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Head-Up Tilt and Lower Body Suction: Comparison of Hormone Responses in Healthy Men

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Summary

The purpose of this study was to compare, in the same subjects, hormonal responses to 30-min head-up tilt (HUT) and lower body suction (LBNP) of different intensity (24° and 70°, and 15 and 35 mm Hg, respectively). Basal pooled individual data from –10 min (n=32) were within normal reference limits: norepinephrine (NE) averaged 318±23 pg/ml; epinephrine, 34.0±5.5 pg/ml; plasma renin activity (PRA), 0.72±0.08 ng ATII/ml/h; aldosterone, 164±20 pg/ml; atrial natriuretic peptide (ANP), 29.9±2.0 pg/ml; cGMP, 6.29±0.59 mmol/l; cortisol, 95.7±5.8 ng/ml; and ACTH, 50.3±2.6 pg/ml. The low-level stimuli failed to induce consistent changes in hormone levels. From the onset of the stimulus (minute 0) to its termination (minute 30), norepinephrine (NE) increased by 101 % with LBNP–35, and by 70 % with HUT70, respectively. The NE increase with LBNP–35 was higher ($p<0.05$) than with HUT70. Epinephrine rose with HUT70 (by 162 %) only. PRA increased by 157 % with LBNP–35, and by 119 % with HUT70, respectively; these responses were not significantly different. Aldosterone rose equally (by 85 and 89 %) with LBNP–35 and HUT70 but not with the low-level stimuli. No consistent changes were observed in ANP, c-GMP or ACTH concentrations. Cortisol values fell during the LBNP and HUT24 situations but rose transiently after HUT70. We conclude that the hormones investigated respond differently to head-up posture and lower body suction and in a specific manner. Greater effects of high-level stimuli (HUT70, LBNP–35) were noted as compared to low-level stimuli (HUT24, LBNP–15). The application of combined sets of models stimulating the cardiovascular system may aid in the analysis of responses of hormonal systems in man.

Key words

Simulated orthostasis – Cardiovascular stimulus – Catecholamines – Volume-regulating and stress dependent hormones

Introduction

Reflex and hormonal mechanisms activated by cardiopulmonary and arterial baroreceptors in response to changes in blood pressure and cardiac filling pressure play an important role in cardiovascular homeostasis. Passive head-up tilt (HUT) or lower body suction (LBNP) are well-known models frequently used to simulate an increase in gravitational load. Both stimuli cause acute volume depletion by venous blood pooling, redistribution of blood from the intrathoracic region to the lower part of the body and decrease in central blood volume (Blomqvist and Stone 1983, Gauer and Thron 1965, Norsk 1992). During HUT, fluid shift is induced by gravitational forces along the longitudinal axis of the body whereas with LBNP, fluid shifts are induced by pressure changes imposed on the subcutaneous tissue and muscles of the lower limb. Thus, these two models cannot be considered to be equal but rather to represent two situations inducing specific changes in cardiovascular and endocrine functions.

Considerable amount of data has accumulated on the changes of volume regulatory hormones during LBNP or HUT (Tuck *et al.* 1975, Sancho *et al.* 1976,

Tatár *et al.* 1986, Sander-Jensen *et al.* 1986, 1988, Haller *et al.* 1987, Huber *et al.* 1988, Baily *et al.* 1991, Matzen *et al.* 1992, Norsk 1992, Stewart *et al.* 1992, Debrah *et al.* 1995) and some information is also available on changes of other hormonal systems (Vigaš *et al.* 1984, Sander-Jensen *et al.* 1988, Matzen *et al.* 1992). In these studies, a variety of different protocols was used, and the hormone responses to LBNP and to HUT were investigated separately. Many of the results obtained are inconsistent and it is difficult to evaluate the neuroendocrine responses to cardiovascular stress in relation to their specific features and intensity.

The aim of the present study was to follow volume regulatory and stress hormone responses to a low or a high level of LBNP as well as to a low or a high degree of HUT. All experiments were performed in the same group of subjects to enable a direct comparison of hormone responses to defined loads on the cardiovascular system.

Methods

Eight healthy male volunteers (25±4 yr, 76±8 kg body weight) were fully informed about the test procedure and gave their written consent. Each of them participated in 4 investigations, namely 24° HUT (HUT24), 70° HUT (HUT70), −15 mm Hg LBNP (LBNP−15), and −35 mm Hg LBNP (LBNP−35). Single trials were separated by at least one week. The subjects abstained from the use of tobacco, caffeine and alcohol on the day before the study. They had a light breakfast 2 h before the investigations which were performed between 09.00 and 12.00 h. After voiding, horizontal position was assumed for 40 min before the trial was started. None of the 8 subjects felt dizzy or nauseated during either test.

