Non-epileptic paroxysmal disorders / Imitators of epilepsy

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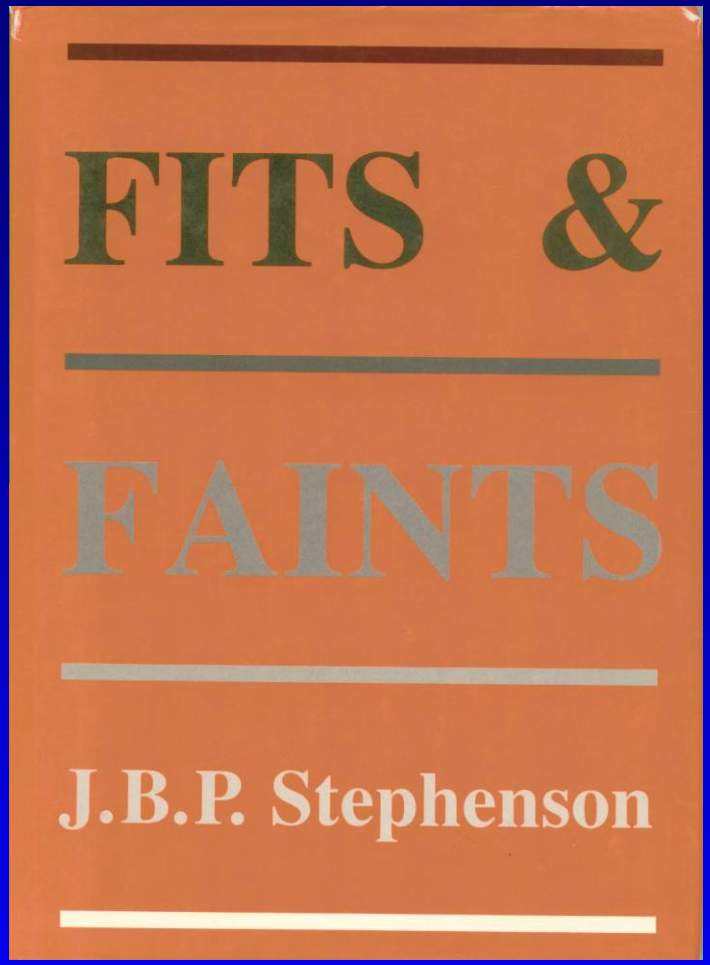

Published 1990

The borderland of epilepsy: clinical and molecular features of phenomena that mimic epileptic seizures

Douglas E Crompton, Samuel F Berkovic

Lancet Neurol 2009; 8: 370–81

ORIGINAL ARTICLE

Diagnoses made in a secondary care "fits, faints, and funny turns" clinic

D Hindley, A Ali, C Robson

Arch Dis Child 2006;**91**:214–218. doi: 10.1136/adc.2004.062455

Authors' affiliations
D Hindley, Fairfield General Hospital, Bury, UK
A Ali, C Robson, University of Manchester, UK

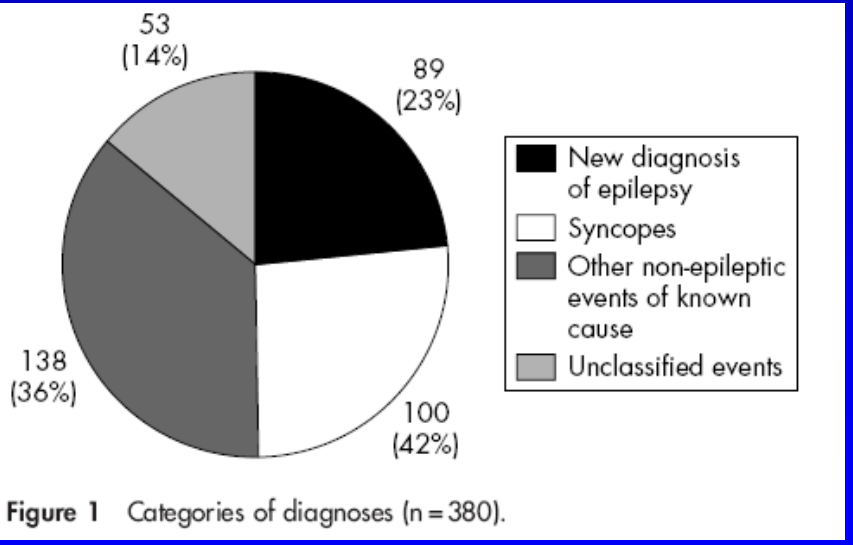

Figure 1 Categories of diagnoses (n = 380).

