Chapter 17

Non-epileptic paroxysmal neurological and cardiac events: the differential diagnosis of epilepsy

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An accurate clinical diagnosis requires differentiation between epilepsy and other causes of transient neurological disturbance and collapse, but the manifestations of epileptic seizures are diverse and there are many imitators, ranging from convulsive syncope to parasomnias. Nevertheless, the diagnosis of epilepsy is frequently straightforward, particularly when precise and detailed personal and eyewitness accounts of the prodrome, onset, evolution and recovery period after the event are obtained.

Misdiagnosis is common, however, and possibly affects up to 2–30% of adults with a diagnosis of epilepsy[1,2]. For example, 74 patients previously diagnosed with epilepsy were investigated with tilt-table testing, prolonged electrocardiogram (ECG) monitoring, blood pressure and ECG-monitored carotid sinus massage and found an alternative, cardiological diagnosis in 31 patients (41.9%), including 13 taking antiepileptic medication[3].

This and other reports highlight the high rate of misdiagnosis of epilepsy, the cause of which is undoubtedly multifactorial. The reasons for misdiagnosis may include a deficiency of relevant semiological information obtained during the ascertainment of the clinical history, lack of understanding of the significance of specific clinical features and over-reliance on the diagnostic value of routine investigations[4]. The attainment of a correct diagnosis is of paramount importance as an erroneous diagnosis of epilepsy has physical, psychosocial[5] and socioeconomic consequences for the patient, and economic implications for the health and welfare services[6].

Syncope

Transient loss of awareness is common, and may affect up to 50% of people at some stage of life[7,8,9]. Elucidating the aetiological basis for an episode of loss of awareness is challenging. Typically, the episode is transient, patients are generally unable to provide an accurate description of the event and there may be a lack of reliable witnesses, particularly in the elderly who, more frequently, live alone. The difficulty in establishing an accurate diagnosis is further hampered by systemic and neurological examinations and subsequent investigations frequently being normal after an episode or between habitual attacks when the patient is seen in the hospital ward or clinic[10].

Transient loss of awareness has three main underlying mechanisms:

1. Transient global cerebral hypoperfusion, i.e. syncope
2. Epilepsy
3. Dissociative (psychogenic, non-epileptic) seizures (discussed in Chapter 19).

Syncope, derived from the Greek ‘syn’ meaning ‘with’ and ‘kopto’ meaning ‘I interrupt’, may be defined as transient, self-limited loss of consciousness, usually leading to collapse, due to cerebral hypoperfusion[11].

Syncope is more prevalent than either epilepsy or dissociative (psychogenic) seizures and is common across all age groups with an overall incidence of 10.5% over a 17-year period[12]. Vasovagal syncope is most frequently encountered in adolescence, whereas syncope due to cardiac causes becomes increasingly prevalent with advancing age. The annual incidence of syncope in the elderly population in long-term care has been reported to be as high as 6%[9]. Recurrence is not unusual, occurring in approximately 30% of patients, typically within the first two years after symptom onset[13]. Recurrence is associated with increased morbidity, such as fractures, subdural haematomas and soft-tissue injuries[14], and impaired quality of life[11].

There are numerous causes of syncope, each resulting in inappropriate systemic hypotension and critical cerebral hypoperfusion. The causes can be divided into two main groups, cardiac and vascular.

Cardiac conditions that cause syncope may be either structural heart disease, such as aortic stenosis, hypertrophic cardiomyopathy, right ventricular dysplasia, some forms of congenital heart disease, severe ischaemic cardiomyopathy and left atrial myxoma, or arrhythmias, such as ventricular tachycardia, ventricular fibrillation, Brugada syndrome, long-QT syndrome, supraventricular tachycardia, atrioventricular block, and sinus node disease causing bradyarrhythmia or asystole. Vascular causes include reflex syncope, such as neurocardiogenic or carotid sinus hypersensitivity, situational syncope, for example, during coughing[15] or micturition, and postural syncope, including orthostatic hypotension or postural orthostatic tachycardia syndrome (POTS).

Neurocardiogenic syncope

Neurocardiogenic syncope is the most common cause of syncope[11] and has many synonyms including vasovagal, reflex, vasodepressor and neurally mediated hypotension. It arises through the provocation of inappropriate reflex hypotension, with a variable degree of bradycardia, or even transient asystole. There is often a precipitating cause such as prolonged standing in a warm environment, or fright, for example, venepuncture or the sight of blood. There may be a family history of ‘fainting’ or recent addition of vasoactive medication targeted at, for example, hypertension or ischaemic heart disease.