At each experimental session, the left antecubital vein was cannulated, using a 17G−1.4x40 mm 3-way stopcock Teflon catheter (MeCath, Codan Steritex ApS, Denmark) with the subject in the control supine position. Tilting was performed manually and took less than 15 s. The tilt table was provided with a footboard and harness. LBNP was applied by enclosing the subject's lower body up to the iliac crest in a transparent box. Pressure within the box was lowered by a vacuum pump and adjusted electronically. A neoprene gasket around the iliac crest and lower thorax provided sufficient sealing. The pressure difference to ambient value was monitored with a high precision manometer (Wallace Tiernan), pressure was adjusted to ±1 mm Hg in less than 10 s. The heart rate and blood pressure were measured by an oscillometric technique (Critikon, 1846 SX, Dinamap, USA). Blood samples for hormone determinations were taken 10 min and immediately before starting orthostasis or suction (min 0); 3, 5, 10, 20, and 30 min of stimulation; and 2, 5, and 20 min after the stimulus had been discontinued (min 32, 35, and 50). Blood was kept on ice in tubes with prechilled EDTA, heparin or glutathione. After rapid centrifugation at 4 °C plasma aliquots were stored at −20 °C not longer than 2 months before analysis.

Commercially available radioimmunoassay kits (Pharmacia) were used for the measurement of plasma renin activity, aldosterone, cGMP and atrial natriuretic peptide (ANP) concentrations. Cortisol in the plasma was determined by a radioimmunoassay procedure described previously (Ježová and Vigaš 1988). Plasma catecholamines were determined by the radioenzymatic method (Peuler and Johnson 1977).

Data are given as means ± S.E.M. Repeated-measures-ANOVA was used to determine differences between the test conditions. A paired non-parametric test (Wilcoxon) was employed for statistical evaluation of both absolute and relative data (Stat View II, Abacus Concepts Inc., USA). The differences in hormone concentrations within individual tests were compared to basal values at time 0 min. Because of the inhomogeneity of variances, median values, which give a better description of the centre of gravity than arithmetical means, are shown in the figures.

Results

Plasma norepinephrine concentrations (NE) (Fig. 1, Table 1)

Basal NE values in the study averaged 318±23 pg/ml (pooled individual data from −10 min, N=32). NE values before the stimulus were somewhat higher in the trial with LBNP−35 compared to those in the other three models (ca 390 vs. 280 pg/ml), however, all initial values were within the normal range (305±39 and 400±85 pg/ml in the LBNP−15 and LBNP−35; 311±37 and 273±36 pg/ml in the HUT24 and HUT70 treatments, respectively). In each of the four experimental situations studied, significant increases in plasma NE were found during the stress phase; the rise in response to LBNP−15 and HUT24 was not consistent and was of small magnitude. The most pronounced activation of NE release was observed throughout LBNP−35; at the beginning of suction, plasma NE levels showed a rapid rise and reached a plateau (80−107 % vs values at 0 min) within 5−30 min of the exposure. The NE rise during HUT70 also showed a rapid increase during the first minutes and the increasing tendency was maintained until the end of exposure (+103 % at 30 min vs the values at 0 min). After the withdrawal of stimuli, NE dropped to basal values immediately. Comparison of the relative NE responses showed that the highest response was elicited by LBNP−35, with significant differences ($p<0.05$) between LBNP−35 vs HUT70 vs low-level stress.

