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Syncope Triggered by Anxiety, Fear, or Pain: Cases and Associated Factors

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Abstract

Background: Receiving a blow, severe pain, having blood drawn, or experiencing intense emotion is known to be able to trigger a vasovagal syncope. In some patients, syncope is even caused by fear of academic situations. Our objective is to describe our cases and what factors are associated with this condition. **Methods**: We present 188 patients with vagal syncope associated with pain or emotion (P/E patients) and compare them with individuals (non P/E patients) in whom vagal syncope is triggered only a period of standing (n: 323/63%). All underwent clinical examination and a tilt test (HUT). **Results**: The age of onset and sex are clearly different between the two groups (P/E group: 20 years old, 29 years old in non P/E patients). 74% of the patients are women. In them, the age of onset is 19 years versus 27 years in men. 44% of patients reported having affected first-degree relatives, and 20% in second-degree relatives. 83% of this inheritance comes from the maternal line. 48% of cases present a significant degree of joint hypermobility. 74% of cases show an important degree of venous pooling in the lower extremities during prolonged standing in the tilt test. The influence of all these factors, is analyzed in our study. **Conclusions**: Factors associated with P/E syncope include female sex, very young age of onset, joint hypermobility, venous pooling during standing, and a hereditary tendency to experience syncope, especially from the maternal line.

Keywords

Dysautonomia, Vasovagal Syncope, Fainting, Tilt Test, Pain, Emotion, Stress

1. Introduction

In clinical practice, we have observed that receiving a blow, intense pain, or a strong emotion, such as fear, can trigger vasovagal syncope [1] [2]. In some patients, syncope occurs by fear of academic situations in some young students. In

these cases, vasovagal syncope occurs when the autonomic system reacts exaggeratedly or paradoxically to certain triggers [3] [4].

We studied 188 patients with this condition and analyzed the specific characteristics of these patients related to the onset of this clinical picture. In the discussion, we present a review of the topic.

2. Materials and Methods

2.1. Definition of the Study Group

This study includes retrospective data analysis of 511 patients (64% female) referred to the Head Tilt Test (HUT) between 2015 and 2024, after suffering a vagal syncope.

The mean age of these patients was 30.8 years (range: 6 - 89 years).

We selected 188 cases (37%) in our study group whose syncopes were associated with pain (somatic, visceral, trauma, blood draws, vaccinations, etc.) or emotional stress.

We compared them with those individuals (control group) in whom vagal syncope is triggered by orthostatism after a period of standing (n: 323/63%) which is not the case in our patients.

More ominous causes, such as those related to arrhythmias and valvular abnormalities, such as ventricular tachycardia, atrioventricular (AV) block, or critical aortic stenosis, were excluded from our study.

Our patients are Chileans, of mixed Hispanic or Latin-European descent.

2.2. Exam Conditions

The exam is performed on an empty stomach, between 8 a.m. and 12 p.m., In a quiet, dimly lit room with a temperature between 20˚C and 22˚C. A neurologist, a cardiologist, and a medical technologist participate. Continuous electrocardiographic monitoring is performed by cardiology staff.

To rule out hypoglycemia, a blood glucose test is performed prior to the exam.

2.3. Tilt Test Protocol

A record of heart rate (HR) and blood pressure (BP) and of symptoms reported by the patient is kept every 5 minutes. The reason for stopping the examination or any important incident is noted and recorded at any time. The sublingual spray nitroglycerin protocol (0.4 ug) is based on Del Rosso [5].

Time line: Initial questioning (15 minutes)/Monitoring installation (digital cuff to measure BP and continuous electrocardiogram) (10 minutes)/Basal HUT (horizontal) for 10 minutes/Passive HUT (standing at 70˚) 45 minutes. Active HUT with 0.4 ug of sublingual spray of trinitrin (without laying the patient down) for 10 minutes/final recovery lying down (10 minutes) Total HUT: 55 minutes. Approximate total, time: 95 minutes.

Carotid massage is performed on all patients over 60 years of age. Previous discard of murmur or carotid stenosis or stroke in the last 6 months. Five minutes on each side (11).

Head-Up Tilt Table Test ends if a "positive HUT" is obtained: This is syncope (loss of consciousness) or presyncope (dizziness, nausea, paleness, etc., announcing that syncope is imminent). Associated with low blood pressure (Systolic BP < 70 mmHg) or low blood pressure plus bradycardia, or if intolerable patient discomfort occurs.

If there are no symptoms, it is terminated due to the end of the protocol.

The equipment consists of: Digital monitor (Ohmeda 2300 Finapres BP Monitor USA). Digital cuff placed on the index or middle finger to measure BP and HR continuously.

Electric tilting table (Magnetic Manumed USA) and electrocardiogram monitor (Quinton Q4500 USA). The patient is fastened to the table with two velcro straps (knees and chest).

Venous congestion with a score ranging from 1 to 5, was measured using a colorimetric method, with visual observation of color and venous congestion in the lower extremities and feet, and comparing these findings with standardized photographs for each range.

2.4. Data Analysis

For the statistical comparison, data is analyzed by χ^2 test, anova and logistic regression, and depending on the sample size, a non-parametric test is used.

2.5. Ethical Approval

Our study was analyzed and approved by the institutional ethics committee of the Hospital Militar, and was carried out in accordance with the ethical standards of the Helsinki Declaration 1964. Patients and controls signed an informed consent before inclusion.

