Spinal Cord (2000) 38, 158–163

www.nature.com/sc

Systemic circulation and cerebral oxygenation during head-up tilt in spinal cord injured individuals

S Houtman*,[1], WNJM Colier[1], B Oeseburg[1] and MTE Hopman[1]

[1]*Department of Physiology, University of Nijmegen, Nijmegen, The Netherlands*

Objective: To compare tilt-induced alterations in cardiovascular homeostasis and cerebral oxygenation of spinal cord-injured (SCI) to able-bodied (AB) individuals.
Design: Subjects underwent 10 min supine rest followed by 10 min 70° head-up tilt. The last 5 min of supine rest and head-up tilt were analyzed, provided a steady state existed.
Subjects: SCI individuals ($n=11$), with lesions between C4 and T4, and AB individuals ($n=10$), all males and balanced for age and weight.
Main outcome measures: Calf circumference, mean arterial pressure (MAP), stroke volume, heart rate and cerebral oxygenated ([O_2Hb]), deoxygenated ([HHb]) and total ([tHb]) haemoglobin concentration changes were measured.
Results: Head-up tilt evoked a greater fall in MAP (mean (SD): −9 (12) *vs* 2 (6) mmHg $P=0.02$) and stroke volume (−43 (12) *vs* −22 (10)%, $P=0.005$), and a greater increase in heart rate (27 (12) *vs* 18 (6) beats, $P=0.04$) in SCI than AB. Cardiac output decreased during head-up tilt in SCI but not in AB (−17 (15) *vs* 1 (15)%, $P=0.01$). The change in cerebral oxygenation ([HHb]: 3.9 (2.8) *vs* 2.8 (1.4) $\mu mol \cdot l^{-1}$, $P=0.1$ and [O_2Hb]: −6.1 (5.0) *vs* −2.1 (5.5) $\mu mol \cdot l^{-1}$, $P=0.1$) was similar in SCI and AB. All variables mentioned showed a change significantly different from zero in both groups, apart from [O_2Hb] in AB and [tHb] in both groups.
Conclusion: SCI demonstrated a greater decrease of MAP and stroke volume with a similar decrease in cerebral oxygenation compared to AB. This suggests that although systemic circulation was less well regulated in SCI compared with AB, cerebral circulation in SCI was maintained as in AB.
Spinal Cord (2000) **38,** 158–163

Keywords: tetraplegia; near-infrared spectroscopy; Portapres

Introduction

In individuals with a spinal cord lesion, passive standing is used to stress the musculo-skeletal system of the lower limbs in order to prevent, among other things, osteoporosis, and attenuate muscle spasms.[1] Unfortunately, spinal cord-injured (SCI) individuals lack muscle pump function and have an impaired sympathetic nervous system causing difficulties in the maintenance of cardiovascular homeostasis during orthostatic challenges caused by postural changes.

In SCI individuals cardiovascular homeostasis during head-up tilt settles at a lower blood pressure,[2] stroke volume and cardiac output[3] compared to able-bodied (AB) individuals, which is supposedly caused by a decreased venous return secondarily to insufficiently opposed orthostasis. Despite the lower blood pressures in SCI individuals during head-up tilt, SCI individuals show a low incidence of presyncope or syncope after rehabilitation, which has raised the idea of an adapted cerebral autoregulation in SCI.[4]

To study the circulation, cardiovascular changes between supine rest and orthostatic challenges like head-up tilt may be divided into changes following immediately (<3 min) upon transition, and steady state-like differences (>3 min). Attaining a steady state not too different from the initial condition indicates a responsive regulation, which has adequately altered the circulation. Although circulatory variables, like a lower blood pressure during head-up tilt, may indicate a risk of syncope, only variables reflecting the cerebral circulation can give information about the final common pathway leading to syncope.