A typical attack commences with prodromal symptoms of nausea, clammy sweating, blurring or greying visual impairment, lightheadedness, and ringing or roaring tinnitus. Occasionally, visual and auditory hallucinations can be more complex, and involve figures or scenes[16]. Many of these individual symptoms are difficult for patients to describe and their description may be vague, but collectively the cluster of symptoms is characteristic. Subsequently, the patient will look pale and be sweaty. Mydriasis, tachypnoea, bradycardia and acral paraesthesia may be present. Muscle tone is reduced, causing the eyes to roll up, and the patient to fall to the ground. In the horizontal position, skin colour, pulse and consciousness usually return within a few seconds, and while the patient may feel briefly unwell, confusion, amnesia and drowsiness are not prolonged. Injury and incontinence are rare but may occur. Tongue biting in syncope of any cause is unusual, but frequently seen in epilepsy. The presence of brief myoclonic jerks during a syncopal episode of any cause, observed in approximately 15% of patients[17,16], is often over-interpreted by witnesses, and occasionally health professionals, leading to diagnostic confusion. Such myoclonic jerks are usually multi-focal and are rarely rhythmic, prolonged or of large amplitude. Videotelemetric monitoring shows that the myoclonic jerks rarely last longer than 15–20 seconds[16] and do not have an EEG correlate, unlike true epileptic myoclonus. Rarely, manual and orofacial automatisms may occur, even during the presyncopal stage[18]. If recovery from cerebral hypoperfusion is delayed, for example if the patient is held in an upright position, a secondary anoxic convulsive seizure may occur. These should not be classified as epileptic however.

Orthostatic syncope

Orthostatic syncope is caused by autonomic failure rather than an exaggerated and inappropriate but essentially normal physiological response, as seen in neurocardiogenic syncope. Patients lose the normal vasoconstrictor response to standing, resulting in venous pooling and a postural fall in blood pressure, usually within seconds or minutes of becoming upright. Unlike in neurocardiogenic syncope, the skin stays warm and well perfused, the pulse rate is unchanged and sweating is absent. The causes of autonomic dysfunction are varied and include autonomic neuropathy due to diabetes, alcohol, amyloidosis, genetic abnormalities or complex autonomic failure, such as primary autonomic failure or multiple system atrophy. Medications such as antihypertensives, phenothiazines, tricyclic antidepressants, diuretics and medication for Parkinson's disease may also be implicated.

Postural orthostatic tachycardia syndrome

Postural orthostatic tachycardia syndrome (POTS) is an autonomic disturbance characterised by symptoms of orthostatic intolerance, mainly light-headedness, fatigue, sweating, tremor, anxiety, palpitation, exercise intolerance and syncope or presyncope on upright posture[19]. Patients also have a heart rate greater than 120 beats per minute on standing or an increase in heart rate of 30 beats per minute from a resting heart rate after standing for 1–5 minutes, compared to an increase of only 15 beats per minute in heart rate in the first minute of standing in normal subjects. POTS is most common in females between the ages of 12 and 50 years and may follow surgery, pregnancy, sepsis or trauma[20]. The pathophysiological basis of POTS is not well understood. Hypotheses include impaired vascular innervation, baroreceptor dysfunction and high plasma noradrenalin concentrations, of which impaired innervation of the veins or their response to sympathetic stimulation is probably the most important[21].

Carotid sinus hypersensitivity

Carotid sinus hypersensitivity (CSH) is an exaggerated response to carotid sinus baroreceptor stimulation. Even mild stimulation to the neck results in presyncopal symptoms or syncope from marked bradycardia and a drop in blood pressure causing transiently reduced cerebral perfusion. CSH is found in 0.5–9.0% of patients with recurrent syncope and is observed in up to 14% of elderly nursing home patients and 30% of elderly patients with unexplained syncope and drop attacks[22,23]. It is more common in males. It is associated with an increased risk of falls, drop attacks, bodily injuries, and fractures in elderly patients but rates of total mortality, sudden death, myocardial infarction, or stroke are similar to the general population. Around 30% of cases are classified as cardioinhibitory where the predominant manifestations are sinus bradycardia, atrioventricular block, or asystole due to vagal action on sinus and atrioventricular nodes. Permanent pacemaker implantation is effective at reducing recurrence rate[24]. The vasodepressor type also comprises 30% of cases and results in a marked decrease in vasomotor tone without a change in heart rate. The remaining patients are of a mixed type[25]. Untreated symptomatic patients have a syncope recurrence rate as high as 62% within four years. The diagnosis is established by performing carotid sinus massage with the patient supine, under ECG and blood pressure monitoring.