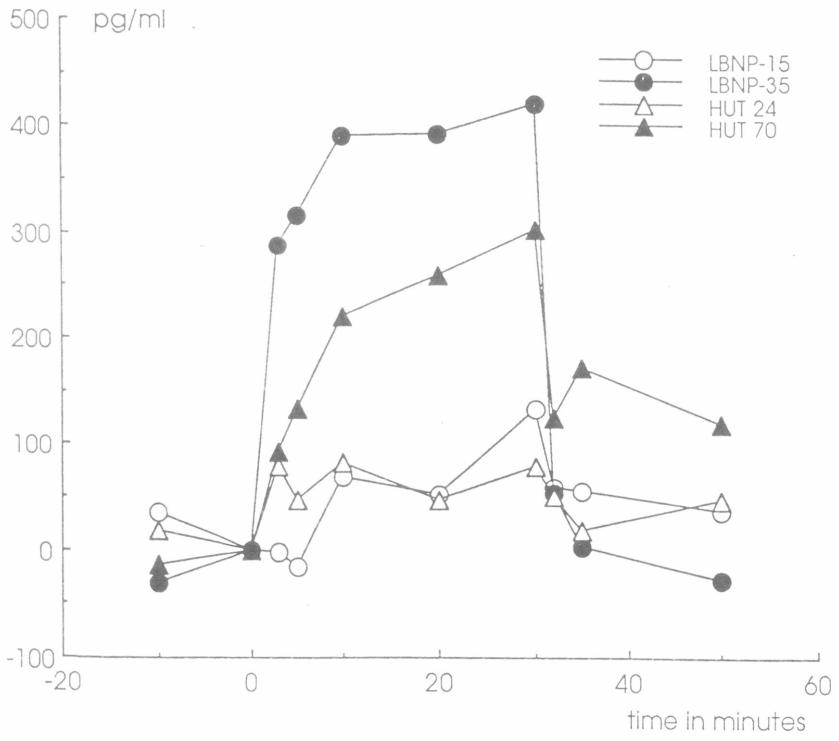

Fig. 1
Time course of plasma norepinephrine (NE) median values relative to NE at time zero.

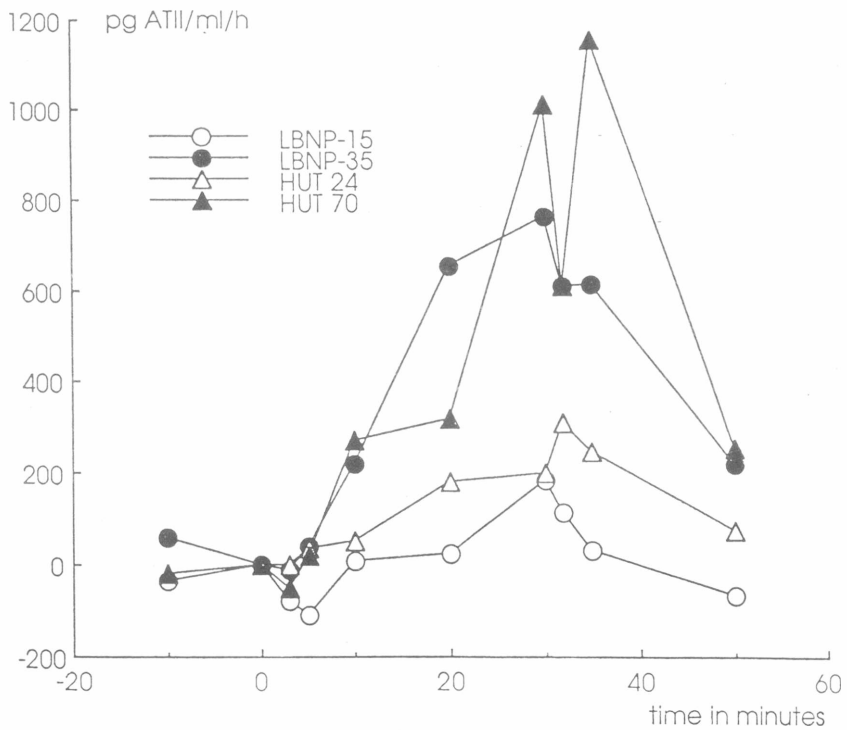

Fig. 2
Time course of plasma renin activity (PRA) median values relative to PRA at time zero.

Plasma renin activity (PRA) (Fig. 2, Table 1)

Basal PRA values averaged 0.72±0.08 ng ATII/ml/h (pooled data at −10 min). The starting levels were 0.68±0.18 and 0.51±0.10 ng/ml/h in the LBNP−15 and LBNP−35; and 0.87±0.17 and 0.97±0.17 ng/ml/h in the HUT24 and HUT70 runs, respectively. The stimuli increased PRA with some delay. Significant responses were not obtained until 20 min of LBNP−35 and HUT70 ($p<0.05$). PRA reached 157 % and 119 % above control levels at 30 min of LBNP−35 and HUT70, respectively, and decreased slowly after stimulus cessation. PRA values were similar at identical times of HUT70 and LBNP−35; they were found to be different ($p<0.05$) when low- and high-load phases were compared.

Table 1
Time course of the changes in norepinephrine (NE, pg/ml), epinephrine (EPI, pg/ml), aldosterone (ALDO, pg/ml), atrial natriuretic peptide (ANP, pg/ml), cyclic guanosine monophosphate (cGMP, mM), plasma renin activity (PRA, ng ATII/ml/h), corticotropin (ACTH, pg/ml) and cortisol (CORT, ng/ml) before (−10 and 0 min), during (3, 5, 10, 20, and 30 min) and 2, 5, and 20 min after the application of lower body suction (LBNP) or head-up tilt (HUT).

