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Paroxysmal Disorders in Neuropsychiatry: Why Episodic Disorders Must be Accounted For

Research Article

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Abstract

Possibly the most under-diagnosed of all medical conditions are the episodic ones linked with the brain. These paroxysmal disorders are often ignored because when the patient presents to the mental health practitioner (MHP) they appear well. Very often, they deny that anything is wrong, and yet their families cry out for the MHP to help them. But this is only one side. These patients may have one or more of several conditions and many are not even listed in diagnostic bibles such as DSM5. They require revised terminology, which is sometimes non-existent. They need to be diagnosed, yet the criteria to evaluate them are usually unknown. The broader impacts on spouses, partner and families must be understood and in return how much role those varying ethicospirituobiopsychofamilioethnicosociocultural considerations may play in alleviating or aggravating these conditions. Episodic phenomena are difficult to evaluate, and the need for appropriate management after the initial and continued evaluations make them a challenge. Additionally, the absence of proper diagnostic listings makes even potential insurance remuneration more difficult.

[a]

The author places these conditions in a varied basket of diagnoses and syndromes, called "paroxysmal disorders". Clearly, the organic elements must be particularly carefully treated, and the underlying psychological conditions handled potentially in a therapeutic relationship or at least with appropriate support.

The author has been fortunate enough to be involved in pioneering the discipline of neuropsychiatry and behavioral neurology having established the first division of neuropsychiatry in the USA in 1986 and having led the first USA and International Delegation in Neuropsychiatry and Psychopharmacology. This has necessitated developing a string of diagnostic questionnaires and standardized follow up historical questions. These various historical measures are 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).

However, I have been fortunate to also have available key, but highly specialized investigations such as Home Ambulatory Electroencephalography with Video Monitoring (VAEEG).

Using these tools, I have over the past two decades recognized several major clinical conditions:

1. Paroxysmal Neurobehavioral Disorder is an important major condition. This condition seldom manifests in frank seizure phenomena, but alternatively in behavioral, cognitive and affective phenomena that may be subtle, or in significant headaches, like migraines.
2. Mesial temporal lobe epilepsy is a specific but important and commonly missed condition.
3. The differentiation of what be abnormal electrocerebral firing, atypical seizure events, temporolimbic instability and non-epileptic events are tabulated in detail.
4. With Dr Neppe, his colleague, Dr Dietrich Blumer regarded the term "Paroxysmal Somatoform Disorder" as far the most appropriate way to describe a whole series of related conditions largely synonymous with the preceding labels of Nonepileptic Seizures, Pseudoseizures, Hysterical epilepsy and Hysteroseizures.
5. A rare controversial condition, Paroxysmal Startle Disorder, may be one specific major manifestation of this Paroxysmal Somatoform Disorder and might demonstrate an important biological mechanism for some kinds of Paroxysmal Somatoform Disorder. This is uncommon enough for us to fit this within the fabric of Paroxysmal Somatoform Disorder.
6. Dr Neppe has also recognized an important variant of electro-cerebral firing, namely Paroxysmal Photosensitive Disorder.
7. Finally, Dr Neppe reports on a new condition that has no organic brain basis and has psychological components which he recognizes as Atypical Episodic Disorder.

The author then describes several useful questionnaires and ways to evaluate the patients.

a) The INSET

b) The SOBIN

Also, Video Ambulatory EEG usage and its advantages over regular EEG are discussed. These new categorizations of paroxysmal disorders create a more standard and easier way to conceptualized these episodic conditions. They remain

[a]This series of articles focuses 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. As with all

controversial because they involve new ways of seeing old phenomena. Many practitioners may claim to have never seen them: But then one only sees what one is aware of.

He describes a clinical retrospective research analysis showing that there appears to be a legitimate condition where patients with ostensible mesial temporal lobe abnormalities as evidenced by severe explosive behavior, marked mood lability and some kinds of blankings with or without headache, or post-event sleepiness or nausea, should respond in every instance to appropriate anticonvulsant medication plus adjuncts as required. This is irrespective of whether these patients have abnormal home ambulatory electroencephalograms on three days of monitoring.

A word of caution: These entities do not officially exist. There are no approved treatments and no marketed drugs for these indications. This makes management controversial. But essentially, this does not make these conditions any less real. We clinicians must solve the dilemma of management of problematic symptoms.

Keywords: Affective; Anticonvulsants; Antipsychotic Medication; Atypical Episodic Disorder 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); Hystero-epilepsy; Hystero seizures; Inventory of Neppe of Symptoms of Epilepsy and the Temporal Lobe (INSET); Irritability; Kindling; Medicine; Lamotrigine; 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; Pseudo seizures; Rage attacks; Recurrent; Refractory; Seizures; Soft Organic Brain Inventory Of Neppe (SOBIN); Somatization; Spells; Standardization; Syncope; Temporal lobe; Temporolimbic instability; Temporal lobe dysfunction; Terminology

Paroxysmal Disorders: The old and the New (Part 1)

My dilemma

I have a dilemma. As an academic, I am used to communicating in two ways. In writing, in professional articles, I like to ensure that everything I say can be justified, generally be referencing any comment in some detail. *This exemplifies the Science of Medicine and of Psychology.* While this is an approach that still exists in this article series, and despite its more than a hundred references, I am mainly communicating in this paper *as if I were doing rounds with my medical residents*. Here the aspect that is pertinent is often *"this in my experience is what I've found, or how I think it works"*. Whereas this is fine in teaching and very valuable, in fact, very appropriate, I am communicating in this article in this way. It is more speculative, more experiential, and more based on the experience of a supposed leading expert in the field. This exemplifies the Art of Medicine and of Psychology. I will use mainly this latter approach—the Art—though I will try wherever possible to integrate some Science in this article. But we're dealing with such a pioneering area, there is at this point, necessarily, more creative, anecdotal Art, than there is well-justified, well-demonstrated Science. If it were the reverse, there would be no need for this pioneering paper!

How anticonvulsant use arose in psychiatry (Part 1A) [1]

In1977, in South Africa, 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 had to be severely sedated, and this produced further side-effects. He did not improve when he had been given even the doses of antipsychotic agent most psychotic patients would improve on. Higher dosage produced intolerable side-effects. He was ostensibly condemned to a life in a mental hospital.

I carefully considered my options. The patient could tolerate low doses of antipsychotic agent without side-effects but without response. Should I also give him low doses of an anticonvulsant? I chose phenytoin. The patient responded dramatically. He effectively normalized and yet he did not have any manifest seizure phenomena.

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 [2].

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, it had a narrow therapeutic spectrum and slightly higher doses than that could produce toxicity. Also it did not improve patients' cognitive functions, had potential paradoxical effects in seizures with too high a dose, and the impression at that time was that it was less effective than a newer anticonvulsant, carbamazepine.

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, and should hypothetically have worked better in these postulated focal paroxysmal (intermittent) abnormal electrical firing. Indeed, there was very

little disturbance of thinking, and on the appropriate doses, every one of these patients improved profoundly clinically. This randomized, crossover design, placebo controlled study became the landmark for research in the area [3], and I presented it at the Epilepsy International Congress in Japan in 1981 [4]. It was the first (and remains the only) double blind study of Carbamazepine as adjunctive medication in patients with temporal lobe abnormalities on EEG [3,5], 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 [6] and also Robert Post at the National Institute for Mental Health in the United States [7], totally changed the face of psychiatry such that millions of patients were being treated with anticonvulsants [8,9] for conditions such as Bipolar Disorder and Nonresponsive Psychosis with irritability and agitation [6,7,10,11].

The controversy [12]

This was a condition without a name and it has still remained so. I had labeled it "temporal lobe dysfunction" [13], 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 "tonic clonic seizures") or with "partial seizures" (seizures that have a specific origin in the higher brain, often 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 slow wave manifestations (e.g. <7 cycles per second in bursts or <4/ second). But not all paroxysms are epileptic seizures: Paroxysms of coughing or sneezing are not 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 (since the 1930s), 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. Alternatively, we would not see firing because it was episodic and we would not see any abnormalities during our short EEG measure [14,15].

Yet, we might have seen some slowing in some focus of the brain, such as the temporal lobe [16]. We would debate what these were. If they were not seizures, 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" were too non-specific. So we tried "atypical spells". But what did this "atypicality" imply?

By 1980, I had linked up these conditions to the phenomenonof "kindling", which Dr. Graham Goddard had characterized as the lighting of an abnormal fire in the brain. In effect, a small stimulus that previously was sub threshold suddenly reached threshold levels and evoked a clinically abnormal response—in the rat model it was seizures. It seemed this was what we were dealing with [17]. 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*" [18,19]. "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. We know that drugs such as cocaine and possibly amphetamine will keep lowering that threshold. These would be examples of chindling. 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 [20]. Given the wealth of recreational drug abuse the likelihood is that this is the most common phenomenon today that causes these abnormal brain firing symptoms.

But we were still looking for a name for my condition I was labeling "temporal lobe dysfunction". I was using the term "non-epileptic temporal lobe dysfunction" to differentiate it from "epileptic temporal lobe dysfunction" so as not to distress my more staid neurological colleagues would not have a non-epileptic seizure! [21]. But already I had delineated 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. I needed to be able to delineate these target symptoms. It was necessary to develop a series of questionnaires. The first such questionnaire was the Neppe Temporal Lobe Questionnaire. This had already become the subject of intensive analysis in my early work (Master's thesis) on the temporal lobe and subjective experience, in the mid- and late-1970s [22] and later on in my and later in my Doctoral thesis on déjà vu [23]. It was embraced by another doctoral student and used thereafter in other research. Subsequently, it was developed by Dr. Michael Persinger in Canada in his research [24], and by Dr. Richard Roberts in Iowa [24], as well as by Dr. Marty Stein in Washington DC [25]. All modified it, though the latest version of 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. Was this adequate? I wanted to have another measure, too, to assist in picking up more static impairments of higher brain function. And so I developed the *SOBIN* (Soft Organic Brain Inventory of Neppe).

Dr. Dieter 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 studying something that was not usual. We were two

neuropsychiatrists trying to understand the science of epilepsy—epileptology. This was a different direction to most neurologists who insisted that anticonvulsants could only be used for seizure disorders and later on for certain kinds of neuralgic pain. 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 [26].

We needed a name for this new condition of "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.

Table 1A: Terminology.

a)	Epilepsy: Two or more seizures separated in time without symptomatic causes.
b)	Chindling: Induction of seizures after repetitive sub-threshold chemical stimulation e.g. cocaine
c)	Electrocerebral: Firing in the brain.
d)	Kindling: Induction of seizures after repetitive sub-threshold electrical stimulation.
e)	Neuralgia: Abnormal pain syndrome in the peripheral nerves.
f)	Paroxysmal: Episodic brain firing.
g)	Seizure: Abnormal electrical episodic cerebral firing.
h)	Temporolimbic instability: Abnormal symptoms based on the mesial temporal lobe and limbic system.