3. Results

Pain, stress, and/or emotion.

188 of our patients reported that syncope is related to pain and/or emotion (P/E in the text). Therefore, it occurs in situations such as a blow or cut, a blood draw, a visit to the dentist, vaccination, or severe emotional stress (an academic exam, an earthquake, or seeing a spider). The number of patients with P/E and non P/E syncope and their characteristics (gender and age at onset of syncope) can be seen in Table 1.

Table 1. Gender and age of onset of syncope.

Syncope triggered by P/E n: 188 (37%) x: 20 years old		**Syncope not triggered by P/E n: 323 (63%) x: 29 years old**	
Females P/E n (%) and x: age of onset	**Males P/E** n (%) and x: age of onset	**Females Non P/E** n (%) and x: age of onset	**Males non P/E** n (%) and x: age of onset
n: 139 (27%) 19 years old	n: 49 (10%) 27 years old	n: 186 (36%) 25 years old	n: 137 (27%) 33 years old

In Figure 1, we show the distribution of patients by decade at onset of the symptoms.

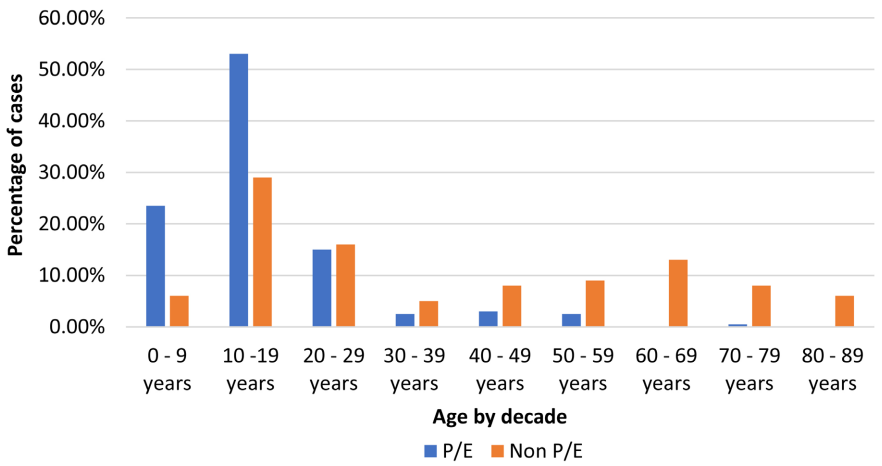

Figure 1. Percentage of patients with and without P/E syncope per decade.

3.1. Triggering Events for Syncope

1) Vaccination or blood extraction n: 36, 2) Insurmountable fear (earthquake or arachnophobia) n: 6, 3) Academic stress n: 140, 4) Fall or strong blow n: 18, 5) Cut or bleeding n: 10, 6) Abdominal or menstrual pain n: 18.

In Table 2, we show the types and number of events triggered by P/E.

Table 2. Types and number of triggering events.

Triggering event*	Male	Female
Fall or strong hit	16	2
Vaccination/Blood extraction	6	30
Academic stress	18	122
Cut or bleeding	4	6
Abdominal/Menstrual Pain	-	18
Arachnophobia	-	4
Fear of earthquakes	-	2
Total events n: 230*	46 (20%)	184 (80%)

*Some different triggering events can occur in the same patient. They are usually female. The most common combinations are: vaccination/blood draw + menstrual pain and vaccination/blood draw + academic stress.

3.2. Female Sex and P/E Syncope

Female patients represented 64% (n: 325) of the total cases sent to HUT (n: 511), compared to 36% (n: 186) in males. This difference was even greater in our patients with P/E-triggered syncope, female (74%) vs. male (26%) (n: 139 vs. 49) ($p \leq 0.05$).

This is exactly the opposite in the male sex, where syncopes not triggered by P/E predominate (42% vs 26%) [6] ($p \leq 0.05$).

Of our P/E patients with a severe level (>5) of joint hypermobility syndrome (JHS), 65% are women. Even more women constitute 68% of those who have severe (grade 4) or very severe (grade 5) of venous congestion (venous pooling) during prolonged standing, versus women whose syncope is not triggered by P/E (orthostatic syncope): 58% ($p \leq 0.05$).

3.3. Age of Onset and P/E Syncope

The average age of onset of syncope in our patients was 20 years old, compared to non P/E patients, where this age was 29 years. In females, the earlier age of onset was even more noticeable in P/E cases: 19 years (female) versus 27 years (male) ($p \leq 0.05$).

In our non P/E patients, the predominance of females was also observed, with a younger age of onset of syncope: 25 years (female) versus 33 years (male) ($p \leq 0.05$).

3.4. Age of Onset in Cases with a Hereditary History

Cases with a hereditary history of P/E syncope have an average onset at 16 years of age, compared to 31 years of age in the hereditary group without P/E ($p \leq 0.05$). Inheritance in our cases with P/E syncope occurs at earlier ages, especially in women (χ: 12 years old).

3.5. Heredity

A history of vagal syncope in first-degree relatives (mother, father, children, siblings) is very common. All patients were given a questionnaire asking if they knew of any other family members affected by vagal syncope or fainting.

In our P/E patients (n = 188), we found a history of syncope in these first-degree relatives (83/188 = 44% frequency). Inheritance occurs mainly through the maternal branch (83%), more often than through both branches (maternal and paternal) (14%), and rarely only through the paternal line (3%) ($p \leq 0.05$).