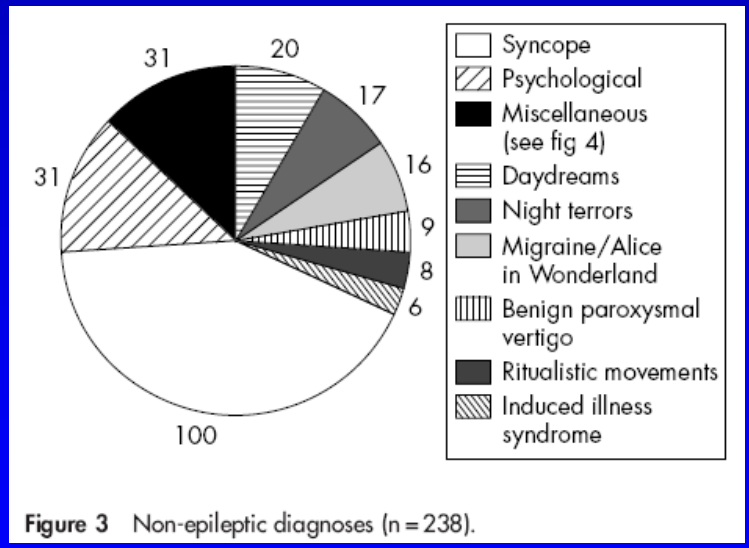

Figure 3 Non-epileptic diagnoses (n = 238).

Study period 1995-2003

ORIGINAL ARTICLE

The misdiagnosis of epilepsy in children admitted to a tertiary epilepsy centre with paroxysmal events

P Uldall, J Alving, L K Hansen, M Kibæk, J Buchholt

Arch Dis Child 2006;**91**:219–221. doi: 10.1136/adc.2004.064477

Authors' affiliations
P Uldall, J Alving, L K Hansen, M Kibæk, J Buchholt, Danish Epilepsy Centre, Kolonivej 1, DK-4293 Dianalund, Denmark

Table 2 Reasons for referral versus diagnosis at discharge among 223 children admitted for possible epilepsy

	Epilepsy confirmed	Epilepsy not confirmed
Doubt about diagnosis of epilepsy in referral note	7 (18%)	32 (82%)
No doubt of epilepsy expressed in referral note	129 (70%)	55 (30%)

Table 3 Diagnosis of 87 children discharged without a diagnosis of epilepsy

Diagnosis	No.
Staring episodes	46
Mental retardation (n=22)	
Autism/Asperger syndrome (n=4)	
Learning disorder (n=3)	
Self stimulation (n=2)	
Abnormal EEG (n=7)	
Normal child (n=8)	
Psychogenic non-epileptic seizures (PNES)	9
Syncope	4
Dystonia	4
Parasomnias	4
Hyperventilation attacks	3
Migraine	3
Breath holding spells	2
Munchhausen by proxy	2
Narcolepsy, Gilles de la Tourette, benign tremor, febrile convulsions	4
Not clarified	6

Study period 1997

Classification of Non-epileptic Seizures and Events

Six broad and sometimes overlapping clinical categories:

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- Psychological / behavioural disorders.
- Derangements of the sleep process.
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- Miscellaneous neurological and non-neurological events

Syncope

The abrupt loss of consciousness and postural tone resulting from transient global cerebral hypoperfusion, followed by complete spontaneous recovery

- *Neurally mediated*
- *Cardiovascular*

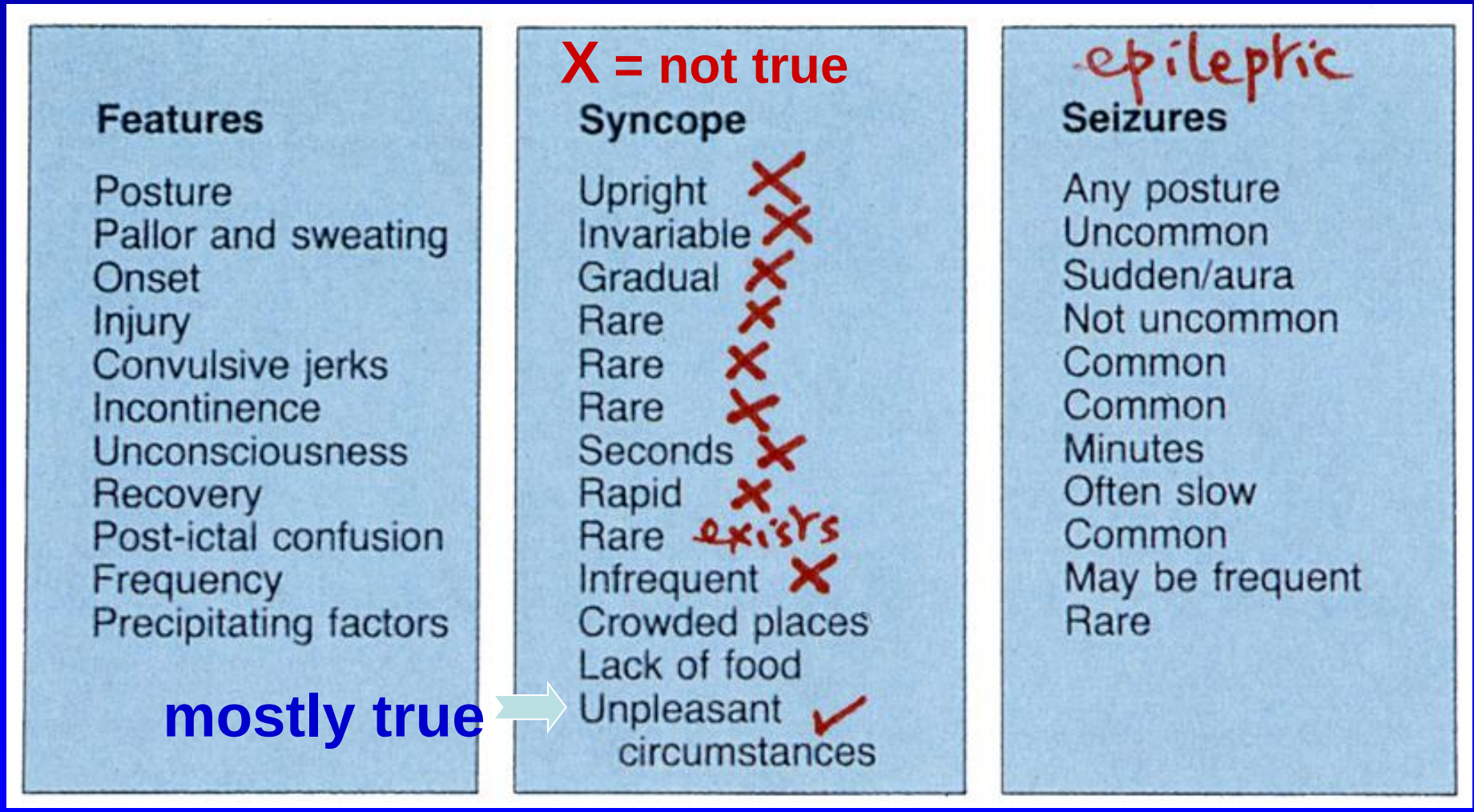
- Syncope occurs when there is an abrupt cutting off of the energy substrates to the cerebral cortex
  - *"A transient loss of consciousness resulting from an insufficient supply of oxygen to the brain"*