The other paroxysmal disorders

But Dr. Blumer and I realized there was a need to clarify such related terminologies. We recognized various other paroxysmal disorders. What about patients who were being labeled as having "hysterical seizures", but which were not epileptic? Do terms like *"paroxysmal somatoform disorder"* and individual *"paroxysmal somatoform spells"* fit [27]? What about that subpopulation of these "hysterical seizures" who were apparently using a "startle" mechanism—so-called *"paroxysmal startle disorder"* [28]?

And what about the underlying symptoms that we needed to analyze to find suitable patients? We recognized we could better improve our yield by using the technology of *Home Ambulatory EEG*, later adapted to include video monitoring of the events as well. 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? And what was its significance? And so the exploration of some remarkable episodic conditions in the brain began.

Paroxysmal Neurobehavioral Disorder: The episodic brain condition (Part 2)

We have named the disorder without a name "Paroxysmal neurobehavioral disorder". Certainly in the neuropsychiatric context it is common. It's important to define the criteria. The essential element is the episodic behavior. Effectively, we've postulated this is due to brain components producing changes in mental state and manifesting in changes in behavior as a consequence of abnormal paroxysmal firing. The exact symptoms depend on the exact location of the symptoms in the brain.

We were in virgin territory. It seems obvious today that we must take episodic disorders seriously, yet this was not so in the 1980s. Certain conditions are episodic based on both logic and empirical observation of response to anticonvulsants. We postulated this related to some kind of electrical pathophysiological firing within the brain. Although, Dr. Blumer and I have described this condition in lectures and in diagnoses, this actual label of Paroxysmal Neurobehavioral Disorder was first written in a chapter relating to this condition but not with the specifics in this article in 1992 for a book, but the book was never published.

Initially we called these conditions "spells". We did not want to label them as: "seizures" or "complex partial seizures" because they were not, and such a label may have been prejudicially harmful to the patients, particularly with them still driving and having no reason to stop. Some years later, I began to call them "atypical spells". Nevertheless, 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 [26].

I have a major dilemma here: Usually, when I publish articles there may be a clinical component but I'm able to justify each and every point, often based on research. Now the information below is different: It is not anecdotal but it relates to the insights of an experience clinician who has pioneered this discipline these part three decades. One could argue about the evidence: Let's just call this a curbside consult with the Attending Physician in this discipline. My experience has been first see what's out there, then do the research. This is the preliminary seeing what's out there. And importantly, my fundamental ideas from 1989 till now have not changed in substance, though the terminology may be clearer. Also the one condition that has arisen out of this has been *Mesial Temporal Seizure Disorder.*

Classification of PND

Paroxysmal Neurobehavioral Disorder (PND) was our attempt at indicating that this broad spectrum of conditions that was not associated with seizures, yet consistently responsive to anticonvulsant medication, based on my extensive experience of three decades, with these conditions, had an episodic quality about them, and yet had a variety of different features.

We hypothesized that this was usually due to temporal lobe abnormalities in general. This is because the temporal lobe the great integrator of the brain, and when there is abnormal functioning this produces "disintegrative symptoms".

These may manifest with abnormal brain firing, or potentially it may manifest as a nonepileptic malfunction. Either way, we

find that consistently certain anticonvulsant medications on their own, or sometimes with other medications, help.

Classification of PND

In 1989, we attempted our first classification of these various paroxysmal disorders. (Table 1 Section A with my 2015 modification in section B). We realized there were many possible symptoms, most frequently occurring in combination.

PND Mood disorder: PND commonly is associated with a *mood disturbance* at times. Here 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 might be misdiagnosed as bipolar because of periods of elevated mood. However, the mood elevations in "PND – mood variant", is not over days, but over seconds and minutes. There are profound fluctuations of mood and the patient can notice the switch on and off of symptoms within seconds. This is a key example of how one has to phenomenologically analyze even the most basic of symptoms to ensure that any later analysis involved evaluating *"like symptoms with like, not with unlike"* [29-31].

Importantly, at one point one of the leading experts on affective disorders and anticonvulsants, Dr Robert Post, analyzed temporal lobe type symptoms and found them as common in bipolar disorder: He concluded this did not differentiate symptoms. In another context, the same group recognized the importance of phenomenology. However, with great respect, unless one phenomenologically analyzes symptoms in detail, the information will end up fallacious because "*like* is compared with *not-like*". I have demonstrated this repetitively including in both a Masters [32] and Doctoral thesis [33], analyzing the phenomenology of déjà vu [34,35], of olfactory hallucinations [36], and of temporal lobe symptomatology [22,37,38], so such analyses are very contextually relevant. Effectively, once one elicits the symptom is present, it must be looked at in sufficient detail, for example:

Are there possible post-ictal type symptoms like headache, sleepiness, nausea, exhaustion or confusion?

Is there some kind of symptom march?

PND Irritability disorder: PND is almost invariably associated the irritability. Patients have explosive outbursts which they cannot fully control. These outbursts may or may be precipitated by the environment or stress or a medical condition. In a minority of cases, they are linked with some amnesia for the anger. The outbursts also often have an impulsive, unplanned component. Patients recognize these events when they are given choices of different kinds of anger and it's often combined with a gradual build-up of stress or a little controlled anger first. These episodes are 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. Today, based on empirical data, we know, indeed, that this constitutes temporolimbic instability.

PND Psychotoform Type: A third but still common variant involves some kind of psychotic presentation. The patients exhibit paranoid delusional or cognitive distortions. Initially they have bizarre transient thoughts that could later become entrenched as delusional, if they are left untreated. They may also experience perceptual distortions, which could be visual where the hallucinations may be full level visions or just distortions, olfactory hallucinatory with episodic smell distortions, or auditory distortions, such as buzzes or hums but sometimes hearing voices. Characteristically, these patients do not have the full self-referential features of a psychosis and the whole episode may last seconds, minutes or hours.

PND with Anxiety Disorder: Another possible manifestation is the anxiety component, which appears less frequent alone than the irritability. Many such patients exhibit any or several agitation related features: ruminations — obsessional thoughts which are repetitive and go on and on, with mulling; panic episodes with acute anxiety—so-called fear of a fear, phobias directed towards avoiding specific events, thoughts or actions; alternatively, they may exhibit generalized anxiety phenomena. These also reflect the limbic elements.

PND with blanking: These patients report fluctuating difficulties with focusing, and will often regard this as "attention deficit disorder", though this more likely involves losing time or blanking out or of difficulties with memory.

PND with confusion: Some patients have real confusional episodes with memory impairments, almost as if they were not registering information because of clouded consciousness.

PND with personality dysfunction: Some families or loved ones report personality changes. For example, these patients may exhibit increased rigidity of thinking, misinterpret information, have difficulties conceptualizing, have difficulties registering and all these features lead to attempted adaptation that produce changes in functioning and personality difficulties that are for the worse.

PND with bodily elements: Pain, fatigue and myalgic features: Originally we had included Paroxysmal Somatoform Disorder as one subtype of PND but I now see this as a separate condition, which could be a form of nonepileptic seizure. However, there are PND expressions in somatization and pain, including headaches.

PND Combined: Most PND manifests with combinations of symptoms and we can list these as such: PND with irritability, blanking and headaches, constitutes a good descriptive way of portraying this.

Table 2A reflects possibly the most common kinds of PND: However, in some patients with Paroxysmal Neurobehavioral Disorder, the episodic phenomena may have idiosyncratic variants. We recognize that these are usually not single entities, and they could be complex and manifest with at least two or three different categories. This is why as with all the prevailing psychiatric nomenclatures, we introduce a "not otherwise specified" category.

Table 2A: Paroxysmal Neurobehavioral Disorder .

	1989 terminology	2015 terminology
1	MOOD (like elated, dysphoric, cyclothymic, bipolar)	PND Mood disorder
2	IRRITABLE, IMPULSIVE (like intermittent organic explosive disorder)	
3	PSYCHOTOFORM (like paranoid, perceptual, delusional, cognitive distortions)	PND Psychotoform Type
4	ANXIETY (like ruminative, panic, phobic, generalized)	PND with Anxiety Disorder
5	BLANKING	PND with blanking
6	AMNESTIC or CONFUSIONAL phenomena (like attentional, paramnesic, clouding, blank outs)	PND with confusion
7	PERSONALITY (like changes in tolerance, skill set, interactions)	PND with personality dysfunction
8	Paroxysmal Somatoform	PND with bodily elements
9	COMPLEX (>3 categories) Stipulated	PND Combined
10	Not otherwise specified	PND Not otherwise specified

(Neppe, Blumer 1989 [39]; modified 2008 [1,12]; updated by Neppe 2015 (in this article).

To answer the initial question: Are these legitimately Paroxysmal Neurobehavioral conditions Disorders or Syndromes? Syndromes involve collections of symptoms with varying causes. In this instance, I believe we can call this condition Paroxysmal Neurobehavioral Disorder because we apparently have one cause namely abnormal brain firing responsive to anticonvulsants with if needed adjunctive medication. Just as in DSM 5 conditions [40], there is sometimes a variation of symptoms and therefore presentations, the core criteria can be applied in PND.

Management of Paroxysmal Neurobehavioral Disorder (PND) Part 3

The recognition of this PND disorder is critical. These patients were not being treated before. There was no known treatment and there still is enormous variation of these kinds of conditions without a name. Yet, I believe there are principles to apply.

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.

Despite there being no marketed drugs for these kinds of indications, these patients invariably appear to respond to anticonvulsant medications. This is our broader experience. The most common ones we've used have been lamotrigine (Lamictal) and carbamazepine (Tegretol, Carbatrol and others). My colleagues and I have not had as much success with efficacy with

i. Gabapentin, which, nevertheless, many seem to be using;

ii. Topiramate, because of toleration and side-effect issues; and with

iii. Valproate (Depakote) which was a great drug in its time, but tends to cause weight gain, and also, in our experience, has not been successful for this specific condition; and with

iv. Phenytoin (Dilantin), which sometimes seems to induce irritability and has a low therapeutic to toxic range variation.

So the choice of anticonvulsant, and the principles of starting low, and then monitoring for response of certain of the target symptoms above or side-effects.

We do not have double blind studies on this and these are not likely. The clinical changes are not slight but profound, and I wonder about the ethics of such studies versus placebo at this point. More pragmatically, these compounds are generic. Consequently, allocation of the requisite large amounts of funds comparing Drug A with Drug B would be unlikely. But even if funded, 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.