On the contrary, of the patients with orthostatic syncope (not triggered by P/E): 323 cases, only 13% (n: 42) ($p < 0.05$) had a history of syncope in first-degree relatives. A main predominance of female inheritance was also observed in these patients.

See data on inheritance patterns in first degree relatives in **Figure 2**.

We found data on the parents (29 mothers, 9 fathers) of our P/E patients who recalled the presence of emotionally/pain triggered fainting spells in their own parents, siblings, aunts, or uncles (second-degree relatives): 20%.

In cases of orthostatic syncope (non P/E), we found only 9 mothers and 3 fathers who recalled the presence of P/E-triggered syncope in their ancestors (4%). ($p \leq 0.05$).

See these data in **Figure 3**.

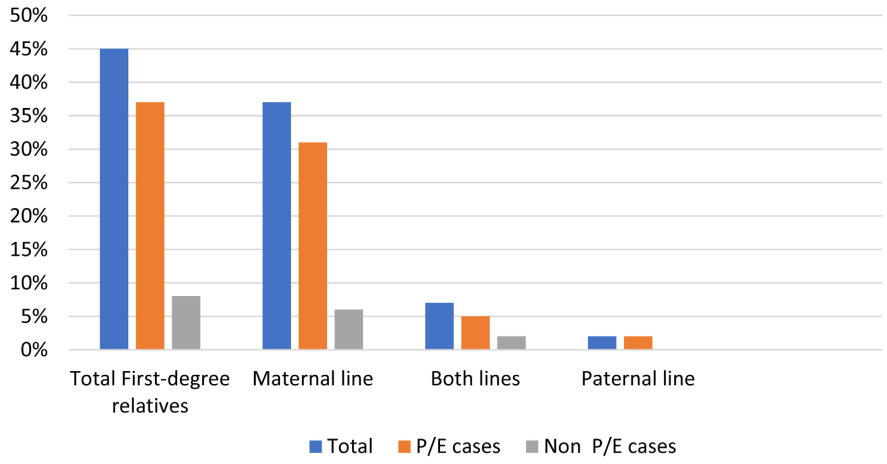

Figure 2. Inheritance patterns of emotionally/pain triggered syncope in first degree relatives of patients with syncope P/E v/s non P/E patients.

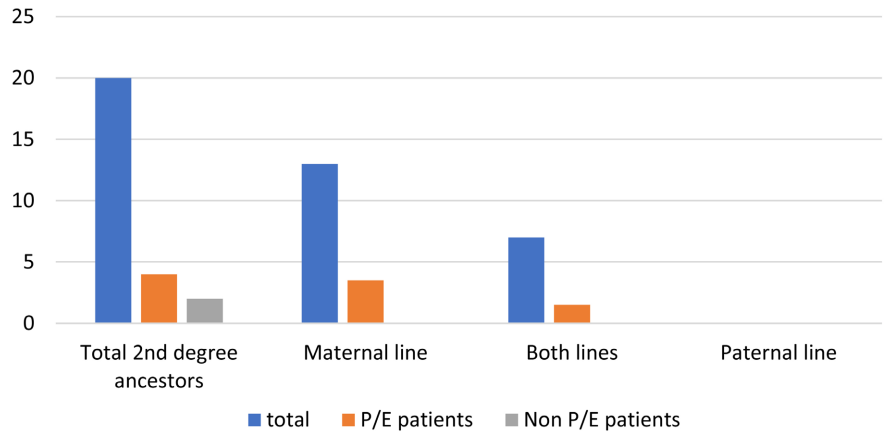

Figure 3. Inheritance patterns of emotionally/pain triggered syncope in second degree relatives of patients with syncope P/E v/s non P/E patients.

We thus postulate a certain hereditary continuity of syncope triggered by P/E. Especially through the maternal line. Even in our non P/E cases (orthostatic syncope), maternal branch is the main line of inheritance of vasovagal syncope.

Even maternal inheritance is closely linked to the presence of joint hypermobility syndrome in our female patients (n: 56 = 61%).

3.6. Joint Hypermobility Syndrome

Of the 511 patients studied, 235 (46%) had joint hypermobility (score 5 or ≥ on the "Beighton Scale") [7].

We notice a hereditary tendency of joint hypermobility syndrome in our patients P/E = 48% versus in non P/E cases: 35% ($p \leq 0.05$).

3.7. Venous Congestion in the Lower Extremities and Prolonged Standing

We observed a relationship between the accumulation of "venous pool" in lower

extremities and syncope during the passive phase (45 minutes) of HUT. Venous congestion was measured by visual observation of the color and congestion in lower extremities and feet with a score ranging from 1 to 5. And compared to a standard set of photographs for each range.

1 = nothing (little or no change in color of feet), 2 = mild (pinkish feet), 3 = moderate (reddish feet), 4 = severe (dark reddish feet) and 5 = very severe (acrocyanosis and purple feet). This system has been already explained in our previous publication [8]. In **Table 3**, we show the colorimetric scale with our classification for the different degrees of venous pooling.

Table 3. Grades of venous pooling: Colorimetric scale.