Cardiogenic syncope

Cardiogenic syncope arises from either a rhythm disturbance or structural cardiac defects. The identification of a cardiac cause of syncope is of paramount importance because the prognosis is poor if untreated[10,13,26,27]. A family history of sudden cardiac death may be present, indicating the possibility of Brugada syndrome, long-QT syndrome or an inherited cardiomyopathy, for example, hypertrophic cardiomyopathy, familial dilated cardiomyopathy or arrhythmogenic right ventricular dysplasia. Typically, presyncopal symptoms will be absent, and the circumstances of the syncope may be important. Syncope *after* exercise is a manifestation of neurocardiogenic syncope, whereas syncope *during*

exercise is more suggestive of cardiomyopathy or primary electrical disturbance such as Wolff-Parkinson-White syndrome or right ventricular dysplasia.

Cerebrogenic cardiac dysfunction has also been observed. Arrhythmias, conduction block, and repolarisation ECG abnormalities have been reported in up to 56% of epileptic seizures. Abnormalities appear to be more common in nocturnal, prolonged, and generalised seizures than in focal seizures or those occurring during wakefulness[28-32].

Differentiation

The differentiation between epileptic seizures and syncopal attacks can be difficult. Typically, patients with epilepsy have more episodes of loss of consciousness and a longer history than patients with syncope. Clinical features that are most strongly predictive of syncope of any cause versus seizures are a postural component, a prior history of presyncopal episodes with unpleasant situations, diaphoresis, dyspnoea, chest pain, palpitations, a feeling of warmth, nausea, and vertigo. Patients are also more likely to have hypertension and ischaemic heart disease.

In a study evaluating the utility of a diagnostic questionnaire, epilepsy was predicted by the presence of tongue biting, urinary incontinence, prodromal déjà vu, post-ictal confusion, mood disturbance, muscle pain, headaches, witnessed convulsive movements, head turning and cyanosis[17]. The application of the questionnaire resulted in a diagnostic accuracy of 86%, suggesting that the careful evaluation of the history from the patient and witness is of principal importance in attaining the correct diagnosis. It is important to note that syncope due to primary cardiac disease may present with sudden collapse and have a less well defined, or often completely absent, prodromal period compared to vasovagal syncope[18,16,33].

In patients with syncope, neurological and cardiological examinations are frequently unrewarding. Further investigations may be necessary and are dependent on the history obtained. Extensive investigation is not mandatory, however, in patients with, for example, a typical history of neurocardiogenic syncope. A 12-lead ECG should, however, be undertaken in all patients. Patients with an abnormal cardiological examination or 12-lead ECG or those patients with a family history of sudden cardiac death or a personal history that is atypical for neurocardiogenic syncope, for example, episodes during exercise, while lying flat or with palpitations, warrant more extensive cardiac investigations including a transthoracic echocardiogram, prolonged ECG monitoring and, frequently, tilt-table testing.

In conditions such as Brugada syndrome, the ECG abnormalities may be intermittent. Serial ECGs in undiagnosed syncope may, therefore, be helpful. In patients with infrequent episodes, one- to seven-day prolonged, Holter-type, ECG recordings have a yield of less than 1%[11] and implantable loop recorders, which can monitor cardiac rhythm for up to 18 months, are more appropriate, with a yield in unexplained syncope of up to 50%[34-36]. Autonomic function testing, and more specifically tilt-table testing (for example, 70º tilt for 45 minutes) also has high sensitivity (approaching 70%) for identifying patients with a syncopal tendency, particularly in patients over the age of 50 years with recurrent syncope and no structural cardiac pathology[37,38], but reproducibility has been reported to be poor[39]. Measures to induce syncope, such as isoprenaline, provoke syncope more rapidly and provide additional sensitivity (10–15%), but at the expense of reduced specificity[40].

