Syncope : an integrative physiological approach

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Defining and classifying syncope

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Chapter 3

Abstract

There is no widely adopted definition or classification of syncope and related disorders. This lack of uniformity harms patient care, research, and medical education. In this article, syncope is defined as a form of transient loss of consciousness (TLOC) due to cerebral hypoperfusion. Differences between syncope and other causes of TLOC such as epilepsy, and disorders mimicking TLOC are described. A pathophysiological classification of syncope is proposed.

Introduction

The terminology used to define episodes of transient loss of consciousness is inconsistent and frequently inaccurate. Lack of pathophysiological understanding of syncope is perhaps the main culprit. Patients with these disorders are seen by physicians with different specialties, including cardiologists, neurologists, internists, emergency physicians, pediatricians and psychiatrists, all with different customs and practices. Inconsistent terminology complicates research, as results cannot be generalized because study populations may differ. Lack of pathophysiological understanding hampers patient care, leading to misuse of resources and unnecessary tests.[28,39] It also affects medical education by failing to emphasize essential diagnostic features. Here, we define syncope and related terms, briefly discuss differential diagnosis and propose a pathophysiological classification of syncope.

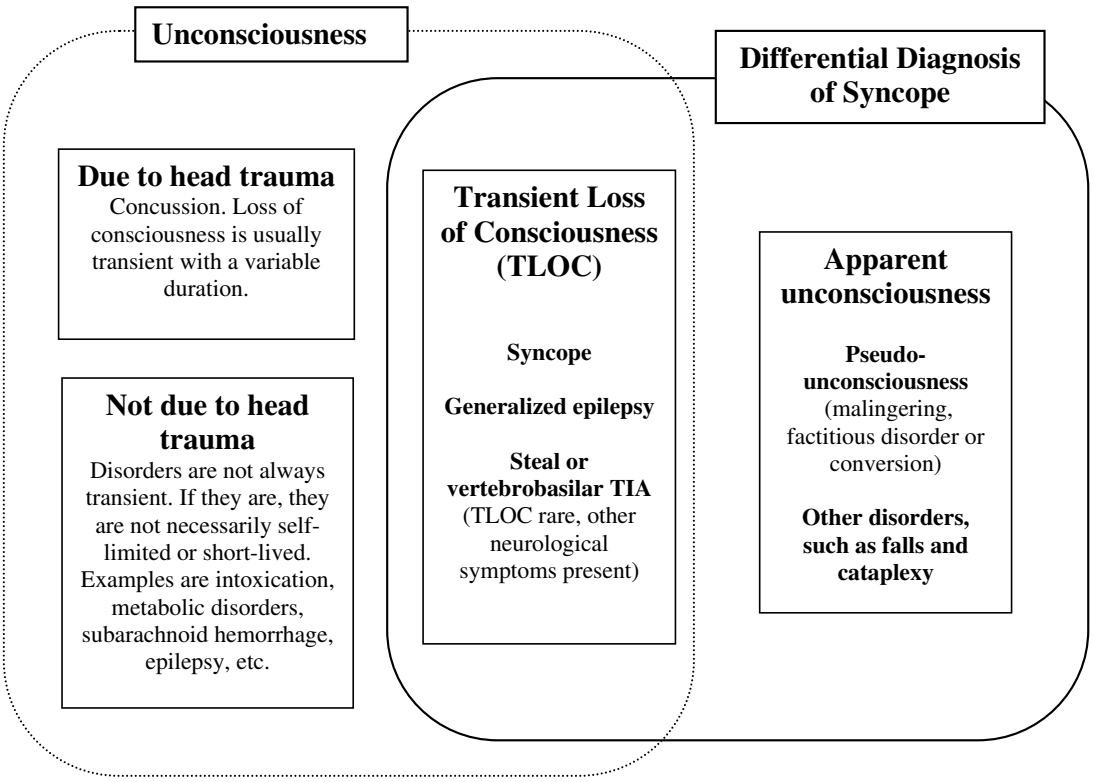
Defining a pathophysiological framework for syncope

Syncope

Syncope should be distinguished from conditions characterized by transient loss of consciousness and from conditions in which consciousness only appears lost (Figure 1). Widely used definitions of syncope are unhelpful. For example, in the Framingham study, and in many medical textbooks, syncope is defined as “a sudden loss of consciousness associated with the inability to maintain postural tone, followed by spontaneous recovery".[233] This definition of syncope is so wide that it encompasses almost all causes of transient unconsciousness, including concussion and several types of epileptic seizures. TIA's and strokes were also included under the syncope heading.