Grade of pooling	Visual scale
1) None	Pale, whitish feet
2) Mild	Pink feet
3) Moderate	Reddish feet
4) Severe	Dark reddish feet
5) Very Severe	Purple feet

Of the patients with P/E syncope, 74% presented moderate, severe, or very severe (grades 3, 4 or 5) venous pooling during the passive HUT. Of these, 82% had a positive HUT for vasovagal dysautonomia. Of the patients with non P/E syncope, 65% presented equivalent grades of venous pooling and, of these, only 68% had a positive HUT for vagal syncope ($p \leq 0.05$).

The increase in venous congestion during prolonged standing in our patients is related to:

1) Female sex: Venous pooling is much higher in women (55%) than in men (33%) ($p \leq 0.05$). In female patients with orthostatic episodic syncope, it was 47%.

2) Joint hypermobility: Venous congestion during standing is higher in our patients with joint hypermobility (74%) versus non P/E cases (65%). ($p \leq 0.05$).

3) Inheritance: We observed a higher frequency of hereditary history of P/E syncope in patients with greater venous congestion during prolonged standing, 78% of patients with severe venous congestion and hereditary history, versus non P/E cases: 62% ($p \leq 0.05$).

This may be greatly influenced by the high proportion of people with joint hypermobility and Ehlers-Danlos syndrome type 3 in Chile [9].

4. Discussion

4.1. Stress and Vagal Syncope

There is a positive association between anxiety and panic and a positive HUT [2] [10] [11], and between recurrent vagal syncope and emotional stress [11].

Intense fear can motivate us to act (fight or run away) or, conversely, it can paralyze us and prevent us from acting, triggering fainting, postural dizziness, or

even urinating or defecating (in extremely frightened people) [12] [13].

In nature, it is seen in animals that "play dead," such as the opossum, some snakes, and some birds, because this confers a survival advantage during periods of unavoidable threat [14].

This applies to humans in what is known as the "Paleolithic threat hypothesis," which postulates that, in fear-induced fainting, genomes associated with life-threatening situations, such as encountering "a stranger holding a sharp object," are selected and inherited [15].

Thus, there would be an enhanced heritable predisposition to abruptly increase vagal tone and collapse flaccidly, rather than attempting to flee or fight in response to fear or threat. Even a minor injury or the sight of blood may have evolved as a response associated with this fear circuit. Such a "paradoxical" hemodynamic predisposition will increase the chances of survival for some individuals [15] [16].

There are cases of soldiers in battle or about to be shot who survive after fainting [16]. Or young women who, when they faint, are kidnapped alive to be enslaved, and the fainting prevents them from being killed [15] [16].

Therefore, we believe the Paleolithic threat hypothesis fits perfectly with some of our findings, such as the strong female predominance (74% vs 26% in male) and strong maternal inheritance in our patients (83% for us).

Thus, we propose that the maintenance of this mainly maternally inherited reflex in evolution supports the survival of the female sex, which is essential for the survival of the human species.

The Paleothreat hypothesis is consistent with our observation of a pattern of fear-induced fainting at a young age, primarily in women, which could explain what is observed in disasters such as earthquakes, terrorism against civilians, or traumatic events, where epidemics of fear-induced fainting or imitation of others occur in very young women [15] [17]-[21].

Ultrasound scans show how stress induces left ventricular sympathetic hypercontractility, but the reduced venous return that occurs in the HUT activates an inhibitory vagal reflex in some individuals, slowing the heart rate. This would constitute a beneficial cessation of the heart's pumping function, since it would reduce myocardial oxygen consumption, allowing better diastolic filling and coronary perfusion [22] [23].

4.2. Injection or Blood Extraction and Arachnophobia

Functional MRI studies have investigated arachnophobia versus injection or blood draw phobia. The degree of anxiety and disgust is greatly enhanced by activation in some regions common to both groups, such as the thalamus, cerebellum, and occipitotemporal regions [24]-[26].

The group with a phobia of injection or blood draw is characterized by greater activation in the thalamus and visual/attention areas (occipitotemporoparietal cortex). Patients with arachnophobia show greater activation in the dorsal anterior cingulate cortex and anterior insula compared to injection-phobic patients

and healthy controls [27]-[29].

4.3. Female Hormones and Syncope Triggered by Stress, Pain, or Emotion

Sex hormones play an important role (with an explosion during adolescence) in shaping neuronal structure and connections in the thalamus and visual/attention areas (occipitotemporoparietal cortex), dorsal anterior cingulate cortex, amygdala, and anterior insula [30]-[32] and the high presence of progesterone receptors on noradrenergic neurons in the nucleus of the solitary tract (vagal nerve), in the region whose connections project to the supraoptic nucleus of the hypothalamus [33]. And from the hypothalamus, there are connections that regulate the stress responses of the sympathetic and parasympathetic systems in the brainstem and spinal cord [34] [35].

This may explain some rapid and automatic emotional reactions that override rational thought and occur in situations of great fear or risk. This is known as "amygdala hijacking," where emotional reactions become disproportionate to the actual threat [36], and these are more frequent and intense in women [37] [38].

4.4. Genetics and Vagal Syncope

The genetic tendency to suffer from vasovagal syncope is clear [39]-[41]. Family history is described in about 20% of these patients [42] [43]. The presence of vasovagal syncope shows much higher concordance in monozygotic twins than in dizygotic twins [44]. Klein [44] believes that the tendency to experience vasovagal syncope is inherited in an autosomal dominant manner, via genes on chromosome 15. This would bring us closer to understanding the biological basis of syncope and maybe allow for future gene therapies [44].