Studies on the cerebral circulation indicated a similar relation between systemic blood pressure and cerebral flow in AB individuals and individuals with paraplegia in supine and sitting position using the

*Correspondence: S Houtman, Department of Physiology 237, University of Nijmegen, PO box 9101, 6500 HB Nimegen, The Netherlands

$_{133}$Xenon technique to measure cerebral flow.[5] Gonzalez and co-workers, using transcranial Doppler, reported that in individuals with tetraplegia cerebral autoregulation, but not systemic blood pressure, seemed to be crucial in the prevention of syncope during tilt.[6] The latter study did not include able-bodied individuals, and we are not aware of a study simply comparing cerebral flow in individuals with and without a high spinal cord injury during head-up tilt. Possibly more relevant than cerebral flow detected by transcranial Doppler, near infrared spectroscopy (NIRS) reflects the match between oxygen delivery to and consumption by the cerebrum.[7,8]

The aim of this study therefore, was to compare AB individuals with SCI individuals with a lesion above T4 regarding changes in cardiovascular variables and cerebral oxygenation induced by tilt.

Methods

Eleven SCI and ten healthy AB males (mean (SD): age: 34 (9) years; weight 78 (12) kg and age: 31 (9) years; weight (82 (7) kg, respectively) participated in this study after an informed consent was signed. Three outlying SCI individuals between 40- and 50-years old, one of them having a body mass of 106 kg, were matched with comparable AB individuals. All spinal cord lesions were sustained by trauma more than 2 years previously, at or above T4 and were complete except for two subjects (C5 ASIA B and C4 ASIA C). Individuals with a spinal cord-lesion above this level have an impaired sympathetic innervation of the heart, splanchnic area and adrenal gland and have been reported to show a similar lowered blood pressure stability.[9] None of the participants was hypertensive or suffered from cardiovascular or renal diseases, or from inflammation of the bladder. None of our AB participants used any medication, four of our SCI participants are using centrally-acting medication against muscle spasms for many years: Two participants used Lioresal, one Sirdalud (a Tizanidine), and one used Valium. They continued to do so during the experiment. The Faculty Ethics Committee approved the study.

Protocol

Subjects visited the laboratory in the morning. All participants emptied their bladder directly before the experiment. After approximately 15 min supine rest, when steady state levels of heart rate and blood pressure were attained, calf circumference increase following inflation of a thigh cuff to 40 mmHg was determined. Thereafter, the actual experiment was performed consisting of 10 min supine rest and 10 min 70° head-up tilt. The room where the experiment was performed was quiet and kept at a constant temperature of 22°C. Participants were not allowed to speak or sleep during the experiment.

Measurements

During the whole experiment cerebral oxygenation was assessed by measuring changes in oxy- and deoxyhaemoglobin concentration ([O_2Hb] and [HHb], respectively) using NIRS. NIRS monitors changes in light absorption of tissue *in vivo*, which are mainly caused by oxygenation dependent [O_2Hb] and [HHb] changes. The sum of [O_2Hb] and [HHb] changes is a measure of the total blood volume ([tHb]) change in the monitored tissue. This non-invasive method has been described in greater detail in earlier studies.[7,8] Optodes were placed above the left eyebrow, using an interoptode distance of 4.5 cm. A pathlength factor of 6 was used. The NIRS equipment (Radiometer Medical, Copenhagen, Denmark) used was a four wavelength, continuous wave instrument. NIRS data was sampled at 1 Hz, displayed in real time and stored on disk for off-line analysis. The NIRS apparatus was fixed to the tilt table and the optodes were firmly fixed to the head to avoid measurement artefacts due to tilting. We found that slight movement or vibration of the optode cables did not cause any signal disturbance.