We have empirically and consistently seen success happen, repetitively many hundreds of times. These might reflect fundamental, yet unapproved principles of pharmacological management.

a) Management of PND spectrum is always out of labeling whatever anyone prescribes, because no medications are specifically indicated for it.

b) The anticonvulsants are often used in conjunction with other medications depending on the symptoms. I understand the anticonvulsants to effectively be potentially more curative, treating the underlying causes. The other psychopharmacological and systemic medications were often to for symptomatic management.

c) This postulated cerebral firing should theoretically respond to appropriate anticonvulsant medication if indeed this reflects abnormal electrical firing. So this is a diagnostic test based on what I call "Axis VI of DSM-V", namely pharmacological responsiveness.

The most common pertinent anticonvulsants in this context are in Table 3A.

Table 3A: Common Anticonvulsants.

Name	Key take home feature
Acetazolamide (Diamox)	Specialized and seldom used
Carbamazepine (Tegretol, Carbatrol, Epitol)	Remarkably effective, but complex pharmacokinetics
Clobazam (Onfi)	1-5 benzodiazepine; seems to retain efficacy
Clonazepam (Klonopin)	Excellent acutely but used out of labeling in anxiety and like the other 1-3 benzodiazepines may lose efficacy
Felbamate (Felbatol)	Excellent drug but threatening potential side-effects and some cognitive variations
Gabapentin (Neurontin)	Commonly used out of label for certain neuralgias and for sleep but appears less effective as an anticonvulsant
Lamotrigine (Lamictal)	Outstanding anticonvulsant, often of choice but careful dosing needed, including to avoid potential allergic reactions
Levetiracetam (Keppra)	Outstanding anticonvulsant, but varying dosing and cognitive effects limit its use.
Oxcarbazepine (Trileptal)	Daughter of carbamazepine, but easier to use, though clinically may vary more in efficacy, and more hyponatremia?
Phenobarbital	Oldest anticonvulsant available, sedative, depressive, significant interactions, not used much
Phenytoin (Dilantin)	Old anticonvulsant, significant interactions, small range of toxicity and clinical effects, varied cognitive effects
Pregabalin (Lyrica)	Excellent but sedative for some neuropathies particularly, but not caught on as much with seizures
Primidone (Mysoline)	Excellent early drug, daughter to phenobarbital
Tiagabine (Gabitril)	Neglected but excellent potential
Topiramate (Topamax)	Some inconsistent cognitive side-effects, dosing can vary from tiny to large, possible weigh loss
Valproate (Depakote as divalproex sodium)	Wonderful in its time, limited side-effects except sometimes significant weight gain and tremor, but in our experience not as good for these atypical PND symptoms
Valproic acid (Depakene)	Mother of valproate, similar features
Zonisamide (Zonegran)	Very long half life, some inconsistent cognitive side-effects

There is most frequently a need for appropriate adjunctive medications. This means that based on the symptoms above, almost every patient also need other medications in addition to the anticonvulsants.

a) I have been using the only marketed azapirone medication, namely buspirone, extremely frequently, as by far the most common adjunctive medication [18]. When used appropriately, it has few side-effects and is literally a life-saver because of its normalizing effects. This compound, buspirone, is a "normalizer" of serotonin [41]. It regulates the serotonin 1A receptor at both autoreceptor levels (at doses of 10 to 25mg/day in 2 or 3 divided doses), as well as post-synaptically (at doses of 30-60mg daily. I build the does gradually by e.g. 7.5mg/day every 4 days to 30mg bid, unless I encounter "non-vertiginous dizziness" [41]—a strange, likely serotonin 1A side-effect indicating a necessity to slightly lower the dose [42], and I ensure that the buspirone is given with meals (as nausea, otherwise, sometimes occurs) [42]. Buspirone is technically marketed for anxiety—I call it "anxioselective" [41] — and pharmacologically, it is much more similar in action and effects to the antidepressants than the "quick-fix" of the benzodiazepines [41].

b) At times when there is a depressive component, patients need antidepressant adjunct: Dr Blumer discovered that this subpopulation, at times, specifically responded to the (now long-forgotten) tricyclic antidepressants, and they are remarkable normalizers. Because my choice has been buspirone, I cannot adequately comment from my personal experience on tricyclics. Other more modern antidepressants, such as SNRI drugs like venlafaxine or desmethylvenlafaxine

(when the 2D6 gene shows marked inhibition) are good choices. These are sometimes used in severe depressions depending on specific symptom circumstances. I would not use SSRIs.

c) Thirdly, 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. My own preference has been doses usually ranging from 1mg to 5mg of aripiprazole (Abilify) daily. Sometimes paranoia, or frank delusional thought or auditory hallucinatory phenomena require higher doses of antipsychotics: These may also be used prophylactically in patients with such histories.

d) I find that if patients still have their post-ictal type headache, or report blankings or confusion, the dose of the lamotrigine should be increased.

e) Commonly systemic conditions must be managed. Hypovitaminosis D is epidemic in cold Northern cloudy climates requiring Vitamin D supplementation. Hypothyroidism clinically with TSH≥2.0 is very common. Overweight and diabetes must be managed.

The choices of exact pharmacology are complex, dose dependent and requires careful assessment. They are 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) [18,19].

Paroxysmal disorders: What is epileptic and non-epileptic? (Part 4)

Frequently those in Psychiatry and Psychology are referred patients for psychotherapy and psychiatric treatment having been labeled as having non-epileptic spells (NES) of some kind. It is our obligation to ensure that these patients indeed do not have seizures. A mistake may potentially be fatal for the patient.

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 or other causes including medications.

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. This can be sometimes determined on electroencephalogram: However, commonly the EEG does not detect abnormalities for many reasons, including location of the focus in the brain.

Importantly, the diagnosis of NES is a positive one: Unfortunately but frequently, neurologists and epileptologists admit patients to hospital for long-term monitoring. When they do not locate an active abnormal focus in the brain or the patient does not active epileptic seizures during EEG monitoring, they are labeled as having NES. 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 and 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 [43,44]. Even more so, in my experience numerous patients have reported to me their frustration at not having seizures during these times of monitoring while lying in a comfortable bed without stress, even off their anticonvulsants at times. "The doctors wanted me to have seizures so I tried my best and then they said what I was having was not epilepsy."

These patients may reflect a sub-population of NES patients who also have genuine seizure phenomena.

Case history: Sometimes this label of NES is dangerous and I remember a patient who almost died, going into status epilepticus, while her neurologist was busy saying "it's all hysterical". Fortunately, her brain was abnormally firing on EEG when she came into the hospital, and intravenous anticonvulsant stopped her "hysterical episodes". The neurologist went back and reviewed the ambulatory EEG and was then was big enough to admit he had made a mistake!

Principles

a) ***NES is a positive psychiatric diagnosis*** because there are invariably good psychological reasons why the events are occurring at those times and under those specific circumstances. These have logical predisposing psychopathology [45]. The most quoted of these has been predisposing sexual or physical abuse [45] and the underlying psychodynamics need attention [45].

b) ***NES is not a diagnosis of exclusion***. It is primarily not a neurological diagnosis. The NES label is often made after the EEG monitoring (sometimes prolonged, in the hospital, off medication) has been "negative" reflecting an ostensibly normal record. And such diagnostic labels are often pontificated as a gold standard. But there needs to be a context of why the symptoms are occurring at that specific time: What are the predisposing, precipitating and perpetuating features.

c) ***NES is often underdiagnosed:*** I personally have seen a large number of patients labeled with NES on this basis, who turn out to have atypical but genuine electrical firing. And these patients do very well with anticonvulsants but not without.

d) ***When uncertain, err on the diagnosis that does not kill if you're wrong:*** Sometimes NES or seizure simply cannot be made as a diagnosis. And often a combination diagnosis of both conditions is correct. But missing the seizures may result in significant mortality (e.g. status epilepticus can be fatal) and profound morbidity (these patients can be helped).

e) ***Always look for underlying systemic conditions:*** One common one is hypoglycemic episodes that have been missed and trigger "spells" which respond to anticonvulsants.

In Table 4A we list the pertinence of what is "stereotypical", "normal" on EEG and how normal EEG tracings are interpreted.

Table 4A: Special terminology and key interpretations.

"*Stereotypical features*" *often reflect a specific "march"* of the same symptoms and signs every single time, to the extent that the patient can predict what will happen next, unless the real seizure is aborted. The brain begins firing abnormally in particular area and continues to electrically fire moving in order from point A to point B every time. "**Normal"** in Table 4A implies that the feature is statistically no different from the general population: It does not mean absence of the feature if properly and extensively investigated. I have utilized much of the pertinent literature, and incorporated my experience over the past three plus decades, to produce as extensive information as possible for Table 4A. **Interpretation of 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 [43,44,46]. A normal EEG means "*no abnormality detected of sufficient kind for a label of seizures or abnormal foci in the brain*." A normal EEG should never be interpreted as "the definitive absence of seizures".

In Table 4B, the author tabulates some key differentiating features of NES from regular epileptic seizures and from syncope (faints). The features listed reflect general rules and are not specific. However, some features, like the variability of NES compared with the stereotypical features of epileptic seizures, are more specific than others. The value of such tabulation is of core relevance.

Table 4B: Differentiation of Epileptic Seizures, Pseudoseizures (Nonepileptic Seizures) and Syncope.

Quality During the event	Epileptic seizure	PSD (NES)	Syncope
Consistency between events	Stereotypical sometimes but not always	Variable in quality and sequencing	Often consistent, but does not have a march of several symptoms.
Explaining variations	Not always because, inter alia the patient may not be able to recognize it or remember the event.		May not be a consistent march because the underlying cause may be subtly different.
Eyes [47]	Open and may or may not be deviated	Frequently closed	Open deviated
Neurological deficit	Corneal reflex absent or plantar extensor but often normal and any primitive reflex expression		
Lab tests	Prolactin level within a short period (e.g. 10-20 minutes) after a tonic clonic seizure or CPS and controversially simple partial may be elevated (inconsistent in 60%) [48-53].		Can be raised in syncope particularly postural.
Interpretation of a negative	Non-elevation if not tonic-clonic and immediately done does not mean NES. Prolactin should be at baseline after 6 hours. Measure should be early at 20 minutes possibly not at 6 hours [49,50,52].	A normal prolactin level does not imply NES.	A normal prolactin level does not rule out syncope
Rouse during episode	Not usually	Yes, but not invariable	No, but very quick
Duration	10 –180 seconds usually	Variable, longer	Brief
Afterwards	Perplexed, disorientated	Surprised Sometimes crying or emotional	
Color skin [47]	Normal or blue	Normal	Pale
Breathing [47]	Normal	Increased or normal	Shallow

Pain [27]	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. Indicative or real event. May be others e.g. night terrors	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 [54,55]	No different	May yield event [56]	No different
Hypnotizability [57-60]	"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

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Psychological gains	None. Distressing to the patient and family	Frequent. Others controlled by it	None. Distressing to the patient and family
Kind of patient[8,9]	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	May or may not show any events	Events frequently occur in first 48 hours; video not correlated with epileptic seizures [61].	No epileptic events: usually normal as lying down. Important because rarely cardiac abnormalities are associated with seizure phenomena.
Post-traumatic stress disorder	Rare	Common	Normal

PSD: Paroxysmal Somatoform Disorder; NES: Non-Epileptic Seizures.

