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Incidence and Hemodynamic Characteristics of Near-Fainting in Healthy 6- to 16-Year Old Subjects

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Objectives. **We studied the incidence and hemodynamic characteristics of near-fainting under orthostatic stress in healthy children and teenagers.**

Background. **Orthostatic stress testing is increasingly used to identify young subjects with unexplained syncope. However, the associated incidence of syncope and hemodynamic responses in normal young subjects are not well known.**

Methods. **Eighty-four healthy subjects 6 to 16 years old performed forced breathing, stand-up and 70° tilt-up tests. An intravenous line to sample blood for biochemical assessment of sympathetic function was introduced between the stand-up and tilt-up tests. Finger arterial pressure was measured continuously. Left ventricular stroke volume was computed from the pressure pulsations.**

Results. **Sixteen of the 84 subjects were excluded because of technical problems. The incidence of a near-fainting response in the remaining 68 subjects was 10% (7 of 68) for the stand-up test and 40% (29 of 68) for the tilt-up test. Baseline parasympathetic and sympathetic activity of nonfainting and near-fainting subjects was not different. Near-fainting was characterized by attenuated systemic vasoconstriction and exaggerated tachycardia that occurred as early as 1 min after return to the upright position. On tilt-up, plasma adrenaline levels increased by a factor of 2, with slightly higher increments in the near-fainting subjects.**

Conclusions. **Inadequate vasoconstriction is the common underlying mechanism of near-fainting in young subjects. The remarkably high incidence of near-fainting during the tilt-up test after intravascular instrumentation raises serious doubts about the utility of this procedure in evaluating syncope of unknown origin in young subjects.**

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Fainting originates from a precipitous decline in blood pressure with an inadequate flow of blood to the brain and is associated with reflex systemic arteriolar vasodilation and cardiac vagal slowing (1–4). In children and teenagers fainting is a relatively common but poorly documented phenomenon.

We investigated healthy young subjects intended to serve as a control group for studies dealing with true autonomic and cardiovascular dysfunction in children and teenagers. The present study reports the high incidence and hemodynamic characteristics of near-fainting in these healthy subjects during tilt-up testing with intravascular instrumentation for blood sampling. These data are needed because of the increased use of tilt-table testing in young subjects with syncope of unknown origin (5,6).

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Methods

Subjects. Eighty-four young subjects (48 girls, 36 boys; 6 to 16 years old) were studied at the University Hospital for Children and Youth, "Het Wilhelmina Kinderziekenhuis." They were recruited from primary and high schools in the city and region of Utrecht, The Netherlands. All subjects were in good health, did not smoke, ate a normal diet without salt restriction, used no medication and did not visit a hospital clinic regularly. They had no history of postural complaints or frequent fainting. Sixteen girls and nine boys had physical signs of puberty according to the criteria of the Tanner score system.

Subjects and parents gave written informed consent. The study protocol was approved by the Ethics Committee of the hospital. When it appeared that the incidence of near-fainting was unexpectedly high, we communicated our findings to the Ethics Committee, after consultation it was decided to complete the study.

Measurements. Blood pressure was measured continuously by noninvasive recording of finger arterial pressure with an Ohmeda 2300 Finapres monitor (7). This instrument measures blood pressure changes during orthostatic stress testing as well as during hypotensive periods with sufficient accuracy (8,9). A black Ohmeda cuff was wrapped around the right middle finger. Cuff size was chosen according to the manufac-

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turer's recommendations. The cuffed finger was held at heart level to avoid hydrostatic pressure errors. An electrocardiogram was obtained (Hewlett-Packard model 78905A) and connected to a cardiotachometer to obtain instantaneous heart rate responses. Blood pressure, heart rate and an event marker were displayed on a Nihon Kohden WS 681G thermal array recorder (Tokyo, Japan) to monitor cardiovascular changes during the experiments. The signals were digitized on-line and stored in a personal computer for off-line analysis.

Free catecholamine levels were determined radioenzymatically (10). The interassay coefficients of variation for noradrenaline and adrenaline levels determined previously (10) were 10.1% and 10.3%, respectively. The intraassay coefficients of variation for noradrenaline and adrenaline levels were 4.1% and 5.4%, respectively.

