UDC 616.8-009.832-079.4

M. J. Hilz

DIFFERENTIAL-DIAGNOSIS OF TRANSIENT LOSS OF CONSCIOUSNESS

University of Erlangen-Nuremberg, Erlangen, Germany,
New York University, New York, NY, USA

УДК 616.8-009.832-079.4
М. Хильц
ДИФФЕРЕНЦИАЛЬНАЯ ДИАГНОСТИКА ТРАНЗИТОРНОЙ ПОТЕРИ СОЗНАНИЯ
Университет Эрлангена-Нюрнберга, Эрланген, Германия,
Нью-Йоркский университет, Нью-Йорк, США
Транзиторная потеря сознания (ТПС) определяется как внезапная, очевидная потеря сознания. После короткой длительности (от нескольких секунд до нескольких минут) отмечается спонтанное и полное выздоровление. Транзиторная потеря сознания может быть связана с травматическими причинами, такими как сотрясение мозга, или причинами нетравматической этиологии, такими как синкопа, генерализованные эпилептические припадки, функциональные (или «психогенные») «псевдоприпадки» и «псевдосинкопы», и редко с заболеваниями, которые могут включать в себя вертебробазиллярные транзиторные ишемические атаки, подключичный синдром обкрадывания, катаплексии и чрезмерную дневную сонливость, нарушение обмена веществ (например гипогликемии) или «дроп-атаки». Характеризуется ТПС: 1) потерей нормального контроля движений, которая сопровождается вялостью или ригидностью; 2) потерей постурального контроля с падениями; 3) отсутствием реакции и амнезии на событие. Хотя симптомы ТПС хорошо известны, есть потребность в повышении уровня дифференциального диагноза данной патологии.
Ключевые слова: транзиторная потеря сознания, сотрясение мозга, синкопия, эпилептические припадки.

UDC 616.8-009.832-079.4
M. J. Hilz
DIFFERENTIAL-DIAGNOSIS OF TRANSIENT LOSS OF CONSCIOUSNESS
University of Erlangen-Nuremberg, Erlangen, Germany,
New York University, New York, NY, USA
Transient loss of consciousness (TLOC) is defined as abrupt onset of apparent loss of consciousness. After a short duration (of a few seconds to minutes), there is spontaneous and complete recovery. TLOC can be due to a traumatic cause, such as a concussion, or to nontraumatic etiologies, such as syncope, generalized epileptic seizures, functional (or “psychogenic”) “pseudoseizures” and “pseudosyncopes”, and rare miscellaneous disorders that may include vertebrobasilar transient ischemic attacks, the subclavian steal syndrome, cataplexy and excessive daytime sleepiness, metabolic disorders (e.g. hypoglycemia) or “drop attacks”. TLOCs are characterized by 1) loss of normal motor control with either flaccidity or stiffness, 2) loss of postural control with falls, and 3) unresponsiveness and amnesia for the event. Although sympthoms of TLOC are well known, there is still a need in improving the level of differential-diagnosis of this pathology.
Key words: transient loss of conciousness, concussion, syncope, epileptic seizures.

Transient loss of consciousness (TLOC) is defined as abrupt onset of apparent loss of consciousness. After a short duration (of a few seconds to minutes), there is spontaneous and complete recovery [1–4].

TLOC can be due to a traumatic cause, such as a concussion, or to non-traumatic etiologies [2]. Non-Traumatic TLOC is most frequently caused by syncope: Syncope may be neurally mediated (such as so-called reflex-syncope), due to orthostatic hypotension, or due to cardiac arrhythmias or structural heart diseases [3]. Other causes of (non-traumatic) TLOC are primary or secondary generalized epileptic seizures, functional (or “psychogenic”) “pseudoseizures” and “pseudosyncopes”, and rare miscellaneous disorders that may include vertebrobasilar transient ischemic attacks, the subclavian steal syndrome, cataplexy and

excessive daytime sleepiness, metabolic disorders (e.g. hypoglycemia) or "drop attacks" [3].

TLOCs are characterized by 1) loss of normal motor control with either flaccidity or stiffness that may be accompanied by jerking movements, 2) loss of postural control with falls, and 3) unresponsiveness and amnesia for the event [3].