Time	−10	0	3	5	10	20	30	32	35	50
LBNP−15										
NE	304±31	305±39	313±35	341±63	384±52	394±53	426±45	399±55	375±53	377±51
EPI	40±12	41±11	36±9	36±9	45±14	35±7	43±11	36±7	43±8	40±10
ALDO	183±33	149±24	146±29	151±34	136±33	140±32	159±39	155±39	161±37	173±33
ANP	39±3	37±3	36±2	35±2	36±2	34±2	37±2	35±1	35±2	37±3
cGMP	7.7±1.3	6.9±1.3	6.8±1.2	7.1±1.1	6.1±1.3	6.7±1.3	6.1±0.7	6.0±0.7	5.9±0.7	6.2±1.0
PRA	0.65±0.19	0.68±0.18	0.69±0.16	0.57±0.15	0.71±0.18	0.74±0.19	0.95±0.24	0.88±0.20	0.79±0.14	0.68±0.13
ACTH	50±4	45±3	51±6	51±5	49±6	46±5	41±3	45±4	43±4	53±4
CORT	99±10	98±10	93±10	95±12	93±13	84±11	82±12	76±9	76±9	68±8
LBNP−35										
NE	378±72	400±85	662±125	719±121	762±128	828±140	805±137	507±125	428±75	371±64
EPI	47±13	46±14	70±28	47±10	51±8	46±6	56±10	41±9	46±11	38±9
ALDO	161±30	164±24	173±14	153±18	178±15	231±34	304±36	334±45	332±34	288±29
ANP	25±2	24±2	22±1	24±2	24±2	25±2	23±2	23±2	23±2	24±2
cGMP	5.1±0.4	6.6±0.9	5.8±0.5	5.8±0.6	5.6±0.7	5.8±0.7	5.6±0.6	5.1±0.6	4.3±0.5	4.2±0.4
PRA	0.58±0.11	0.51±0.10	0.53±0.10	0.59±0.13	0.85±0.21	1.13±0.11	1.31±0.13	0.99±0.15	0.96±0.08	0.67±0.07
ACTH	54±5	54±6	57±11	51±7	54±6	50±6	59±5	52±8	51±7	45±5
CORT	96±11	91±10	90±11	87±11	86±12	87±13	79±11	80±10	75±9	69±8
HUT24										
NE	308±25	311±37	355±51	358±38	316±27	393±31	377±24	344±33	337±40	325±23
EPI	26±9	19±4	27±7	28±5	29±7	27±6	47±15	38±15	30±4	25±2
ALDO	121±30	111±25	98±18	96±21	73±18	123±27	153±32	150±32	160±33	158±31
ANP	23±3	26±4	24±4	23±3	20±2	23±2	21±2	22±3	23±3	24±4
cGMP	7.1±1.4	5.0±0.9	4.5±0.8	4.1±0.6	4.7±0.7	3.8±0.6	3.9±0.6	3.7±0.6	3.4±0.4	3.4±0.5
PRA	0.77±0.13	0.87±0.17	0.87±0.17	0.94±0.16	0.97±0.24	1.15±0.29	1.15±0.27	1.17±0.25	1.05±0.17	1.04±0.27
ACTH	50±4	45±3	51±6	51±5	49±6	46±5	41±3	45±4	43±4	53±4
CORT	109±12	110±15	115±15	108±15	104±18	102±16	104±18	105±16	93±15	88±11
HUT70										
NE	278±29	273±36	386±45	429±26	492±26	537±31	553±47	464±62	443±47	366±34
EPI	21±6	23±7	38±7	44±9	49±14	43±14	61±19	39±9	45±15	46±16
ALDO	145±30	158±54	148±35	130±24	177±62	239±75	299±81	315±64	333±82	308±55
ANP	32±5	34±5	37±5	32±4	34±4	33±4	34±5	31±3	27±2	–
cGMP	5.1±1.3	4.8±0.7	5.0±0.8	4.7±0.8	5.0±0.8	4.9±0.6	3.8±0.7	3.5±0.6	3.8±0.4	4.0±0.5
PRA	0.99±0.19	0.97±0.17	0.88±0.14	1.00±0.20	1.19±0.21	1.67±0.39	2.12±0.47	2.04±0.44	1.97±0.40	1.14±0.24
ACTH	54±5	54±6	57±11	51±7	54±6	50±6	49±5	52±8	51±7	45±5
CORT	80±11	84±15	84±14	81±13	81±14	94±17	102±18	101±17	94±18	95±15

Data are means ± S.E.M.