Protocol. At least 1 h before the start of the study, the subjects consumed a light breakfast without coffee or tea. The investigation began at 9 AM in a room with a constant ambient temperature of 22°C. The subject's age, gender, height and weight were recorded. A general medical investigation was performed next, and the results were normal in all subjects. The subjects then had a 30-min period to become familiar with the equipment and the maneuvers.

Maneuvers. The experiment began at about 10 AM and was always performed in the same order. Forced breathing and stand-up tests were performed first as an initial evaluation of neurocardiovascular function (11). This part of the protocol was performed without the venous catheter because intravascular instrumentation may itself influence the responses studied (1). Next, a venous catheter was inserted, and the tilt-up test was performed. Tilt-up testing is preferred to stand-up testing because the experimenter has more control and allows rapid return to the supine position in case of impending syncope in the upright position.

Forced breathing. After 5 min of supine rest, the subjects performed six maximal inspirations and six expirations at a rate of six breaths a minute to evaluate cardiac vagal control (11).

Stand-up testing. After another 5 min of supine rest, subjects were given a verbal command to stand up. The subjects stood up in 2 to 3 s and remained standing for 5 min. If premonitory symptoms or signs of near-fainting occurred (see later), or if an abnormally large decrease in blood pressure was observed, the subjects were instructed to lie down immediately.

Venipuncture. A 20-gauge polyethylene catheter was placed in the antecubital vein of the left arm. Local anesthesia was not used. The subjects then watched a calming nature movie in the supine position. After 30 min, a 10-ml venous blood sample was collected for biochemical assessment of sympathetic function. After blood sampling, another 5-min rest period was instituted to obtain baseline values of blood pressure and heart rate.

Tilt-up testing. A 70° tilt-up test was then performed for 3 s on a tilt table with foot support. After 5 min in the head-up position, a second venous sample was taken. Because of the time needed for blood sampling, subjects remained in the upright position for 6 to 7 min. However, subjects who experienced near-fainting were tilted back immediately, and a second blood sample was obtained immediately after tilt-back.

Premonitory symptoms and signs of near-fainting included nausea, abdominal discomfort, light-headedness, weakness, blurred vision, pallor, yawning, sighing and sweating. A persistent decrease in blood pressure on orthostatic stress >20 mm Hg for systolic blood pressure or >5 mm Hg for diastolic blood pressure was considered abnormal (11). Postural tachycardia was defined as an increase in heart rate above its age-adjusted 95% confidence interval of >35 beats/min after 2 min of standing (11).

Analysis of data. Heart rate variation during forced breathing was expressed as the inspiration–expiration difference in beats/min and used to assess efferent vagal cardiac control (11). We evaluated the recordings continuously during a 30-s supine control period before and during the first 30 s immediately after the start of the two orthostatic stress tests. During the 5 min in upright posture, we also evaluated 10-s averages of variables at the end of each minute. During the tilt-up test we additionally analyzed the last minutes before termination of the test.

The arterial pressure signal was analyzed by software developed by the physiology department of the Academic Medical Centre (12). The finger arterial pulsewave was analyzed by a pulse contour method that computes changes in left ventricular stroke volume from the pulsatile systolic area. We used the improved pulse contour method of Wesseling et al. (13) in which pulsatile systolic area is considered proportional to stroke volume. The proportionality constant is the aortic characteristic impedance, and its value is taken as the group mean statistic only, not for each individual. The method therefore lacks absolute individual calibration, but changes from baseline set at 100% can be determined with precision (12–16). Cardiac output was computed as the product of stroke volume and heart rate. Systemic vascular resistance was computed as mean blood pressure divided by cardiac output. A 5-s moving average was used in the computation of systemic vascular resistance to account for the delays between changes in instantaneous cardiac output at the aortic root and their transformation to changes in tissue perfusion flow due to the Windkessel buffering effect of the arterial system (15).

Statistics. Results are expressed as differences from baseline (supine) measurements for heart rate in beats/min; for systolic and diastolic blood pressure in mm Hg; for stroke volume, cardiac output and total systemic vascular resistance as percent change. Paired and unpaired Student t tests were performed when appropriate. As a correlation measure, we used the Pearson product moment correlation (r). Results are presented as mean value ± SD; $p < 0.05$ was considered significant.