A more precise definition of syncope should be narrower, as was recently agreed upon by the Task Force on Syncope of the European Society of Cardiology (ESC): "a transient, self-limited loss of consciousness, usually leading to falling. The onset of syncope is relatively rapid, and the subsequent recovery is spontaneous, complete, and relatively prompt. The underlying mechanism is a transient global cerebral hypoperfusion".[28] 'Global' does not necessarily imply that the loss of consciousness is due to dysfunction of the entire brain; this may be due to brain stem dysfunction, dysfunction of a major part of both hemispheres, or both.

Figure 1 Syncope in relation to real and apparent loss of consciousness**.** 'Transient Loss of Consciousness' (TLOC) concerns a self-limited transient short-lived loss of consciousness not due to head trauma. Syncope is a form of TLOC caused by cerebral hypoperfusion. The differential diagnosis of syncope primarily includes other disorders within TLOC. Sometimes it is not clear whether consciousness was truly lost. Disorders that cause 'apparent unconsciousness' then also feature in the differential diagnosis of syncope. Causes of unconsciousness that are either due to head trauma, or are not transient, not self-limited or not short-lived, can usually be distinguished from syncope and other forms of TLOC.



Transient loss of consciousness (TLOC)

The term syncope should only be used to describe transient loss of consciousness caused by a specific pathophysiology. In clinical practice, however, the cause of a particular episode of unconsciousness is not always clear. Disorders other than syncope, such as epilepsy, then need to be considered (Figure 1). Until the cause is clarified, the episode should be labeled in a way that does not restrict thinking to one particular cause. The phrase 'transient loss of consciousness (TLOC)' may be used for this purpose.[28] Apart from unconsciousness it has four key features that together describe a common presentation pattern: a transient, self-limited nature, a short duration (minutes), and the absence of an external cause. The last item is meant to exclude concussion.

Consciousness is 'the state of awareness of the self and the environment'.[196] Consciousness has content and arousal. While content denotes the awareness itself, arousal describes a degree of wakefulness ranging from fully awake to deeply unconscious. The two aspects are not independent, as it is not possible to be aware (the content aspect) without being awake. Taking this definition to its logical conclusion suggests that unconsciousness might also be divided into content and arousal, but this is not done in daily practice. If 'unconsciousness' would also be used for content, then the word would also cover the mental state during absence epilepsy and partial complex seizures: patients have impaired awareness of themselves and their surroundings, so content is affected. The arousal aspect is however normal in the sense that these patients do not fall and appear 'awake'. Not many people will use 'unconsciousness' for such states, meaning that use of the term is restricted to the arousal aspect and describes an abnormal sleep-like state. The International League Against Epilepsy (ILAE) uses 'impaired' to describe consciousness in these states. We will conform to this use by reserving 'loss of consciousness' or 'unconsciousness' for the arousal part of consciousness. Partial complex seizures and absences do not therefore fall under the TLOC heading. 'Falling' or 'loss of postural tone' is often added to a definition of syncope, and may therefore also be considered to belong in the definition of TLOC. However, unconsciousness as defined above leads to a complete loss of all voluntary motor activity, meaning that falling is a logical consequence of TLOC and does not need to be added to its definition.

Epilepsy

Generalized seizures produce TLOC and should be distinguished from syncope. Generalized seizures may be tonic, clonic, myoclonic, tonic-clonic, or atonic, depending on the predominant muscle activity observed during the seizure. A generalized seizure is a seizure 'whose initial semiology indicates, or is consistent with, more than minimal involvement of both hemispheres'.[20] Although loss of consciousness is not included in the definition, abnormal neuronal activity of major parts of both hemispheres generally results in loss of consciousness. Myoclonic seizures are the sole exception, as these seizures usually present without affecting consciousness. 'Tonic' refers to a sustained increase in muscle contraction lasting a few seconds to minutes. Myoclonus is defined as 'a sudden, brief (<100ms) involuntary single or multiple contraction(s) of muscle(s) or muscle groups of variable topography (axial, proximal limb, distal)'. Clonic refers to 'a myoclonus that is regularly repetitive, involves the same muscle groups, at a frequency of ~2-3 /s, and is prolonged'. Tonic-clonic refers to 'a sequence consisting of a tonic followed by a clonic phase'. Finally, atonic seizures are characterized by 'a sudden loss or diminution of muscle tone without apparent preceding myoclonic or tonic event lasting 1 to 2 s, involving head trunk jaw, or limb musculature'. Atonic attacks are rare and occur almost only in small children.

