Dynamic time course of hemodynamic responses after passive head-up tilt and tilt back to supine position

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Toska, Karin, and Lars Walløe. Dynamic time course of hemodynamic responses after passive head-up tilt and tilt back to supine position. J Appl Physiol 92: 1671–1676, 2002. First published December 7, 2001; 10.1152/japplphysiol.00465.2000.—Mechanisms involved in the control of arterial pressure during postural changes were studied by analysis of the dynamic time course of cardiovascular changes during head-up tilt (HUT) and tilt back to supine position (TB). Beat-to-beat values of cardiovascular variables were recorded continuously before, during, and after passive HUT to 30° in seven healthy humans. Left cardiac stroke volume (SV), Doppler ultrasound, mean arterial blood pressure (MAP), heart rate (HR), cardiac output (CO), and total peripheral conductance (TPC) were recorded. During HUT, MAP at the level of the carotid baroreceptors decreased by ~5 mmHg. There was a striking asymmetry between the time courses of cardiovascular changes on HUT and on TB. Adjustments generally took up to 30 s after HUT, whereas most changes were completed during the first 10 s after TB. Cardiovascular reflex adjustments of HR and TPC were more symmetrical. After HUT, SV was maintained during the first 4–6 s and then decreased steadily during the next 30 s to a stable level ~25% below its pretilt value. However, after TB, SV increased rapidly to its pretilt value in <10 s. This asymmetry in SV dynamics may be explained in part by a more rapid change in left cardiac filling after TB than after HUT. On TB, there must be a rapid inflow of stagnant blood from the legs, whereas venous valves will impede backward filling of veins in the lower body on HUT. In conclusion, we have revealed a characteristic asymmetry in cardiovascular responses to inverse variations in gravity forces in humans. This asymmetry can be explained in part by nonlinear, hydrodynamic factors, such as the one-way effect of venous valves in the lower part of the body.

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THE DYNAMIC TIME COURSE OF CARDIOVASCULAR RESPONSES TO RAPID POSTURAL CHANGES REFLECTS BOTH CHANGES MECHANICALLY INDUCED BY THE INFLUENCE OF GRAVITY ON THE CIRCULATORY SYSTEM AND THOSE CAUSED BY THE RESULTING NERVOUS REFLEX RESPONSES. WHEN POSTURE CHANGES, SO DOES THE POSITION OF THE MAIN ARTERIAL PRESSOR RECEPTORS IN THE CAROTID ARTERIES RELATIVE TO THE HEART, AND THIS MIGHT INDUCE REFLEX CHANGES IN ARTERIAL PRESSURE AT HEART LEVEL. IF ARTERIAL PRESSURE AT THE LEVEL OF THE HEART STAYED CONSTANT DURING A POSTURAL CHANGE FROM SUPINE TO UPRIGHT POSITION, ARTERIAL PRESSURE IN THE ARTERIES ENTERING THE SKULL WOULD DECREASE BY ~20 mmHg, THEREBY DECREASING THE PERFUSION PRESSURE OF THE BRAIN. THE CAROTID BARORECEPTORS, ~25 cm ABOVE HEART LEVEL, WOULD SENSE ARTERIAL PRESSURE TO BE ~18 mmHg LOWER THAN AT HEART LEVEL, GIVEN THAT ARTERIAL FLOW RESISTANCE IS CLOSE TO ZERO. WITH A HIGH BAROREFLEX GAIN, ARTERIAL PRESSURE AT HEART LEVEL WOULD THEN BE EXPECTED TO INCREASE BY ~15 TO 20 mmHg FROM THE SUPINE TO THE STANDING POSITION. HOWSOEVER, AORTIC AND CAROTID BARORECEPTORS, WHICH SENSE A HIGHER ARTERIAL PRESSURE THAN CAROTID BARORECEPTORS, MIGHT PARTLY COUNTERACT SUCH AN INCREASE IN MAP. ON THE OTHER HAND, FILLING OF THE HEART IS IMPEDED BY THIS CHANGE IN POSTURE BECAUSE THE ARTERIES AND ESPECIALLY THE VEINS BELOW THE HEART ARE FILLED TO A MUCH HIGHER DEGREE IN THE STANDING POSITION. THE INCREASE IN VOLUME IN THE LOWER PART OF THE BODY IS ESTIMATED TO BE ~700 ml (13). THIS SUBSTANTIAL DECREASE IN CENTRAL FILLING PRESSURE WOULD CAUSE A SIGNIFICANT FALL IN STROKE VOLUME (SV) AND POTENTIALLY A DECREASE IN CARDIAC OUTPUT (CO), EVEN IF ARTERIAL BAROREFLEX MECHANISMS INDUCED AN INCREASE IN HEART RATE (HR). THUS, TO KEEP ARTERIAL PRESSURE FROM DECREASING, SIGNIFICANT PERIPHERAL VASOCONSTRICTION TAKES PLACE WHEN BODY POSITION CHANGES FROM SUPINE TO STANDING.