Results

In 16 of 84 subjects finger arterial pressure measurement on stand-up or tilt-up testing was of poor quality as a result of

Table 1. Supine and Hemodynamic Value Changes After 1 min of Stand-Up and 1 min of Tilt-Up Testing

	Stand-Up Test		Tilt-Up Test	
	Nonfainting Group (n = 61)	Near-Fainting Group (n = 7)	Nonfainting Group (n = 39)	Near-Fainting Group (n = 29)
Gender (M/F)	33/28	3/4	24/15	12/17
Supine SBP (mm Hg)	102 (13)	99 (12)	112 (3)	109 (11)
Supine DBP (mm Hg)	51 (9)	49 (5)	59 (9)	57 (6)
Supine HR (beats/min)	75 (9)	78 (6)	74 (11)	72 (9)
ΔSBP	10 (11)	3 (12)	8 (12)	2 (10)*
ΔDBP	15 (7)	10 (7)†	17 (8)	11 (9)*
ΔHR	19 (10)	26 (8)†	15 (10)	25 (11)*
SV (% change)	−35 (9)	−36 (7)	−38 (10)	−37 (7)
CO (% change)	−19 (9)	−13 (10)	−25 (10)	−16 (11)‡
SVR (% change)	46 (18)	27 (15)§	60 (26)	34 (20)‡

*$p < 0.05$, †$p < 0.005$, ‡$p < 0.001$, §$p < 0.01$, nonfainting versus near-fainting subjects. Data presented are mean value (SD) or number of patients. CO = cardiac output; DBP = diastolic blood pressure; F = female; HR = heart rate; M = male; SBP = systolic blood pressure; SV = stroke volume; SVR = systemic vascular resistance; Δ = absolute difference from supine level; % change = percent change to supine level.

artifacts caused by movements of the finger or hand. These subjects were excluded from analysis. In 4 of the remaining 68 subjects insertion of the intravenous line was not successful for technical reasons. However, these 4 subjects remained in the study group. Of the 16 subjects excluded from the study, 1 developed a near-fainting response during stand-up testing and 2 during tilt-up testing.

Stand-up testing. After 3 to 5 min of stand-up testing, near-fainting was observed in 7 of the 68 subjects (3 girls, 4 boys), of whom 6 had premonitory symptoms or signs and a large decrease in blood pressure. Only one subject had a large decrease in blood pressure without signs or symptoms. None of the subjects actually fainted. Age, gender and supine control values for blood pressure and heart rate did not differ between the near-fainting and nonfainting groups (Table 1). Height (146 ± 9 cm in the near-fainting group, 153 ± 15 cm in the nonfainting group) did not differ, but body weight was significantly lower in the near-fainting group (35 ± 5 vs. 44 ± 14 kg, $p < 0.005$).

In general, the initial circulatory patterns were similar in the near-fainting and nonfainting groups (Fig. 1). However, differences in some hemodynamic responses to the orthostatic stress of active stand-up testing could be observed within 20 s after the onset of the maneuver. After 1 min of standing, diastolic blood pressure in the near-fainting group was significantly lower and heart rate higher (Table 1). Systemic vascular resistance increased in both groups in response to stand-up testing. In the non-fainting group the average increase was 46% after 1 min of standing, whereas in the near-fainting group the increase was only 27% ($p < 0.01$). No differences in cardiac output were observed. During continued standing, the differences in arterial blood pressure and systemic vascular resistance continued to increase slowly. The difference in heart rate remained unchanged during prolonged standing. In 2 of 7 subjects in the near-fainting group and in 5 of 61 in the nonfainting group, postural tachycardia was observed.

Venipuncture. None of the subjects developed a near-fainting response during the insertion of the intravenous line or during the supine sampling of blood.

Tilt-up testing. After 1 to 7 min of tilting, 29 (12 girls, 17 boys) of the 68 subjects developed a near-fainting response. In the seven subjects with near-fainting during stand-up testing, near-fainting also occurred during tilt-up testing. In the four subjects that did not receive an intravenous line, near-fainting was not observed. In 26 of the 29 near-fainting subjects, a large decrease in blood pressure was accompanied by premonitory symptoms or signs. In three subjects a large decrease in blood pressure without premonitory symptoms or signs was observed. None of the subjects actually fainted. As in the stand-up test, supine control values, gender, age and height did not differ. In contrast to the stand-up test, there was also no difference in body weight. The inspiration–expiration differences during forced breathing were almost identical at 28 ± 6 beats/min in the near-fainting group and at 29 ± 7 beats/min in the nonfainting group.