Stiffness and myoclonus are not restricted to epilepsy. They were observed in 90% of healthy subjects who intentionally provoked syncope using the so-called 'fainting lark'.[148] Jerking movements are probably less frequent in spontaneous syncope. Estimates in fainting blood donors of movements vary from 12%[152] to 46%.[186]

Finally, caution is needed regarding the word 'seizure'. Whereas most physicians probably equate seizure with 'epileptic attack', this use is not universal. The ILAE in fact does not restrict its use to epileptic attacks, and disorders such as 'reflex anoxic seizures' are not epileptic but syncopal in nature.

Regional cerebral hypoperfusion: transient ischemic attacks (TIA's) and steal syndrome

TIA's and steal syndromes cause a temporary regional cerebral hypoperfusion and should not be confused with syncope. A TIA is defined as 'a clinical syndrome characterized by an acute loss of focal cerebral or monocular function with symptoms lasting less than 24 hours, and which is thought to be due to inadequate cerebral or ocular blood flow, arterial thrombosis or

embolism associated with disease of the arteries, heart, or blood'.[262] A TIA might theoretically cause TLOC, but in practice the clinical presentation of a TIA differs so markedly from syncope that a TIA almost never features in the differential diagnosis of syncope. A regional cerebral perfusion deficit can lead to unconsciousness only if it affects the ascending reticular activating system in the brainstem. This excludes TIA's in the territory of the carotid arteries for the differential diagnosis of syncope. Only TIA's in the vertebrobasilar territory might cause TLOC, but it will then almost invariably be associated with signs and symptoms of brainstem dysfunction such as vertigo, diplopia, dysarthria, hemiparesis or ataxia, features that are never found in syncope. Moreover, about 75% of all TIA's have a duration of over 5 minutes,[262] considerably longer than the duration of syncope. Whether or how often a vertebrobasilar TIA causes TLOC without neurological deficit is not known. Experience suggests that TIA's produce neurological deficit without unconsciousness and syncope produces unconsciousness without neurological deficit.

Steal syndrome refers to the condition in which stenosis or occlusion of an artery causes such low blood pressure beyond the stenosis that blood is diverted from another artery to the low-pressure region. Stenosis of the subclavian artery, in which the post-stenotic artery receives an additional blood supply through the ipsilateral vertebral artery, may cause hypoperfusion of the vertebrobasilar territory during vigorous muscle activity of the affected arm. Here too, it is not known whether or how often a steal syndrome gives rise to unconsciousness without any neurological deficit.

Apparent transient loss of consciousness

Occasionally the description of a presumed syncopal episode fails to clarify whether there was true loss of consciousness, a prerequisite for TLOC and syncope. Whether this category can mimic syncope largely depends on the quality of the account by the patient or an eyewitness. Two factors in the history are particularly important: true loss of consciousness precludes actively staying upright, and is associated with amnesia for the event.

Psychogenic and psychiatric disorders.

The term 'psychogenic syncope' is a misnomer. The proper term is 'psychogenic pseudo-syncope', as 'psychogenic syncope' would imply that there was a true loss of consciousness. 'Psychogenic syncope' could in principle be used for true syncope that is self-induced for some psychological reason, but 'self-induced syncope' is clearer.

A 'psychogenic' cause for an event may be difficult to prove. Epidemiological or individual studies on real or apparent TLOC should be critically scrutinized, as psychogenic conditions should be based on proper psychiatric criteria, not solely on excluding other disorders. Estimates of the frequency of 'psychogenic' attacks are probably unreliable if they are not based on such criteria.

'Psychogenic pseudosyncope' refers to episodes when patients appear unconscious but are not. Related conditions are 'psychogenic seizure', 'psychogenic coma' or 'pseudo-unconsciousness', depending on the clinical presentation.