In a multi-centric, prospective study, the so-called Group for Syncope Study in the Emergency Room (GESINUR) study, Baron-Esquivias et al. have prospectively analyzed the admissions of patients (14 years and older) to 19 Spanish emergency departments over a 1 month period: 1419 patients were admitted because of TLOC (prevalence, 1.14%). 37.3% of these patients had electrocardiogram abnormalities, 12% had abnormal orthostatic test results, 76% were diagnosed with syncope, 24% had a diagnosis of non-syncopal TLOC, and 25% of the TLOC patients were admitted to hospitals [5].

Syncope is the major cause of TLOC (33–88% of TLOCs) [3; 6–9]. Syncope is defined as a temporary interruption of cerebral perfusion with a sudden and transient loss of consciousness and spontaneous recovery.

Typically, syncopal episodes are brief. They can be as short as only seven seconds [4], and mostly last only up to 20 seconds [10]. The differential diagnosis may be difficult in the rare cases of longer syncope duration, lasting even up to several minutes [10].

Approximately one third of the population experiences syncope at least once during lifetime. Presyncopal signs and symptoms, including weakness, headache, blurred vision, diaphoresis, nausea, and vomiting are sometimes present for seconds or minutes prior to loss of consciousness. After syncope, there is rapid reorientation: while patients may present with persisting drowsiness, headache, dizziness, nausea, there is usually no prolonged confusion or disorientation.

Causes of syncope have been categorized as cardiovascular, non-cardiovascular, and unexplained. Cardiovascular causes can be subdivided into structural heart disease, coronary heart disease, and arrhythmia. Non-cardiovascular causes include neurological, metabolic, psychiatric and other disorders. Orthostatic hypotension — one of the most frequent causes of syncope — has manifold etiologies comprising various neurological and internal diseases. Orthostatic hypotension usually can be attributed to an impairment of peripheral vasoconstriction or to a reduction of the intravascular volume. Signs and symptoms, including the above prodromi are often present upon rising from supine or sitting to the standing position. Frequently, blood pressure decreases significantly without an increase in heart rate as autonomic cardiovascular modulation is often reduced. Many of the patients with "unexplained" syncope experience neurally mediated (i.e. neurocardiogenic or vasovagal) syncope. In contrast to orthostatic hypotension that shows a rather rapid onset of drop in blood pressure, patients with neurally mediated syncope usually have stable heart rate and blood pressure for an extended period of orthostatic challenge; then, after prolonged standing, patients with neurally mediated syncope manifest a sudden decrease in blood pressure and heart rate due to withdrawal of sympathetic activity [11].

Neurocardiogenic or neurally mediated syncope can be induced by painful or emotionally stressful situations, such as anxiety or fear, but also by prolonged standing or by specific situational triggers that induce a so-called reflex syncope. Such triggers of reflex syncope include micturition, defecation, coughing or sneezing, visceral stimulation, or pain in areas with trigeminal or glossopharyngeal innervation [11].

Epileptic seizures may be tonic, clonic, tonic-clonic or atonic in nature [2; 3]. In contrast to syncope, seizures are rarely trigger-induced [3]. However, reflex epilepsies can be triggered e.g. by flashing, stroboscopic lights or startling [3; 12; 13]. Seizures may be accompanied by auras such as a rising sensation in the abdomen [3; 14]. Seizures usually last longer than syncope, i.e. mostly at least 1 minute or longer. In contrast to syncope, epileptic seizures may be accompanied by muscle jerks that can occur already prior to the fall. In epileptic seizures, jerks are usually symmetrical and rhythmic. In contrast, syncope may be associated with jerks that are irregular, not symmetrical and not synchronous, and usually last for only a few seconds [3].

During epileptic seizures, the patient's eyes are usually open with the gaze directed to one side [3]. However, in syncope, eyes are also open even if they were closed prior to loss of consciousness; moreover, eyes may be turned upwards (or straight ahead) during syncope [2; 3].