Mean arterial pressure (MAP) and heart rate were measured continuously with Portapres (TNO-BMI, Amsterdam, The Netherlands), the portable version of Finapres. This instrument samples finger arterial pressure at 200 Hz based on the method of Penaz.[10] It has been shown that changes in arterial blood pressure are accurately reflected by Finapres and Portapres.[11–13] Stroke volume and cardiac output were calculated off-line using Modelflow, a pulse contour method described by Wesseling *et al*.[14,15] This method requires the compliance of the individual's aorta, which may be estimated from information on the height, weight, gender and age of each subject. However, our main aim being the head-up tilt induced alterations, all cardiovascular variables calculated by Modelflow during head-up tilt were expressed relative to supine rest. Cerebral perfusion pressure was calculated by correcting MAP for the estimated orthostatic pressure difference (between heart and eyebrow) induced by tilt.

Relative calf cross-sectional area changes were measured in order to detect excessive venous blood pooling, using a home-built strain gauge plethysmograph. The mercury-filled silicon tubes were stretched around the thickest part of the left calf. The plethysmograph was calibrated as described by Brakkee and Vendrik.[16] Relative changes in calf volume during cuff inflation and head-up tilt were expressed as percentages of those during supine rest, which method is supposed to reflect changes in venous volume.[17]

Analysis

Averaged values of circulatory variables during head-up tilt and supine rest periods and the corresponding cerebral oxygenation changes were calculated from data gathered during the last 5 min of each period, provided a steady state existed. Differences between head-up tilt and supine rest were calculated for each individual. The relative change in calf volume from steady state supine rest to both the last minute of head-up tilt, and to a steady state circumference during thigh cuff inflation, were used for further analysis.

Statistics
The differences between head-up tilt and supine rest in circulatory and cerebral oxygenation variables were tested to be different from zero (95% confidence interval). All variables were normally distributed. However, sometimes, for example in case of the change in MAP of AB (Figure 1), visual inspection of the distribution raised doubts. Since a non-parametric test yielded the same results, significance based on normal distributions are presented. So, differences between supine rest and head-up tilt of SCI and AB were compared using a Student's *t*-test, assuming a *P*-value smaller than 0.05 as an indication of a significant difference.

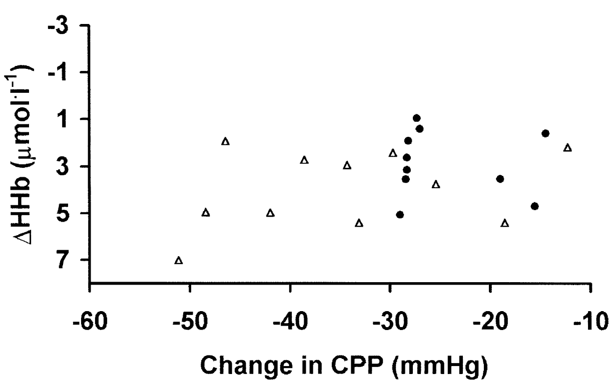

Figure 1 The relation between the cerebral perfusion pressure (CPP) and deoxygenated haemoglobin concentration [HHb] change in all spinal cord-injured (triangles) and able-bodied (circles) individuals. The scaling of the [HHb]-axis is inverted in order to get values indicating proper oxygenation at the top and values indicating a poorer oxygenation at the bottom

Results

SCI and AB had similar MAP and heart rates during supine rest, but SCI showed lower map during head-up tilt than AB (Table 1). Although two SCI individuals experienced transient mild presyncope symptoms, all subjects completed 10 min of head-up tilt. In one SCI individual [HHb] and [O_2Hb] drifted slightly from equilibrium during the entire 10 min of head-up tilt, in the other subjects a steady state was attained. This steady state showed in some SCI more fluctuation than in AB.