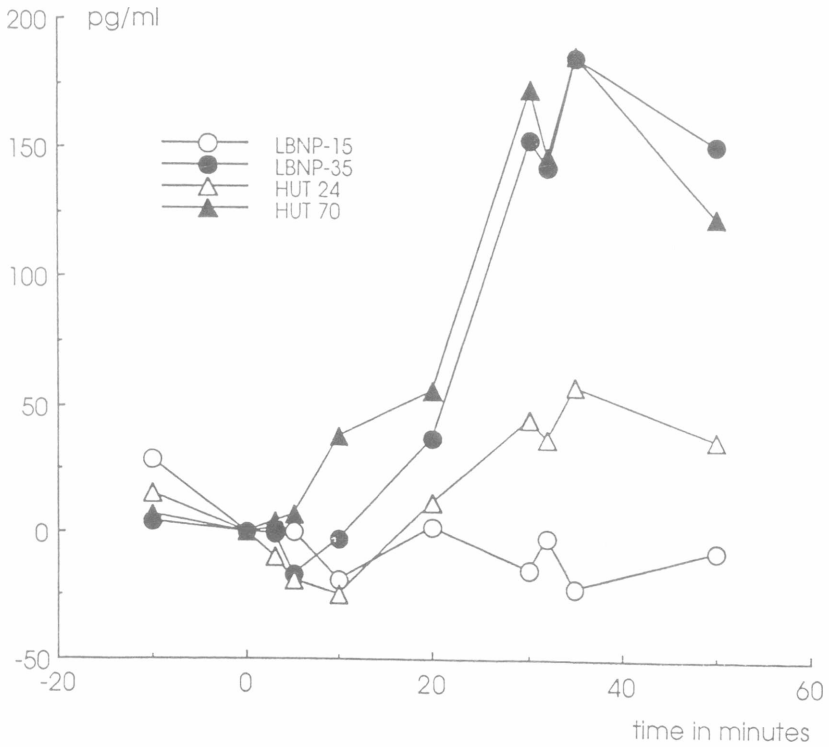

Fig. 3
Time course of plasma aldosterone median values relative to aldosterone at time zero.

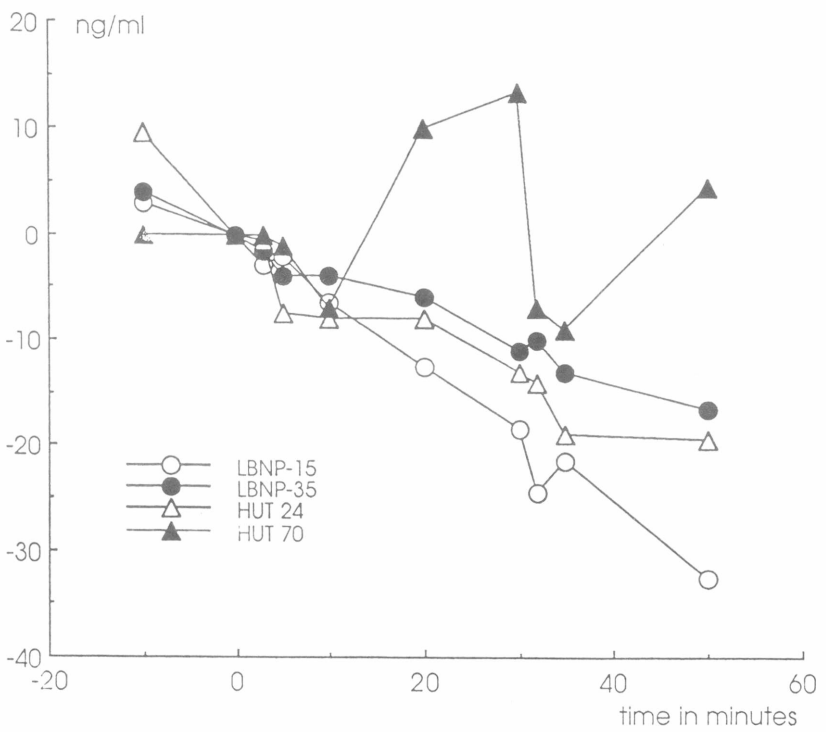

Fig. 4
Time course of plasma cortisol median values relative to cortisol at time zero.