Perspective

Importantly, there are major clinical differences between patients who exhibit pure seizure disorders with atypical presentations, paroxysmal somatoform disorder with non-epileptic events and those with syncope. However, commonly, there are overlaps: For example patients with non-epileptic events often have a history of real epilepsy or of organic brain disease as a base for their ostensible psychological condition.

In my opinion, the most important features related to the psychogenic seizure or somatoform conditions almost always having special psychological precipitators or triggers. On the other hand those labeled with non-epileptic seizures who in reality have seizures do not exhibit la belle indifference. They are clearly distressed about the label, sometimes to the extent of feeling helpless and suicidal. Response to appropriate anticonvulsant and reassurance sometimes might even save their lives.

Paroxysmal somatoform disorder or Pseudoseizures—misdiagnosis or appropriate terminology (Part 5)

The term "seizure", although not regarded as synonymous with epilepsy by specialists, is often incorrectly perceived as synonymous with epilepsy. Epilepsy is a condition in which the patient has two or more events separated in time, without relevant precipitators, such as high fevers, medication induced, systemic disease or hypoglycemia. Moreover, not all seizures are associated with the paroxysmal abnormal electrical firing in the brain.

The manifestations of epilepsy are variable, involving some impairment of consciousness (we refer to these as complex partial seizures) all the way through to total impairments (as in tonic clonic seizures [synonymous with grand mal seizures] and other usually generalized manifestations). There may also be no impairment of consciousness: These are simple partial seizures and may manifest in many ways, often relating to firing in the temporal lobe producing literally simple symptoms like burning smells. Epilepsy may also manifest variably with alterations in perception, awareness, emotionality, or behavior, and the diagnostic features sometimes relate to manifestations on electroencephalogram confirming such a diagnosis. However, often the EEG does not detect abnormalities particularly in mesial parts of the brain, and this does not mean there are no seizures. This is where tests like Neppe's INSET questionnaire are particularly useful [62-64].

We should remember that we are trying to ensure that our relationship with patients is not compromised. Whereas occasionally patients need to be told that their "events" are entirely psychologically based, in most instances this produces distress and possible therapeutic rejection. If they were prepared to accept the pure dynamics of their events, they would likely not have seizures. Therefore, the way their condition is couched must be carefully considered, particularly as sometimes, they may not be having "psychological events" or those events are superimposed upon an organic base such as brain damage, seizures or mental retardation.

This is a special condition: Slavney [65] emphasizes the *active role of the experient* in the pseudoseizure—the patients are *doing it to themselves,* it's not just happening to them. This is a fine differentiating point. Such events are generally not consciously motivated: The patient is not malingering his illness, nor is he / she consciously producing the symptoms. The condition does not appear to have direct environmental gain —it is not consciously factitious. And yet, the condition does not just arise out of nothing, unlike real epileptic seizures which may or may not have triggers. And it's these triggers of seizures that sometimes make interpretations of whether these events are psychological. Alternatively, it is always important to establish whether these events are associated with abnormal brain firing. That makes diagnosis more difficult.

Terminology

We can debate what an appropriate but descriptive non-prejudicial term would be 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.

Ironically, too, the names invariably become "psychiatric". This should not be important except that these patients are then billed for a psychiatric not a medical condition, and insurance companies often remunerate differently.

Spells / Atypical spells: 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. I like this term, as it is non-prejudicial. It does not make a diagnosis but says something is wrong. Patients appreciate the lack of judgment of the physician or psychologist who is busy further investigating the condition. It allows for epilepsy, it allows for brain dysfunction, and it allows for psychodynamic elements. In a way, this is a "camouflage term". This reflects an example of a non-prejudicial framework, yet emphasizing the connection with the body, have led to the whole area of Somatoform disorders being studied. Several other alternatives exist [66].

Nonepileptic seizures (NES): Why NES as is a common term: Possibly the most common term today, is "Nonepileptic Seizure" (NES). 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) [67,68]. NES is a commonly used diagnostic label.

Pseudoseizures: NES followed pseudoseizure, but this attempt was neutral in connotation and acceptable in denotation [69]. 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. "Pseudo", has implications in primary and secondary gains, such as sick role and attention [65]. Yet, "pseudoseizure" may currently be the most common term used today [69,70]. But it raises a new specter 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 very 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 that pseudo sense and that they sometimes feel they are being actively accused of causing it. Whereas this may or may not be true, this perception is unhealthy and inappropriate.

Hysterical / Hystero-epilepsy /seizures: Three decades ago, clinicians were calling these events "hysterical epilepsy", "hysteroepilepsy", or "hysterical seizures" [71]. The term hysteria then went out of favor in psychiatry and with it, thankfully, the entity of "hysterical seizures".

Psychogenic seizures: 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.

Conversion fits: The conversion nature of these atypical events suggests "conversion fits". The problem is, "conversion" 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 and mutism, and these NES phenomena are classically positive activities.

Doxogenic seizures: A different term is Doxogenic Seizures. This introduces the esoteric term, doxogenic, implying the patient's own mental conceptions. 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 [66]. Doxogenic as a term has seldom been taken seriously as a contender.

The suffix "seizure": 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[65]. 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, and also even hypoglycemic episodes or panic attacks or even cardiac events, 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 "seizure" to epileptic firing.

Pseudo-attacks: 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 (Neppe and Blumer) felt badly about adding to this debate new terms, but clearly the old ones are unacceptable or borderline or limiting, at best.

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. It should also 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. Moreover, we should recognize that real seizures commonly co-exist in patients with NES (maybe as high as 50% to 80% or as low as 12%-18%) [45]. We want to emphasize the essential episodic nature of the events, which are usually sudden and have onsets over seconds. And the events usually last a short time - generally seconds or minutes, but occasionally hours or days.

Consequently, they are paroxysmal. We and others have used the term "spell" for a non-prejudicial 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 so revisiting "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. It 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 may ultimately lead to a diagnosis of a syndrome or disorder cluster.*

Paroxysmal Somatoform Disorder: 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 [66].

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 [72,73]. This has been introduced into psychiatric classifications since about the 1990s, as in the Diagnostic and Statistical Manual-IV (DSM-IV) and somatoform [40] remains a useful term, but used somewhat differently, and not in the diagnostic nomenclature of DSM-V.

Table 5

Dr David Kupfer, Chair of the DSM-5 Task Force explains [74]:
"Somatoform disorders are characterized by symptoms suggesting physical illness or injury, but which may not be fully explained by a general medical condition, another mental disorder, or by medication or substance side effects. The symptoms are either very distressing or result in significant disruption of an individual's ability to function in daily life. People suffering from somatoform disorders are often initially seen in general medical settings as opposed to psychiatric settings.

The DSM-5 makes a significant change to the diagnostic criteria from previous editions by shifting the emphasis from medically-unexplained symptoms to the impact of those symptoms on a person's thoughts, feelings and actions. In DSM-IV, it was required that somatic symptoms be medically unexplained -- that is, if symptoms could be traced to an identifiable underlying medical disorder like depressive symptoms in hypothyroidism, the diagnosis of somatoform disorder could not be made. The problem with this exclusion is that it did not take into account some patients who exhibit an unusually negative reaction to their symptoms (like excessively-high anxiety) even when symptoms are medically-explained. Such patients may benefit from treatment.

Thus, the DSM-5 diagnosis of somatic symptom disorder (which subsumes several DSM-IV's somatoform disorders, like pain disorder and somatization disorder) removes this requirement and instead focuses on the degree to which patients' thoughts, feelings and behaviors about their somatic symptoms are disproportionate or excessive. However, in cases where somatic symptoms are medically-explained, DSM-5 requires that all other criteria for the disorder be met. In addition, the narrative text notes that it is not appropriate to make a somatic diagnosis solely because the symptoms are medically-unexplained.

When Dr Blumer and I originally wrote about the Somatoform element [45], we believed to be useful because it emphasized 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 [27]. Hence, Somatoform Spells would allow differentiation from syncopal or pain episodes. But we wanted to be more specific: What of people who have repetitive somatoform spells—they would have PSD or Paroxysmal Somatoform Disorder (PSD) [27,75]. We respectfully, therefore, added this term to the tumult of terms.

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 some 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 [27,28]. Exaggerated startle reflexes are well-demonstrated in classic post-traumatic stress disorder patients who have experienced sexual abuse or been traumatized in war [27]. Certainly, therefore, a subpopulation of PSD may be startle episodes (paroxysmal startle disorder), as well as the various pain related phenomena or other atypical spells [76,77].

The problem is over the years, I've not even found a necessity to use it. Instead, most commonly, I'm using "atypical spells" or "spells" and sometimes the prejudicial pseudoseizures!

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, and Hysterical seizures. Certainly, Paroxysmal Somatoform Disorder (PSD) is a term to use for this controversial entity and that individual episodes would then be called somatoform spells [75]. This eliminates previously involved prejudicial or inaccurate labeling and diagnostic features.

But I have to admit to a major problem: Even though I introduced the term in Paroxysmal Somatoform Disorder (PSD) in 1992 [75], and again in 1998, I seldom find a need to use it! That I think, is the bottom line. We still do not have a perfect term for these atypical spells or maybe non-epileptic seizure phenomena.

Paroxysmal Photosensitive Syndrome: The neglected condition (Part 6)

We recognize the Americans for Disabilities Act (ADA) and provide wheelchairs and onramps for those who are physically disabled. In the United States, we also provide special education for those who are in need. However, there is a subpopulation of patients who appear to have been entirely neglected. I call the

condition of 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, or profound fatigue or impaired concentration or any of the manifestations of paroxysmal neurobehavioral disorder. The commonality is an intense dislike of flashing lights, such as discotheque 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 whereby flashing episodic and repeated lights produces an EEG response, called Photic Paroxysmal Response (PPR). PPRs are well documented in both epileptic and non-epileptic subjects. The equivalent of IPS can be induced by other visual stimuli of daily life, such as flashing holiday lights, and yet seldom does one see any assistance being offered in regard to this disability. A minor exception is that we are sometimes warned about being exposed to flashing lights during a theatrical presentation.

