Classificazione, fisiopatologia ed epidemiologia

Paolo Alboni

U.O. di Cardiologia
Centro Aritmologico
Ospedale Civile
Cento (FE)
Guidelines for the diagnosis and management of syncope (version 2009)

The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC)

Developed in collaboration with, European Heart Rhythm Association (EHRA)¹, Heart Failure Association (HFA)², and Heart Rhythm Society (HRS)³

Endorsed by the following societies, European Society of Emergency Medicine (EuSEM)⁴, European Federation of Internal Medicine (EFIM)⁵, European Union Geriatric Medicine Society (EUGMS)⁶, American Geriatrics Society (AGS), European Neurological Society (ENS)⁷, European Federation of Autonomic Societies (EFAS)⁸, American Autonomic Society (AAS)⁹

Authors/Task Force Members, Angel Moya (Chairperson) (Spain)⁸, Richard Sutton (Co-Chairperson) (UK)⁸, Fabrizio Ammirati (Italy), Jean-Jacques Blanc (France), Michele Brignole¹ (Italy), Johannes B. Dahm (Germany), Jean-Claude Deharo (France), Jacek Gajek (Poland), Knut Gjesdæ² (Norway), Andrew Krahn³ (Canada), Martial Massin (Belgium), Mauro Pepi (Italy), Thomas Pezawas (Austria), Ricardo Ruiz Granell (Spain), François Sarasin⁴ (Switzerland), Andrea Ungar⁶ (Italy), J. Gert van Dijk⁷ (The Netherlands), Edmond P. Walma (The Netherlands), Wouter Wieling (The Netherlands)
Syncope is a transient loss of consciousness (T-LOC) due to global cerebral hypoperfusion characterized by rapid onset, short duration, and spontaneous complete recovery.
CLASSIFICATION OF T-LOC

- Reflex (neurally-mediated)
  - Syncope Due to orthostatic hypotension
  - Cardiac (cardiovascular)

- Disorders with partial or complete T-LOC, but without global cerebral hypoperfusion
REFLEX (NEURALLY-MEDIATED SYNCOPE)

Typical vasovagal

- triggered by emotional distress
- triggered by orthostatic stress

Situational

- gastrointestinal stimulation (swallow, defecation)
- micturition
- post-exercise
- post-prandial
- others (laught, brass instrument playing)

Carotid sinus syncope

Atypical forms
SYNCOPE DUE TO ORTHOSTATIC HYPOTENSION

Primary autonomic failure
- Pure autonomic failure, Parkinson’s disease

Secondary autonomic failure
- Diabetes, amyloidosis, uraemia, spinal cord injury

Drug-induced orthostatic hypotension
- Alcohol, vasodilators, diuretics, phenothiazines, antidepressant

Volume depletion
- Haemorrhage, diarrhoea, vomiting, etc.
CARDIAC SYNCOPE

Arrhythmia as primary cause

- Bradycardia (SN dysfunction, AV block)
- Tachycardia (supraventricular, ventricular)

Structural heart disease

- Valvular heart disease, acute MI/ischemia, hypertrophic cardiomyopathy, atrial mixoma, pericardial disease/tamponade, pulmonary embolus, pulmonary hypertension, acute aortic dissection, etc.
DISORDERS WITH PARTIAL OR COMPLETE T-LOC BUT WITHOUT GLOBAL CEREBRAL HYPOPERFUSION

- Epilepsy
- Metabolic disorders (hypoglycaemia, hypoxia)
- Intoxication
- Vertebrobasilar TIA

DISORDERS WITHOUT IMPAIRMENT OF CONSCIOUSNESS

- Cataplexy
- Drop attack
- Falls
- Functional (psychogenic pseudosyncope)
- TIA of carotid origin
Epidemiology
PREVALENCE OF SYNCOPE IN THE YOUNG

394 students
mean age 21 yrs
Prevalence of syncope: 39%

Ganzeboom KS et al, Am J Cardiol 2000
Pathophysiology
Pathophysiology

Cardiac syncope
PATIENTS WITH PAROXYSMAL AF

AF and syncope  
(n=38 pts)

AF without syncope  
(n=16 pts)

Positive tilt test during SR

17 (45%)  
1 (6%)  
0.005

Brignole M et al, J Am Coll Cardiol 1993
Pathophysiology

Vasovagal syncope
Efferent part of the reflex circuit

- Inhibition of the sympathetic system → Hypotension
- Activation of the vagal system → Bradycardia
OPINION

Is vasovagal syncope a disease?

Paolo Alboni¹*, Michele Brignole², and Ettore C. degli Uberti³

¹ Division of Cardiology and Arrhythmologic Center, Ospedale Civile, Via Vicini 2, 44042 Cento (FE), Italy; ² Department of Cardiology and Arrhythmologic Center, Ospedali del Tigullio, Lavagna, Italy; and ³ Section of Endocrinology, Department of Biomedical Sciences and Advanced Therapies, University of Ferrara, Italy
Distribution of age and cumulative incidence of the first episode of syncope

2009 ESC guidelines
VASOVAGAL SYNCOPE IN THE YOUNG

No disease

- Triggers
- Very frequent
- Benign
- No evidence of underlying heart, neurological disease or other autonomic disturbances
- Normal BP regulation outside the syncopal episodes
- In astronauts
- Frequent spontaneous disappearance in middle/advanced age
VASOVAGAL SYNCOPE STARTING IN OLD AGE

Very likely a disease

- No triggers

- Frequent overlap with other autonomic disturbances (CS hypersensitivity, orthostatic hypotension, post-prandial hypotension, abnormal sweating, etc.)