The characteristic blood pressure and systemic vascular resistance decrease observed in the first 20 s of active standing (Fig. 1) were attenuated or not present on tilt-up testing (Fig. 2). These differences in the initial circulatory adjustments between active standing and passive tilting are well known (15,17) and are not discussed further. The hemodynamic deviations from control in the near-fainting group after 1 min in the tilt-up position were similar to those during stand-up testing; blood pressure increased less and heart rate increased more than in the nonfainting group (Table 1). The decrease in cardiac output in the near-fainting group after 1 min of tilt-up testing was significantly less than that in the nonfainting group ($p < 0.001$). Systemic peripheral resistance increased in both

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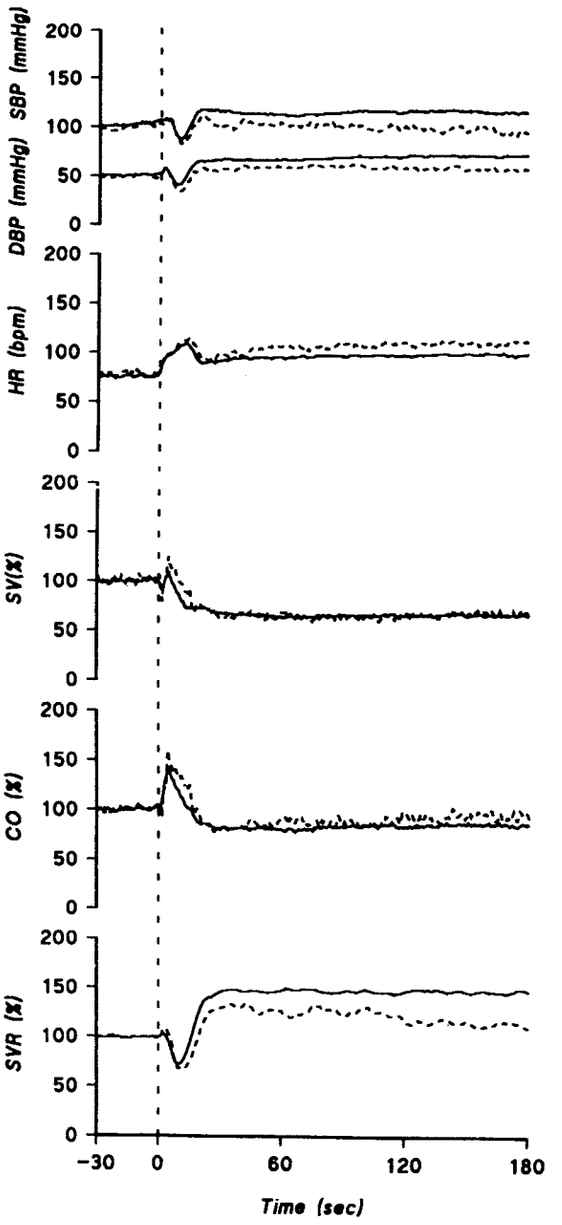

Figure 1. Characteristic hemodynamic responses to stand-up testing are plotted as group averages for 61 nonfainting subjects (**solid line**) and 7 near-fainting subjects (**dashed line**). Systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) are expressed in absolute values, whereas stroke volume (SV), cardiac output (CO) and systemic vascular resistance (SVR) are expressed in relative changes to supine control values. The maneuver started at 0 s. None of the subjects had premonitory signs or symptoms of near-fainting within the first 3 min after the onset of stand-up testing. bpm = beats/min.