Multiple genetic variants associated with hypotension and/or vasovagal syncope have been described. For example, variants exist in the chromosomes that regulate blood pressure control mechanisms [45] [46], in neurotransmitters related to the synthesis of norepinephrine [47], in the absorption of salt in the renal tubule, as seen in the hereditary salt wasting of Gitelman syndrome [48], or in alleles related to serotonin signaling [49] [50], some of them associated with a decrease in syncope in men but an increase in women or vice versa [49].

4.5. Inheritance in Vagal Syncope: Maternal vs. Paternal Branch

Studies support our observation about the heritability of vagal syncope in first-degree relatives [43] [49]-[53], especially through the maternal line [41] [49]. It can also be inherited from the paternal side, but with a significantly lower frequency [49].

4.6. Joint Hypermobility: Inheritance and Syncope

Hypermobile patients experience significant venous congestion in their lower extremities when standing. This leads to impaired venous return, creating condi-

tions for syncope due to systemic hypotension and cerebral circulatory deficit [54]. Skin biopsies show that the connective tissue in hypermobile individuals has a much higher proportion of type III collagen, which is more distensible. Their veins are much more congested when standing [9] [54] [55]. Furthermore, the hereditary tendency to ligament hyperlaxity is recognized as a risk factor for being a carrier of vagal syncope. This fact is known in the literature [9] [54]-[58].

5. Clinical Implications

The clinical implications of these findings are important. Our patient should avoid contact sports (boxing, martial arts, soccer, hockey, rugby, etc.). Other activities, such as cycling or running, should be performed with a helmet and protective gear on vulnerable areas such as knees and elbows. Blood draws and vaccinations should be done with the patient lying down. To receive emotionally important news (for example, exam grades) the patient must be sitting. In periods where syncopes are frequent or in risk situations, the patient could be medicated with drugs such as midodrine, fludrocortisone or droxidopa.

In this way, these patients could have a normal life for a long time and their syncopes would occur very infrequently, and could even be a less expressed dysautonomia [8].

6. Final Conclusions

Factors that we have found associated with P/E syncope include female sex, very young age at onset of syncope, significant joint hypermobility, severe venous congestion during prolonged standing, and a hereditary tendency to experience syncope, especially if inherited from the maternal line. A continuous pattern of cases was observed in first- and second-degree relatives. But syncopes do not occur unless there is some potentially manageable environmental factor that acts as a trigger (got hit, pain, and/or emotion), triggering an autonomic reflex that produces syncope.

7. Limitations of the Study

First, our study is retrospective, so it is difficult to obtain patients' recollection of the age at which their symptoms began and information about affected family members. In some cases, the patient, after a second interrogation, remembers having suffered episodes during childhood or adolescence. Added to this is the lack of knowledge about their ancestors, especially in some patients who have not lived with or met their male parents.

Second: It is difficult to draw statistically valid conclusions due to the small number of patients studied in our sample and the fact that the study was conducted at a single center.

We understand that a larger sample size and a more collaborative study are necessary in the future.

Third: Our visual scale, used to assess venous congestion of the lower extremi-

ties, is not yet internationally validated. It was our creation, documented with photos and statistically closely related [59] [60] to prolonged standing and joint hypermobility.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Kato, K., Kakisaka, Y., Jin, K., Fujikawa, M., Nakamura, M., Suzuki, N., *et al.* (2017) Stressful Medical Explanation May Cause Syncope in Patients with Emotion-Triggered Neurocardiogenic Syncope. *Pacing and Clinical Electrophysiology*, **41**, 96-98. https://doi.org/10.1111/pace.13199

[2] Gracie, J., Newton, J.L., Norton, M., Baker, C. and Freeston, M. (2006) The Role of Psychological Factors in Response to Treatment in Neurocardiogenic (Vasovagal) Syncope. *EP Europace*, **8**, 636-643. https://doi.org/10.1093/europace/eul073

[3] Abuzainah, B., Gutlapalli, S.D., Chaudhuri, D., Khan, K.I., Al Shouli, R., Allakky, A., *et al.* (2022) Anxiety and Depression as Risk Factors for Vasovagal Syncope and Potential Treatment Targets: A Systematic Review. *Cureus*, **14**, e32793. https://doi.org/10.7759/cureus.32793

[4] Shaposhnikov, E.A., Ioseliani, K.K., Chugunov, V.S. and Narinskaia, A.L. (1992) [The Asthenic Syndrome and Mental Work Capacity]. *Aviakosmicheskaia i Ekologicheskaia Meditsina*, **26**, 59-65. https://pubmed.ncbi.nlm.nih.gov/1297495/

[5] Del Rosso, A., Bartoli, P., Bartoletti, A., Brandinelli-Geri, A., Bonechi, F., Maioli, M., *et al.* (1998) Shortened Head-Up Tilt Testing Potentiated with Sublingual Nitroglycerin in Patients with Unexplained Syncope. *American Heart Journal*, **135**, 564-570. https://doi.org/10.1016/s0002-8703(98)70268-6

[6] Wang, S., Peng, Y., Zou, R., Wang, Y., Cai, H., Li, F., *et al.* (2023) The Relationship between Demographic Factors and Syncopal Symptom in Pediatric Vasovagal Syncope. *Scientific Reports*, **13**, Article No. 22724. https://doi.org/10.1038/s41598-023-49722-w