Cardiovascular variables altered following the transition from supine rest to head-up tilt in all subjects, but AB seemed to maintain cardiovascular homeostasis better than SCI. Compared to AB, SCI showed a greater decrease in MAP and stroke volume. In SCI, cardiac output and stroke volume decreased more than in AB, while heart rate increased more in SCI than AB individuals (Table 2). In contrast, alterations in cerebral oxygenation between head-up tilt and supine rest during steady state in cerebral oxygenation were similar in SCI and AB

Table 1 Blood pressure and heart rate during supine rest and head-up tilt

Variable	*Spinal cord injured*	*Supine rest* *Able bodied*	*Probability*
MAP (mmHg)	72 (16)	75 (7)	
Heart rate (min^{-1})	59 (7)	59 (7)	
		Head up tilt	
MAP (mmHg)	63 (13)	77 (11)	0.018
Heart rate (min^{-1})	86 (15)	76 (10)	

Mean and SD of mean arterial pressure (MAP) and heart rate during supine rest and head-up tilt in spinal cord-injured and able-bodied individuals

Table 2 Differences between head-up tilt and supine rest

Variable	*Spinal cord-injured* *Difference*	P-*value*	*Able-bodied* *Difference*	*P-value*	P-*value between groups*
[O_2Hb] ($\mu mol \cdot l^{-1}$)	−6.1 (5.0)	0.000	−2.1 (5.5)		
[HHb] ($\mu mol \cdot l^{-1}$)	3.9 (2.8)	0.000	2.8 (1.4)	0.000	
[tHb] ($\mu mol \cdot l^{-1}$)	−2.1 (5.0)		0.8 (5.1)	0.09	
MAP (mmHg)	−9 (12)	0.013	2 (6)		0.02
Heart rate (min^{-1})	27 (12)	0.000	18 (6)	0.000	0.03
Stroke volume (%)	−43 (8)	0.000	−22 (10)	0.000	0.000
Cardiac output (%)	−17 (15)	0.008	1 (13)		0.01

Mean and SD of the alteration from supine rest to head-up tilt in oxygenated ([O2Hb]), deoxygenated ([HHb]) and total ([tHb]) haemoglobin concentration, stroke volume, mean arterial pressure (MAP), heart rate and total peripheral resistance (TPR) in spinal cord-injured and able-bodied individuals. A listed '*P*-value' indicates a significant alteration during the transition from supine rest to head-up tilt, a listed '*P*-value between groups' indicates a significant difference between groups

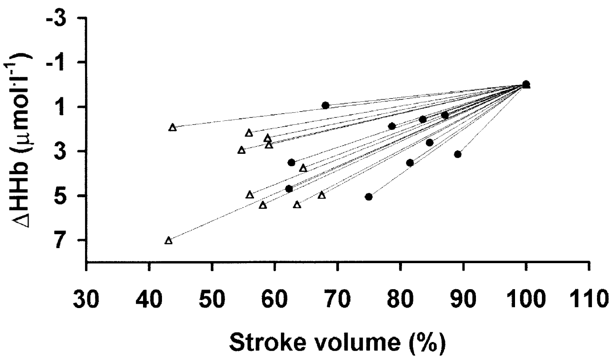

Figure 2 The relation between stroke volume, as an indicator of orthostatic stress, and deoxygenated haemoglobin concentration [HHb] change of all spinal cord-injured (triangles) and able-bodied (circles) individuals. The scaling of the [HHb]-axis is inverted in order to get values indicating proper oxygenation at the top and values indicating a poorer oxygenation at the bottom

(Table 2). The relation between the alteration in [HHb] and cerebral perfusion pressure (change in MAP corrected for change in orthostatic pressure at eyebrow level; 25–30 cmH_2O) was similar in SCI and AB (Figure 1). The relation between stroke volume, as an indicator of orthostatic stress, and [HHb] is shown in Figure 2. In SCI who showed very small tilt-induced changes in MAP the experiment was repeated on another day, which confirmed the findings in these subjects. The SCI participants with lower lesion levels or those using spasmolytic medication could not be distinguished from the other SCI participants regarding their changes in systemic circulation or cerebral oxygenation. The three SCI participants with the smallest change in MAP (Figure 1) had complete cervical lesions and one of them was using Lioresal.