Prognosis and treatment

The prognosis and treatment of syncope is entirely dependent on the underlying aetiology. Structural heart disease significantly increases the risk of death in patients with syncope[11]. For example, patients with syncope and severe left ventricular failure have a one-year mortality rate of 45% compared to a similar group of patients with cardiac failure but no syncope[10,26,27]. In contrast, patients with neurocardiogenic syncope, aged 45 years or less,

without structural heart disease have no increase in mortality rate. Even patients who remain undiagnosed following extensive investigations have a good prognosis[10,13]. It is therefore of paramount importance, from a prognostic and interventional point of view, to identify those patients with syncope due to an underlying cardiac cause.

Drop attacks

Neurological causes of sudden collapse other than epilepsy and autonomic dysfunction include intermittent obstructive hydrocephalus caused by, for example, a colloid cyst of the third ventricle or a craniocervical junction abnormality such as an Arnold-Chiari malformation. Colloid cysts present with syncope and sudden death, particularly with changes in posture, are readily identified on neuroimaging and are amenable to neurosurgical intervention[41,42].

Diencephalic attacks, as sequelae of diffuse brain injury, are extremely rare and manifest as autonomic dysfunction with diaphoresis, sinus tachycardia, collapse and intermittent hypertension[43].

Brainstem and spinal cord lesions or lower limb weakness of any cause may present with unexplained falls without impairment of consciousness. There are usually fixed neurological signs which will guide appropriate investigations and the episodes are rarely confused with atonic or tonic seizures of epilepsy. Cataplexy usually occurs in association with the narcoleptic tetrad of excessive daytime somnolence, hypnagogic hallucinations, and sleep paralysis, although it may be the presenting feature. Further details regarding this condition are found in Chapter 18 on epilepsy and sleep.

Idiopathic drop attacks are most commonly seen in middle-aged women. They take the form of a sudden fall without loss of consciousness, and patients frequently remember hitting the ground. Recovery is instantaneous but injury often occurs. Neurological, cardiac and autonomic investigations are unrewarding.

It is likely that vertebrobasilar ischaemia is overdiagnosed and probably accounts for only a small proportion of drop attacks. Typically, the attacks occur in the elderly, with evidence of vascular disease and cervical spondylosis, both commonly occurring conditions which frequently co-exist in the elderly population. Furthermore there is clinical overlap with other more commonly occurring but benign conditions such as benign paroxysmal positional vertigo. The attacks may be precipitated by head turning or neck extension resulting in distortion of the vertebral arteries and haemodynamic ischaemia, although embolic events are probably a more frequent cause. Drop attacks are accompanied by features of brainstem ischaemia such as diplopia, vertigo and bilateral facial and limb sensory and motor deficits[44].

Hyper- and hypokalaemic periodic paralyses (PP) are rare autosomal dominant disorders of sodium and calcium ion channel dysfunction characterised by episodic flaccid weakness secondary to abnormal sarcolemmal excitability and rapid changes in serum potassium levels. Cranial musculature and respiratory muscles are usually spared. Attacks last from between minutes in hyperkalaemic PP to hours and occasionally days in hypokalaemic PP. Precipitants include fasting, alcohol, resting following exercise, stress (hyperkalaemic PP) and a high carbohydrate meal, cold and exertion the previous day (hypokalaemic PP). Acute treatment is directed at supportive care and normalisation of the serum potassium. Effective prophylaxis of hypokalaemic PP, like many of the channelopathies, is with acetazolamide[45]. Thyrotoxicosis is the commonest cause of secondary periodic paralysis.

Convulsive movements and transient focal hypermotor episodes

Convulsive limb movements commonly accompany episodes with transient loss of awareness and are most commonly due to epilepsy, syncope or dissociative seizures. Transient, episodic limb movements without loss of awareness are also frequently misdiagnosed as epilepsy. There is often a degree of overlap with myoclonus as the clinical manifestation of a variety of pathophysiological processes embracing the subspecialty fields of both epilepsy and movement disorders. Epileptic myoclonus, which is cortical in origin, can be confused with other hyperkinetic movement disorders, including myoclonus originating from subcortical structures, brainstem, spinal cord or peripheral nerves, tics, chorea, dystonia and tremor. Definitive localisation of the myoclonic focus requires electrophysiology, specifically a time-locked back-averaged EEG. Careful neurological examination is also often helpful in this regard, for example, in identifying spinal cord pathology or evidence of a cortical process.