- Anoxic seizure – the collapse, stiffening, +/- jerking that occurs as a result of the syncope

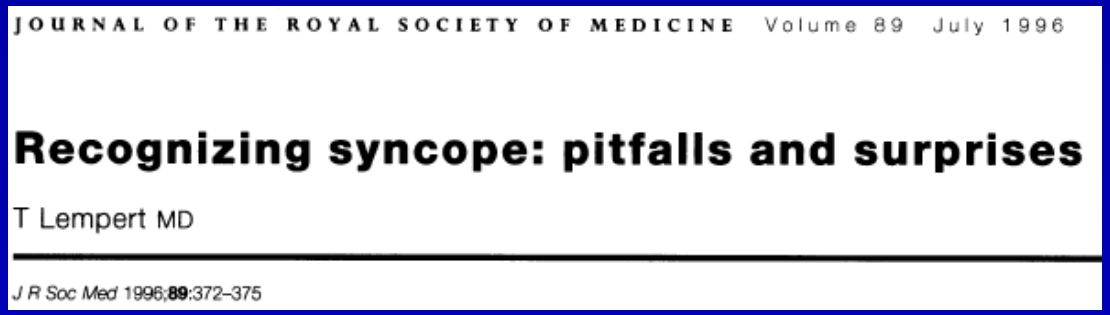
Syncope in the differential diagnosis of paroxysmal events

Syncope as a manifestation of neurological disorders

"The difference between syncopes and seizures"



Do not believe everything you read in a textbook



JOURNAL OF THE ROYAL SOCIETY OF MEDICINE Volume 89 July 1996

Recognizing syncope: pitfalls and surprises

T Lempert MD

J R Soc Med 1996;**89**:372–375

- 50% flaccid fall, 50% hips and knees extended
- Convulsive moments in >70%
- Eyes open with vertical downbeating nystagmus and then upward turning of eyes, can then deviate laterally
- Automatisms in 80%, moaning or growling in 40%
- Hallucinations- dreamlike in 60%. Visual and sometimes auditory, colours lights or complex images. Out of body experiences. Weightlessness, peace, detachment – near death experience.

Lifetime prevalence of neurally mediated syncope is 40%

Reflex anoxic seizure

- reflex asystolic syncope

Reflex anoxic seizures or reflex asystolic syncope occurs from early infancy onwards, either remitting pre-school age or evolving into vasovagal syncope. Alternative names include pallid breath holding and pallid syncope. In these events an unpleasant, typically sudden stimulus such as a bump, knock on the head, cut or abrasion leads to a profound vagal discharge with a dramatic drop in the heart rate and transient asystole. These events are not due to temper tantrums. The child may cry very briefly or let out a couple of grunts and then becomes exceedingly pale and loses consciousness. Decerebrate posturing with extensor stiffening may mimic atonic seizure and be followed by flexor spasms and irregular convulsive movements however the whole sequence of abnormal movements will just last a few seconds. Recovery of consciousness may be rapid but some children may sleep for hours after an event. The events appear very frightening for carers but have a good prognosis. When reflex anoxic seizures are very frequent, atropine or cardiac pacing may be considered. There is an uncommon situation in which an anoxic seizure may trigger a secondary prolonged convulsive seizure; the anoxic-epileptic seizure. The two phases of the event can be distinguished by a careful history, as in most events infants will have syncope without the epileptic component.

