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The impact of gravity during head-up tilt

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Abstract— **The impact of gravity during head-up tilt, a test often used in the clinic to diagnose patients who suffer from dizziness or frequent episodes of syncope, is not well described. This study uses mathematical modeling to analyze experimental blood pressure data measured at the level of the aorta and the carotid sinuses in a healthy volunteer. During head-up tilt the head is lifted above the heart stimulating gravitational pooling of blood in the lower extremities. This shift in volume is followed by an increase in blood pressure in the lower body, while the pressure in the head decreases, while the pressure at the level of the heart is either constant or increases. At the same time, the normal response to head-up tilt is an increase in heart rate. The change in posture, and subsequent change in heart rate, is believed to be mediated via baroreflex inhibition. Traditional understanding of the baroreceptor system is that inhibition is a result of a blood pressure drop. However, only the carotid sinus blood pressure is decreased during head-up tilt, suggesting that the receptors at this location are more prominent than the receptors in the aortic arch. To explore this hypothesis further, we developed a model predicting hydrostatic height between the two locations. Results from this model were compared with measurements. Furthermore, we show, using a differential equations model predicting blood pressure, that it is possible to predict blood pressure measured at the level of the carotid sinuses using heart rate as an input. Finally, we discuss our results in relation to measurements obtained at the two locations.**

I. Introduction

Head-up tilt is a test commonly performed to asses patients who are suffering from dizziness or frequent episodes of syncope [3]. This test is performed by having patients lie on their back on a flat tilt-table. Continuous measurements of blood pressure and heart rate are obtained for a period of 10-15 minutes to obtain a steady recording. The table is then tilted to a 60-70^o degree angle for another 5-10 minutes after which the table is tilted back to horizontal position (before the subject experiences any symptoms of dizziness or syncope). During the tilt, blood pressure in the lower body (including at the level of the heart) increase due to gravitational pooling of the blood in the lower extremities, while blood pressure in the head, above the hydrostatic center, decreases. The typical response to head-up tilt is an increase in heart rate, and it is believed [4], that the heart rate response is mediated via the autonomic nervous system, in particular via inhibition of the arterial baroreceptors. According to current understanding of baroreceptor function, a baroreceptor mediated increase in heart rate is a response to a decrease of blood pressure.

Several previous studies (e.g. [10], [9], [5], [6]) have studied baroreflex regulation, and several of these studies have found that the baroreceptor function was difficult to asses. However, most of these studies were based on analysis of blood pressure measurements obtained at the level of the heart. At the same time, baroreceptor studies in animals where the head is located at the level of the heart, have been more successful, e.g. the study [1] designed to assess hypertension in rats have showed that the receptors in the aortic arch play a more important role than carotid sinus receptors.

In this study, we will show that in humans, whose head is on top of the heart, blood pressure increases at the level of the heart, while it decreases (as expected) at the level of the carotid arteries. Using these observations, we show, that if blood pressure is measured at the level of the carotid sinuses the anticipated heart rate increase can be predicted using a mathematical model. These results motivated us to hypothesize that during head-up tilt, the carotid sinus baroreceptors play a more prominent role than the baroreceptors located in the aortic arch.

II. Methods

A. Experimental studies

Experimental data analyzed in this study include heart rate and arterial blood pressure measured during head-up tilt to a 60^o angle (see Fig. 1). During the tilt blood pressure was measured simultaneously (with two Finapres devices) at two locations: at the level of the heart and at the level of the carotid sinuses (see Fig. 2). At both locations blood pressure was measured in the middle finger of the left and right arm, respectively. The exact location of the heart (or more precisely, the aortic arch) and the carotid sinuses were found using Doppler imaging and echocardiography. At the same time heart rate was recorded from a standard 3-lead ECG. Data were sampled at 1000 Hz and processed using the Chart analysis program, ADInstruments. Finally, the distance between the aortic arch and carotid sinus was measured using a ruler.

B. The baroreceptor control system

The body aims to maintain homeostasis: within the cardiovascular system the aim is to maintain blood pressure and

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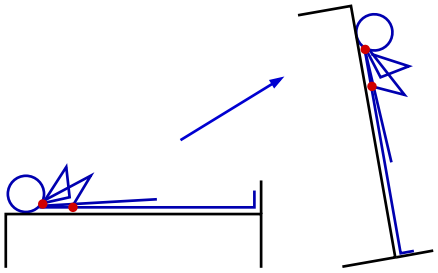

Fig. 1. Head-up tilt procedure. The subject is tilted to an angle of 60^o over a period of 7 sec. Blood pressure (mmHg) and heart rate (betas/min) is measured using a Finapres devise at the level of the heart and carotid sinuses, marked by two red circles in the figure. Heart rate was measured using a standard 3-lead ECG.