Cortical myoclonus arises from a hyperexcitable focus within the sensory-motor cortex, and involves an arm, leg or the face. In general, it is typically arrhythmic, although in the setting of epilepsia partialis continua jerks may appear rhythmic. Cortical myoclonus is triggered by action or intention, and is often stimulus-sensitive. Subcortical myoclonus refers to myoclonus without a preceding cortical discharge and arises from structures such as the thalamus, and is usually, although not exclusively, stimulus-insensitive. In practice, it is frequently difficult to differentiate cortical from subcortical myoclonus on clinical grounds, and neurophysiological investigation is required. Neuroimaging may also be helpful in this regard. Myoclonus arising from the brainstem (startle, palatal and reticular reflex myoclonus), spinal cord (segmental and propriospinal myoclonus) and peripheral nerves are usually recognised and differentiated from epilepsy without difficulty.

Among the hyperkinetic movement disorders, tremor is the entity most often confused with myoclonus and convulsive limb movements. Tremor is habitually rhythmic and oscillatory, and significantly slower than myoclonus; however, occasionally tremor may be jerky and irregular, mimicking clonic jerks to the degree that electrophysiological investigation is required to differentiate between them.

Like myoclonus, tics are also brief; however, they are typically preceded by an urge to perform the movement and can usually be temporarily suppressed, features not seen in myoclonus or simple partial seizures. Tics are usually stereotyped, repetitive and often complex, involving multiple different noncontiguous muscle groups.

Chorea, a brief involuntary ‘dance-like’ movement, is usually easy to distinguish from myoclonus and epilepsy due to the characteristic flowing movements. Dystonia is an involuntary movement disorder characterised by repetitive, sustained movements that typically produce twisting postures. Dystonia rarely mimics myoclonus although it may be confused with epileptic tonic spasms or the dystonic posturing seen in partial seizures of frontal or temporal lobe origin. Many patients with dystonia possess a manoeuvre that attenuates the dystonia, termed a ‘geste antagoniste’.

Paroxysmal dyskinesias are a genetically and clinically heterogeneous group of rare movement disorders characterised by episodic dystonic or choreiform movements. Paroxysmal kinesigenic dyskinesia (PKD) is the most common type, although the precise prevalence is unknown. This condition is characterised by brief attacks of unilateral or bilateral limb dystonia or chorea, lasting less than one minute and with preserved consciousness, triggered by initiation of voluntary movements. An ‘aura’, such as an unusual cephalic or epigastric sensation, may precede the attacks, further adding to the diagnostic confusion[46]. Sporadic cases occur; however, PKD is considered to be an autosomal dominant condition with variable penetrance, linked to the pericentromeric region of chromosome

16[47,48,49]. The underlying pathophysiological mechanism is thought to be a sodium channelopathy because the condition is highly responsive to carbamazepine and there is possibly some overlap with afebrile infantile convulsions and channelopathy-related epilepsies, such as autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE).

Episodic ataxias typically present in childhood or adolescence and manifest as ataxia and myokymia (type 1, potassium channelopathy) or vertigo, ataxia and occasionally syncope (type 2, calcium channelopathy). These events are commonly diagnosed as epilepsy and EEG recordings can show sharp and slow waves. Moreover, true epileptic seizures can occur, confounding the diagnosis further.

Painful tonic spasms of multiple sclerosis and other upper motor neuron disorders are involuntary, unilateral dystonic movements that are frequently precipitated by movement. The clinical history and neurological examination should usually provide sufficient evidence to differentiate between tonic spasms of, for example, multiple sclerosis, epileptic seizures and paroxysmal dyskinesias.

Startle syndromes are a heterogeneous group of disorders, comprising hyperekplexia, startle epilepsy and neuropsychiatric syndromes, which are characterised by an abnormal motor response to startling events. Despite some clinical overlap, a carefully recorded history is frequently sufficient to accurately differentiate these entities[50]. Hyperekplexia is characterised by an exaggerated startle response consisting of forced closure of the eyes and an extension of the extremities followed by a generalised stiffness and collapse. It can be mistaken for cataplexy in patients with narcolepsy, or atonic or tonic epileptic seizures. More minor forms of hyperekplexia display an exaggerated startle response without tonicity and collapse. Hyperekplexia may be hereditary, due to a genetic mutation in the alpha-1 subunit of the glycine receptor on chromosome 5, sporadic or symptomatic, secondary to widespread cerebral or brainstem damage. Clonazepam may be helpful in reducing both the severity of the startle response and degree of tonicity[51].