Photosensitive synchronization at certain frequencies is almost invariable in everyone. In my experience, almost everyone, for example, will synchronize their brain waves when exposed to a 13 per second flashing stimulus. 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) [78]. But such stimuli are 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 [79]. Twenty years ago it was pertinent too with computer monitors with cathode ray tubes (CRTs), but this is now less pertinent with predominantly liquid crystal displays (LCDs). The mechanisms of generation of PPR are poorly understood, but genetic factors likely play an important role [80].

As background to this, we examine briefly the different brain rhythms. When one performs an electroencephalogram (EEG) on a patient, we sometimes test using this Intermittent Photic Stimulation (IPS) deliberately to pick out who may have electrical seizure type phenomena (though it, sometimes, may not manifest physically in any ways). But the fact that virtually everyone will synchronize at a certain point with the frequency of flashing lights reflects the nature of the brain, as it is so basic. Various names are given for the different rhythms See Table 6A.

This chart is simplistic because at times there are more than one kind of brain wave frequency occurring simultaneously. However, the dominant rhythm at the time may be the one recorded, though with special computerized EEG apparatus, such as quantitative EEG, we can more clearly see the other frequencies.

Table 6A: EEG Primer.

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.

There are many techniques, such as meditative, biofeedback, entrainment, and others, that use the different brain wave rhythms therapeutically. Ultimately, individuals learn to entrain themselves, and these can be used therapeutically with improvements that 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.

a) For example, as indicated, when strobe lights are flashed in the beta range, at 13Hz (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.

b) For many patients, there is also a synchrony occurring around 8 cycles per second (Hz), which is the lower level of the alpha rhythm. This raises possible questions of links with earth events, as an 8Hz rhythm (or more specifically on average 7.83Hz, although this varies enormously), is the earth's own rhythmic ionospheric cycle, the so-called Schumann Resonance [81 p.85]. Could this possibly explain why some may be sensitive to certain natural disasters like earthquakes?

c) 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.

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 and 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 [82,83] and

others who may be nauseated autonomically or become acutely irritable or depressed as part of their paroxysmal neurobehavioral disorder may suffer.

Anecdotally, in my experience, though I don't know of this being officially reported in journals, some schizophrenic patients seem to love flashing lights. These patients, with their generally flat affect, become quite animated when visiting discotheques, for example. This may be another of those physiological indices that we sometimes ignore that suggest the organic neurological bases of a condition like schizophrenia, and it's worth investigating further.

Whereas induction of seizures in many instances are simply called Photosensitive Seizures or Photosensitive Epilepsy, prior to my 2008 paper [79], this entity had not been named in its syndrome (cluster of features form). I hypothesized, controversially, and my further experience since then appears to validate my previous impression, that this is a far broader spectrum[b]. These patients will often respond to anticonvulsants, and in my experience, drugs such as topiramate (Topamax) and also carbamazepine are particularly useful under these circumstances. It is difficult to find appropriate sunglasses or shading of the eyes that help, although this intervention is recommended as it sometimes may assist a little. 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, the patients improve with antiepileptic drugs, sometimes in highish doses [80]. These responses may be pertinent in seizure disorders, 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 of the flashing is unimportant, and sometimes the light is consistently delivered.

I named this condition Paroxysmal Photosensitive Disorder [79]. 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 have seizures, but migraines, and emotional symptoms, such as lability of affect, depression, fatigue, other headaches or irritability, may be alternative manifestations. We as a society should be taking note and improving life for those with this specific disability. And we should certainly, be trying to make flashing lights not a source of pleasure for the holidays, but aware of those who suffer.

Paroxysmal disorders: electrical firing and systems diagnoses (Part 7)

Ethically in the healing professions, we try to improve the patient at every level. We frequently prescribe biological treatments, such as medications, for underlying biological conditions. However, typically some psychological triggers produce or exacerbate conditions which may appear to manifest physically but have an underlying psychological component, most likely predisposed by an underlying biological basis. A pertinent example is Paroxysmal Somatoform Disorder.

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 [12].

Putting these different system levels, 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[c].

One approach to these paroxysmal conditions has, indeed, required ethicofamiliosocioculturality and more. The ethics relates to our need to act to assist individuals who are sensitive to flashing lights 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. This is a classical example of a condition that is often incorrectly labeled psychologically. All paroxysmal conditions, be they epileptic seizures, paroxysmal somatoform disorder, or paroxysmal neurobehavioral disorder have biological bases. These 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; or to elicit chronic conditions such as an underlying heart valve lesion that persists whenever one sees the patient. Contrast this with

[b]We have a great deal of unofficially analyzed data at the Pacific Neuropsychiatric Institute and would gladly work with an independently minded, intelligent graduate student in studying this and many other features of PND in research analyses.

[c] As an aside, the term, ethicobiopsychofamiliosociocultural appears first in my book, Cry the Beloved Mind [81]. 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, biopsychofamiliosociocultural, which originally appeared in 1989 in the first edition of Innovative Psychopharmacotherapy [19]). We had previously commented that "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" [84]. However, subsequent to that Neppe and Close in Reality begins with consciousness: a paradigm shift that works (5th Edition) Fifth Edition. Seattle: Brainvoyage.com, 2014 listed a 299 complex word involving a legitimate meaningful 38 component systems approach [84].

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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 patients' relationships 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, however organic they might be, still 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 seizures or several unnamed 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, possibly a rare manifestation of this Paroxysmal Somatoform Disorder and questionably linked with acute panic attacks; 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. But the management always remains pharmacological as well as non-pharmacological. We are never separated from our environment.

The INSET as an important historical and diagnostic screen in paroxysmal disorders (Part 8)

To evaluate paroxysmal phenomena in the brain—symptomatic of episodic brain firing—one needs to be able to screen for symptoms [63]. Traditionally, in Medical Practice, a history is taken. It is useful to have a series of structured screening 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 [63]. This is a historical probe, just as when we attend a physician, we might fill in forms pertaining to gastrointestinal symptoms, such as nausea, vomiting, diarrhea, and abdominal pains, or be asked about our cardiac or renal status.

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 or four days of recording [62-64]. This implies a far higher yield but more questionable interpretations. On the other hand, the objectivity of an outside and very confirmatory EEG recording cannot be denied [62,64].

The INSET (Inventory of Neppe of Symptoms of Epilepsy and the Temporal Lobe) developed out of necessity. Dr Vernon Neppe authored an early version of this test in the 1977 [85] and adapted it though to 1992 [86]. This has become critically important because there still remains no other test to screen for possible temporal lobe symptoms. We have used it at the Pacific Neuropsychiatric Institute in Seattle, WA as a screen in almost every patient. The availability of being able to use this as a jumping point in more detail in clinical history taking is very relevant.

A written test instrument designed to screen for such symptoms which I use in clinical practice is the INSET. This involves screening for possible temporal lobe, epileptic and organic symptoms, and spells. Thereafter the symptoms are categorized into several headers namely nonspecific symptoms, possible and controversial temporal lobe symptoms, seizure related and other focal features. The test is based on the subject and / or his family responding to questions which are thereafter elaborated in greater clinical detail. Responses are at two time levels: current as well as the most common frequency in the remote past and require the patient to rank frequency from never through less than yearly to more than daily (i.e. 0-6). Questions in the INSET have been based on the earlier Neppe Temporal Lobe Questionnaire which itself derived from an intensive literature review on the topic. The INSET plus medical history is a major determining factor for whether to order follow-up specialized electroencephalograms such as ambulatory EEG. The application of real PTLSs particularly plus seizure phenomena suggests anticonvulsants [87-89].

My suspicion is that many so-called very rapid cycling bipolar patients have temporal lobe disease which is one reason they respond to anticonvulsants. Clearly there is a greater need to pay attention to unusual episodic symptoms [36,63,79,90-96]. Superficial examination of symptoms produces profound misinterpretations [36]. This will ultimately lead to a workable classification and the recognition that certain seizure like features need be treated by psychiatrists. However it is critically important that like is paired with like [97,98].

The INSET as a test involves an inventory that specifically ends "… and the Temporal Lobe". Why do I emphasize the temporal lobe specifically? Simply, this is because this anatomico-physiological area of the higher brain has a particularly high yield for eliciting the symptoms of such conditions as Paroxysmal Neurobehavioral Disorder (PND) and of other paroxysmal brain conditions.

The temporal lobe of the brain is the great integrator [21,22,37,99]. This means that when the patient exhibits impairments in the temporal lobe, he/she manifests *disintegrative* symptoms. Many of these symptoms are paroxysmal (episodic) in nature. Therefore, the INSET questionnaire can be a probe for paroxysmal seizure-like symptoms. This is important as there are very few physical signs 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 because most temporal lobe dysfunction manifestations are symptoms not signs found on examination.

Symptoms have been attributed to the temporal lobe via two main methods: stimulation during neurosurgery and through the clinical features of temporal lobe epilepsy [37,99]. Non-specific symptoms, such as depersonalization, and apparently more specific symptoms, like episodes of olfactory hallucinations, apparently rarely occur without temporal lobe dysfunction, and can be used diagnostically, at times, but with some uncertainty. Nevertheless, symptom specificity is debatable. Consequently, this is why I called such apparently possible pathognomonic symptoms "possible temporal lobe symptoms" (PTLSs) [22].

The INSET or its predecessor, the Neppe Temporal Lobe Questionnaire [32], has been a mainstay of my neuropsychiatric examinations for the last three decades, and is administered in general to all patients with neuropsychiatric or behavioral neurological disorders.

We use a shortened version of the 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. This is relevant because we want to ensure that our interpretations are consistent —that "like is matched with like". Because of this, we began with the "Long INSET". The Long INSET contains the short key questions of the "Short INSET" (now just called the "INSET"). But it allows for decision trees and more detailed questions ensuring greater homogeneity of answers. However, this took time and trained clinicians could apply their history taking skills and elicit differences. The Long INSET [100] requires some expertise for its useful clinical application. Certainly, detailed questions can be used to probe for positive responses by using the Short INSET simply as the first stage for administering the Long INSET.

Realistically, however, given a background training in epileptology, psychology and psychiatry, we need not use this second historical probe except for research. Using the (Short) INSET historical probe, we can link the 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.

These all come together as symptoms that one would probe in an instrument such as the INSET. Essentially, therefore, temporal lobe screens and screens for brain dysfunction are very useful in assessing episodic paroxysmal kinds of conditions.