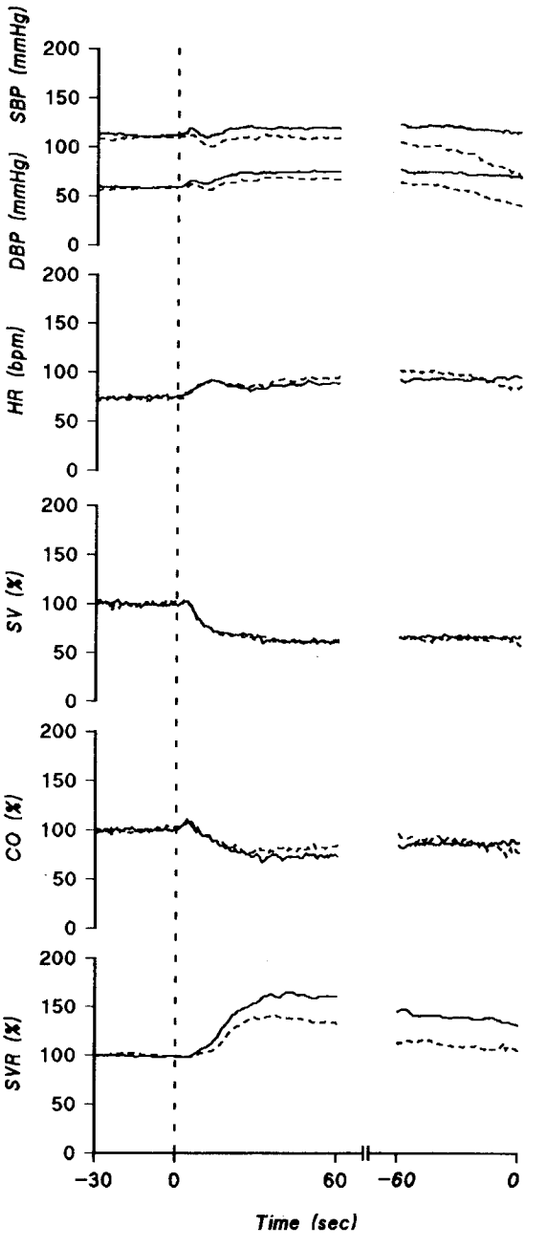

Figure 2. Circulatory responses to tilt-up testing in 39 nonfainting subjects (**solid line**) and 29 near-fainting subjects (**dashed line**). The maneuver started at 0 s. Near-fainting started after 1 min of tilting. **Vertical dashed line** = last 60 s before tilt-back. Abbreviations as in Figure 1.

groups but only 34% in the near-fainting group compared with 60% in the nonfainting group ($p < 0.001$). Eight of the 29 subjects in the near-fainting group developed postural tachycardia compared with 4 of the 39 subjects in the nonfainting group. In the last minute before tilt-back (Fig. 2) in the near-fainting group, blood pressure levels rapidly decreased, heart rate no longer responded with an increase but decreased to a level below that in the nonfainting group. The combination of a constant stroke volume and a decrease in heart rate resulted in a decrease in cardiac output. At the moment of tilt-back, systolic blood pressure in the near-fainting group had decreased to 71 ± 12 mm Hg and diastolic blood pressure to 43 ± 9 mm Hg, whereas in the nonfainting group systolic blood pressure had increased to 118 ± 18 mm Hg and diastolic blood

Table 2. Plasma Noradrenaline and Adrenaline Levels in Nonfainting and Near-Fainting Subjects (mean ± SD)

	Noradrenaline (nmol/liter)		Adrenaline (nmol/liter)	
	Nonfainting Group (n = 36)	Near-Fainting Group (n = 28)	Nonfainting Group (n = 36)	Near-Fainting Group (n = 28)
Supine	1.70 (0.62)	1.52 (0.59)	0.16 (0.11)	0.14 (0.11)
Standing	2.62 (0.75)	2.30 (0.70)	0.34 (0.23)	0.49 (0.48)
Increase	0.93 (0.71)	0.78 (0.67)	0.17 (0.19)	0.35 (0.43)*

*$p < 0.05$, near-fainting versus nonfainting subjects.

pressure to 73 ± 12 mm Hg (all $p < 0.005$). At the moment of tilt-back, systemic vascular resistance had decreased to the supine control level in the near-fainting group but remained 31% above control levels in the nonfainting group ($p < 0.001$).

Biochemical assessment of sympathetic function. Supine plasma noradrenaline levels in nonfainting and near-fainting subjects did not differ, and an identical increase after 5 min of tilt-up testing was observed (Table 2). Supine plasma adrenaline levels were nearly identical, but in the near-fainting group the increment from supine to upright was significantly higher than that in the nonfainting group, with very pronounced increases in two near-fainting subjects (upright levels 1.5 and 2.3 nmol/liter, respectively). The correlation between changes in plasma adrenaline levels and in systemic vascular resistance at the moment of tilt-back was negative and significant ($r = -0.28$, $p < 0.05$) but poor ($r^2 = 0.08$ [i.e., 8% of the variance explained]).

