

## Differential Diagnosis of Epilepsy

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- Once the diagnosis of epilepsy is made it's difficult to be "undone".
- Wrongly diagnosing epilepsy is relatively common.
- Multiple studies have shown that 25-30% of patients previously diagnosed with epilepsy who are not responding to drugs are found to be misdiagnosed, most of them are eventually shown to have PNEA.

## Introduction

- A diagnosis of epilepsy carries with it many important psychosocial issues as well as therapy decisions.
- The consequence of incorrectly diagnosing epilepsy may include unnecessary restrictions on driving, working, and recreational activities.
- Misdiagnosis of epilepsy may lead to the prescribing of potentially toxic and unnecessary antiepileptic drugs (AEDs) and suffering from the stigmatization that is often directed at people with epilepsy.

### Epilepsia

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#### Outcome of Prolonged Video-EEG Monitoring at a Typical Referral Epilepsy Center

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- **Results:** In total, 251 inpatient video-EEG monitoring sessions were performed. **Nonepileptic seizures** were diagnosed in 75 (30%); 58 (23%) were found to be surgical candidates; seven were implanted with the vagus nerve stimulator. In 47 (19%) patients, seizures were recorded, and the diagnosis of epilepsy was confirmed and clarified (symptomatic/cryptogenic generalized epilepsy, seven; localization-related epilepsy, 35; idiopathic generalized epilepsy, five).

Epilepsia, 45(9):1150-1153, 2004



**The misdiagnosis of epilepsy and the management of refractory epilepsy in a specialist clinic**

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**Summary**

We assessed the frequency, causes and consequences of erroneous diagnosis of epilepsy, and the outcome of patients referred with 'refractory epilepsy', by retrospective analysis of the case records of 324 patients. The sample was divided into those exposed to anti-epileptic drugs (n=184), of whom 92 were said to have refractory seizures, and those who had not received treatment (n=140). The latter group is reported elsewhere. The overall misdiagnosis rate was 26.1% (46/184), with incomplete history-taking and misinterpretation of the EEG equally responsible. Side-effects were reported by 19/40, while unnecessary driving restrictions and employment difficulties were encountered by 12/33 and 5/33, respectively. Of those labelled 'refractory epilepsy', 12 did not have epilepsy. Sixteen were rendered seizure-free and 25 significantly improved by the optimal use of anti-epileptic drugs or surgery. Diagnostic and management services for patients with suspected and established epilepsy are suboptimal, with psychological and socio-economic consequences for individual patients. The resulting economic burden on the health and welfare services is probably substantial.

Q J Med 1999; 92:15-23

- Differential diagnosis includes two main groups:
  - Psychogenic nonepileptic attacks/spells.
  - Other (physiologic) non epileptic paroxysmal disorders

Psychogenic spells	Physiologic nonepileptic
Panic attacks	Syncope
Conversion	Complex migraine
Acute Psychosis	TIA
Munchausen	TGA
Malingering	Sleep disorders
Hyperventilation syndromes	Some movement disorders
	Delirium

- ### Suspecting nonepileptic attacks
- Nonepileptic events are initially suspected in the clinic based on the history and exam.
  - Specific features of the episodic spells have the potential to help distinguish epileptic seizures from psychogenic nonepileptic attacks (PNEA) or other physiologic events.
  - Recurrent episodes with consistent clinical features and little to no variation between events and the presence of an aura, favors the diagnosis of epileptic seizures (ES).

## Suspecting nonepileptic attacks

- On the other hand there are some “red flags” that suggest PNEA like:
  - Unusual triggers
  - Spells in the physician’s waiting room
  - Events that occur at high frequency and don’t respond to anti-seizure medications
  - Events occur only in the presence of an “audience”
  - Past medical history includes chronic pain or fibromyalgia.
  - Review of systems has many “positives”

## Suspecting nonepileptic attacks

- There are some red flags also on exam:
  - Give way weakness
  - Over dramatization
  - Event occur during exam

## Confirming the diagnosis

- Routine EEG
- Long term EEG/EMU
- MRI
- Ambulatory EEG

## Routine EEG

- An essential component in the initial workup of the patient with suspected epilepsy.
- The EEG can show many abnormalities, but true epileptiform activity have a high correlation with a tendency for clinical seizures.
- Nonspecific abnormalities such as background slowing, focal slowing, and abnormal-appearing normal variants may be over interpreted as correlating with seizures.