Startle epilepsy usually manifests as an asymmetric tonic seizure, triggered by a sudden stimulus[52,53]. Other ictal patterns such as absences, atonic seizures, or generalised seizures are less common. EEG abnormalities during such seizures may be obscured by profuse electromyographic activity in the pericranial muscles, although occasionally epileptiform activity over the vertex may be seen. Startle-provoked seizures usually become manifest after spontaneous epileptic seizures of the same ictal phenotype have been present for a prolonged period with a high-frequency, possibly due to a kindling-like phenomenon. In the majority of cases, both ictal phenotype and neuroimaging data suggest a seizure onset zone within the supplementary motor area. Other than hyperekplexia, startle-induced conditions which may be confused with reflex startle epilepsy include stiff-person syndrome[54] and progressive encephalomyelitis with rigidity and tetanus, although the presence and nature of concomitant neurological symptoms and signs readily distinguish these conditions from each other.

Transient focal sensory attacks

Migraine and epilepsy are both characterised by paroxysmal cerebral dysfunction and a possible relationship between migraine and epilepsy has been postulated[55,56]. Migraine is frequently mistaken for epilepsy, particularly in acephalgic migraine, when the headache is mild or absent. Epileptic seizures can be accompanied or followed by migraine-like headache[57-59], and attacks of migraine can lead to unconsciousness[60], particularly in basilar migraine[61], and acute confusion[62,63]. Migraine attacks can cause epileptiform EEG abnormalities[64-66], although the EEG changes are usually non-specific. It has been suggested that episodes of migraine with aura may provoke seizures, in a condition termed ‘migralepsy’[67], although this has not been universally accepted[68].

Attacks of migraine and of epilepsy also have various precipitants in common, such as hormonal factors and sleep disturbance[56]. A migrainous aura may have visual, sensory or motor features that may be suggestive of seizure activity and alertness may be impaired. There are, however, a number of important semiological differences. Visual migraine auras are monochromatic, angulated, bright and frequently scintillating. They commence in the centre of the visual field and gradually evolve over several minutes towards the periphery of one hemi-field, often leaving a scotoma. They usually last between 30 and 60 minutes. In contrast, simple partial seizures arising from the occipital lobe are circular, amorphous, multicoloured obscurations that develop rapidly within seconds, and are brief in duration (2–3 minutes). They often appear in the periphery of a temporal visual hemi-field, becoming larger and multiplying in the course of the seizure, while frequently moving horizontally towards the other side[69,70].

Somatosensory migraine commences with unilateral paraesthesias spreading from one area to another over 15–30 minutes, often resolving in the first area before becoming evident in the next. Epileptic sensory symptoms arise quickly and spread rapidly over seconds to involve other somatic areas in summation, often culminating in secondary generalisation. Peripheral neuropathies or radiculopathies also cause sensory symptoms and may be transient if, for example, they are compressive or inflammatory in aetiology. Neurological examination may reveal evidence of a fixed neurological deficit, and the circumstances in which the sensory symptoms develop and lack of associated epileptic semiology rarely result in diagnostic confusion.

Transient ischaemic attacks (TIAs) are broadly distinguished from seizures and migraine by their 'negative' symptoms, that is, sensory loss, weakness or visual impairment, with retained awareness. However, tingling and focal jerking may occur in association with local cerebral hypoperfusion and occasionally with severe bilateral carotid stenosis[71].

Vertigo with brief episodes of disequilibrium is often misinterpreted as seizure activity. More commonly, the symptoms are due to disorders of the peripheral vestibular system, such as benign paroxysmal positional vertigo or Ménière's disease. Vertigo may occur as a feature of focal seizures, arising from the frontal or parietal regions and specifically the intraparietal sulcus, posterior superior temporal lobe, and the temporo-parietal border regions[72-75]. Vertigo observed in epileptic seizures rarely occurs in isolation and other clinical manifestations of seizure activity, such as impaired awareness, are also usually present. Vertigo due to a peripheral vestibular disorder is often accompanied by nausea and vomiting and precipitated by head movement, such as rolling over in bed or on provocation with Hallpike's manoeuvre. Focal onset or generalised epileptic seizures may be provoked by the same manoeuvres in patients with 'vestibular epilepsy', a subtype of the reflex epilepsies.