A useful website – www.stars.org.uk

Prolonged expiratory apnoea (Breath holding)

Breath-holding attacks typically affect pre-school children. The child will begin crying after some form of upset and then stop breathing in expiration with what appears a silent cry or a series of expiratory grunts. With this prolonged expiratory apnoea the child's face becomes blue with deep cyanosis. They may recover at this point and breathe in, or go on to a syncope with transient loss of consciousness. An anoxic seizure identical to that seen in reflex anoxic seizures may occur. Decerebrate posturing with extensor stiffening may mimic a tonic seizure and be followed by flexor spasms and irregular convulsive movements however the whole sequence of abnormal movements will just last a few seconds. Recovery of consciousness may be rapid but some children may sleep for hours after an event. The events appear very frightening for carers but have a good prognosis. In contrast to reflex anoxic seizures there is no asystole, and it is thought the syncope is due to a combination of intrapulmonary shunting, reduced venous return and hypoxia. The attacks are more common if the child has iron deficiency anaemia. There can be clinical overlap between breath-holding and reflex anoxic seizures and distinguishing them is not critical except for the very rare situation when reflex anoxic seizures are so frequent that treatment is considered.

ORIGINAL ARTICLE

Anoxic-epileptic seizures: observational study of epileptic seizures induced by syncopes

I A Horrocks, A Nechay, J B P Stephenson, S M Zuberi

Arch Dis Child 2005;**90**:1283–1287. doi: 10.1136/adc.2005.075408

Also look at Epileptic Disorders website and search under Stephenson or Zuberi for video examples

Compulsive valsalva

Compulsive valsalva can cause frequent syncope in people with learning disability, particularly those with autism. Individuals learn that through hyperventilation, followed by breath holding and a valsalva manoeuvre they can self-induce a syncope. It is presumed that this produces a pleasurable sensation. These children may also have epileptic seizures, a particular example being Rett syndrome. Video is invaluable in making the diagnosis.

16y old with malignant syncope

16 year old boy with 1 year history of collapses

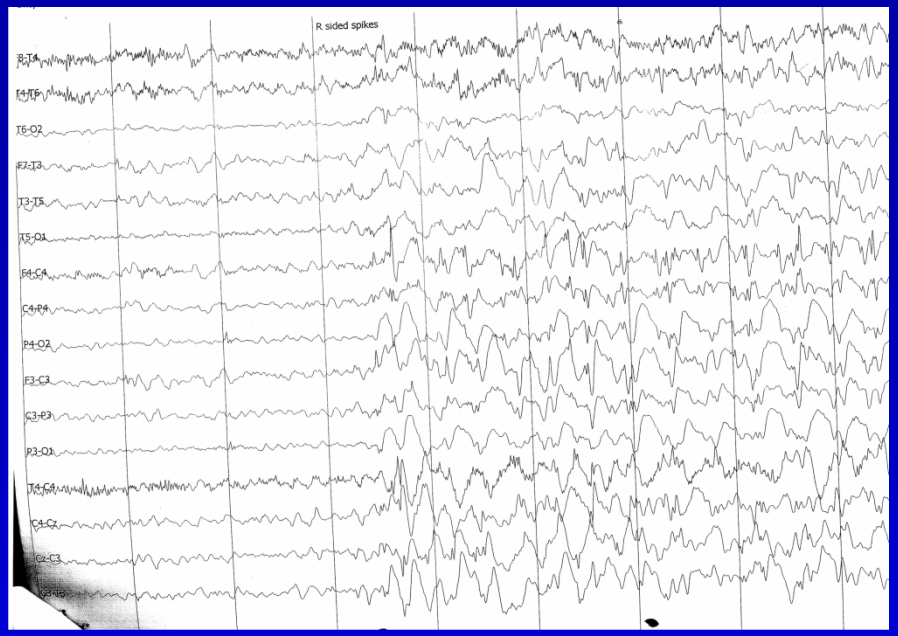
Normal EEG & MRI, during tilt test feels faint with drop in blood pressure