Three psychiatric conditions may underlie 'psychogenic pseudosyncope'. One is conversion disorder, in which patients have unexplained somatic symptoms, suggesting a neurological or general medical condition while psychological factors are judged to be associated with these complaints. As a rule, the symptoms cannot, after appropriate investigation, be fully explained by a general medical condition, direct effects of a substance, or as a cultural sanctioned behavior or experience.[68]

In factitious disorder, these symptoms are, in contrast with the conversion disorder, intentionally produced, with the motivation being to assume the sick role. In malingering, the motivation of symptom production has, in contrast to the factitious disorder, an external incentive (such as economic gain or avoiding legal responsibility).[68]

Usually, pseudo-unconsciousness lasts too long to be confused with syncope. Also, muscle tone differs from that of truly unconscious subjects. For example, when a lifted limb is let go it may hesitate shortly in mid-air before it starts to fall. There may be sudden and active eye closure when the eyes are opened passively. There may be reflexive gaze movements, or the eyes may be turned upwards, downwards or consistently away from the observer. Ice water irrigation of the ears produces eye deviation in comatose subjects but a lively nystagmus in patients who are awake. Unresponsiveness during a tilt table test with preserved blood pressure and heart rate strongly suggests pseudo-unconsciousness. A neurological examination usually shows signs, which are not compatible with true unconsciousness; if more documentation is needed, a normal EEG during the event rules out epilepsy.

Cataplexy

Cataplexy refers to a loss of muscle tone due to emotions, particularly laughter. In complete attacks, the patient is unable to respond at all, although he or she is completely conscious and aware of their surroundings. However, this can only be assessed after the fact. Cataplexy is rare and mostly occurs in narcolepsy, usually accompanied by excessive daytime sleepiness.

Metabolic disorders

While metabolic disorders such as hypoglycemia may cause unconsciousness, these states usually last longer than syncope, and therefore do not cause much diagnostic confusion.

Classification of syncope

We present a classification of syncope that is based on four principle ways of failure of the systemic circulation. It is modified slightly from of the ESC Task Force.[28] The four ways of failure are (Table 1): **1**. Insufficient pumping action of the heart, i.e., reduced cardiac output. Cardiac arrhythmia and structural heart disease fall into this category; **2**. Low blood pressure due to reduced vascular tone, and failure to prevent blood pooling in the legs and abdomen during standing. Syncope in this group is due to orthostatic hypotension. Primary, secondary and drug-induced autonomic failure fall into this category. **3.** Insufficient filling of the circulation, i.e., hypovolemia. **4**. A counterproductive neural influence over the circulation that involves the central nervous system: i.e., reflex or neurally mediated syncope. The dysfunction consists of vagally-mediated bradycardia, sympathetic withdrawal-mediated vasodilatation or both. The autonomic nervous system abnormality in reflex syncope differs fundamentally from that in autonomic failure: in autonomic failure, the autonomic nervous system initiates a normal action but fails to deliver a response of sufficient magnitude, while in reflex syncope the action itself is inappropriate. Examples of reflex syncope are carotid sinus syncope and ocular pressure syncope. The term 'situational syncope' is sometimes used to bundle various forms such as syncope evoked by coughing, swallowing, micturition and defecation, but there is no advantage in separating these forms from other forms of syncope, many of which also tend to occur during specific situations.

This classification is aimed at primary causes affecting the circulation. In many cases, syncope involves a complex chain of events, with different interlocking mechanisms contribu-

Table 1 Classification of syncope

A. Insufficient pumping action of the heart
-Arrhythmia
Examples: paroxysmal (supra)ventricular tachycardia, long QT syndrome
-Structural cardiac disease
Examples: valvular disease, obstructive cardiomyopathy

B. Insufficient vascular tone, leading to orthostatic hypotension
-Autonomic failure
Primary
Examples: multiple system atrophy, pure autonomic failure
Secondary
Examples: diabetic and other neuropathies
Drugs
Examples: antidepressants, alpha-adrenergic blockers

C. Insufficient circulatory volume: hypovolemia
Examples: Addison's disease, diuretics, hemorrhage

D. Inappropriate neural control over the circulation: reflex syncope (= neurally-mediated syncope)
Examples: vasovagal syncope, carotid sinus syndrome, miction syncope

ting to its occurrence. For example, pooling of blood in the lower parts of the body during standing makes syncope due to any primary mechanism more likely. The classification presented here is a broad overview; it could easily be expanded to add further subtypes of syncope. A few subtypes of syncope are mentioned in Table 1.

Conclusion

There is an urgent need for accurate terminology and classification of syncope and related disorders. A few key features are already in place, such as the classification of the primary autonomic failure syndromes and the definition of syncope by the Task Force on Syncope of the European Society of Cardiology.[28,242] Useful precedents are the international classification systems of epilepsy and headache.[20,105] The primary focus should be on the differential diagnosis of TLOC and syncope. Success will require a wide consensus among the various specialties dealing with transient loss of consciousness. The present article attempts to further this goal.