The calf circumference was smaller in SCI than in AB individuals (0.32 (0.02) m and 0.37 (0.02) m, respectively, $P=0.000$). Calf volume change evoked by thigh cuff inflation to 40 mmHg was greater in AB than in SCI (mean (SD): 3.3 (0.6) and 1.0 (0.5), respectively, $P=0.000$). Interestingly, in AB an increase of calf volume similar to that during cuff inflation (3.3 (1.2), $P=0.95$) was observed during head-up tilt, while orthostatic pressure was probably closer to 90 mmHg than the 40 mmHg of the cuff. SCI individuals showed a clearly greater increase (2.3 (0.7), $P=0.000$) in calf volume during head-up tilt than during thigh cuff inflation to 40 mmHg.

Discussion

The relation between systemic circulation and cerebral oxygenation in SCI individuals with a lesion above T4 was studied during an orthostatic challenge. This study did not attempt to assess cerebral autoregulation, instead, it focused on circulatory alterations secondary to a manoeuvre SCI individuals may perform in daily life.

The present study found no difference between groups in MAP in supine position, while most previous studies reported a lower MAP in SCI individuals.[1] This may be explained by MAP in AB individuals being 'low-normal' during supine rest, whereas some SCI individuals had a resting MAP similar to that normally observed in AB. This latter observation was not related to lesion level or medication, but may be caused by chance, since variation in the SCI population, even if stratified for lesion level, is greater than in the ordinary healthy population.

Circulatory responses

Since calf volume changes are considered to reflect changes in venous volume,[17] our plethysmography results point out that cuff induced venous volume change in supine position is greater in AB than in SCI, which is possibly caused by a smaller vascular bed[17] or less compliant veins in SCI. More importantly, the similar increase in calf volume in AB both during head-up tilt and a 40 mmHg cuff inflation suggests a sympathetic nervous system-induced change in venous tone, which is accordingly not found in SCI. Muscle tension effects in AB are unlikely, but cannot be ruled out completely. Finally, the smaller calf circumference, and smaller relative changes in calf volume indicate blood pooling in the legs of SCI to be less than in AB.

Stroke volumes of AB decreased during head-up tilt compared to supine rest, as found in previous studies in AB.[19,20] This is caused by blood pooling in the legs and splanchnic area with the body upright,[19] resulting in a diminished venous return and, consequently, a decreased stroke volume via the Frank-Starling mechanism. The significantly higher HR, found in the present as well as in other studies,[20,21] partly compensates this smaller stroke volume and reduces the decrease in cardiac output. Cardiac output and MAP were unaltered in AB during head-up tilt most likely due to a sympathetic nervous system-induced increase in total peripheral resistance. In some AB individuals MAP increased during tilt, as has been found by other studies.[19]

The decrease in stroke volume of SCI was greater than in AB and its effect on cardiac output was less well compensated for by a higher heart rate, thus leading to a greater decrease in cardiac output compared with AB. The decrease in stroke volume in SCI during head-up tilt, which is in accordance with an earlier study,[3] is probably caused by a greater decrease in venous return due to a lack of vasoconstriction in the legs and splanchnic area. Blood volume and flow in the splanchnic area, important for blood redistribution, cannot be regulated by brainstem commands in SCI with a lesion above T5, although some sympathetic activity below the level of the lesion may still be evoked by reflexes.[22]

The diminished cardiac output and the impaired sympathetic nervous system-induced vasoconstriction in SCI are the most likely causes of the greater fall of MAP in SCI compared with AB, as was observed in other studies.[1] However, some SCI individuals (Figure 1) could repeatedly maintain MAP. Since there seemed to be no relation to medication or lesion level, the vasoconstriction thus shown by some SCI individuals may be explained by an unexpected incompleteness of the sympathetic nervous system lesion. Alternatively, muscle spasms could contribute to maintenance of blood pressure during head-up tilt, but few muscle spasms occurred after the first minutes of head-up tilt. Finally, vasoconstriction below the level of the lesion in SCI individuals may be evoked by sympathetic reflexes,[22] ie independently from brainstem control, even though these reflexes were minimized by ensuring that all SCI participants emptied their bladder before the experiment and that they were comfortable on the tilting table. In general MAP decreased in SCI, and thus, SCI could not maintain circulatory homeostasis like AB, which may be expected in individuals with an impaired sympathetic nervous system.