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- The yield of recording epileptiform activity on the routine EEG can be improved by performing the test with sleep deprivation and recording a brief period of time during light stages of sleep.
- The activation procedures of intermittent photic stimulation and hyperventilation should be used during routine EEG when possible.
- Initial EEG shows epileptiform activity in about 50% of recordings.
- Repeating the EEG improves the yield but to a point.

## Overinterpretation of EEGs and Misdiagnosis of Epilepsy

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- The authors report a series of EEGs on patients who were diagnosed eventually with psychogenic nonepileptic seizures and who had an EEG read as epileptiform.
- Of the 15 actual records available for review, the overread patterns were wicket spikes (n = 1), hypnagogic hypersynchrony (n = 1), and hyperventilation induced slowing (n = 1).
- **In the other 12 records, the overread patterns were simple fluctuations of sharply contoured background rhythms or fragmented [alpha] activity.**

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- Misinterpreting normal EEG as epileptiform activity may lead to:
  1. Unnecessary treatment with anti-seizure medications which are not entirely safe.
  2. Delays the right treatment
  3. The epilepsy diagnosis is harder to undo.
  4. Cost of treatment could be substantial

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## Epilepsy Monitoring Unit

- The gold standard in providing the accurate diagnosis.
- Also used to classify seizure types and to accurately localize the seizure focus when surgical intervention is considered.

- Monitoring in EMU changes the diagnosis in approximately 25% of cases: patients with an initial diagnosis of ES were found to have PNEA in 25% of cases, and those with an initial diagnosis of PNEA were found to have ES in about 25% of the cases.

Adult neurology. 2nd ed. Wiley-Blackwell, 2005

## MRI

- MRI is superior to CT in the evaluation of the person with suspected seizures, as the overall resolution for potential epileptogenic lesion detection is superior.
- Although many patients with epilepsy do not have identifiable lesions on MRI or CT scans; some may have lesions that are considered epileptogenic.
- Common examples include mesial temporal sclerosis(MTS), primary brain neoplasms, evidence of remote trauma, stroke, developmental abnormalities, and other vascular lesions.

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## AMBULATORY EEG

- Allows patients to be in their usual environment where spontaneous events typically occur.
- In theory it appears to be a good alternative to admission to the EMU.
- But the use of ambulatory EEG has several drawbacks compared to an EMU admission, including technical malfunctions, lack of video correlation, and inherently limited recording time.
- Caution in interpreting ambulatory recordings without the video correlation is appropriate as the ambulatory EEG is prone to technical artifact caused by scalp scratching, tooth brushing, chewing, eating, and other artifacts that have potential to be overinterpreted as epileptiform activity.

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## PSYCHOGENIC NONEPILEPTIC ATTACKS

## Some terminology

- The word non epileptic is not synonymous with psychogenic.
- Prefer not to use terms like pseudo seizure.
- The word seizure in psychogenic seizures might indicate epileptic seizures induced by psychological factors.
- The term psychogenic non-epileptic seizures is confusing to patients and families.
- Preferred term is psychogenic non epileptic attacks (PNEA) or spells.

- It has been estimated that 5% to 20% of the cases of suspected epilepsy ultimately turn out to be PNEA.
- In the selected population of patients admitted to an EMU, 25% to 40% of these patients are diagnosed with PNEA.
- Most patients with PNEA are refractory to AEDs, a fact that can alert the practitioner to this possible diagnosis.
- Patients with PNEA often have comorbid personality or psychological disorders, which further complicates making the diagnosis and subsequent management.
- Certain stereotypic movements, including pelvic thrusting and back arching, have been associated with PNEA.

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- In some observational studies, ictal stuttering, bringing a stuffed animal into the EMU, a history of fibromyalgia or chronic pain, a personal history of physical, emotional or sexual abuse, and having a seizure during the outpatient epilepsy clinic visit.
- Ictal eye closure could be a reliable indicator for PNEA

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## Coexisting Epilepsy

- The percentage of patients with PNEA who also has epilepsy ranges in the literature between 10% and 50%.
- However careful review of literature shows that the reports that have found a high percentage are based on loose criteria (like "abnormal" EEG) whereas those that required definite evidence for coexistence found percentages between 9% and 15%

Benbadis, Neurology 2001, 11;57(5):915-7

## PHYSIOLOGIC NONEPILEPTIC EVENTS

- Syncope
- Migraines
- TIA
- TGA
- Some movement disorders
- Sleep disorders

## Syncope

- Convulsive syncope represents the most confusing variant of this condition.
- During the attack of convulsive syncope, abnormal movements, including tonic posturing, myoclonus, or clonic motor activity, occur in response to sudden and transient cerebral anoxia and ischemia.
- The EEG during these attacks does not show epileptiform activity, instead showing diffuse slowing of the background rhythms.
- Many patients with syncope are diagnosed on clinical evaluation based on the comprehensive history and physical examination.