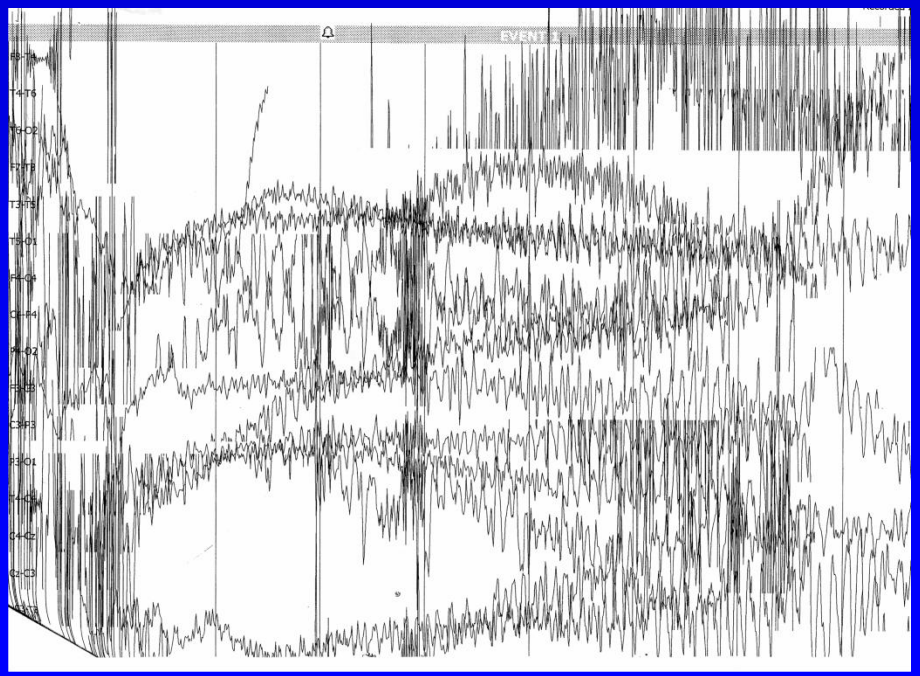
Had implantable cardiac ”Reveal” monitor

Diagnosed with malignant syncope. Taking a good history and asking his father to imitate the seizure allowed a diagnosis of epilepsy to be made.

Tilt test may be misleading if it does not reproduce the exact event you are wortried about.

2 weeks of ambulatory EEG were required to capture a seizure and undiagnose malignant syncope





Red flags

- Exercise-induced syncope, pre-syncope or chest pain
- Family history of sudden death
- Family history of drowning
- Family history of “SIDS”

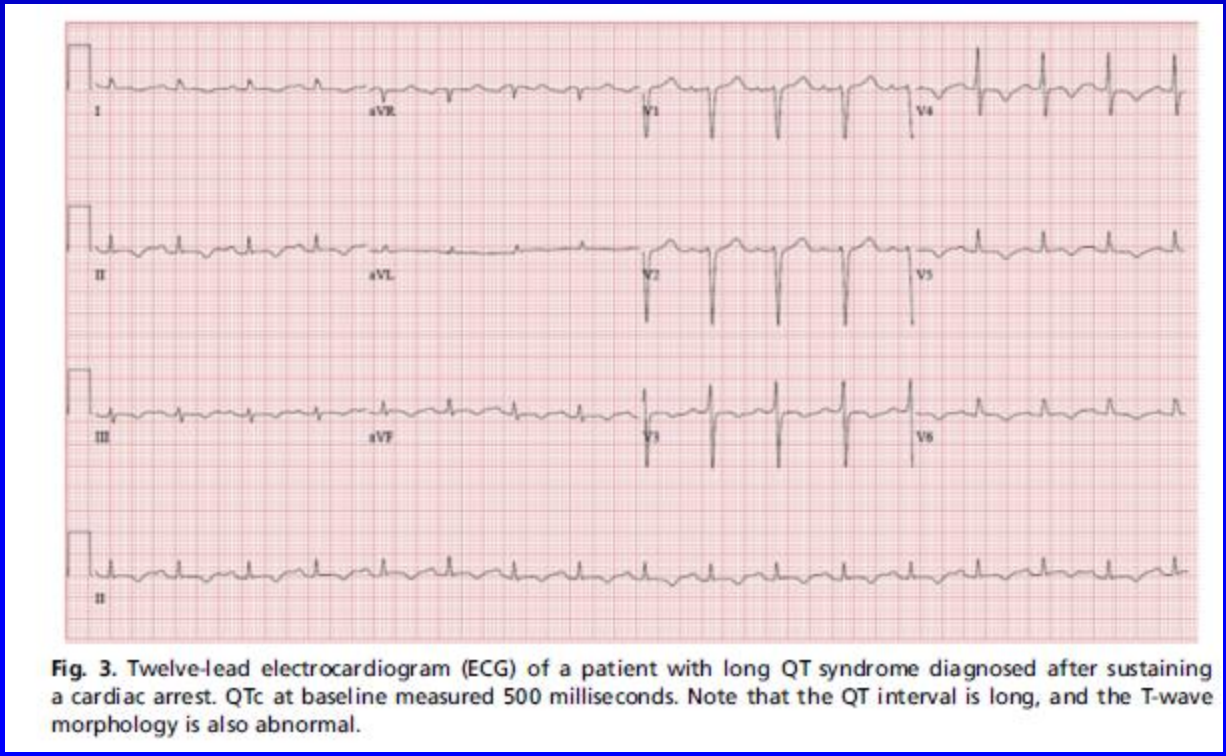


Fig. 3. Twelve-lead electrocardiogram (ECG) of a patient with long QT syndrome diagnosed after sustaining a cardiac arrest. QTc at baseline measured 500 milliseconds. Note that the QT interval is long, and the T-wave morphology is also abnormal.