Psychic experiences

Focal seizures arising from the temporal lobe commonly involve psychic phenomena, including déjà vu, panic and fear, visual, olfactory or auditory hallucinations. Perception of the environment may be altered with derealisation, micropsia and macropsia, and interaction with others may be impaired by abnormal language function and altered thought patterns, seen most commonly in temporal and frontal lobe seizures. Panic attacks, which have a psychological rather than epileptic basis, are associated with feelings of fear and anxiety, hyperventilation and palpitations. The diagnosis is usually clear as they are commonly situational rather than spontaneous, and have a protracted time course with a characteristic evolution. Simple partial seizures arising from the amygdala can, however, be difficult to differentiate from brief episodes of fear and anxiety[76,77].

Hallucinations or illusions can occur in the context of loss of a primary sense. This is well recognised in limb amputees, with phantom limb pain and sensory disturbance. Similarly, patients with visual impairment may develop Charles Bonnet syndrome, with visual hallucinations in the area of visual field loss. This results from damage to the visual system due to, for example, age-related macular degeneration or glaucoma, but it may also arise in patients with intracranial pathology and secondary deafferentation of the visual cortex[78].

Aggressive or vocal outbursts

Episodic dyscontrol syndrome (EDS) and its counterpart, intermittent explosive disorder (IED), are patterns of abnormal, episodic, and frequently violent and uncontrollable social behaviour often in the absence of significant provocation. These events are frequently attributed to epilepsy as they often arise seemingly out of character. Uncontrolled rage occurring in the context of epileptic seizures is also unprovoked, however the anger is usually undirected or reactive, the episodes occur in isolation and other manifestations of a seizure disorder are frequently present. Additionally, routine inter-ictal EEG recordings in EDS have not shown epileptiform activity[79]. Interestingly, however, a significant proportion of patients demonstrate non-specific diffuse or focal slowing not attributable to drowsiness or the effects of medication. There is neuroimaging evidence of frontolimbic involvement in the pathogenesis of EDS and IED and co-existent neurological and psychiatric conditions are frequently seen[80]. So although the rage attacks themselves may not have an epileptic basis, the two conditions may be pathogenetically linked.

Prolonged confusional or fugue states

Acute neurological conditions, such as non-convulsive status epilepticus, intracranial infections, head injuries, ischaemic events and drug intoxication or withdrawal may result in an acute confusional state. Systemic disorders may also give rise to episodes of acute encephalopathy and transient loss of consciousness such as renal or hepatic failure and endocrine and metabolic abnormalities, the most common of which is hypoglycaemia related to insulin therapy in diabetes mellitus. Other precipitants of hypoglycaemia include alcohol, insulinomas, rare inborn metabolic abnormalities, such as congenital deficiencies of gluconeogenic enzymes, and renal or hepatic disease. The symptoms of hypoglycaemia are protean, and include visual disturbance, diaphoresis, confusion, unconsciousness, and altered behaviour including irritability and aggression. Peri-oral and acral paraesthesias, ataxia, tremor and dysarthria are common features, leading to diagnostic confusion unless an accurate history and appropriate laboratory investigations are performed. The rare disorders of phaeochromocytoma, carcinoid syndrome and hypocalcaemia may also present with confusion, presyncope or syncope and the hypocalcaemic sensory disturbance may be mistaken as an epileptic aura[81].

Transient global amnesia (TGA) usually occurs in middle-aged or elderly people and is characterised by the abrupt onset of anterograde amnesia, accompanied by repetitive questioning[82]. With the exception of the amnesia, there are no neurological deficits. There is neither clouding of consciousness nor loss of personal identity. Attacks last between minutes and hours, with six hours being the average duration. The ability to lay down new memories gradually recovers, leaving only a dense amnesic gap for the duration of the episode and a variable degree of retrograde amnesia. The attacks are often associated with headache, dizziness and nausea. The duration and number of attacks are important in distinguishing TGA from transient epileptic amnesia and transient ischaemic events affecting mesial temporal lobe structures. Unlike the epileptic form of amnesia, TGA rarely lasts less than one hour, and recurrences occur in less than 10% of patients. The aetiological basis of TGA is uncertain. Possible underlying mechanisms include cortical spreading depression or venous

congestion. Most likely, however, TGA may refer to a single expression of several pathophysiological phenomena[82,83].