Plasma aldosterone concentration (Fig. 3, Table 1)

Basal aldosterone levels as calculated from all individual data at −10 min were 164±20 pg/ml. LBNP−15 did not stimulate any release of aldosterone, whereas HUT24 caused a slight but significant decrease of aldosterone concentrations 5 and 10 min after exposure. The aldosterone increase at the end of HUT24 was not significant as compared to pre-stress levels. Higher loads significantly raised plasma aldosterone levels starting at 20 min of exposure: 85 % (from 164±24 pg/ml) with LBNP−35; and 89 % (from 158±54 pg/ml) with HUT70. Maximal concentrations were reached 5 min after cessation of both experimental situations. The recovery period was too

short to observe the return of aldosterone levels to basal concentrations, and at the end of observation plasma aldosterone levels were still significantly increased. There were no differences in the course and magnitude of plasma aldosterone responses to LBNP−35 and HUT70. A higher increase ($p<0.05$) in plasma aldosterone was found for LBNP−35 vs LBNP−15 from min 20, and for HUT70 vs. HUT24 from min 30, until the end of observation.

Plasma cortisol and ACTH concentrations (Fig. 4, Table 1)

Basal concentrations of plasma cortisol showed great variability. However, the differences were not statistically significant and all values were within the physiological range. Plasma cortisol levels significantly decreased in time during and after LBNP−15, LBNP−35 as well as HUT24. A similar tendency though with less significant differences was found in plasma ACTH levels. In contrast, cortisol concentrations in response to HUT70 increased ($p<0.05$) at min 20 and 30. The relative values of plasma cortisol showed a decrease in all experimental situations with the exception of HUT70.

Plasma epinephrine (EPI) concentration (Table 1)

Basal, pooled (−10 min) EPI values in the study averaged 34.0±5.5 pg/ml. Hormone levels at both −10 and 0 min were higher in the LBNP trials compared to those in the HUT studies. EPI concentrations were not influenced by the stimuli used with the exception of HUT70 in which EPI levels increased by 162 % from 23.3±6.6 pg/ml.

Plasma atrial natriuretic peptide (ANP) and cGMP concentrations (Table 1)

Plasma ANP levels showed very high variability. Although a tendency to decrease in response to cardiovascular stress situations could be noted, a fall in ANP levels clearly under the range of pre-test values was found only during HUT24 at 10 min. The overall response of cGMP during the cardiovascular load was also a decrease in its concentrations, but the detailed changes were different from those of ANP. In this parameter, the high variability also complicated the evaluation of the small differences observed.

Table 2
Time course of the changes in heart rate (HR, beats/min), systolic (SBP) and diastolic (DBP) blood pressure (mm Hg) during and after the application of lower body suction or head-up tilt.

Time	0	3	5	10	20	30	32	35	50
LBNP−15									
HR	66±2	71±3	72±3*	72±3*	71±3*	71±3	65±3	65±3	63±3
SBP	128±3	117±3*	117±2*	121±3	122±3	124±3	121±3*	118±3*	123±3
DBP	71±3	63±3*	64±3*	68±3*	70±3	77±2	69±3	64±3*	73±3
LBNP−35									
HR	72±2	87±3*	92±4*	91±3*	88±3*	89±3*	65±3*	67±2*	69±2
SBP	124±3	119±3	115±3*	116±3*	116±2	118±3	123±2	122±2	124±3
DBP	69±2	68±3	68±3	70±3	69±3	72±2	70±3	69±3	72±2
HUT24									
HR	65±3	68±3	69±3*	71±6*	72±2*	71±3*	64±3	63±3	62±3
SBP	116±3	116±3	115±4	119±4	118±3	115±3	116±3	109±3*	115±3
DBP	66±3	66±3	63±3	66±3	66±3	66±3	61±3	62±3	64±3
HUT70									
HR	63±3	86±5*	86±2*	88±2*	86±3*	89±3*	65±4*	63±4*	66±2
SBP	115±3	119±3	119±4	121±4	122±4	119±4	116±4	113±4	114±4
DBP	61±3	63±3	61±3	70±4*	72±3*	71±4*	60±3	58±3	63±3

*Data are means ± S.E.M. The "zero" value is the mean of the two measurements done just before starting the HUT/LBNP phase. * indicates $p<0.05$ compared to control (0) value*

Heart rate and blood pressure (Table 2)

Heart rate increased slightly but significantly during both low-level protocols (LBNP−15, HUT24) and markedly during both high-level protocols (LBNP−35, HUT70). In all trials, it returned to basal levels immediately after cessation of the stimulus. During LBNP−15 and LBNP−35, systolic blood pressure (SBP) significantly decreased. In the case of LBNP−15, the fall in SBP persisted for 20 min post-LBNP while after termination of LBNP−35, it returned to basal values. No changes of SBP were observed during tilting in HUT24 or HUT70. After bringing the subjects back to the supine position, a decrease in SBP was observed during both HUT protocols. Diastolic blood pressure fell during the first minutes of LBNP−15, was increased from min 10−30 during HUT70, and remained unchanged during the other trials.