Mortality risk in syncope

- Long QT
- Hypertrophic cardiomyopathy
- Structural heart disease
- Brugada syndrome

- 15% mortality at 1 year in patients with cardiac syncope
- Risk not increased in neurocardiogenic syncope

Causes of severe infantile / childhood syncope

- Hyperekplexia
- Paroxysmal extreme pain disorder
- Imposed upper airways obstruction
- Chiari malformation
- Cardiac arhythmias

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CLINICAL INFORMATION

History of presenting complaint

Presenting complaint

Description: infantile spasms

Comment: 9/12 old otherwise healthy child,clenches both arms and legs go rigid can last between 2 mins and 90 mins ,more marked on recent visit to America where he had a normal EEG
Mum has good video footage of the event. during the event the pattern can be physically broken but child returns to the behavior and cannot be distracted. child looks distressed during the events. he has not had any scanning

Reason for referral

Care type requested: Out Patient

Expected outcome: Not Specified

Past medical history

Current medication (Active Repeat medication issued within the last 12 months)

No current medications recorded

Recent medication (Any medication issued within last 90 days not shown above)

Clinical warnings

Additional relevant information

Administrative information

OK to send correspondence to home address?:Yes

Patient will accept any site:Yes

Patient will accept cancellation or short notice appointment (within 1-6 days):Yes

Patient has disability or requires wheelchair access:No

Referred By:Referring GP

Electronic Attachment Present:No

Signature of referring doctor (or other professional) **Date**

If the referral suggests gratification ask families to bring a video to the clinic

Self-gratification

Self-gratification or self-stimulation includes behavior which may be seen from infancy onwards, more so in pre-school girls. Rhythmic hip flexion and adduction may be accompanied by a distant expression, a flushed face and sometimes followed by sleepiness. The distant expression, sometimes associated with straining and head turning, may be confused with focal dyscognitive seizures. The diagnosis is more difficult when the infant or young child seems unhappy during or after the rhythmic movements. The relative frequency of events and occurrence in specific circumstances, such as when bored or in a car seat or high chair, lends this behavior to home video recording. Self-gratification or self-stimulation rather than terms such as masturbation are preferred by parents and better reflect the mechanism.

www.epilepsy diagnosis.org – Imitators section

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Benign neonatal sleep myoclonus

Benign neonatal sleep myoclonus is a normal sleep phenomenon which can be very frequent in some infants leading to misdiagnosis as myoclonic seizures or generalised convulsive seizures. The movements may begin in the neonatal period and be observed for many months and sometimes years. The myoclonus only occurs in sleep and the infants have a normal neurological examination, with normal feeding and behavior. Benign neonatal sleep myoclonus can be identified reliably on parental home video. Video is usually easily obtained as events are frequent, at predictable times and prolonged (often occurring over 30 minutes or so). An EEG is not required. On video, myoclonus is seen to affect all limbs and close observation reveals that there may be synchronous myoclonus of upper limbs, of lower limbs or all limbs. Sometimes one arm or one leg may be affected. The face is only exceptionally affected. The myoclonus occurs in brief flurries lasting a second or so with pauses of variable duration. The myoclonus also varies in amplitude. Waking the child abolishes the movements. A dramatically exaggerated form of sleep myoclonus is seen in infants of opiate-dependent mothers. The differential diagnosis for benign neonatal sleep myoclonus is myoclonic seizures, however neonates with myoclonic seizures would be expected to have a severe early onset epilepsy, with associated neurological deficits - such neonates would not be expected to feed and behave normally.

***"That's it!" – show a video* and use a doll**

Held-Egli K *et al* Benign neonatal sleep myoclonus in newborn infants of opioid dependent mothers. *Acta Paediatr* 2008

67% of neonatal abstinence cases had flurries of myoclonus

Narcolepsy-cataplexy – www.epilepsydiagnosis.org - Imitators

Narcolepsy-cataplexy is a lifelong neurological disorder of state boundary control in which the distinctions between sleep states, particularly REM sleep, and wakening are blurred. Onset is typically in the teenage years though it can occur in younger children and begin later in life. It is thought to be an acquired disorder with an autoimmune mechanism in individuals with a genetic predisposition. There is a very strong HLA association, evidence of reduced levels of a neuropeptide called orexin in CSF as well as post mortem evidence of damage to orexin producing neurons in the hypothalamus. Diagnosis is often delayed for several years and misdiagnosis with epilepsy can occur for several reasons. The condition is characterised by excessive daytime sleepiness, cataplexy (loss of tone in response to strong emotion), hypnagogic hallucinations, sleep paralysis and disturbed night time sleep. Cataplexy comprises a sudden onset of physiological REM atonia associated with a strong emotion, particularly laughter. This may cause a head drop, sagging of facial features, buckling of knees and a fall. All or some of these may occur in an event. The individual remains conscious, though the eyes may close, and through a degree of motor control try not to fall. This may give the appearance of repetitive jerks. The falls and head drops may be misdiagnosed as myoclonic seizures, the sagging of the face and lack of response may lead to a diagnosis of absence seizures. Attacks of sleep or the desire to sleep may lead to a variable level of responsiveness and a misdiagnosis of focal dyscognitive seizures may be made. The hypnagogic hallucinations, dreamlike often frightening visions in the awake state may be misdiagnosed as focal dyscognitive seizures. A good sleep history and if possible video of cataplexy can be sufficient to make a secure diagnosis but most individuals would require further evaluation including polysomnography, multiple sleep latency testing, HLA status and in selected cases CSF orexin estimation. Any association with learning disability or abnormalities on neurological examination should make the clinician consider Niemann Pick Type C, a brainstem lesion or Coffin Lowry syndrome.