THE DETAILED TIME COURSE OF THE IMMEDIATE CARDIOVASCULAR RESPONSES TO CHANGES IN BODY POSITION IS NOT WELL KNOWN. THIS IS PROBABLY BECAUSE OF A LACK OF METHODS FOR NONINVASIVE MEASUREMENT OF BEAT-TO-BEAT CARDIAC SV. OUR LABORATORY HAS PREVIOUSLY DEVELOPED AN IMPROVED ULTRASOUND DOPPLER METHOD FOR RECORDING BEAT-TO-BEAT SV CONTINUOUSLY FOR LONG PERIODS OF TIME AND IN SEVERAL BODY POSITIONS (2). TO ANALYZE THE EFFECT OF CHANGES IN BODY POSITION IN THIS STUDY, WE APPLIED THIS METHOD IN ADDITION TO OTHER STANDARD MEASUREMENT TECHNIQUES AND CONTINUOUSLY RECORDED BEAT-TO-BEAT VALUES OF SV AND OTHER CARDIOVASCULAR VARIABLES IN HEALTHY HUMANS DURING PASSIVE HEAD-UP TILT TO 30°, THEREBY INTRODUCING A MILD POSTURAL STRESS. IN THIS SITUATION, THE CAROTID BARORECEPTORS ARE LIFTED TO A POSITION SOME 25 cm ABOVE HEART LEVEL, MIGHT INDUCE REFLEX CHANGES.
cm $\times$ sin 30° (i.e., 25 cm $\times$ 0.5) above heart level, and
the pressure at the level of the carotid is thus $\sim$10
mmHg lower than at heart level. Passive tilting was
chosen to prevent interference from muscular reflexes.
The low tilt angle was chosen to make sure that the
quality of the ultrasound Doppler signal was satisfac-
tory during and after tilt. The aim of this study was
thus to analyze the dynamic time course of cardiovas-
cular changes during head-up tilt and that this
baroreflex compensatory mechanisms are symmetrical
during head-up and head-down tilt. We also hypothe-
sized that mechanical factors may have a different
impact on the time course of cardiovascular changes
during head-up and head-down tilt.

METHODS

Subjects. Seven volunteers, three men and four women
between the ages of 22 and 24 yr, were studied (Table 1). All
were healthy medical students, nonsmokers, and in good
physical shape. None was taking any medication or had any
signs of cardiovascular disease. Written, informed consent
was obtained from all participants, and the study was ap-
proved by the regional ethics committee.

Experimental design. Subjects were lightly dressed, and the ambient temperature was kept between 20 and 24°C. To
minimize cardiovascular variations induced by digestion, all
experiments were run at least 3 h after a light meal (20).
Subjects were familiarized with the test situations in several
pilot experiments, and none reported any discomfort during
tilting. During a period of 2–3 wk, two to three 1-h sessions
consisting of two to four experimental runs were held with
each subject.

On a manually driven tilt table, each subject was tilted
from supine to a 30° head-up position in $\leq$2 s. This position
was maintained for 2 min, and the subject was then tilted
back to a supine position in $\leq$2 s. Between tilting sessions,
subjects rested on the tilt table for $\sim$10 min. To minimize any
muscular activity, the subject was stabilized on the tilt-table
bed by a vacuum mattress preformed to the body. Cardiovas-
cular variables were continuously recorded during a period of
3 min before tilt, during tilt-up and the 2 min head-up tilted
position, during tilt back to supine position, and during the
following 3 min in the supine position. Great care was taken
to ensure that the fingers of the left hand, where arterial
pressure was recorded, stayed exactly at the level of the right
atrium throughout the tilting procedures.