Discussion

Head-up tilt and lower body suction induce central hypovolaemia and, by unloading of cardiopulmonary receptors alone, or in combination with arterial baroreceptors, give rise to neural and hormonal counter-regulation (Abboud *et al.* 1976, Blomqvist and Stone 1983). LBNP of less than −20 mm Hg results in selective unloading of central "volume" receptors, whereas higher levels also affect arterial "pressure" receptors (Abboud *et al.* 1979, Egan *et al.* 1983, Joyner *et al.* 1990, Rea and Wallin 1989, Thompson *et al.* 1991, Zoller *et al.* 1972) as head-up tilt generally does due to hydrostatic effects (Gauer and Thron 1965, Smith and Ebert 1991). The presented results confirm the activation of several hormonal systems known to occur in response to cardiovascular stress and, in addition, allow for direct comparison of hormonal responses to various loads. To our knowledge, this is the first study directly addressing the question of endocrine responses to different kinds of orthostatic stress − HUT and LBNP − and of its different intensity in the same group of volunteers.

In our investigation, the changes in the cardiovascular variables were complete within 5 min after the onset of orthostasis or negative pressure. A similar time course was observed in other studies with LBNP (Lightfoot *et al.* 1991). Intravascular pooling is thought to be essentially completed within one minute after the onset of LBNP. Therefore, it is suggested that the signal for neuroendocrine responses to the stimuli is generated within the first minutes of HUT or LBNP. The actual increase in plasma concentrations of hormones which respond by increased secretion depends on the rate of their release. "Quick" hormones, such as catecholamines, show a change within the first five minutes. NE levels increase after about 2 min of orthostatic challenge (Blomqvist and Stone 1983, Huber *et al.* 1988); the most pronounced rapid response observed in this study was that of NE during LBNP.

The sympathetic nervous system plays an important role in maintaining homeostatic conditions. In several models of increased gravitational stress including HUT and LBNP, an increased sympathetic activity has been described (Baily *et al.* 1991, Norsk 1992, Sander-Jensen *et al.* 1986, 1988). During stress situations, epinephrine and NE are released almost synchronously from the adrenal medulla; 20 % of the secretion is NE (Mannelli *et al.* 1982). We observed no or only moderate increases in epinephrine which is in line with findings of others (Huber *et al.* 1988, Sander-Jensen *et al.* 1986, Tatár *et al.* 1986). In contrast, a significant rise in NE concentrations was observed with HUT70 and LBNP−35. During the low loads of both HUT and LBNP, a noticeable elevation in NE levels failed to reach significant levels and might be considered as biologically unimportant. Nevertheless, this moderate increase probably represents a response to the experimental situations rather than an accidental variation in plasma levels as shown by the rapid decrease after cessation of the stimulus. Moreover, the increases in NE levels during LBNP and HUT of low intensity seem to be related to actual changes in the cardiovascular system, and not to reflect a non-specific stress response, as a variety of stress models have been shown to induce much higher sympathetic-adrenomedullary activation (Ježová *et al.* 1985, Vigaš *et al.* 1984). In a study on healthy volunteers using arterial blood sampling, a 70 % NE increase in response to one-hour of 30° HUT, and a 100 % increase with 60° HUT was observed (Sander-Jensen *et al.* 1986). A threshold seems to exist for catecholamine responses to LBNP since with −10 mm Hg, NE did not change in another study of Hirsch *et al.* (1989). Venous and arterial sampling may yield different catecholamine findings. Further, it has been shown that changes in cardiac output *per se* can alter NE by changed hormone clearance from the bloodstream (Baily *et al.* 1991).

In our study, higher LBNP and HUT load in the same group of subjects elicited significant sympathetic activation as shown by increases in NE levels and heart rate. The increase of NE in LBNP−35 is considered to be a specific response to decreased blood pressure rather than a non-specific response to stress connected to the experimental procedure, since there was no concomitant elevation of plasma cortisol

values. The increase in plasma NE during LBNP−35 was the only condition in which hormone concentrations were greater during negative pressure compared to orthostasis (HUT70). Since no significant hypotension occurred during HUT70, there was no reason to expect pronounced sympathetic activation (Giorgino 1988). Other hormones responded either similarly to both stronger stimuli (LBNP−35 and HUT70) − e.g., aldosterone − or, as cortisol, by a more pronounced release in response to HUT70.