- Sometimes progressively worsening over time
Typical vasovagal syncope

What is the vasovagal reflex?
What is its origin?
The origin of vasovagal syncope: to protect the heart or to escape predation?
Vasovagal reaction in vertebrates

- Vasovagal reflex during hemorrhagic shock

- Fear and threat bradycardia ("alarm bradycardia"), mainly during tonic immobility
Vasovagal reflex during hemorrhagic shock
Cat - Vasovagal reflex during hemorrhagic shock

Fear and threat bradycardia ("alarm bradycardia"), mainly during tonic immobility
Animal responses to fear or threat

“Fight-or-flight” response

Tonic immobility (playing dead, death-feint, freezing response)
Tonic immobility – Red deer
“Alarm bradycardia” during tonic immobility in vertebrates

Mammals
- Deer, ground squirrel, chipmunk, mouse, opossum

Birds
- Willow grouse

Reptiles
- Caiman

Amphibians
- Salamander

Fishes
- Plaice, cod, salmon
Mammals. Opossum. "Alarm bradycardia" during tonic immobility

Gabrielsen GW et al, Acta Physiol Scand 1985
Mammals. Wild rodents. “Alarm bradycardia” during tonic immobility

Hofer MA, Psychosom Med 1970
Birds. Wild grouse hen. “Alarm bradycardia” during tonic immobility

Reptiles. Caiman. “Alarm bradycardia” during tonic immobility

Gaunt AS et al, Nature 1969
Amphibians. Salamander. "Alarm bradycardia" during tonic immobility

Fishes. Cod. “Alarm bradycardia” during tonic immobility

Kanwisher J et al, Fishery Bull 1974
"Fear and threat bradycardia" in carnivores

Investigation carried out in 3 cats, during preparation for fighting in response to an attack by another cat

Variables: heart rate, intra-arterial blood pressure

Adams DB et al, Nature 1968
Cat – Vasovagal reflex during emotional situation

Adams DB et al, Nature 1968
Similarities between emotional VVS in humans and “alarm bradycardia” in the other vertebrates

1. The same trigger (emotion/threat) evokes the same response (bradycardia)
2. Both emotional VVS in humans and “alarm bradycardia” in animals are more frequent in young individuals than in older ones
3. Both emotional VVS in humans and “alarm bradycardia” in animals are preceded by an increase in sympathetic activity (shown by an increase in heart rate)
4. The few data available suggest that in animals the slowing in heart rate is associated with a decrease in blood pressure as in emotional VVS in humans
Origin of vasovagal reflex

The vasovagal reflex is predisposed in mammals and in the other vertebrates (fishes, amphibians, reptiles, birds).

These similarities suggest a common evolutionary root for the vasovagal reflex. Accordingly, classical VVS would not have evolved recently in the modern human lineage, but it should be regarded as an advantageous response which originated in the ancient past within some ancestral group(s) of vertebrates.
If the vasovagal reflex has persisted for millions of years along the vertebrates evolutionary history, we can reasonably assume that it has (or, for some groups, it may have had in the past) a function. Also, since the vasovagal reflex occurs sporadically, a possible role as a “defense mechanism” is likely.
Vasovagal reaction

“Defense mechanism”

Emotional stress

Orthostatic stress
(thoracic hypovolemia)

High sympathetic activity

Withdrawal of sympathetic activity
Increase in vagal tone

Vasovagal reflex

Increase in myocardial O₂ consumption

Decrease in myocardial O₂ consumption
and improvement in diastolic filling
Spontaneous loss of consciousness, appears to be absent (or extremely rare) in animals during the vasovagal reflex, whereas man looses consciousness

Why?
No loss of consciousness in animals during the vasovagal reflex

1. Quadruped or recumbent position reduces the risk of cerebral hypoperfusion and, consequently, of loss of consciousness. Alexander RM, 1991

2. The metabolic demand for the brain is lower in monkeys than in humans (4-7% of cardiac output is destined for the brain in monkeys versus ~ 20% in humans) and lower in the other animals. van Dijk PG, 2003

3. Monkeys’ legs are relatively much more thinner than those of man and muscle pump appears more active. van Dijk PG, 2003
Syncope in the context of T-LOC

Transient loss of consciousness (T-LOC)?

Yes

Falls, altered consciousness

No

Transient?

Rapid onset?

Short duration?

Spontaneous recovery?

Yes

No

Coma, Aborted SD, Other

Yes

Syncope

No

Non syncopal T-LOC

ESC Guidelines 2009
CAUSES OF SYNCOPE IN SPECIALIZED CLINICAL SETTING

- Neurally mediated: 65%
- Cardiac: 13%
- Orthostatic: 10%
- Syncope-like conditions: 6%
- Unexplained/not available: 11%

Brignole M et al, Europace 2006