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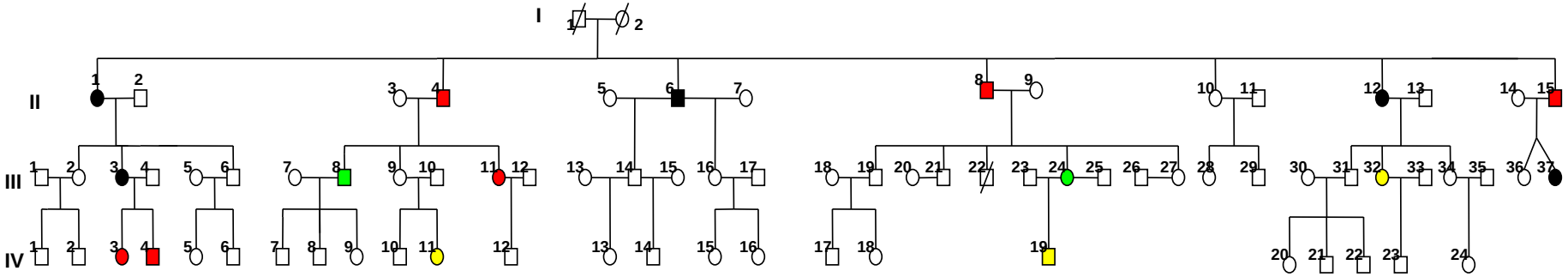
Paroxysmal kinesigenic dyskinesia is a hyperkinetic movement disorder characterised by brief (less than 1 minute) attacks of abnormal movements triggered by a sudden normal movement. The triggering movements are typically whole body movements and can include standing up from sitting or getting out of a car. Some individuals describe a feeling prior to the abnormal movement. This may be described as a "rush" through the body or a feeling of tightness or numbness. The abnormal movements are usually dystonic in nature, though they can appear choreiform, and can affect limbs on one or both sides of the body. Paroxysmal kinesigenic dyskinesia can be sporadic or familial, inherited in an autosomal dominant fashion, and may co-exist with epilepsy in the syndrome of familial infantile epilepsy (familial infantile epilepsy and paroxysmal kinesigenic dyskinesia syndrome, also known as ICCA syndrome). The movement disorder typically has its onset in mid-childhood or adolescence and may remit in the third decade. Paroxysmal kinesigenic dyskinesia with or without associated epilepsy is associated with mutations in the PRRT2 gene. Attacks may mimic frontal lobe seizures however movement as a trigger is the key differentiating feature in the history. Paroxysmal kinesigenic dyskinesia can respond dramatically to low dose carbamazepine.

www.epilepsydiagnosis.org - Imitators

Benign infantile familial convulsions and paroxysmal dyskinesia in a Scottish family



Unaffected male

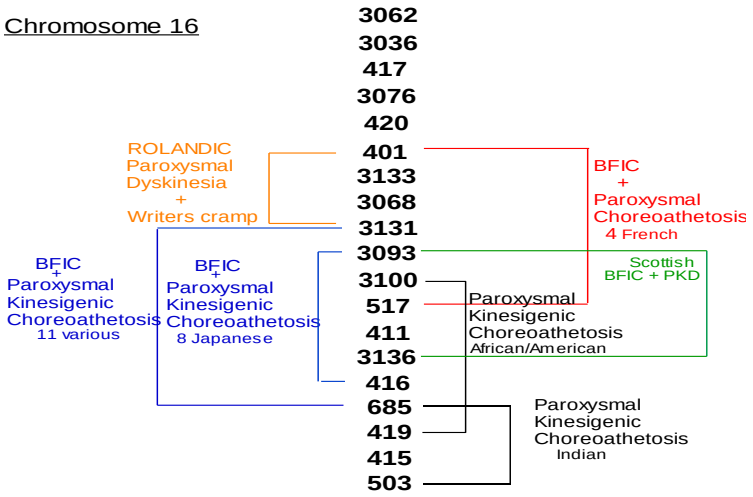
Unaffected female

Infantile convulsions and paroxysmal dyskinesias

Infantile convulsions

Paroxysmal dyskinesias

Other paroxysmal disorder



PRRT2 Mutations Cause Benign Familial Infantile Epilepsy and Infantile Convulsions with Choreoathetosis Syndrome

