A, Fried, I, Engel, J, Jr. Sleep states differentiate single neuron activity recorded from human epileptic hippocampus, entorhinal cortex, and subiculum. *J Neurosci*. 2002, 22:13, 5694-5704.

49. Cummings, JL, Trimble, M.R. *Concise Guide to Neuropsychiatry and Behavioral Neurology*. Washington, DC: American Psychiatric Press. 2002.

50. Walczak, TS, Papacostas, S, Williams, DT, Scheuer, ML, Lebowitz, N, et al. Outcome after diagnosis of psychogenic nonepileptic seizures. *Epilepsia*. 1995, 36:11, 1131-1137.

51. Kuyk, J, Spinhoven, P, van Dyck, R. Hypnotic recall: a positive criterion in the differential diagnosis between epileptic and pseudoepileptic seizures. *Epilepsia*. 1999, 40:4, 485-491.

52. Kuyk, J, Jacobs, LD, Aldenkamp, AP, Meinardi, H, Spinhoven, P, et al. Pseudo-epileptic seizures: hypnosis as a diagnostic tool. *Seizure*. 1995, 4:2, 123-128.

53. Goldstein, LH, Drew, C, Mellers, J, Mitchell-O'Malley, S, Oakley, DA. Dissociation, hypnotizability, coping styles and health locus of control: characteristics of pseudoseizure patients. *Seizure*. 2000, 9:5, 314-322.

54. Barry, JJ, Atzman, O, Morrell, MJ. Discriminating between epileptic and nonepileptic events: the utility of hypnotic seizure induction. *Epilepsia*. 2000, 41:1, 81-84.

55. Parra, J, Kanner, AM, Iriarte, J, Gil-Nagel, A. When should induction protocols be used in the diagnostic evaluation of patients with paroxysmal events? *Epilepsia*. 1998, 39:8, 863-867.

56. Moore, DP. Non-epileptic seizures and depth recording. *Neurology*. 1998, 50:3, 832-833.

57. Finke, J. [Non-epileptic seizures]. *Z Allgemeinmed*. 1972, 48:32, 1486-1491.

58. McDade, G, Brown, SW. Non-epileptic seizures: management and predictive factors of outcome. *Seizure*. 1992, 1:1, 7-10.

59. Parraga, HC, Kashani, JH. Treatment approach in a child with hysterical seizures superimposed on partial complex seizures. *Can J Psychiatry*. 1981, 26:2, 114-117.

60. Guberman, A. Psychogenic pseudoseizures in non-epileptic patients. *Can J Psychiatry*. 1982, 27:5, 401-404.

61. Gates, JR, Ramani, V, Whalen, S, Loewenson, R. Ictal characteristics of pseudoseizures. *Arch Neurol*. 1985, 42:12, 1183-1187.

62. Slavney, PR. In defense of Pseudoseizure. *Gen Hosp Psychiatry*. 1994, 16:4, 248-250.

63. Merskey, H. Commentary: conversion fits, pseudo-attacks, or doxogenic seizures. *Gen Hosp Psychiatry*. 1994, 16:4, 246-247.

64. Kuyk, J, Swinkels, WA, Spinhoven, P. Psychopathologies in patients with nonepileptic seizures with and without comorbid epilepsy: how different are they? *Epilepsy Behav*. 2003, 4:1, 13-18.

65. Binder, LM, Salinsky, MC, Smith, SP. Psychological correlates of psychogenic seizures. *J Clin Exp Neuropsychol*. 1994, 16:4, 524-530.

66. Neppe, VM. Pseudoseizures or somatoform spells; hysteroepilepsy or somatoform spell disorder. *http://www.pni.org/neuropsychiatry/seizures/epilepsy/pseudo_seizure.html*. 1992, 1992,

67. Ahern, GL, Howard, GFd, Weiss, KL. Posttraumatic pilomotor seizures: a case report. *Epilepsia*. 1988, 29:5, 640-643.

68. Neppe, VM, Kaplan, C. Short-term treatment of atypical spells with carbamazepine. *Clin Neuropharmacol*. 1988, 11:3, 287-289.

69. Angus-Leppan, H. Seizures and adverse events during routine scalp electroencephalography: a clinical and EEG analysis of 1000 records. *Clin Neurophysiol*. 2007, 118:1, 22-30.

70. Verrotti, A, Tocco, AM, Salladini, C, Latini, G, Chiarelli, F. Human photosensitivity: from pathophysiology to treatment. *Eur J Neurol*. 2005, 12:11, 828-841.

71. Kroner-Herwig, B, Ruhmland, M, Zintel, W, Siniatchkin, M. Are migraineurs hypersensitive? A test of the stimulus processing disorder hypothesis. *Eur J Pain*. 2005, 9:6, 661-671.

72. Lai, CW, Dean, P, Ziegler, DK, Hassanein, RS. Clinical and electrophysiological responses to dietary challenge in migraineurs. *Headache*. 1989, 29:3, 180-186.