Other important features of epileptic seizures are a lateral tongue bite [15], head deviation [16], and emission of a cry at the onset of the seizure [3]. Patients recover slowly and may show prolonged disorientation and confusion [3; 17].

Increased levels of serum prolactin cannot definitely distinguish between epileptic seizure

and syncope because serum prolactin but may be increased not only after a seizure but also after syncope [18]. In contrast, increased serum levels of creatine phosphokinase (CPK) are typically seen after a seizure [18].

Functional or "psychogenic" TLOC occur in somatisation or conversion disorders and may present as "pseudo-epilepsy" ("pseudo-seizure") or as "pseudo-syncope".

"Pseudo-seizures" are functional or psychogenic TLOCs resembling epileptic seizures [3]. According to Dijk et al. [3], up to 20% of patients in tertiary epilepsy clinics might have "pseudo-seizures" [3]. There may be a history of preceding psychological problems, physical or sexual abuse [3; 19]. According to Dijk et al., "pseudo-seizures" occur more frequently in women than men and in younger than older individuals [3]. Functional attacks may be induced by verbal suggestion or various provocations [20; 21], and may be distinguished from epileptic seizures by simultaneous video-monitoring of the electroencephalogram and the patient [21; 22].

Although tongue-biting and incontinence are rare in pseudo-seizures [23], trauma is more common than usually assumed and may occur in 50% or pseudo-seizure cases [3; 19; 22]. Bizarre body movements, including the "arc de cercle", or pelvic thrusting [22], alternating or waxing and waning limb movements can be seen during a "pseudo-seizure" [3].

In contrast to syncope or epileptic seizures, the patient almost always keeps his or her eyes always closed during the "pseudo-seizure" attack [3].

In **"pseudo-syncopes",** patients seem to be unconscious although they are not unconscious [2]. Often, the muscle tone differs from the muscle tone in patients who are actually unconscious [2]. As an example, a passively raised arm or leg will not drop immediately as in an unconscious patients but might be shortly held in the elevated position before it starts falling [2].

Patients may close their eyes suddenly and actively when they are passively opened [2]. "Pseudo-syncopes" may be accompanied by reflexive gaze movements, and the eyes may show strange movements, upwards, downwards or away from the observer [2]. While caloric stimulation with ice water irrigation of the ears induces a tonic eye deviation in a comatose patient, awake patients presenting with pseudo-unconsciousness show a prominent and vivid nystagmus [2]. During tilt-table testing, unresponsiveness that is associated with stable blood pressure and heart rate also strongly suggests pseudo-unconsciousness. A normal electroencephalogram during an event rules out syncope. Moreover, the neurological examination of a patient presenting with "pseudo-unconsciousness" usually shows signs that are not compatible with real unconsciousness [2].

"Pseudosyncopes" may account for 6% of presumed syncope events [24; 25]. They can last longer than regular syncope, often many minutes, and may recur many times during one day. Frequently, recovery is slow and can be accompanied by weeping [3].

During **vertebrobasilar transient ischemic attacks** (TIAs), perfusion of the brainstem is temporarily reduced [2; 3]. As a rule of thumb one can assume that TIAs usually cause a neurological deficit without unconsciousness while syncope causes unconsciousness without neurological deficit [2]. Theoretically, vertebrobasilar TIA may induce loss of consciousness if the reduced perfusion involves the ascending reticular activating system (ARAS) [2]. However, signs and symptoms of brainstem dysfunction such as vertigo, diplopia, dysarthria, alternating hemiparesis or ataxia, facilitate the diagnosis of TIA because syncope does not cause these neurological deficits [2]. Moreover, most TIAs last more than five minutes (but less than 24 hours), i.e. the TIAs last significantly longer than syncope [2].

Loss of consciousness in patients with **subclavian-steal syndrome** also only occurs in the presence of neurological symptoms [2]. Depending on the degree of the stenosis of the proximal subclavian artery, physical activity and effort of the ipsilateral arm causes a redirection of ipsilateral vertebral artery blood flow and induces hypoperfusion of the vertebrobasilar territory which in turn causes neurological symptoms, such as dizziness, vertigo, pain or pallor in the arm and hand. The stenosis or occlusion of the proximal subclavian artery causes post-stenotic low blood pressure in the arm and results in a difference in blood pressures between the left and right arm [2].