Instrumentation. Beat-to-beat SV was recorded by using
an ultrasound Doppler method (2). A bidirecional ultra-
son Doppler velocimeter (model SD-100, GE Vingmed Ul-
trasound, Horten, Norway) was operated in pulsed mode at 2
MHz with a handheld transducer. The ultrasound beam was
directed from the suprastral notch toward the aortic root.
The sample volume range was adjusted so that measure-
ments were made 1–2 cm above the aortic valve. The sample
volume was positioned centrally in the aorta by searching for
the highest obtainable velocity signal. An angle of 20° be-
tween the directions of the sound beam and the bloodstream
was assumed in the calculations. To remove vessel wall and
valve motion artifacts, together with any recorded diastolic
movement of blood, the built-in high-pass filter in the SD-100
was set to remove signals originating from velocities $<0.275
m/s. The output of the SD-100 maximal velocity estimator
and a three-lead surface electrocardiogram were on-line in-
terfaced to a recording computer running a dedicated data
collection and analysis program (program for real-time data
acquisition, written by Morten Eriksen, Oslo, Norway).

In a separate session, the diameter of the rigid aortic ring
was determined by parasternal sector-scanner imaging
(model CFM-750, GE Vingmed Ultrasound, Horten, Nor-
way). On the assumption that the orifice was circular, this
diameter was used to calculate the area of the aortic valvular
orifice. SV was calculated by multiplying the value obtained
by numerical integration of the recorded instantaneous max-
imal velocity during each R-R interval by the area of the
orifice. The calculation is based on the assumption that the
velocity profile in the aortic valvular orifice is rectangular
and that this velocity is conserved as the central maximal
velocity of a jet 3–4 cm downstream (2).

The ultrasound Doppler transducer was handheld in the
suprasternal notch by one of the authors (K. Toska), who
stood beside the subject and followed the movement of the tilt
table during tilt up and tilt down. Blood flow velocity in the
ascending aorta was thus continuously recorded before, dur-
ing, and after tilt. Great care was taken to ensure that the
backscattered ultrasound signal was of good quality and that
the angle of insonication did not vary much during the
experiment. The quality of the signal was monitored and was
good in all the experiments included. Some 10% of the trials
were excluded because it was not possible to maintain a good
quality signal during tilt up.

Instantaneous HR was obtained from each R-R interval of
the electrocardiogram signal, and beat-to-beat CO was cal-
culated from the corresponding HR and SV values.

Finger arterial pressure was recorded continuously from
the third finger of the left hand (model 2300 Finapres blood
pressure monitor, Ohmeda, Madison, WI). Instantaneous
pressure output was transferred on-line to the recording
computer, and beat-to-beat MAP was calculated by numeri-
cal integration. Arterial pressure obtained by this method
has been shown to be in accordance with central, intra-
arterial pressure in various situations (4, 5, 11). Distortion of
the pressure waveform caused by pulse-wave transmission
and reflection in the brachial arteries will be canceled in the
process of beat-synchronous averaging for mean arterial
blood pressure (MAP) calculation.

Total peripheral conductance (TPC) as CO/MAP presupposes that the beat-to-beat averaged
flow into the aorta (CO) is equal to the averaged flow through the
resistance vessels. This is not the case during rapid
changes in arterial pressure, because the amount of blood

Table 1. Characteristics of the subjects and number of
experiments involving each of them

<table>
<thead>
<tr>
<th>Initials</th>
<th>Age, yr</th>
<th>Height, cm</th>
<th>Weight, kg</th>
<th>Number of Experiments</th>
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<td>IA</td>
<td>22</td>
<td>167</td>
<td>56</td>
<td>6</td>
</tr>
</tbody>
</table>

Letters in initial column are subjects’ initials. M, male; F, female.
stored in the aorta varies, depending on the changes in arterial pressure and the compliance of the aorta and the large arteries (9). However, changes in MAP were relatively small, and the beat-to-beat changes in TPC during larger changes in MAP were not evaluated. We also calculated TPC by using a value of 0.150 ml/mmHg for compliance of the aorta (14) to take blood storage into consideration.

All recorded signals, including the instantaneous angle of the tilt table, were on-line transferred to a recording computer running a dedicated data collection and analysis program.