[7] Grahame, R. (1990) The Hypermobility Syndrome. *Annals of the Rheumatic Diseases*, **49**, 199-200. https://doi.org/10.1136/ard.49.3.199

[8] Jiménez-Cohl, P., Aspeé, M., Sepúlveda, M., Lepe, B., Godoy, J.I. and Jiménez-Castillo, S. (2022) Minimal Vasovagal Dysautonomia in Patients with Rare or Unique

Syncope. *International Journal of Clinical Medicine*, **13**, 262-275. https://doi.org/10.4236/ijcm.2022.137022

[9] Bravo, J.F. (2010) Síndrome de Ehlers-Danlos tipo III, llamado también Síndrome de Hiper-laxitud Articular (SHA): Epidemiología y manifestaciones clínicas. *Reumatología*, **26**, 194-202.

[10] Zysko, D., Melander, O. and Fedorowski, A. (2013) Vasovagal Syncope Related to Emotional Stress Predicts Coronary Events in Later Life. *Pacing and Clinical Electrophysiology*, **36**, 1000-1006. https://doi.org/10.1111/pace.12138

[11] Cohen, T.J., Thayapran, N., Ibrahim, B., Quan, C., Quan, W. and Von Zur Muhlen, F. (2000) An Association between Anxiety and Neurocardiogenic Syncope during Head-up Tilt Table Testing. *Pacing and Clinical Electrophysiology*, **23**, 837-841. https://doi.org/10.1111/j.1540-8159.2000.tb00852.x

[12] Mawer, S. and Alhawai, A.F. (2023) Physiology, Defecation. StatPearls. https://www.ncbi.nlm.nih.gov/books/NBK539732/

[13] Shafik, A., El-Sibai, O. and Ahmed, I. (2002) Parasympathetic Extrinsic Reflex: Role in Defecation Mechanism. *World Journal of Surgery*, **26**, 737-740. https://doi.org/10.1007/s00268-002-6285-9

[14] Peterson, C. (2021) Many Animals Play Dead Not Just to Avoid Predators. National Geo-Graphic. https://www.nationalgeographic.com/animals/article/many-animals-play-dead-not-just-to-avoid-predators

[15] Bracha, H.S., Bracha, A.S., Williams, A.E., Ralston, T.C. and Matsukawa, J.M. (2005) The Human Fear-Circuitry and Fear-Induced Fainting in Healthy Individuals. *Clinical Autonomic Research*, **15**, 238-241. https://doi.org/10.1007/s10286-005-0245-z

[16] Van Dijk, N. and Wieling, W. (2009) Fainting, Emancipation and the 'Weak and Sensitive' Sex. *The Journal of Physiology*, **587**, 3063-3064. https://doi.org/10.1113/jphysiol.2009.174672

[17] Turk, D. (2025) Vasovagal Syncope as Social Signal: An Evolutionary Perspective. *Medical Hypotheses*, **203**, Article 111751. https://www.sciencedirect.com/science/article/pii/S0306987725001902

[18] Levine, R.J. (1977) Epidemic Faintness and Syncope in a School Marching Band. *JAMA*: *The Journal of the American Medical Association*, **238**, 2373-2376. https://doi.org/10.1001/jama.1977.03280230037017

[19] Mohr, P.D. and Bond, M.J. (1982) A Chronic Epidemic of Hysterical Blackouts in a Comprehensive School. *BMJ*, **284**, 961-962. https://doi.org/10.1136/bmj.284.6320.961

[20] Etchells, P. (2015) The Ripon 'Ripple of Anxiety' and Mass Hysteria. The Guardian. https://www.theguardian.com/science/head-quarters/2015/nov/12/the-ripon-ripple-of-anxiety-and-mass-hysteria

[21] Perlmutter, L. (2023) Was Mass Hysteria Behind the Mysterious Case of 227 Middle School Students Fainting Last Fall? Business Insider. https://www.businessinsider.com/was-mass-hysteria-behind-a-mysterious-middle-school-fainting-epidemic-2023-6

[22] BBC News (2015) Who, What, Why: Can a 'Ripple Effect' Cause Mass Fainting? BBC News. https://www.bbc.com/news/magazine-34793710

[23] Joo, E.Y., Hong, S.B., Lee, M., Tae, W.S., Lee, J., Han, S.W., *et al.* (2010) Cerebral Blood Flow Abnormalities in Patients with Neurally Mediated Syncope. *Journal of Neurology*, **258**, 366-372. https://doi.org/10.1007/s00415-010-5759-1

[24] Moon, J., Kim, H., Kim, J., Chung, S., Choi, E., Min, P., *et al.* (2010) Left Ventricular Hypercontractility Immediately after Tilting Triggers a Disregulated Cardioinhibitory Reaction in Vasovagal Syncope: Echocardiographic Evaluation during the Head-Up Tilt Test. *Cardiology*, **117**, 118-123. https://doi.org/10.1159/000320141

[25] Caseras, X., Giampietro, V., Lamas, A., Brammer, M., Vilarroya, O., Carmona, S., *et al.* (2009) The Functional Neuroanatomy of Blood-Injection-Injury Phobia: A Comparison with Spider Phobics and Healthy Controls. *Psychological Medicine*, **40**, 125-134. https://doi.org/10.1017/s0033291709005972