Loss of consciousness due to **metabolic disorders,** is related to a loss or critical reduction in cerebral energy supply, for example during hypoglycemia, hypoxia or prominent hypercapnia, and mostly lasts longer than syncope [2; 11].

Cataplexy is often misdiagnosed as reflex syncope or as complex partial or even tonic-clinic seizure as it may mimic transient loss of consciousness [26; 27]. However, patients do not loose consciousness but are awake and aware of the event, i.e. they have no amnesia for the

cataplectic event [2]. Triggered by an emotional stimulus, such as laughter, or unexpected emotional events, such as suddenly meeting a friend, patients partially or fully loose muscle tone and therefore fall (or are still able to prevent a complete fall if there is partial preservation of muscle tone) [2; 3; 28]. When cataplexy progresses into sleep, patients may however not remember the end of the cataplexy. If cataplexy is combined with prominent daytime sleepiness, the diagnosis of narcolepsy is quite certain [3].

"Drop attacks" are also not associated with a transient loss of consciousness. These rare events mainly affect middle-aged individuals and consist of a sudden fall, patients usually land on their knees and hands, usually without any loss of consciousness. The pathophysiology of "drop attacks" is unknown [3; 29].

The diagnostic workup of TLOC should be initiated with a detailed history including the patients' age, the frequency of attacks, possible causes or triggers, precipitating events, the time course of attacks (prodromal phase, duration, reorientation), witnesses, other symptoms or injuries (autonomic or motor symptoms, tongue bite), awareness or amnesia for the event, the history of other diseases, drug and family history (particularly sudden cardiac death among relatives) [2; 3; 11]. During the physical examination, the state of hydration should be assessed and blood pressure measurements should be performed at both arms in supine and standing position. A simple test that is widespread in German speaking countries is the Schellong test: The patient is at rest, in lying position, supine heart rate and blood pressure values are taken every minute and averaged as values at rest. After 5–10 minutes, the patient is asked to stand up and to remain standing for 10 minutes. Again, heart rate and blood pressure are measured every minute and compared to values in the supine position [11; 30].

Up to 50% of patients with syncope may show some electrocardiographic abnormalities which are however non-specific and poorly correlated with symptoms. In patients with arrhythmias or any suspected cardiogenic etiology, a detailed cardiologic work-up is essential, continuous ambulatory (Holter) monitoring of the electrocardiogram for up to 72 hours or longer is recommended (11).

Finally, the 2010 guidelines of the British National Clinical Guideline Centre, NICE [31], emphasize that patients should undergo a special examination by a cardiologist within 24 hours of the TLOC if there was any of the following "red flag" signs or symptoms:

— transient loss of consciousness during exertion;

— new or unexplained breathlessness;

— heart failure;

— family history of sudden cardiac death in people younger than 40 years and/or an inherited cardiac condition;

— a heart murmur;

— any of the following abnormalities in a 12 lead electrocardiogram:

atrial arrhythmia (sustained),

— inappropriate persistent bradycardia,

— conduction abnormality (for example, complete right or left bundle branch block or any degree of heart block),

— left or right ventricular hypertrophy,

— long QT interval (corrected > 450 ms) and short QT interval (corrected < 350 ms),

— pathological Q waves,

— ventricular pre-excitation,

— any ventricular arrhythmia (including ventricular extrasystoles),

— Brugada syndrome,

— paced rhythm,

— any abnormalities in ST segment or T wave, especially abnormal T wave inversion [31].

REFERENCES

1. Soteriades E.S., Evans J.C., Larson M.G., Chen M.H., Chen L., Benjamin E.J., et al. Incidence and prognosis of syncope. *N Engl J Med.* 2002; 347 (12): 878-885.

2. Thijs R.D., Wieling W., Kaufmann H., van Dijk G. Defining and classifying syncope. *Clin Auton Res.* 2004; 14 Suppl 1: 4-8.

3. Van Dijk J.G., Thijs R.D., Benditt D.G., Wieling W. A guide to disorders causing transient loss of consciousness: focus on syncope. Nat. Rev. Neurol. 2009; 5 (8): 438-448.