Very relevant in the INSET is the ability to monitor changes 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? This is key in the proper management. We know almost immediately, for example, if the patient has no significant side-effects but still has some symptoms, even when they are somewhat better, that we should (unless there are specific reasons why not such as allergy) increase the dosage and, so to say, test the limits.

The INSET is an example of a remarkable historical instrument that is, therefore, particularly useful in monitoring change, and the change that occurs can, at times, can be quite profound with appropriate medications. The patient psychologically also feels better when noting the changes that occur. The earliest origins of looking at temporal lobe symptoms were in the 1977 [101]. 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 [102]. I followed this through with further research [23,103]. The INSET is, in my opinion, the best historical screen. This follow on my initial Neppe Temporal Lobe Questionnaire. With respect, the INSET because of its adaptations has become far more clinically relevant and usable than other derivations from this NTLQ (such as separately, Persinger [104,105], Roberts, Stein) [63] Persinger has done a great deal of research in this area using his adaptation, but he is not using it mainly as a clinical instrument. And the adaptation from the NTLQ is not as good as one derived from the INSET which is far more stable. Subsequently others have use the INSET too to the extent that there are three PhDs going on at this time in three different countries outside the USA. And at the Pacific Neuropsychiatric Institute in Seattle, WA, we have applied the INSET as a screen in almost every patient.

The INSET has become greatly important in management as well. Together with ambulatory electro-encephalography (AEEG), we are able to clinically delineate with high accuracy, which patient will require prescriptions of anticonvulsants. The AEEG may not show abnormalities, and the INSET might. This is because the INSET can detect mesial temporal symptoms more commonly, and also the AEEG, even when four days in duration, is still a short period to show up acute abnormalities.

These are reflected in Table 8A[62].

Possible Temporal Lobe Symptoms

Seizure disorders with behavioral disturbance, may initially be interpreted as psychiatric in origin. Many such problems relate to the temporal lobe of the brain. The features of temporal lobe epilepsy and non-epileptic dysfunction of the temporal lobe are so varied and so protean that it is necessary to classify them.

At the start, we needed new additional terms. I called and continue to call the most specific symptoms *Possible Temporal Lobe Symptoms* (PTLSs) [21,32,37,99]. These are symptoms that appear to derive from the temporal lobe of the brain [33,34]. 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 upward towards the chest, and unrelated to meals.

"Possible temporal lobe symptoms" (PTLSs) [107] relate to features which can be induced by stimulating areas of the temporal lobe during neurosurgery. These symptoms only become specific symptoms of temporal lobe dysfunction if their occurrence is validated empirically during a seizure - either through observation or by the electroencephalogram (hence the word "possible" in possible temporal lobe seizures).

Great care must be taken in interpretation of such features: We have seen that using a phenomenological analysis, I demonstrated that the symptom of déjà vu commonly regarded as symptomatic of temporal lobe epilepsy is not in general so. However, a particular subtype a very special phenomenological quality in patients with temporal lobe epilepsy [108,109]. Like many other such focal symptoms, this involves its association with post-ictal features such as sleepiness, headache, profound fatigue, and clouded consciousness and its link in time with these features. This association provides an excellent clue to the existence of temporal lobe epilepsy. However, déjà vu is a normal phenomenon occurring in 70 percent of the population and unless such phenomenological detail is obtained, patients' symptomatology may be misinterpreted [23,110-114]. And when

I similarly studied olfactory hallucinations, a specific definitive type of temporal lobe epilepsy olfactory hallucination could not be demonstrated, although there were suggestive features [22,115,116].

Table 8A: 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. Profound mood fluctuations in seconds;

Signs:

10. Receptive (Wernicke's) aphasia;
11. Superior quadrantic homonymous hemianopia;
12. 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:

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. Complex visual hallucinations linked to other qualities of perception such as voices, emotions, or time.
11. 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:

- Profound mood changes within hours;
- Frequent subjective paranormal experiences e.g., Telepathy, mediumistic trance, writing automatisms, visualization of presences or of lights/colors around people, dream extrasensory perception, out-of body experiences, alleged healing abilities;
- Intense libidinal change;
- Uncontrolled, lowly precipitated, directed, non-amnesic aggressive episodes;
- Recurrent nightmares of stereotyped kind;
- Episodes of blurred vision or diplopia [106].

A major message, therefore, may be the relevance of adequately assessing the symptomatology of patients presenting with epilepsy. It may be that this is a direction as relevant as electroencephalographic monitoring.

Most of all it reminds us how slender our interpretations of other related but different symptoms such as "he experiences strange smells" might be and the fact that it is critical to elicit whether these are episodic in quality and linked with other symptomatology particularly epileptic or temporal lobe.

I distinguished between "disintegrative temporal lobe symptoms" (DPTLSs) and "not necessarily disintegrative ones" (NDPTLSs), 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. Disintegrative features need treatment because they cause problems.

"Not necessarily disintegrative symptoms" are still serious, likely reflecting seizure disorders. But in and of themselves, they need not be treated except we would treat them because they are reflecting seizure symptoms, and as Hughlings Jackson has said in the late 19th century: "Seizures beget seizures" [31,117]. These therefore should be treated. NDPTLSs are also useful in monitoring conditions.

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 extrasensory 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 [22]. Then there are non-specific kinds of symptoms such as depression or anxiety or non-explosive irritability triggered by stressors which can occur in temporal lobe disease or ins seizures but also occur in multiple psychiatric conditions.

Difficulties and research

Major difficulties exist in interpreting the pathophysiological origins of even 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 [22,23,115]. 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 where I found four phenomenologically distinct kinds of déjà vu and these all had different causes: Only one was temporal lobe epileptic déjà vu [23]. Finally, we correlate these findings with the EEG and anticonvulsant response.

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!

We have used other instruments to assist us as well. For example, we have had significant experience with the SOBIN (Soft Organic Brain Inventory of Neppe) since 2002. 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). With the INSET we also use the SOBIN [62,64]. It has become extremely important to evaluate differences in events, particularly if any specific brain injury is involved.

The SOBIN is the only available clinical neuropsychiatric inventory screening for soft organic type symptoms and learning disabilities.

Vernon Neppe authored an early version of this test in 2002 and adapted it in 2005, both times at the Pacific Neuropsychiatric Institute, where it's used extensively. The SOBIN developed out of necessity and is critically important because there remains no other detailed test to screen for subtle organic brain symptoms.

The SOBIN integrates five major directions: Primarily eliciting soft organic brain pathology which is particularly important in neuropsychiatric cases evaluating subtle difficulties like prosopagnosia and dysproccia. Secondly, monitoring changes including after significant pathology like head injury or encephalitis. Thirdly, establishing subjective cognitive areas of special strengths. Fourthly, eliciting and monitoring ordinal severity fluctuations in higher brain function. Fifthly, obtaining ancillary baseline data ranging from laterality to personality to symptom triggers, additional to the INSET. By scoring 74 main items plus 24 ancillary items, the SOBIN compares past and present, and evaluates degrees of severity. The SOBIN has proven critical in both clinical and forensic contexts, including patients with questionable organic or brain pathology or neurological conditions with possible psychiatric elements, previous head injury or encephalitis or tumor or other brain insult or possible seizure disorders or paroxysmal neurobehavioral disorders [64].

The SOBIN screens in a consistent and standardized manner such symptoms also ensuring there are no indicators of invalid responses so as to be able to better interpret neuropsychiatric tests properly. The SOBIN's neuropsychiatric use and applications are discussed.

The SOBIN is very important for both clinical and forensic use in Neuropsychiatry and Behavioral Neurology. It also has enormous relevance in assisting directions for cognitive rehabilitation. These symptoms can be clustered together, for example, to allow more detailed evaluations such as "dysproccia" (a disorder of processing afferent and efferent information) [118,119], attentional disturbances, focal disturbances such as dyspraxia and dysgnosia, as well as prosopagnosia, right-left, directional and many other subtle disturbances.

Apparently, almost everyone has some difficulties but we all compensate.

Particularly important are changes that occur e.g. "normal" to "gross" after cerebral insults. Also pertinent are utilizing any self-rated "exceptional" abilities. Additionally, there is great value in assessing such accessory features as mixed laterality, responses to stimuli like lights, and the patients self-evaluations like intelligence.

Paroxysmal disorders: Home ambulatory EEG with video monitoring as an objective screening (Part 9)

When one does an electroencephalogram (EEG) measuring brain waves, a major 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 of sharp waves and spiking. However, in psychiatric disorders, this very often involves a certain slowing. A second component may be detection of abnormalities despite the absence of any paroxysmal episodes: there are focal areas of difference, for example in the temporal lobe of the brain. This clarifies further management, as many of these patients, when combined with clinical data suggestive of temporal lobe pathology, respond to anticonvulsants in our experience [12].

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. 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 [120]. 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.

The yield rate of abnormalities on short office regular EEGs has been small —possibly only a few percent higher yield, questioning whether such uncomfortable procedures are ethical

and worth the trouble [8]. 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 [121-123].

However, in patients with atypical paroxysmal conditions, the yield appears to be far, far lower. Indeed, one has to be lucky to find abnormalities. Sometimes, interpretations are backward: "most patients with seizures can be detected on regular EEG." How do we know if EEG abnormalities are used as a gold standard? In our experience, patients with paroxysmal neurobehavioral disorder have a much lower yield and need to be monitored in their home environment for a prolonged period of time.

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 [124-126].

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) [127,128] with or without video monitoring. Patients go home after they are hooked up via a complex, very expensive, battery operated recording device looking rather like a Sony Walkman recorder, weighing 1.2lbs and about 3inches^3. A computer records the brain waves in 23 plus channels. Additionally, they are set up with video monitoring. To ensure privacy these can be switched off. Because at this point, the video is heavier and somewhat bulky (weight 18lbs, and about 10inches^3), it's recommended that this be used in one room during the day and switched on before sleep.

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 "push buttons" 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 through to Stage 4 and rapid eye movement sleep. This contrasts with just the Stages 1 and 2 sleep we mainly see in regular Sleep EEGs because the patient in a half-an-hour or so has not achieved deeper sleep. This increases the potential yield of positive results—a normal record does not mean that it would not have been abnormal at another time. Sleep records are of great relevance in increasing the yield of abnormalities [95] and their environment of being at home is helpful, as well.

We monitor patients with atypical paroxysmal conditions for a prolonged period of time, such as 3 or 4 days, so as to maximize picking up abnormalities. The yield is reasonably high, particularly with sophisticated apparatuses.