[26] Bracha, H.S., Bienvenu, O.J. and Eaton, W.W. (2007) Testing the Paleolithic-Human-Warfare Hypothesis of Blood-Injection Phobia in the Baltimore ECA Follow-Up Study—Towards a More Etiologically-Based Conceptualization for DSM-V. *Journal of Affective Disorders*, **97**, 1-4. https://doi.org/10.1016/j.jad.2006.06.014

[27] Straube, T., Mentzel, H. and Miltner, W.H.R. (2007) Waiting for Spiders: Brain Activation during Anticipatory Anxiety in Spider Phobics. *NeuroImage*, **37**, 1427-1436. https://doi.org/10.1016/j.neuroimage.2007.06.023

[28] Hermann, A., Schäfer, A., Walter, B., Stark, R., Vaitl, D. and Schienle, A. (2007) Diminished Medial Prefrontal Cortex Activity in Blood-Injection-Injury Phobia. *Biological Psychology*, **75**, 124-130. https://doi.org/10.1016/j.biopsycho.2007.01.002

[29] Caseras, X., Mataix-Cols, D., Trasovares, M.V., López-Solà, M., Ortriz, H., Pujol, J., *et al.* (2010) Dynamics of Brain Responses to Phobic-Related Stimulation in Specific Phobia Subtypes. *European Journal of Neuroscience*, **32**, 1414-1422. https://doi.org/10.1111/j.1460-9568.2010.07424.x

[30] Çavuşoğlu, M. and Dirik, G. (2011) Fear or Disgust? The Role of Emotions in Spider Phobia and Blood-Injection-Injury Phobia. *Türk Psikiyatri Dergisi*, **22**, 115-122.

[31] Matteoli, M. (2017) The Brain: What Relationship Does It Have with Female Hormones? All Medical Sciences Student life. https://www.hunimed.eu/news/brain-relationship-female-hormones/

[32] Hornung, J., Lewis, C.A. and Derntl, B. (2020) Sex Hormones and Human Brain Function. *Handbook of Clinical Neurology*, **175**, 195-207. https://www.sciencedirect.com/science/article/abs/pii/B978044464123600014X

[33] Barth, C., Villringer, A. and Sacher, J. (2015) Sex Hormones Affect Neurotransmitters and Shape the Adult Female Brain during Hormonal Transition Periods. *Frontiers in Neuroscience*, **9**, Article 37. https://doi.org/10.3389/fnins.2015.00037

[34] Diaz-Brinton, R., Thompson, R.F., Foy, M.R., Baudry, M., Wang, J.M., Finch, C.E., Morgan, T.E., Stanczyk, F.Z., Pike, C.J. and Nilsen, J. (2009) Progesterone Receptors: Form and Function in Brain. *Frontiers in Neuroendocrinology*, **29**, 313-339. https://pmc.ncbi.nlm.nih.gov/articles/PMC2398769/

[35] Benarroch, E.E. (2014) Hypothalamus: Autonomic Pattern Generator for Homeostasis and Adaptation. Oxford University Press, 3-14.

[36] Sawchenko, P.E., Li, H.-. and Ericsson, A. (2000) Circuits and Mechanisms Governing Hypothalamic Responses to Stress: A Tale of Two Paradigms. *Progress in Brain Research*, **122**, 61-78. https://doi.org/10.1016/s0079-6123(08)62131-7

[37] Poláčková Šolcová, I. and Lačev, A. (2017) Differences in Male and Female Subjective Experience and Physiological Reactions to Emotional Stimuli. *International Journal of Psychophysiology*, **117**, 75-82. https://doi.org/10.1016/j.ijpsycho.2017.04.009

[38] Domes, G., Schulze, L., Böttger, M., Grossmann, A., Hauenstein, K., Wirtz, P.H., *et al.* (2009) The Neural Correlates of Sex Differences in Emotional Reactivity and Emotion Regulation. *Human Brain Mapping*, **31**, 758-769.

https://doi.org/10.1002/hbm.20903

[39] Cooper, C.J., Ridker, P., Shea, J. and Creager, M.A. (1994) Familial Occurrence of Neurocardiogenic Syncope. *The New England Journal of Medicine*, **331**, 205. https://www.nejm.org/doi/10.1056/NEJM199407213310316?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

[40] Lewis, S.L. and O'Toole, M. (1994) Familial Occurrence of Neurocardiogenic Syncope. *The New England Journal of Medicine*, **331**, 1529. https://www.nejm.org/doi/10.1056/nejm199412013312219?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

[41] Camfield, P.R. and Camfield, C.S. (1990) Syncope in Childhood: A Case Control Clinical Study of the Familial Tendency to Faint. *Canadian Journal of Neurological Sciences/Journal Canadien des Sciences Neurologiques*, **17**, 306-308. https://doi.org/10.1017/s0317167100030626

[42] Newton, J.L., Kerr, S., Pairman, J., McLaren, A., Norton, M., Kenny, R.A. and Morris, C.M. (2005) Familial Neurocardiogenic (Vasovagal) Syncope. *American Journal of Medical Genetics Part A*, **133A**, 176-179. https://doi.org/10.1002/ajmg.a.30572

[43] Newton, J.L., Kenny, R., Lawson, J., Frearson, R. and Donaldson, P. (2003) Prevalence of Family History in Vasovagal Syncope and Haemodynamic Response to Head up Tilt in First Degree Relatives. *Clinical Autonomic Research*, **13**, 22-26. https://doi.org/10.1007/s10286-003-0077-7