Discussion

Incidence and predictive indexes of near-fainting. Fainting is a common phenomenon in young subjects but is rare in adulthood (1,2,18). It has been estimated that as many as 15% of young subjects will have a fainting experience before reaching adulthood (19). There is no explanation for the high incidence of fainting in children. In two recent studies (6,17) dealing with the incidence of fainting under orthostatic stress in 42 healthy children and teenagers, a 17% near-fainting response was observed. When the shorter duration of our test (5 vs. 10 to 20 min) is considered, the incidence of near-fainting responses of 10% in the stand-up test in our study is in accordance with previous studies. The absence of any incidence of near-fainting in two other recent studies (20,21) can probably be explained by the small number of young subjects involved. In young patients with a suspected condition called neurocardiogenic syncope (22), the incidence of near-fainting during orthostatic stress ranged from 43% to 57% (6,20,21). A slightly higher incidence was calculated in a recent comprehensive data review (23).

The high incidence (40%) of near-fainting in our study during a tilt-up test of only 5 min in duration can be attributed to the intravascular instrumentation and blood sampling accompanying the tilt-up testing (emotional faint response) (1,2,24). Previous investigators (1) have also demonstrated that invasive methods predispose subjects to fainting during orthostasis. Stevens (25) found a near-fainting response in 41 (50%) of 82 healthy men (23 to 43 years old) during a 20-min tilt-up test with instrumentation compared with 15 (10%) of 152 subjects without instrumentation (25). We cannot exclude the possibility that the passive change in posture contributed to the high incidence of near-fainting. However, this factor is not expected to be of great consequence because the static increase in skeletal muscle tone during passive 70° tilting and quiet standing is likely to be similar. Moreover, orthostatic responses on stand-up and 70° tilt-up testing are reported to be comparable in young adults (1). A separate study will be needed to determine whether active or passive changes in posture without instrumentation evoke different orthostatic responses in children and teenagers.

The present findings imply that the use of tilt-up testing in combination with intravascular instrumentation as a diagnostic procedure in young patients with unexplained syncope will result in many false positive test results. Thus, a positive tilt-table test result cannot be interpreted as solid proof of an innocent cardioinhibitory fainting response as the underlying cause of the syncope.

In agreement with previous studies in healthy young subjects (17), no significant differences in incidence of near-fainting responses were observed between genders. Physical height, in contrast to a previous report (1), was not a predictive index for orthostatic tolerance in our study. Body weight correlated with near-fainting only in the active stand-up test before venipuncture. Thus, gender and body build appear to have at most only a small influence on orthostatic tolerance in normal young subjects. Heart rate variations during forced breathing did not differ between near-fainting and nonfainting subjects and were normal for age (11,26). Thus, we could not confirm with this test a recent observation (27) that faint-prone young subjects have a high vagal activity. Control values for blood pressure, heart rate and plasma catecholamine levels were comparable in the near-fainting and nonfainting groups, again suggesting similar average basal sympathetic outflow before the orthostatic stress test.

Hemodynamic characteristics of near-fainting. The key factor responsible for the gradual decrease in arterial pressure before an impending faint was early progressive decrease in systemic vascular resistance (Fig. 1 and 2, Table 1). However, this phenomenon is not easily explained because there is strong circumstantial evidence that sympathetic outflow before the actual faint is high (28–31). It has been suggested that a reflex triggered by ventricular receptors stimulated by the combination of a low ventricular volume and a high inotropic state is involved in vasovagal fainting (2,22). Such a reflex mechanism could theoretically be responsible for the progressive decrease in systemic vascular resistance. However, we did not find a pronounced decrease in stroke volume in the early phase of near-fainting. Moreover, the link between ventricular receptor

activation and neurally mediated syncope has not been firmly established (2,4,24,32).

Adrenaline has been proposed as a humoral vasodilating agent in the vasovagal response (3,33) and has been reported to be elevated during fainting induced by tilt-up testing in adults (3,30,33,34). In the present study the increase in venous plasma adrenaline levels after 5 min in the upright position was marked (Table 2). However, pronounced increases in adrenaline levels were also found in the nonfainting group, and the correlation between adrenaline level and systemic vascular resistance responses in both groups was poor. On the whole, the data suggest that the elevated upright adrenaline level reflects arousal (35) but does not act as an important mediator of fainting.