4. Wieling W., Thijs R.D., van Dijk N., Wilde A.A., Benditt D.G., van Dijk J.G. Symptoms and signs of syncope: a review of the link between physiology and clinical clues. *Brain: a Journal of Neurology* 2009; 132 (Pt 10): 2630-2642. Epub 2009/07/10.

5. Baron-Esquivias G., Martinez-Alday J., Martin A., Moya A., Garcia-Civera R., Paz Lopez-Chicharro M., et al. Epidemiological characteristics and diagnostic approach in patients admitted to the emergency room for transient loss of consciousness: Group for Syncope Study in the Emergency Room (GESINUR) study. *Europace.* 12 (6): 869-876.

6. Bartoletti A., Fabiani P., Bagnoli L., Cappelletti C., Cappellini M., Nappini G., et al. Physical injuries caused by a transient loss of consciousness: main clinical characteristics of patients and diagnostic contribution of carotid sinus massage. *Eur Heart J.* 2008; 29 (5): 618-624.

7. Martikainen K., Seppa K., Viita P., Rajala S., Laippala P., Keranen T. Transient loss of consciousness with and without injuries: where to treat these patients? *Eur. J. Gen. Pract.* 2003; 9 (3): 91-95.

8. Martikainen K., Seppa K., Viita P., Rajala S., Laippala P., Keranen T. Transient loss of consciousness as reason for admission to primary health care emergency room. *Scand. J. Prim. Health. Care.* 2003; 21 (1): 61-64.

9. Thijs R.D., Granneman E., Wieling W., van Dijk J.G. [Terms in use for

transient loss of consciousness in the emergency ward; an inventory]. *Ned Tijdschr Geneeskd.* 2005; 149 (29): 1625-1630. Gebruikte termen voor Voorbijgaande bewusteloosheid' op de Eerste Hulp; een inventarisatie.

10. Brignole M., Alboni P., Benditt D., Bergfeldt L., Blanc J.J., Bloch Thomsen P.E., et al. Guidelines on management (diagnosis and treatment) of syncope. *Eur. Heart. J.* 2001; 22 (15): 1256-1306. Epub 2001/07/24.

11. Hilz M.J., Marthol H., Neundorfer B. [Syncope — a systematic overview of classification, pathogenesis, diagnosis and management]. *Fortschr Neurol Psychiatr.* 2002; 70 (2): 95-107. Synkopen — eine systematische Ubersicht zur Klassifikation, Pathogenese, Diagnostik und Therapie.

12. Bakker M.J., van Dijk J.G., van den Maagdenberg A.M., Tijssen M.A. Startle syndromes. *Lancet Neurol.* 2006; 5 (6): 513-524.

13. Trenite D.G. Photosensitivity, visually sensitive seizures and epilepsies. *Epilepsy Res.* 2006; 70 Suppl 1: 5269-5279.

14. Van Donselaar C.A., Geerts A.T., Schimsheimer R.J. Usefulness of an aura for classification of a first generalized seizure. *Epilepsia* 1990; 31 (5): 529-535.

15. Sheldon R., Rose S., Connolly S., Ritchie D., Koshman M.L., Frenneaux M. Diagnostic criteria for vasovagal syncope based on a quantitative history. *Eur Heart J.* 2006; 27 (3): 344-350.

16. Sheldon R., Rose S., Ritchie D., Connolly S.J., Koshman M.L., Lee M.A., et al. Historical criteria that distinguish syncope from seizures. *J Am Coll Cardiol.* 2002; 40 (1): 142-148.

17. Hoefnagels W.A., Padberg G.W., Overweg J., van der Velde E.A., Roos R.A. Transient loss of consciousness: the value of the history for distinguishing seizure from syncope. *J. Neurol.* 1991; 238 (1): 39-43.

18. Kowalik A., Bauer J., Elger C.E. [Asystolic seizures]. *Nervenarzt* 1998; 69 (2): 151-157. Asystolische Anfalle.

19. Reuber M., Howlett S., Khan A., Grunewald R.A. Non-epileptic seizures and other functional neurological symptoms: predisposing, precipitating, and perpetuating factors. *Psychosomatics* 2007; 48 (3): 230-238.