[44] Klein, K.M., Xu, S.S., Lawrence, K., Fischer, A. and Berkovic, S.F. (2012) Evidence for Genetic Factors in Vasovagal Syncope. *Neurology*, **79**, 561-565. https://doi.org/10.1212/wnl.0b013e3182635789

[45] Newton, J. (2003) A15-3 Angiotensin-Converting Enzyme Insertion/Deletion Polymorphism and Tilt Diagnosed Vasovagal Syncope. *Europace*, **4**, B23. https://doi.org/10.1016/s1099-5129(03)91587-x

[46] DeStefano, A.L., Baldwin, C.T., Burzstyn, M., Gavras, I., Handy, D.E., Joost, O., *et al.* (1998) Autosomal Dominant Orthostatic Hypotensive Disorder Maps to Chromosome 18q. *The American Journal of Human Genetics*, **63**, 1425-1430. https://doi.org/10.1086/302096

[47] Man in't Veld, A.J., Moleman, P., Boomsma, F. and Schalekamp, M.A.D.H. (1987) Congenital Dopamine-β-Hydroxylase Deficiency. *The Lancet*, **329**, 183-188. https://doi.org/10.1016/s0140-6736(87)90002-x

[48] Cruz, D.N., Simon, D.B., Nelson-Williams, C., Farhi, A., Finberg, K., Burleson, L., *et al.* (2001) Mutations in the Na-Cl Cotransporter Reduce Blood Pressure in Humans. *Hypertension*, **37**, 1458-1464. https://doi.org/10.1161/01.hyp.37.6.1458

[49] Sheldon, R., Rose, M.S., Ritchie, D., Martens, K., Maxey, C., Jagers, J., *et al.* (2019) Genetic Association Study in Multigenerational Kindreds with Vasovagal Syncope. *Circulation*: *Arrhythmia and Electrophysiology*, **12**, e006884. https://doi.org/10.1161/circep.118.006884

[50] Sheldon, R.S. and Sandhu, R.K. (2019) The Search for the Genes of Vasovagal Syncope. *Frontiers in Cardiovascular Medicine*, **6**, Article 175. https://www.frontiersin.org/journals/cardiovascular-medicine/articles/10.3389/fcvm.2019.00175/full

[51] González-Hermosillo, A., Márquez, M.F., Vallejo, M., Urias, K.I. and Cárdenas, M. (2006) Familial Vasovagal Syncope: Clinical Characteristics and Potential Genetic Substrates. In: Raviele, A., Ed., *Cardiac Arrhythmias* 2005, Springer-Verlag, 701-708. https://doi.org/10.1007/88-470-0371-7_87

[52] Matveeva, N., Titov, B., Bazyleva, E., Pevzner, A. and Favorova, O. (2021) Towards Understanding the Genetic Nature of Vasovagal Syncope. *International Journal of Molecular Sciences*, **22**, Article 10316. https://doi.org/10.3390/ijms221910316

[53] Titov, B., Matveeva, N., Kulakova, O., Baulina, N., Bazyleva, E., Kheymets, G., *et al.* (2022) Vasovagal Syncope Is Associated with Variants in Genes Involved in Neurohumoral Signaling Pathways. *Genes*, **13**, Article 1653. https://doi.org/10.3390/genes13091653

[54] Gazit, Y., Nahir, A.M., Grahame, R. and Jacob, G. (2003) Dysautonomia in the Joint Hypermobility Syndrome. *The American Journal of Medicine*, **115**, 33-40. https://doi.org/10.1016/s0002-9343(03)00235-3

[55] Bohora, S. (2010) Joint Hypermobility Syndrome and Dysautonomia: Expanding Spectrum of Disease Presentation and Manifestation. *Indian Pacing and Electrophysiology Journal*, **10,** 158-161. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2847865/pdf/ipej100158-00.pdf)

[56] Grahame, R. (1999) Joint Hypermobility and Genetic Collagen Disorders: Are They Related? *Archives of Disease in Childhood*, **80**, 188-191. https://doi.org/10.1136/adc.80.2.188

[57] Malfait, F., Hakim, A.J., De Paepe, A. and Grahame, R. (2006) The Genetic Basis of the Joint Hypermobility Syndromes. *Rheumatology*, **45**, 502-507. https://doi.org/10.1093/rheumatology/kei268

[58] The Ehlers-Danlos Society: Genetics and Inheritance of EDS and HSD. https://www.ehlers-danlos.com/genetics-and-inheritance/

[59] Stewart, J.M., Medow, M.S., Sutton, R., Visintainer, P., Jardine, D.L. and Wieling, W. (2017) Mechanisms of Vasovagal Syncope in the Young: Reduced Systemic Vascular Resistance versus Reduced Cardiac Output. *Journal of the American Heart Association*, **6**, e004417. https://www.ahajournals.org/doi/10.1161/JAHA.116.004417#:~:text=The%20majority%20of%20syncope%20is,that%20reduces%20central%20blood%20volume

[60] Skoog, J., Zachrisson, H., Länne, T. and Lindenberger, M. (2016) Slower Lower Limb Blood Pooling Increases Orthostatic Tolerance in Women with Vasovagal Syncope. *Frontiers in Physiology*, **7**, Article 232. https://doi.org/10.3389/fphys.2016.00232