Cerebral oxygenation change

A previous study[23] indicated [HHb] changes being more reproducible and more closely related to the operating variable in the regulation of cerebral flow than [O_2Hb] changes. Therefore, this study used [HHb] changes as a measure for cerebral oxygenation. [HHb], reflecting the change in match between oxygen consumption and delivery,[7,8] was significantly increased in both groups during head-up tilt. Since cerebral oxygen demand is expected to be independent of body position, the increased [HHb] found indicates a decrease in oxygen delivery, ie cerebral blood flow, while meeting cerebral oxygen demand as indicated by the general absence of presyncope symptoms. The [HHb] increase (<4 mmol·l^{-1}) found in this study is very small (4–6%) compared to the estimated total blood volume of approximately 70–100 mmol·l^{-1} in the cerebrum.[24] Levine *et al*[25] also reported a small decrease in cerebral flow during orthostatic challenges in able-bodied individuals using transcranial Doppler. Although MAP and consequently cerebral perfusion pressure decreased more in SCI than AB, the [HHb] decrease was similar in both groups. These results suggest that although systemic circulation shifts further from homeostasis in SCI compared to AB (Figures 1 and 2), cerebral oxygenation was compromized to a similar extent in SCI and AB.

There may be two lines of reasoning to explain this observation. Firstly, the decreased cerebral oxygenation during tilt may have been caused by the same mechanism in both groups. Then, the similar alteration in [HHb] in the face of different systemic circulation might be explained by different cerebral autoregulation responses, although this study did not attempt to provide evidence for this. Alternatively, although cerebral autoregulation may be operative in both groups, the mechanisms behind the similar alteration in cerebral oxygenation may be different in SCI and AB. It may be argued that cerebral oxygenation decreased in AB due to a sympathetic nervous system-induced vasoconstriction in the cerebrum.[25] In contrast, in SCI individuals with a lesion above T1 (nine of the participants) this vasoconstriction may be absent,[26] while a similar decrease in cerebral oxygenation is caused by the greater decrease in perfusion pressure.

Conclusion

The present study showed that SCI may not maintain systemic circulatory homeostasis as well as AB do during head-up tilt, while alterations in cerebral oxygenation were similar in AB and SCI. This suggests that in SCI cerebral oxygenation was well regulated since it was able to compensate for considerable alterations in the systemic circulation.

Acknowledgements

The authors wish to express their gratitude towards Dr Ralph Houston for critical reading of the manuscript.