The forearm plasma noradrenaline samples taken from nonfainting and near-fainting subjects at the moment of near-fainting did not differ significanty. This seems inconsistent with the finding that in muscle sympathetic nerve recordings in adults, sympathetic silence has been observed at the moment of a near-fainting, indicating complete cessation of sympathetic drive to skeletal muscle vessels (2,28–30). A striking reduction in noradrenaline spillover to plasma is also noted in other major vascular areas, such as the mesenteric, renal and cardiac beds (35,36). This inconsistency was noted earlier (33,34) and has been attributed to two factors: 1) Changes in plasma levels of noradrenalin are too sluggish to document sudden changes in sympathetic nerve firing rates (4,34,35); and 2) not only adrenaline (Table 2), but also noradrenaline is released from the adrenal medulla during hypotensive stress (34,37).

Conclusions. The mechanism leading to near-fainting in healthy young children and teenagers is complex and uncertain and needs to be considered in any investigation of the role of the autonomic nervous system in pathologic conditions. Tilt-table testing with intravascular instrumentation results in false positive (i.e., nonspecific) results. Therefore, there are serious doubts with respect to the utility of this procedure in evaluating syncope of unknown origin in young subjects.

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References

1. Smith JJ, Ebert J. General response to orthostatic stress. In: Smith JJ, editor. Circulatory Response to the Upright Posture. Boca Raton (FL): CRC Press, 1990:1–46.
2. Van Lieshout JJ, Wieling W, Karemaker JM, Eckberg DL. The vasovagal response. Clin Sci 1991;81:575–86.
3. Rowell LB. Orthostatic intolerance. In: Rowell LB, editor. Human Cardiovascular Control. Oxford (UK): Oxford Univ Press, 1993:118–61.
4. Ludbrook J. Haemorrhage and shock. In: Hainsworth R, Mark AL, editors. Cardiovascular Reflex Control in Health and Disease. Philadelphia: Saunders, 1993:463–90.
5. Grubb BP, Temesy-Armos P, Moore J, Wolfe D, Hahn H, Elliott L. The use of head-upright table testing in the evaluation and management of syncope in children and adolescents. PACE 1992;15:742–48.
6. Fouad FM, Sitthisook S, Vanerio G, et al. Sensitivity and specificity of the tilt-table test in young patients with unexplained syncope. PACE 1993;16: 394–400.
7. Wesseling KH. Finapres, continuous noninvasive finger arterial pressure based on the method of Peñáz. In: Meyer-Sabellek W, Anlauf M, Gotzen R, Steinfeld L, editors. Blood pressure measurements. Darmstadt (Germany): Steinkopff-Verlag, 1990:161–72.
8. Imholz BPM, Settels JJ, Van der Meiracker AH, Wesseling KH, Wieling W. Non-invasive continuous finger blood pressure measurement during orthostatic stress compared to intra-arterial pressure. Cardiovasc Res 1990;24: 214–21.
9. Tanaka H, Thulesius O, Yamaguchi H, Mino M, Konishi K. Continuous non-invasive finger blood pressure monitoring in children. Acta Pediatrica 1994;83:57–63.
10. Odink J, Van der Beek EJ, Van den Berg H, Bogaards JJP, Thissen JTNM. Effect of work load on free and sulfate-conjugated plasma catecholamines, prolactin, and cortisol. Int J Sports Med 1986;7:352–57.
11. Wieling W. Non-invasive continuous recording of heart rate and blood pressure in the evaluation of neurocardiovascular control. In: Bannister R, Mathias CJ, editors. Autonomic Failure: A Textbook of Clinical Disorders of the Autonomic Nervous System. Oxford (UK): Oxford Univ Press, 1992: 291–311.
12. Stok WJ, Baisch F, Hillebrecht A, Schultz H, Meyer M, Karemaker JM. Noninvasive cardiac output measurement by arterial pulse analysis compared to inert gas rebreathing. J Appl Physiol 1993;74:2687–93.