Sarah E. Heron,[1] Bronwyn E. Grinton,[2] Sara Kivity,[3] Zaid Afawi,[4] Sameer M. Zuberi,[5] James N. Hughes,[6] Clair Pridmore,[7] Bree L. Hodgson,[1] Xenia Iona,[1] Lynette G. Sadleir,[8] James Pelekanos,[2,9] Eric Herlenius,[10] Hadassa Goldberg-Stern,[3] Haim Bassan,[11] Eric Haan,[12] Amos D. Korczyn,[4] Alison E. Gardner,[13] Mark A. Corbett,[13] Jozef Gécz,[6,13,14] Paul Q. Thomas,[6] John C. Mulley,[6,14,15] Samuel F. Berkovic,[2,*] Ingrid E. Scheffer,[2,16,17] and Leanne M. Dibbens[1,17]

The American Journal of Human Genetics *90*, 152–160, January 13, 2012

Proline Rich Transmembrane protein 2

c.629-630insC (p.P210fsX224)

Startle

- A sudden involuntary movement caused primarily by surprise.
- Seen at 10 weeks in the fetus
- Bilateral synchronous shock like movements including closure of the eyes, raising of the bent arms above the head, flexion of the neck (can be head retraction), trunk, elbows, hips and knees.
- In hyperekplexia (startle disease) there is an exaggerated normal startle with increased gain

Hyperekplexia – www.epilepsydiagnosis.org - Imitators

Hyperekplexia is characterised by an exaggeration of the normal startle response and has several genetic associations (GLRA1, GPHN, GLRB, ARHGEF9 and SLC6A5) all linked to dysfunction of the inhibitory glycinergic pathway in the nervous system. Symptoms are evident from the neonatal period or early infancy. Infants are commonly hypertonic, with rigidity, rather than spasticity, which is relieved by sleep. In response to normal touch, noise or any unexpected stimulus they can startle excessively with flexion of the limbs and retraction of the head. A gentle tap using the tip of the examiner's finger on the tip of the individual's nose should trigger an excessive startle that does not habituate with repeated nose taps. The startle may be a rapid jerk or series of jerks, which can mimic a myoclonic, tonic or convulsive seizure. If an EEG is performed during an episode of stiffening, rhythmic muscle action potentials may be misdiagnosed as spikes. A severe startle response may be associated with apnoea and cyanosis. Severe attacks are particularly linked to SLC6A5 mutations and may be linked sudden infant death in this syndrome. Severe attacks can be aborted by flexing the trunk and neck of the child - the Vigevano manouvre. Clonazepam may be effective in reducing the startle and increased tone. The symptoms tend to resolve after infancy, but adults may have increased startle-induced falls and/or experience nocturnal muscle jerks. There are rarer subtypes of hyperekplexia associated with mutations in the gephyrin and collybistin genes in which epilepsy can co-exist. The onset of excessive startle in later childhood or adult life may be associated with development of autoantibodies to the glycine receptor.

Episodic ataxias

Episodic ataxias are rare autosomal dominant disorders divided into two major categories: episodic ataxia type 1 (EA1) and 2 (EA2) both of which are channelopathies in which a movement disorder and epilepsy may co-exist.

EA1 is associated with mutations in a potassium ion channel gene KCNA1. Brief episodes of cerebellar ataxia lasting seconds or minutes are triggered by sudden movements, emotion or intercurrent illness. Onset is typically in mid childhood with attacks occurring throughout life, though frequency may vary significantly with long periods of remission. During the episodes the individual may have dysarthria, limb and gait ataxia and titubation (coarse tremor) of the head. The movements may appear dystonic or choreiform in some individuals therefore misdiagnosis as paroxysmal kinesigenic dyskinesia or focal seizures may occur. The potassium channel mutation also causes peripheral nerve hyperexcitability which results in continuous stimulation of muscles. This may give the appearance of subtle rippling of muscles (myokymia) seen best under the eyelids or as continuous side to side movements of the fingers seen when the hands are outstretched. With intercurrent illness, particularly vomiting illnesses, the continuous stimulation of muscles may cause generalised stiffness (neuromyotonia). This may also be seen independent of illness in early infancy, with apparent (non-fixed) flexion contractures of the limbs and fisting of hands which gradually lessens over the first year. About 10% of people with EA1 have epileptic seizures, these may be focal seizures which can evolve to a bilateral convulsion. These epileptic seizures are a manifestation of the ion channel mutation causing neuronal hyperexcitability.

EA2 is characterised by periods of cerebellar ataxia lasting minutes to hours, which are triggered by physical and emotional stress. Gait and upper limb ataxia may be accompanied by dysarthria, nystagmus, vertigo, nausea and headache. EA2 can be distinguished from seizures by recognition of triggers, family history and retention of awareness during events. EA2 is associated with mutations in the calcium ion channel gene CACNA1A. Variants in this gene are associated with familial hemiplegic migraine and spinocerebellar ataxia type 6 and some phenotypic overlap with these disorders may occur. There may be gaze-evoked nystagmus in between episodes and over time vertical nystagmus may develop. As events are prolonged it should be possible to capture them on home video. Acetazolamide can be a very effective treatment.

www.epilepsydiagnosis.org – Imitators section

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History, history, history, history, history,history, history, history, history,…….

…..and video helps too.

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