References

1 Figoni SF. Cardiovascular and haemodynamic responses to tilting and to standing in tetraplegic patients: a review. *Paraplegia* 1984; **22:** 99–109.
2 Corbett JL, Frankel HL, Harris PJ. Cardiovascular responses to tilt in tetraplegic man. *J Physiol* 1971; **215:** 411–431.
3 Corbett JL, Debarge O, Frankel HL, Mathias CJ. Cardiovascular responses in tetraplegic man to muscle spasm, bladder percussion and head-up tilt. *Clin Exp Pharm Physiol* 1975; **2:** (suppl) 189–193.
4 Mathias CJ. Cardiovascular control in spinal man. *Ann Rev Physiol* 1988; **50:** 577–592.
5 Nanda RN, Wyper DJ, Harper AM, Johnson RH. Cerebral blood flow in paraplegia. *Paraplegia* 1974; **12:** 212–218.
6 Gonzalez F *et al*. Autoregulation of cerebral blood flow in patients with orthostatic hypotension after spinal cord injury. *Paraplegia* 1991; **29:** 1–7.
7 Colier WNJM. Near infrared spectroscopy: toy or tool? PhD thesis. University of Nijmegen 1995, The Netherlands.
8 Colier WNJM, Binkhorst RA, Hopman MTE, Oeseburg B. Cerebral and circulatory haemodynamics before vasovagal syncope induced by orthostatic stress. *Clin Physiol* 1997; **17:** 83–94.
9 Guttman L *et al*. Effect of tilting on the cardiovascular responses and plasma catecholamine levels in spinal man. *Paraplegia* 1963; **1:** 4–18.
10 Imholz BPM *et al*. Feasibility of ambulatory, continuous 24-hour finger arterial pressure recording. *Hypertension* 1993; **21:** 65–73.
11 Jellema WT *et al*. Finger arterial versus intrabrachial pressure and continuous cardiac output during head-up tilt testing in healthy subjects. *Clin Sci* 1996; **91:** 193–200.
12 Imholz PM *et al*. Non-invasive continuous flow blood pressure measurement during orthostatic stress compared to intra-arterial pressure. *Cardiovasc Res* 1990; **24:** 214–221.
13 Rongen GA *et al*. Comparison of intrabrachial and finger blood pressure in healthy elderly volunteers. *Am J Hypertens* 1995; **8:** 237–248.

14 Wesseling KH, de Wit B, Weber JAP, Smith NT. A simple device for the continuous measurement of cardiac output. Its model basis and experimental verification. *Adv Cardiovasc Phys* 1983; **5** (Suppl II): 16–52.
15 Wesseling KH, Jansen JRC, Settels JJ, Schreuder JJ. Computation of aortic flow from pressure in humans using a nonlinear, three-element model. *J Appl Physiol* 1993; **74:** 2566–2573.
16 Brakkee AJM, Vendrik AJH. Strain-gauge plethysmography: theoretical and practical notes on a new design. *J Appl Physiol* 1966; **21:** 701–704.
17 Struckmann JR, Vissing SF, Hjortso E. Ambulatory strain-gauge plethysmography and blood volume scintimetry for quantitative assessment of venous insufficiency. *Clin Physiol Oxf* 1992; **12:** 277–285.
18 Hopman MTE *et al*. Properties of the venous vascular system in the lower extremities of individuals with paraplegia. *Paraplegia* 1994; **32:** 810–816.
19 Rowell LB. Human Cardiovascular Control. Oxford University Press 1993, New York.
20 Wieling W *et al*. Pathophysiological mechanisms underlying vasovagal syncope in young subjects. *PACE* 1997; **20** [Pt. II]: 2034–2038.
21 Wang JJ *et al*. Hemodynamic mechanism of vasovagal syncope. *Jpn Heart J* 1996; **37:** 361–371.
22 Henriksen O. Sympathetic reflex control of blood flow in human peripheral tissues. *Acta Physiol Scand Suppl* 1991; **603:** 33–39.
23 Houtman S, Colier WNJM, Oeseburg B, Hopman MTE. Reproducibility of the alterations in circulation and cerebral oxygenation from supine rest to head-up tilt. *Clin Physiol* 1999; **19:** 169–177.
24 Hawtazawa J *et al*. Regional cerebral blood flow, blood volume, oxygen extraction fraction, and oxygen utilization rate in normal volunteers measured by the autoradiographic technique and the single breath inhalation method. *Ann Nucl Med* 1995; **9:** 15–21.
25 Levine BD *et al*. Cerebral versus systemic hemodynamics during graded orthostatic stress in humans. *Circulation* 1993; **90:** 298–306.
26 Corbett JL, Eidelman BH. Studies on cerebral circulation in man indicating presence of neurogenic control. *Proc Aust Assoc Neurol* 1973; **9:** 133–144.