Data analysis. Figure 1 shows a primary recording of the cardiovascular variables during one typical experiment. Throughout the recording period, there is considerable beat-to-beat variation in the recorded variables. These variations have previously been reported (1, 3) and are primarily due to the influence of respiration (3, 15). Variation in the recorded variables, which was unrelated to the experimental procedure, was eliminated partly by calculating the averaged response from a number of identical experimental runs in each subject (5–7). This was done by coherent averaging (12), using the onset of tilt up and tilt back for synchronization. Because the original beat-by-beat sampling was irregular, all recorded variables were first converted to a 10-Hz sampled signal by interpolation, and the averaged response was then calculated as the arithmetical mean of each set of synchronous samples for each 10-Hz time step (16, 18).

The individual baseline values for MAP, HR, and SV differed considerably from one subject to another, whereas the time courses of the cardiovascular responses during tilting were rather similar (Fig. 2). All individual response curves were therefore also pooled and normalized for calculation of the interindividual averaged responses (Figs. 3 and 4). The difference in the time course of changes during head-up and head-down tilt was statistically tested by the paired sign test.

RESULTS

The normalized, average responses of the recorded cardiovascular variables from 30 s before to 60 s after tilt up or tilt back are shown in Fig. 3 and are shown in higher time resolution in Fig. 4.

There was a clear asymmetry between the time course of cardiovascular changes during head-up tilt and tilt back. Adjustments generally took up to 30 s after head-up tilt, whereas most changes were com-
The asymmetry between tilt up and tilt back was most striking in the time course of changes in SV. After head-up tilt, SV was maintained for 4–6 s and then decreased steadily during the next 30 s to a stable level 25% below its pretilt value. However, after tilt back, SV increased rapidly to its pretilt value in <10 s. The individually averaged responses in SV are shown for each subject in Fig. 2, and the difference in time course between tilt up and tilt back was statistically significant ($P = 0.016$).

CO is determined as the product of beat-to-beat HR and SV. During head-up tilt, CO, after an initial small increase, decreased to a stable level of 4.8 l/min from 5.8 l/min during the first 30 s. During tilt-back, CO increased to its pretilt value in ~10 s, again with an initial overshoot.

After an initial small increase, TPC started to decrease ~5 s after head-up tilt and reached a stable level after ~30 s. During tilt back, TPC started to increase after ~3–4 s and was almost back to its pretilt level.

Fig. 3. Averaged responses based on normalized, pooled data from 5–7 identical experiments with each of 7 subjects. Total number of experiments = 41. Vertical, dashed lines indicate HUT (left) and tilt back to supine position (right).

Fig. 4. Same recordings as in Fig. 3, showing the initial 30 s of HUT (left) and tilt back to supine position (right) at a higher time resolution.
value after ~15 s. Both MAP and TPC showed a slow dampened oscillation of low amplitude after tilt back. All the variables returned to their control (pretilt) levels after tilt back.

DISCUSSION

The main finding in this study is the clear asymmetry in the time course of cardiovascular changes during head-up tilt and tilt back. Adjustments generally took up to 30 s after head-up tilt, whereas most changes were completed during the first 10 s after tilt back to a supine position. The fact that HR changes were equally rapid during both head-up tilt and tilt back supports our hypothesis that the time constants in the neural reflexes involved do not change significantly between the two situations. Thus the asymmetry may well be caused by mechanical factors. In the present study, we are able to describe the differences in detail, using absolute changes in CO and TPC. Some asymmetry in the response in CO has previously been observed even with the use of a much slower tilt and a lower time resolution in the recordings (10), and relative changes were studied in a recent study by using a pulse-contour method (21). The asymmetry between tilt up and tilt back was most striking in the time course of changes in SV. After head-up tilt, SV was maintained during the first 4–6 s and then decreased steadily during the next 30 s to a stable level 25% below its pretilt value. However, after tilt back, SV increased to its pretilt value in ~10 s.

This asymmetry may be partly explained by a more rapid change in left cardiac filling after tilt back than after tilt up. During tilt back, there must be a rapid inflow of stagnant blood from the legs and visceral regions, whereas venous valves will impede the backward filling of veins in the lower body during tilt up. An abrupt decrease in HR during tilt back may also contribute to a rapid change in cardiac filling by increasing filling time. In addition, MAP decreased rapidly during tilt back, which probably led to an abrupt decrease in left ventricular afterload and thus an increase in cardiac ejection fraction. During head-up tilt, MAP changed gradually.