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## Syncope

- Confirmatory testing can include simple bedside tests such as checking for orthostatic blood pressure changes, simple pulse check, cardiac auscultation, tilt table testing, cardiac event monitors, and cardiac structural tests.
- A combination of tests (hyperventilation test, tilt table test, and carotid sinus massage) has provided a diagnosis and etiology in 81% of cases of syncope.
- The two main causes of syncope are changes in vasovagal tone and cardiac arrhythmia.

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## Migraine

- Features of migraine that are similar to seizures are the transient nature of symptoms, stereotypy, and episodic occurrence.
- Migraine and ES both may have auras consisting of positive symptoms, such as visual obscuration or an evolving sensory march.
- Either condition may also less commonly be associated with negative symptoms, such as hemiplegia.
- Weakness associated with seizures (Todd paralysis) occurs after the event, usually lasting from minutes to hours but is often not associated with headache as in hemiplegic migraine.

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## Migraine

- Additional clues that can distinguish migraine from seizures include the time it takes for the symptoms to develop.
- Typical migraine-associated phenomena develop over minutes compared to seizure-related symptoms, which typically evolve and last seconds

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## Migraine

- A history of having a classic evolving headache with typical migraine features of throbbing unilateral head pain with photophobia and phonophobia favors migraine.
- Typical ES last approximately 1 to 2 minutes followed by a variable duration of postictal symptoms, compared to migraine symptoms tending to last hours to days.

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## TIA's

- Generally, the differentiation between TIA and epilepsy is evident by a detailed history.
- TIA is associated with a sudden loss of neurologic function (negative symptoms), lasting minutes to hours.
- Seizure duration, on the other hand, is typically shorter, lasting seconds to a few minutes.
- TIA's are not as likely to have the repeated occurrence and stereotypy associated with seizures, a fact the practitioner can use to help distinguish between the two entities.

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## TIA's

- On very rare occasions, TIA can have positive symptoms, as in limb-shaking TIA.
- These events consist of the patient having brief myoclonic or rhythmic motor activity corresponding to transient cerebral ischemia secondary to a focal critical arterial stenosis supplying the appropriate motor cortex.
- It is important to note that stroke remains the leading known cause of epilepsy in older adults, when an etiology can be determined.

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## Transient Global Amnesia

- Transient global amnesia (TGA) presents with a sudden onset of confusion and memory impairment.
- TGA often occurs in a person who is seemingly healthy prior to the attack.
- The typical duration of these attacks is less than 24 hours.
- During the event, patients report feeling confused and disoriented rather than being amnesic.
- They are usually able to perform activities of daily living, such as eating, walking, and driving.

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## Transient Global Amnesia

- After the attack resolves, patients recall nothing that happened during the event as they are unable to acquire new information during the attack.
- Many different precipitants and potential etiologies have been proposed, but none have been proven to be definitive.
- The EEG during the TGA attack is normal.
- The overall incidence of TGA is estimated to be 5 to 10 cases per 100,000, with between 10% and 25% of patients suffering from recurrent events.

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## Movement Disorders

- Movement disorders can mimic seizures, especially if they are episodic or transient.
- The common movement disorders, such as essential tremor, chorea, and Parkinson disease, are more persistent and less episodic when compared to seizures.
- The persistence of symptoms in these conditions makes the distinction between movement disorders and seizures easier.

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## Movement Disorders

- Hemifacial spasm tends to be more transient with waxing and waning of symptoms.
- This variability may lead to hemifacial spasm potentially being mistaken as ongoing simple partial seizures.
- A possible distinguishing feature of hemifacial spasm is that over time it may be progressive.

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## Movement Disorders

- Myoclonus can be either epileptic or nonepileptic as defined by its location of origin, with nonepileptic myoclonus being of noncortical origin.
- Typically nonepileptic myoclonus shows no correlative epileptiform activity on the routine scalp EEG during the myoclonus.

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## Sleep Disorders

- Several sleep disorders have the potential to be confused with seizures, especially when the events under evaluation are exclusively nocturnal.
- Parasomnias are disruptive sleep-related disorders that are manifest by arousals or partial arousals from REM or non-REM sleep.
- The most common of these disorders are nightmares, night terrors, sleepwalking, and confusional arousals.
- Occurring at night, these entities may be confused with nocturnal epilepsy.
- Parasomnias are relatively uncommon and account for about 15% of the referrals to a sleep center.

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