13. Wesseling KH, De Wit B, Weber JAP, Smith NT. A simple device for the continuous measurement of cardiac output. Adv Cardiovasc Phys 1983;5(Pt II):16–52.
14. Jansen JRC, Wesseling KH, Settels JJ, Schreuder JJ. Continuous cardiac output monitoring by pulse contour during cardiac surgery. Eur Heart J 1990;11 Suppl 1:26–32.
15. Sprangers RLH, Wesseling KH, Imholz ALT, Imholz BPM, Wieling W. Initial blood pressure fall on stand-up and onset of exercise explained by changes in total peripheral resistance. J Appl Physiol 1991;70:523–30.
16. Wieling W, Veerman DP, Dambrink JHA, Imholz BPM. Disparities in circulatory adjustment to standing between young and elderly subjects explained by pulse contour analysis. Clin Sci 1992;83:149–55.
17. Dambrink JHA, Imholz BPM, Karemaker JM, Wieling W. Circulatory adaptation to orthostatic stress in healthy 10–14 year old children investigated in a general practice. Clin Sci 1991;81:51–8.
18. Lewis T. Vasovagal syncope and the carotid sinus mechanism. Br Med J 1932:873–6.
19. Ruckmann RN. Cardiac causes of syncope. Ped Rev 1987;9:101–8.
20. Ross BA, Hughes S, Anderson E, Gillette PC. Abnormal responses to orthostatic testing in children and adolescents with recurrent unexplained syncope. Am Heart J 1991;122:748–54.
21. Lerman-Sagie T, Rechavia E, Strasberg B, Sagie A, Bleden L, Mirnourni M. Head up tilt for the evaluation of syncope of unknown origin in children. J Pediatr 1991;118:676–9.
22. Abboud FM. Neurocardiogenic syncope. N Engl J Med 1993;328:1117–20.
23. Kapoor WN, Smith MA, Miller NL. Upright tilt testing in evaluating syncope: a comprehensive literature review. Am J Med 1994;97:78–88.
24. Hainsworth R. Syncope and fainting. In Ref 11:761–81.
25. Stevens PM. Cardiovascular dynamics during orthostasis and the influence of intravascular instrumentation. Am J Cardiology 1966;17:211–18.
26. Perry JC, Garson A. The child with recurrent syncope: autonomic function testing and beta-adrenergic hypersensitivity. J Am Coll Cardiol 1991;17: 1168–71.
27. Barron SA, Rogovski Z, Hemli Y. Vagal cardiovascular reflexes in young persons with syncope. Ann Intern Med 1993;118:943–46.
28. Wallin BG, Sundlof G. Sympathetic outflow to muscles during vasovagal syncope. J Auton Nerv Syst 1982;6:287–91.
29. Sanders JS, Ferguson DW. Profound sympathoinhibition complicating hypovolemia in humans. Ann Intern Med 1989;111:439–41.
30. Rowell LB, Seals DR. Sympathetic activity during graded central hypovolemia in hypoxemic humans. Am J Physiol 1990;259:H1197–1206.
31. Ten Harkel ADJ, Baisch F, Karemaker JM. Increased orthostatic blood pressure variability after prolonged head down tilt. Acta Physiol Scand 1992;604 Suppl:89–99.

32. Fitzpatrick AP, Banner N, Cheng A, Yacoub M, Sutton R. Vasovagal reactions may occur after orthotopic heart transplantation. J Am Coll Cardiol 1993;1132–7.
33. Robinson BJ, Johnson RH. Why does vasodilation occur during syncope. Clin Sci 1988;74:347–50.
34. Sander-Jensen K, Secher NH, Astrup A et al. Hypotension induced by passive head-up tilt: endocrine and circulatory mechanisms. Am J Physiol 1986;251:R742–48.
35. Hjemdahl P. Plasma catecholamines—analytical challenges and physiological limitations. In: Bouloux PMG, editor. Clinical Endocrinology and Metabolism. London: Balliere Tindall, 1993: Vol. 7, Number 2:307–353. Catecholamines.
36. Esler M, Jennings G, Lambert G, Meredith I, Horne M, Eisenhofer G. Overflow of catecholamine neurotransmitters to the circulation: source fate and function. Physiol Rev 1990;70:963–85.
37. Victor RG, Thoren P, Morgan DA, Mark AL. Differential control of adrenal and renal sympathetic nerve activity during haemorrhagic hypotension in rats. Circ Res 1989;64:686–94.