The 25% decrease in SV during head-up tilt is in accordance with previous reports (10). The asymmetry between SV changes after tilt up and tilt back was recently described (21). The authors used a pulse-contour method to calculate relative changes in SV. In accordance with their findings, we found that SV started to fall after ~4–6 s. SV remains high for a few seconds because reduced filling of the right ventricle still allows maintained filling of the left side of the heart during a few heartbeats because blood is pumped out from the lungs, indicating that the lungs serve as a reservoir of blood during head-up tilt. There is a similar delay in the increase in SV during tilt back, and this is probably caused by the time it takes to circulate the increased blood volume of the right atrium through the lungs to the left side of the heart. The initial small dip in SV during tilt back may be caused by interventricular interaction because the increased filling of the right ventricle causes a decrease in filling of the left ventricle for a few heartbeats.

During head-up tilt, HR showed an immediate increase and initial overshoot, and it stabilized slightly above its pretilt value after ~30 s. After this, a very slight, linear increase in HR was seen. After tilt back, an increase in HR was seen initially in some subjects; this may have been a nonspecific reaction to the movement. After some initial fluctuations, HR decreased during the next few minutes and returned to its baseline level. The rapid changes in HR are consistent with previous findings that the parasympathetic HR response is almost immediate (18).

During head-up tilt, TPC decreased to a stable level after ~30 s. However, TPC showed an initial increase, which may have been caused by an increased perfusion pressure due to the effect of gravity on arterial pressure before the veins were filled with blood, thus distending the arteries. This may, in turn, have provoked a local, myogenic vasoconstriction response, but our methods do not allow us to distinguish between different effects such as a myogenic response and a peripheral vasoconstriction caused by baroreflexes.

The reflex adjustments of TPC start after 4–5 s, which is in accordance with our laboratory’s previous findings (17, 18). The results also clearly show that the slower responses in TPC compared with HR are the main cause of the longer term control of arterial pressure during both tilt up and tilt back to supine position. The adjustments in TPC are completed ~15 s after the tilting procedures.

In addition, we found the increase in arterial pressure at the level of the heart to be less than expected, taking into consideration the tilt-induced fall in arterial pressure at the level of the carotid baroreceptors. To our knowledge, this phenomenon has not been discussed in any depth in previous publications. In the present experiments, we took great care to measure arterial pressure at the level of the heart throughout the tilt. During head-up tilt, MAP at the level of the carotid baroreceptors will be 8–10 mmHg lower than MAP recorded at heart level. However, during head-up tilt, MAP increased by only 5 mmHg, from 79 to 84 mmHg. There are several possible explanations for this result. First, arterial pressure is known to be controlled by neurally mediated baroreflexes triggered by information both from carotid baroreceptors and from receptors in the aortic arch, which are situated just a few centimeters above heart level. Thus the signals from the aortic baroreceptors may counteract the unloading of carotid baroreceptors. The difference in pressure at the two sets of receptors, which give information on body position, may be integrated in a linear or nonlinear fashion in the central nervous system. Because of the rapidly adjusting cerebral autoregulation, the cerebral perfusion is not affected by the relative hypotension after head-up tilt. Recent studies have also shown that vestibular inputs lead to complex patterns of cardiovascular changes and signals from the vestibular otolith may modulate the baroreflex re-
sponses (7, 8). Carotid baroreflexes may show rapid adaptation or there may be other influences on the reflex control of arterial pressure during tilt, such as a change in the set point for arterial baroreflex control. Our laboratory has previously shown that the gain in arterial baroreflexes is very high at this level of arterial pressure (18) in the supine position, and thus it is not likely that the slight decrease in pressure at the level of the carotid baroreceptors is caused by an inability to adjust arterial pressure. However, a recent study (6) did show a slight decrease in baroreflex sensitivity in the 60° head-up tilted position, but the study did not directly estimate the efficiency of the control of arterial pressure.

In conclusion, we have revealed a characteristic asymmetry in the cardiovascular responses to inverse variations in gravity forces in humans. This can be partly explained by nonlinear hydrodynamic factors. The rapid changes in HR and slower changes in TPC are probably very similar in the two situations and are probably caused by nearly linear neural mechanisms in the two inverse tilting procedures. However, the decrease in MAP at the level of the carotid baroreceptors indicates that the set point or the gain in this reflex decreases during head-up tilt (6).

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Preliminary results from this study have already been presented in abstract form (19).

REFERENCES