Fugue states may also be psychogenic, as a dissociative state symptom. Inconsistencies in cognition and mental state are often elucidated if the patient is examined during an episode, which may be prolonged, lasting days or even weeks.

Summary

In conclusion, there are a large number of neurological and cardiac conditions which result in paroxysmal clinical events and although the causes are multiple and diverse, the clinical manifestations may be similar. The attainment of an accurate and detailed history from the patient and a witness is essential in differentiating these conditions. The application of appropriate investigations frequently increases clinical yield and directs apposite therapy. Nevertheless, misdiagnosis is common and may have profound physical, psychosocial and socioeconomic consequences for the patient, and economic implications for the health and welfare services

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Table. Non-epileptic paroxysmal neurological and cardiac events.

Syncope

Neurocardiogenic (also known as vasovagal, reflex, vasodepressor syncope)

Cardiac

Structural
Cardiomyopathies (obstructive, dilated, restrictive, right ventricular dysplasia)
Valvular disease (mitral and aortic stenosis and mitral valve prolapse)
Other (atrial myxoma)

Arrhythmia
Inherited (long-QT, Brugada and Wolff-Parkinson-White syndromes)
Acquired (SVT, VT, atrioventricular block, sinus node disease)

Orthostatic

Autonomic failure
Neuropathy
Complex autonomic failure (primary, multiple system atrophy)

Postural orthostatic tachycardia syndrome

Carotid sinus hypersensitivity

Situational
Tussive, micturition, swallowing

Neurological
Cerebrogenic cardiac arrhythmias

Drop attacks

Cardiac (as above)

Neurological

Cerebrospinal fluid dynamics
Colloid cyst of 3rd ventricle, Arnold-Chiari malformation

Diencephalic attacks

Lower limb weakness
Brainstem and spinal cord lesions and lower motor neuron disorders

Cataplexy

Idiopathic drop attacks

Vertebrobasilar ischaemia

Periodic hypo- and hyperkalaemic paralyses

Transient hypermotor episodes

Myoclonus

Cortical, subcortical, brainstem, spinal cord and lower motor neuron disorders

Table. Continued

Tics

Dystonia

Tremor

Chorea

Paroxysmal dyskinesia
Kinesigenic, non-kinesigenic, exertion-induced, choreoathetosis with spasticity

Episodic ataxia
Type 1 and 2

Startle syndromes
Hyperekplexia

Culture specific syndromes
Jumping Frenchmen of Maine, Latah, Myriachit

Acquired
Stiff person syndrome, progressive encephalomyelitis with rigidity

Tonic spasms
Upper motor neuron disorders
Multiple sclerosis, cerebral palsy

Cerebral ischaemia

Transient focal sensory attacks

Migraine

Transient ischaemic attacks

Lower motor neuron disorders
Radiculopathies, neuropathies

Vertigo
Ménière's disease, benign paroxysmal positional vertigo

Psychic experiences

Panic attacks

Loss of primary sense
Charles Bonnet syndrome

Post-amputation

Aggressive or vocal outbursts

Table. Continued

Episodic dyscontrol syndrome

Episodic phenomena in sleep

Sleep wake-transition disorders
Hypnic jerks

Rhythmic movement disorders
Jactatio Capitis Nocturna

Restless legs syndrome

Periodic limb movements in sleep

Non-REM parasomnias
Somnambulism, night terrors, confusional arousals

REM parasomnias
Nightmares, sleep paralysis, REM sleep behaviour disorder

Sleep apnoea
Obstructive

Central

Prolonged confusional or fugue states

Encephalopathy
Neurological
Intracranial infection, ischaemia, head injury

Systemic
Infection, hypoxia, hypercapnia, hypoglycaemia, hypocalcaemia, hyponatraemia, hepatic and renal failure, drug and alcohol intoxication, endocrine dysfunction including thyroid disorders, phaeochromocytoma, carcinoid

Transient global amnesia