There are several very good monitoring apparatuses. We currently use the Sleep-Med Digitrace AEEG machine with correlative Video Monitoring using a 27 channel apparatus and utilizing 23-channel bipolar EEG connections examining particularly coronal over temporal over parasagittal montage, using all standard 10-20 electrode placements as well as T1 and T2. Additional channels are available for EOG or areas of special interest [81]. Recording was at a sampling rate of 200 samples per second, per channel. Data is converted to a Cz referential montage which can be re-montaged using an on-screen review program (Insight DT or DigiView). EEG may be recorded at the direction of the patient by the pressing of a pushbutton. Additional EEG may be stored at the direction of automated seizure and interictal epileptiform (spike) detection programs. Digital video and audio is also recorded, synchronized with push-button, seizure, and time sample EEG files, whenever the patient maintained a connection to the video unit. Electrode placements include ECG monitoring concomitantly. Playbacks are done with digital high frequency filters. Both a seizure computer and push-button events plus background EEG for 20 seconds every 10 minutes at night monitor storage are used. At times, where necessary, recordings are slowed to 50 samplings per second.

The patient or family member presses a push button mounted on a waist worn EEG recording device and the EEG is recorded at the direction of the patient by the depression of the button: A record of the details of the event are written down and the video picture-audio sounds recorded. The EEG is stored two minutes prior to and two minutes following each push button event. Importantly, the EEG is additionally stored at the direction of a seizure computer designed to detect and record EEG abnormalities including seizure and spike discharges during sleep. The seizure computer stores files described as automated seizure detections, automated interictal epileptiform detections (spikes), and timed EEG samples. The patient has the opportunity to temporarily suspend the video unit monitoring for convenience and privacy but sufficient sampling is obtained on a daily basis. Medications and any special events of pertinence during the AEEG are recorded.

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 [54]. However, we have used both options (with and without video) and our preference is to use video if available. The reason is because any component that clarifies the diagnosis and assessment is valuable, and the ability of the patient to switch the video on or off, and to unhook from the video recordings makes it less restrictive.

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 or four day period of time may not always pick up abnormalities. But there is fortunately an upside: 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) [63]. 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 [95]. 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 70cycles/second (Hz). Playbacks are done with digital high frequency filters noted at the top of each page, and 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. The seizure computer stores all automated seizure detection files—we humans still have a job, because for the next several years anyway we may be better at reading what is artifact and what is not! This is unlike electrocardiograms (ECGs) which have become almost exclusively the domain of the computer.

The advent of computerized Ambulatory Electroencephalography 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* [18,19], where I recognized that some of these episodic kinds of conditions were treatable by appropriate anticonvulsants. This has 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.

Indications for ambulatory EEG

Long-term EEG in adults includes three modalities: sleep deprived-EEG lasting 1- 3 hours—a modality that is problematic for those with potential for manic episodes and where there is limited yield; 24 hours of ambulatory-EEG and continuous more prolonged EEG lasting from several hours to several days with video. The main indications of long-term EEG *in the possible PND population* include positive diagnosis of paroxysmal clinical events or of focal abnormalities and search for interictal discharges when epilepsy is suspected or for the purpose of therapeutic evaluation. The other areas such as classification of an epilepsy syndrome, and to analyze electro-clinical correlations in a pre-surgical evaluation context, pre-surgical evaluation of drug-resistant epilepsy are not pertinent.

The patient's clinical condition should appropriately suggest the need to amplify for a prolonged period of time whether there were any episodic or paroxysmal episodes occurring in the brain and whether there were any focal abnormalities of any kind. This can be based on the detailed history and evaluation done including the listings of possible temporal lobe symptoms and of possible paroxysmal events occurring on the standardized screen for such events, The Inventory of Neppe of Symptoms of Epilepsy and the Temporal Lobe (the INSET), and a reason for referral. Additionally the history was suspicious for possible paroxysmal events relating to predisposing features.

Although there are many who prefer admitting the patient to the hospital and monitoring as inpatients, we prefer the more natural environment of outpatient monitoring. However, the inpatient monitoring is often for taking patients off medication to locate the focus, for example, for possible surgery, or to establish if the kind of atypical spells that might exist.

Often the standard EEG does not detect abnormalities. But even when it does, it may require AEEG to further delineate the pathology plus the frequency and times of occurrence (e.g. at night; detections by push-buttons). These allow for evaluating treatment efficacy, especially when clinical evaluation is difficult, and to refine a positive diagnosis when paroxysmal clinical events are frequent.

Is AEEG valuable? The International League Against Epilepsy guidelines recommend the use of prolonged EEG where the diagnosis of epilepsy or the classification of the seizure syndrome is proving difficult, and we could add for conditions like PND. Video EEG monitoring is often unavailable to many patients. When analyzing outpatient ambulatory EEGs lasting 72-96 h (3-4 days), without medication withdrawal, even in seizures about two thirds of studies gave positive data, and in our experience it is about half. These studies change management of diagnosis in about a quarter and of classification by another quarter. This kind of study confirms the diagnostic utility of outpatient ambulatory EEG in the diagnosis of paroxysmal events. Outpatient ambulatory EEG is relatively inexpensive and widely available and the demand for long term EEG monitoring is increasing with the emphasis on recording patients' attacks. When video is unavailable, interpretations of an ictus may be more difficult. We investigated whether patients, if offered home video equipment, would take it, if this resulted in simultaneous EEG-video capture of an ictus and if interpretation of the recording was facilitated by the video. This is pertinent because about half (50%) of attacks are captured successfully on video, and this may be particularly pertinent in children.

Regular sleep and wake EEG in this instance should be regarded as inadequate to establish the exact focal abnormalities, number and frequency of daily paroxysmal events, and to delineate links to events to push-button symptomatology and extent of control of seizure or atypical spell or electrical events on the current medication regimen.

There is another component of relevance in AEEGs: Seizures represent a potential source of accidents/death and permission

to drive may require a seizure-free period. Laws and regulations regarding this issue vary widely, and the onus of reporting seizures ultimately rests on the individual. But some patients are legitimately unaware of their seizures, so their reports may be unreliable. The Fattouch study showed an "apparently" seizure-free group of patients who drove regularly and yet were having episodes on AEEG.

Basics of these reports

Particularly pertinent to analyze features are:

Background: Normal would be well-developed posterior alpha rhythm at midHz range present bilaterally over the occipital poles and parietal central regions.

Sleep: the patient should achieve adequate sleep with approximately normal sleep cycles several times during the night. Sleep patterns should appear within normal limits with normal architecture during the routine time sampled EEG

Push button detections should be recorded: These are correlated where possible by the video recordings showing the patient experience and additionally allowing further differentiation of questionable intracranial versus extracranial events and interpretations of the appearance of the events with clinical perspectives. They should be corresponded with *the typical feelings the patient experiences. Also we should examine if* the patient had any episodes where the button should have been pressed but was not. We should look specifically for episodes of paroxysms or spikes that are detected and any focal abnormalities.

The occurrence of events during push-button recording are always significant to consider although clinical relevance is dependent on these events actually having a causal relationship with electrical firing in the brain.

Normally, *automated spontaneous spike (seizure) detection files* should show no episodes of paroxysms or spikes with no intracranial focal abnormalities. The occurrence of events in the spontaneous spike detection file EEG is significant to consider. The clinical relevance is dependent on these events actually having a causal relationship with electrical firing in the brain and whether or not these are causing damage or/ and functional impairment e.g., in the push-button events. These are correlated where possible by the video recordings showing the patient experience and additionally allowing further differentiation of questionable intracranial versus extracranial events and interpretations of the appearance of the events with clinical perspectives.

Background EEG evaluation during routine time sampled EEG should be evaluated for.

Automated Interictal Detections: No episodes of paroxysms or spikes should be normally detected with no focal abnormalities.

The occurrence of events during routine time-sampled EEG are significant to consider although clinical relevance is dependent on these events actually having a causal relationship with electrical firing in the brain and whether or not these are causing damage or / and functional impairment as would be attributable to push button events. These were correlated where possible by the video recordings showing the patient experience and additionally allowing further differentiation of questionable intracranial versus extracranial events and interpretations of the appearance of the events with clinical perspectives.

Finally, these tests should have a cardiac monitor. This should shows a regular sinus rhythm throughout monitoring with a relatively consistent rate of say 66 to 80 beats per minute. The *ECG* should show no arrhythmias and showed no specific abnormalities. However, these can be correlated where possible by the video recordings showing the patient experience and additionally allowing further differentiation of questionable intracranial versus extracranial events and interpretations of the appearance of the events with clinical perspectives, and correlates with possible anoxic episodes and EEG abnormalities.

Video Monitoring during the nighttime recording and intermittently while awake (as the patient would disconnect as needed during e.g. private needs) should reveal no significant pathological behavior.

The ambulatory EEG findings might strongly support the seizure / temporolimbic / organic elements of the diagnostic formulation and suggest inadequate anticonvulsant control during this period the seizure / temporolimbic / organic elements of the diagnostic formulation outlined in the clinical report. This might strongly support the *prescription* of anticonvulsant medication. Or the support may be weaker. Most interesting is the interpretation of so-called "normal" EEGs where the seizure or temporolimbic or organic elements are within normal limits. This might suggest adequate anticonvulsant control during this period or

suggest that the mesial temporal symptoms, recorded on pushbutton did not transmit to the scalp electrodes, or suggest that the benzodiazepine or other medication taken may have blocked records of abnormality. Benzodiazepines can profoundly normalize the EEG and patients should optimally be off them for three weeks pre-AEEG, but most times this is not practical. The prescriptions here should be based on clinical impressions including the INSET.

Further investigations on the basis of the findings in the context of clinical picture may include MRI of the head if there are suggestions of structural abnormalities. This is common, for example, after head injury and usually suggests physiological or anatomical scarring (gliosis) but may require exclusion of an intracranial tumor. Sometimes, extra days of monitoring are required or simply wake and sleep EEG with photic stimulation and hyperventilation to clarify findings. Finally, some patients may require repeat AEEG in six to twelve months after interventions.

Which patients respond to anticonvulsants? The role of mesial temporal lobe firing (Part 10)

We have looked at the INSET and SOBIN as ways to evaluate patients with paroxysmal neurobehavioral disorders. And we have recognized the "Rolls Royce" using Home Ambulatory EEG monitoring with video. But all of these sometimes fail. Is there a way to utilize the INSET and AEEG and measure who responds to anticonvulsants?