20. Ribai P., Tugendhaft P., Legros B. Usefulness of prolonged video-EEC monitoring and provocative procedure with saline injection for the diagnosis of non epileptic seizures of psychogenic origin. *J. Neurol.* 2006; 253 (3): 328-332.

21. Zaidi A., Crampton S., Clough P., Fitzpatrick A., Scheepers B. Head-up tilting is a useful provocative test for psychogenic non-epileptic seizures. *Seizure* 1999; 8 (6): 353-355.

22. LaFrance W.C., Jr. Psychogenic nonepileptic seizures. *Curr. Opin. Neurol.* 2008; 21 (2): 195-201.

23. Oliva M., Pattison C., Carino J., Roten A., Matkovic Z., O'Brien T.J. The diagnostic value of oral lacerations and incontinence during convulsive "seizures". *Epilepsia* 2008; 49 (6): 962-967.

24. Van Dijk N., Boer K.R., Colman N., Bakker A., Stam J., van Grieken J.J., et al. High diagnostic yield and accuracy of history, physical examination, and ECG in patients with transient loss of consciousness in FAST: the Fainting Assessment study. *J Cardiovasc Electrophysiol.* 2008; 19 (1): 48-55.

25. Petersen M.E., Williams T.R., Sutton R. Psychogenic syncope diagnosed by prolonged head-up tilt testing. *Qjm.* 1995; 88 (3): 209-213.

26. Zeman A., Douglas N., Aylward R. Lesson of the week: Narcolepsy mistaken for epilepsy. *Bmj.* 2001; 322 (7280): 216-218.

27. Macleod S., Ferrie C., Zuberi S.M. Symptoms of narcolepsy in children misinterpreted as epilepsy. *Epileptic Disord.* 2005; 7 (1): 13-17.

28. Overeem S., Mignot E., van Dijk J.G., Lammers G.J. Narcolepsy: clinical features, new pathophysiologic insights, and future perspectives. *J. Clin. Neurophysiol.* 2001; 18 (2): 78-105.

29. Stevens D.L., Matthews W.B. Cryptogenic drop attacks: an affliction of women. *Br. Med. J.* 1973; 1 (5851): 439-442.

30. Diener H.C., Weimar C. Leitlinien fur Diagnostik und Therapie in der Neurologie. Stuttgart, Thieme Verlag; 2012.

31. Westby M., Bullock I., Cooper P.N., Davis S. Transient loss of consciousness-initial assessment, diagnosis, and specialist referral: summary of NICE guidance. *Bmj.* 2010; 341: c4457. Epub 2010/09/04.

Submitted 6.06.2013

UDC 613.84:614.23:616-053.2(477.74)

J. B. Lowe[1], N. L. Aryayev[2], T. V. Kuzmenko[2]

PREVALENCE AND ATTITUDES TO TOBACCO USE AND CONTROL AMONG PEDIATRICIANS IN THE ODESA REGION

[1] University of Sunshine Coast, Sippy Downs, Qeensland, Australia,
[2] The Odessa National Medical University, Odessa, Ukraine

УДК 613.84:614.23:616-053.2(477.74)

Дж. Б. Лоу[1], Н. Л. Аряев[2], Т. В. Кузьменко[2]

РАСПРОСТРАНЕННОСТЬ, ОТНОШЕНИЕ К ТАБАКОКУРЕНИЮ И ЕГО КОНТРОЛЬ СРЕДИ ВРАЧЕЙ-ПЕДИАТРОВ ОДЕССКОГО РЕГИОНА

[1] Университет Саншайн-Коста, Квинслэнд, Австралия,
[2] Одесский национальный медицинский университет, Одесса, Украина

Целью исследования было изучение распространенности табакокурения среди врачей Одесского региона (Украина) с различным стажем и содержанием профессиональной деятельности, а также оценка их профилактической работы по прекращению табакокурения. Врачи, особенно педиатры, в значительной степени могут способствовать борьбе против табакокурения.