The renin-angiotensin-aldosterone system plays an important role in blood pressure regulation. The activity of plasma renin, which cleaves angiotensin I from its plasma substrate angiotensinogen, is a good indicator of the activity of this system. In many stress situations, the changes in PRA were found to parallel those of the sympathetic system (Kvetňanský *et al.* 1990). PRA and angiotensin II levels were found elevated within 5−7 min of assuming upright posture (Huber *et al.* 1988, Tuck *et al.* 1975), and a slight but significant rise in PRA has been observed with −10 mm Hg LBNP (Hirsch *et al.* 1989). PRA increased only in response to more intensive stimuli of both models in our investigation, and even the response to LBNP−35 was rather moderate. In contrast to the test subjects studied by Hirsch *et al.* (1989), the low intensity stimuli during LBNP−15 and HUT24 seemingly did not reach the threshold to stimulate PRA, although they may have been sufficient to induce NE release. With −55 mm Hg LBNP, a significant 160 % PRA increase in arterial blood plasma was observed by Sander-Jensen *et al.* (1988). The strongest stimulus for PRA activation in our study seemed to be HUT70, although the values failed to be statistically different compared to those during LBNP−35.

Angiotensin II is an effective regulator of aldosterone release and indeed, aldosterone levels exhibited similar changes compared to those of PRA, with the exception of a transient aldosterone decrease at the beginning of HUT24. The delayed aldosterone response in both models may reflect a slower degradation of this hormone compared to PRA. It has been shown that passive head-up tilt of only 30° can increase arterial plasma aldosterone levels to 5-fold levels (Sander-Jensen *et al.* 1986); in other studies (Norsk 1992, Sancho *et al.* 1976, Stewart *et al.* 1992) much lower aldosterone responses were found in venous blood with postural changes, however. It can be assumed that arterial sampling increases reflex-induced hormone reactions, since invasiveness of the used instrumentation adds considerably to the cardiovascular stress imposed onto the subject (Stevens 1966).

We failed to observe a consistent decrease in ANP release described in several models of increased gravitational stress (Haller *et al.* 1987, Norsk 1992). Our data show a high individual variability of the ANP response during increased cardiovascular load; the same is true for cGMP responses. Actual plasma concentrations are the result of both hormone release and withdrawal; the orthostatic rise in NE levels may, *via* adrenergic receptors, blunt the expected fall in circulating ANP (Sonnenberg 1985, Uehlinger *et al.* 1986), and the upright position may modify metabolic clearance of the hormone (Epstein *et al.* 1986, Gnädinger *et al.* 1986).

The above mentioned hormones are known to be involved in general stress responses having several physiological functions, including a role in the maintenance of body fluid and electrolyte balance. Glucocorticoids also belong to typical stress hormones but not to volume regulatory hormones and their secretion increases in response to stressors with both emotional and somatic components (Whitnall 1993). During all experimental situations studied, with the exception of HUT70, a regular decrease of plasma cortisol concentrations was observed, consistent with endogenous circadian rhythm of this hormone (Ježová and Vigaš 1988). This decrease was absent during HUT70 indicating more general stress response than during the other trials. This suggestion is strengthened by simultaneous increase in plasma epinephrine release observed with HUT70, but not during other trials. In persons receiving saline infusion, Matzen *et al.* (1992) observed an increase of both venous cortisol and ACTH which was significant after less than 30 min of 50° HUT.

Some authors used LBNP as a model of haemorrhage. Pitts *et al.* (1990) showed increased ACTH values 2−10 min and cortisol concentration 15−20 min after the cessation of LBNP in subjects experiencing a presyncope or a drop of blood pressure of more than 20 mm Hg with a rise of heart rate of 30 beats per min or more. These circulatory changes are consistent with the physiological effect of acute haemorrhage corresponding to approximately 15 % of the intravascular volume. The negative pressure in our model was slightly less intensive (−35 vs −40 mm Hg), however, no syncopal or presyncopal symptoms appeared. Pitts *et al.* (1990) summarized the variation in tolerance to negative pressure which was ascribed to several factors, such as the ability to maintain total peripheral resistance and baroreceptor sensitivity. The group of subjects participating in our investigation showed high tolerance as no pronounced blood pressure decrease was found. Therefore, no significant increase of plasma cortisol had occurred.

In conclusion, the application of subatmospheric pressure onto the lower body and passive head-up tilting induce specific changes in volume regulatory hormones related to the particular model and its intensity. Norepinephrine, PRA and aldosterone were significantly increased with high-level stimuli. The time courses were different between hormones, however, and norepinephrine responses were larger with LBNP (−35 mm Hg) than with HUT

(70°), although the heart rate responses were similar. The signals for neuroendocrine activation seem to include not only a challenge of the cardiovascular and fluid-electrolyte systems but also additional components which require clarification in further studies.

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