Whereas frontal lobe dysfunctions can often be measured objectively, most temporal lobe dysfunction involves symptoms: The literature-based INSET (Inventory of Neppe of Symptoms of Epilepsy and the Temporal Lobe 1992 with modifications thereafter) is the only adequate, standardized, brief, historical bedside or waiting-room questionnaire, eliciting pertinent

history-taking detail on seizures, peri-ictal symptoms, and temporal lobe features [62]. And whereas 3 to 4-day Ambulatory Electroencephalography (AEEG) objectively measure focal and ictal events, these evaluations are sometimes limited e.g. in mesial temporal dysfunction (particularly absences; smells; rapid mood/thought fluctuations; explosive irritability), when no pushbutton or nocturnal ictal events occurred, or with some medications (e.g. benzodiazepine). This limits the sensitivity of AEEG during routine use [62-64].

We can evaluate how the INSET and SOBIN apply:

— facilitating more adequate clinical history taking?

—detecting potentially abnormal symptoms?

—allowing more complete additions to the standardized answers?

—amplifying detail to optimize eliciting clinically pertinent symptoms?

To do this we need to examine the difficult diagnostic cases: What happens when we utilize the INSET plus AEEG to identify anticonvulsant responsive patient subpopulations plus mislabeled "seizures" or temporolimbic instability? Can we combine this with the "SOBIN" (Subtle Organic Brain Inventory of Neppe) to overlap broader neuropsychiatric symptom screens, including higher cortical frontotemporoparietal dysfunction, headache, anger, depression, anxiety, fatigue, sleepiness, flashing lights, and overall functioning?

The Research

We evaluated the diagnostic and clinical validity, and reliability of the INSET and SOBIN as adjunct to 3-day AEEG compared with anticonvulsant responsiveness, quantitative clinical improvement and "control" patients.

The INSET and SOBIN diagnostically combines with 72-hour AEEG to easily facilitate diagnostic higher cortical and ictal screening.

Hypotheses and questions:

i. The clinical utility and applicability of the INSET as a historical questionnaire technique applying construct, content, criterion, internal and diagnostic validity and reliability analysis of the INSET compared with 1. Surface electrode AEEG, anticonvulsant response.

ii. Several psychiatric and neurological quantified historical questionnaire monitoring (called the DS-10) as applicable; to the SOBIN (expected not to change); and to a symptomatic patient cohort in a similarly derived "control" population.

iii. The utility of the application of mesial temporal lobe symptoms (MTLs) even in the absence of AEEG abnormalities to use of anticonvulsants. This allows justification of the constructs underlying the INSET.

iv. Establish specific MTLs as indicators.

We knew based on our previous experience that the AEEGs would be normal for one or more of several reasons: benzodiazepines on board; or rarely anticonvulsant medication; mesial temporal abnormalities with no spread to the surface scalp electrodes; and absence of abnormal firing during the 3-4 days.

This therefore produced another population to examine.

Additionally the attending physician evaluated clinically the responses.

Measures:
This consisted of 10 questionnaires (The Diagnostic Screen 10 [DS-10]) [88]. These have been used clinically at the PNI and are in part directly comparable with related modifications of research questionnaires and that clinically work.
a. MD Ranked:
—depression: "SHADES" (derivation: HamD-21, last week and month),
—anxiety: "SHARMS" (derivation: HamA-14)
b. Patient ranked:
—social anxiety (fears, avoidance): "LSAS-24-SR-MPNI" (24*2=48 items) (derivation: Liebowitz)
—obsessive compulsive: "Y-BOCS" (derivation Yale-Brown-10)
—sleepiness: "ESS-R8" (derivation Epworth)
c. Derivative questionnaires have significant extra additions:
—fatigue: "FISS-R (10+4 items) (derivation Fatigue-Severity-Scale 10)
—attention deficit: "PNI M-CAARS" (14=6=20) (derivation Connors 14)
d. Questionnaires fill recognized clinical voids with no previous equivalents.
—PTSD: "PRICE-20" (derivation DSM4R)
—Stress, Insomnia, Pain, Anger /ictal: "SIPAS" (26+6=32 frequency and severity)
—Extended symptoms: "NESS" (40 items): patient ± family-ranked)

Methods

Sample: The population used was complex, in that many had previous refractory psychopathologies and most had multiple medical conditions. Specifically, this was a physician referred, neuropsychiatrically screened, outpatient, non-emergency population of both sexes ranging in age from adolescence to the sixties, who were as yet undiagnosed and not clinically stable but with no formal history of seizure disorder labels.

Routinely patients sign consent for anonymous data use in research: The sample included all those consenting patients (in which a single neuropsychiatrist / epileptologist (Neppe) regarded as having clinical indications for Home 3-4 day AEEG (scalp recordings only T1 – T2 with lateral temporal montage array and lateral temporal placements with electrocardiograms; 16 channels or more). The AEEG was read blind by an internationally respected electroencephalographer.

"Comparative" control group: Comparisons, were performed with "control" patients, who did not exhibit possible temporal lobe features or firing on INSET or EEG abnormalities.

Ongoing measure*s:* Clinical, DS-10 changes (a series of scoring screens involving about 200 items), changes in INSET symptoms with treatment.

Results

All data was analyzed retrospectively because these patients were treated clinically based on the best available approaches for the patients.

These are reflected in Table 10A. The following groups were derived:

MTLs with N AEEG: *20 subjects; 17 of 17 prescribed ACDs (anticonvulsants: Lamotrigine / Carbamazepine) responded to them. 1 patient has an abnormal temporal lobe focus on SPECT. Of the 3 remaining, 1 had no follow up, and 2 did not receive ACDs; 1 was controlled without; 1 was poorly compliant.*

Abnormal AEEGs (ambulatory electroencephalograms): *23 subjects, of which 12/23 had MTLs. 21 of 23 on ACDs. 2 non-MTLs did not require ACDs.*

Responses were measured though the clinical responses in all the patients (AEEG and MTLs alone). All patients receiving anticonvulsants in these two groups demonstrated marked improvements. These responses in both these groups were reflected consistently on the DS-10 (particularly the 40 item NESS score which overall reflects individual symptoms), the INSET and the clinical changes as carefully monitored at each appointment. Remarkably, all patients improved clinically significantly such that their symptoms were much less, and their functioning improved. However, importantly, almost always other medications were clinically necessary. These additional medications sometimes preceded the evaluation, and sometimes were further prescribed sequentially during the evaluation. Therefore, exact measures of the anticonvulsant effects were slightly confounded as interpretations were more difficult as to what the ACDs alone would have been doing. However, because the ACDs were added individually, excellent measures of responses could still be obtained, and essentially, most patients in this group required all their medical conditions to be monitored and treated. Psychiatrically, the most common adjunct medication appears to have been buspirone. The responses were consistently dramatic, not slight, and therefore tabulated as "significantly clinically relevant enough to induce changes in life-style quality and functioning"; in Table 4 this is "Clin ++". There were no "Clin +" (slightly positive), or "Clin 0" (no-change), or "Clin –"or "Clin ––"(where negative consequences resulted).

As postulated, 20 of 43 AEEGs with MTL symptoms (roughly half) did not detect abnormalities.

Comparison population

These patients had "normal" AEEG tracing and clinically no MTLs. They did not need ACDs but 7 of the 12 received ACDs but all with no response. 9 of the 12 responded to other pharmacological medications. Of the remaining 3: 1 is as yet unknown; 1 has had limited response; 1 is poor. The results obtained are overall statistically overwhelming ($p<0.001$) in MTLs group vs no MTLs for both AEEG abnormalities and for ACD responses but we have limited this to significance at the one in a thousand level ($p <0.001$ is designated in Table 10A although these significance levels are much higher).

Table10 A: Analysis of Results.

New Parameter	Size	# Abn. AEEG	# MTLs	Prescr. of ACD	Prescription Responses	Other RX	Clinical Response	P<
Normal AEEG with MTLs	20	0	20	17	17	All	All	*
Abnormal AEEG without MTLs	11	11	0	9	9	All	All	*
Total MTLs	31	11	20	26	26	All	All	*
Abnormal AEEG with MTLs	12	12	12	12	12	All	All	*
Normal AEEG without MTLs	12	0	0	7	0	9 RX	0 vary	NS
Sz disorders	7	varied	Vary	7	7	Vary	0 to ++	*
Totals	62	30+	32+	52	45			

Legend: Abn. AEEG = number of subjects with abnormal ambulatory electroencephalograms.
MTLs = number of subjects with abnormal clinical mesial temporal lobe symptoms involving profound rapid mood fluctuations plus severe explosive type unprecipitated or disproportionate irritability / rage plus some subjective or objective description of "blanking" episodes from the patient or a family member. Not invariable, but frequent were extra symptoms, namely one or more of sudden onset headache and sleepiness,
Prescr of ACD = number of subjects receiving anticonvulsants
Other RX = number of subjects receiving adjunctive medications other than anticonvulsants.
P<: Frequentist probabilistic non-parametric statistic; *reflects 2-tailed responses $p<0.001$; NS: not significant. Fisher's exact test.

Discussion

Table 10A list the past 62 consenting patients attending the PNI who had INSET tests and three days of ambulatory EEG monitoring. Clearly, based on this small sample, patients respond to anticonvulsants if they have abnormal EEGs of any kind — paroxysmal or temporal lobe foci were sufficient to be admitted here; or if they have some defined mesial temporal symptoms namely profound rapid mood fluctuations and severe explosive type unprecipitated or disproportionate irritability / rage with one or more of sudden onset headache and sleepiness.

The data is so overwhelming clinically that it does not require statistical analysis, but clearly, we can easily predict responders to anticonvulsants. In this instance, the anticonvulsant used in this sample was lamotrigine in clinically appropriate doses, sometimes as small as 12.5mg bid, sometimes large such as 150mg bid or higher (or equivalents for the extended release) with a mode of 50mg bid. All patients required adjunctive medication, and the most common was buspirone, again in varying doses, varying from 5mg bid to 45mg bid, with a mode of 30mg bid.

We have described a clinical retrospective research analysis showing that there appears to be a legitimate condition where patients with ostensible mesial temporal lobe abnormalities as evidenced by severe explosive behavior, marked mood lability and some kinds of blankings with or without headache, or post-event sleepiness or nausea, should respond in every instance to appropriate anticonvulsant medication plus adjuncts, as required. This response is irrespective of whether these patients have abnormal home ambulatory electroencephalograms on three days of monitoring.

These results are very encouraging suggesting there is a cohort of patients with paroxysmal neurobehavioral disorder who likely have seizure phenomena with foci in the mesial temporal lobe (laterality not stipulated). They will respond to anticonvulsants provided they are symptomatic and irrespective of whether their ambulatory electroencephalograms are abnormal.

Paroxysmal disorders: Are these seizures or electrocerebral firing? (Part 11)

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