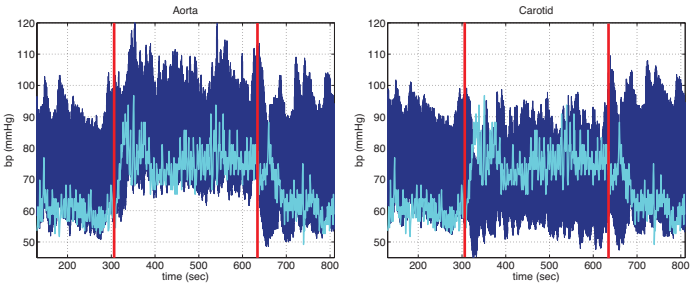

Fig. 2. Blood pressure (mmHg, dark blue) and heart rate (beats/min, cyan) measurements from the finger held at the level of the heart (aortic arch) (left) and carotid (right) sinuses. The vertical (red) lines mark the beginning and end of the tilt.

flow at constant levels. Several control systems contribute to maintaining homeostasis. Immediately following head-up tilt, one of the important controls is mediated by stimulation of the arterial baroreceptors located in the aortic arch and the carotid sinuses (see Fig. 3). Baroreceptors are stretch receptors that when stimulated modulate the firing rate in the afferent baroreceptor nerves. It is believed, that the stretch receptors are stimulated via modulation of arterial blood pressure. The receptors' are inhibited during head-up tilt [4], where a blood pressure decrease causes a decrease of the afferent firing rate. The afferent impulses are integrated in the nucleus solitary tract, from this location efferent stimuli emanate. A decrease in the afferent firing rate leads to parasympathetic withdrawal and sympathetic activation, which both in turn lead to an increase in heart rate. When the subject is tilted blood is pooled in the lower extremities. Typically blood pressure is constant or increased at the level of the heart, because the heart for most people is located below the center of gravity. At the same time, blood pressure is decreased near the carotid sinuses that are located above the center of gravity. Experimental data analyzed in this study (see Fig. 2) follow this trend. Similarly, the heart rate typically increases during head-up tilt, a trend also observed in the experimental data analyzed in this study (see Fig. 2). These observations suggests that during head-up tilt baroreceptors in the carotid sinuses play a more important role than the receptors in the aortic arch.

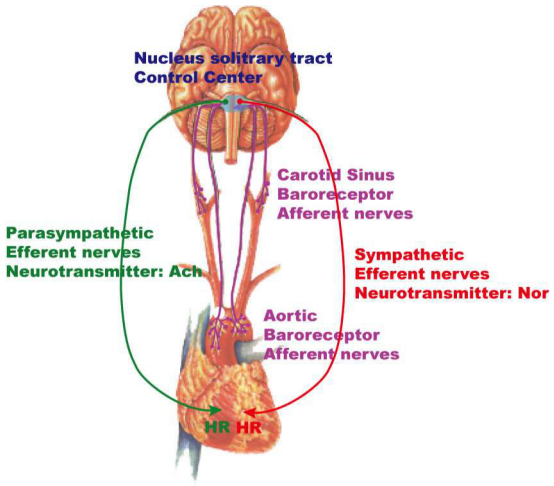

Fig. 3. Baroreceptor feedback system. A drop in blood pressure causes a decrease in the afferent firing rate. The afferent impulses are integrated in the nucleus solitary tract. From here parasympathetic innervation and sympathetic stimulation via a decrease in concentration of acetylcholine (parasympathetic) and an increase in the concentration of noradrenaline (sympathetic) stimulate an increase in heart rate.

C. Mathematical modeling

In this study, two results will be presented, first we show that it is possible to predict the distance between the two measurement locations using the measured pressure as an input. Second we show using a compartmental model, that the response to head-up tilt observed in the carotid artery can be predicted by the model.

1) Impact of hydrostatic gravity: For this analysis, we assume that the vessels in the cardiovascular system can be represented by compliant cylinders. The head-up tilt can then be modeled by tilting the cylinders from horizontal to vertical position. If no other forces impact the system, the hydrostatic difference between the aorta and the carotid sinuses can be predicted by

$$\rho g h \sin(\theta) = \overline{p}_{ao} - \overline{p}_{ca}, \tag{1}$$

where $\rho = 1.06$ g/cm^3 is the blood density, $g = 981$ cm/sec^2 is the gravitational acceleration, and $h\sin(\theta)$ cm is the hydrostatic height difference between the two locations at the tilt angle θ. In our study, $0 < \theta \leq 60$. Finally $\overline{p}_{ao}$ denotes the mean pressure measured at the level of the heart and $\overline{p}_{ca}$ denotes the mean pressure measured at the level of the carotid sinuses. Mean pressures are obtained by integrating continously measured blood pressures over each cardiac cycle. Using the beat-by-beat meanpressures obtained at the level of the heart and the carotid sinuses, we solved (1) to predict the height h.

2) Modeling blood pressure dynamics during head-up tilt: In our second study we used the compartmental model including arteries and veins in the systemic circulation shown in Fig. 4 to predict blood pressure measured at the level of the carotid artery. For simulations done with this model we used the measured heart rate as an input to the model.

The compartmental model assumes conservation of vol-

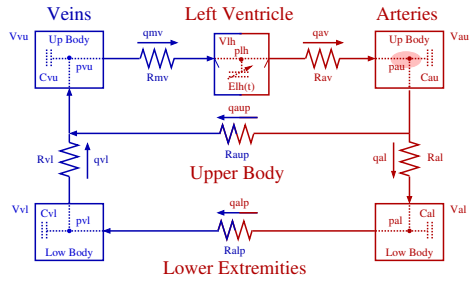

Fig. 4. Compartment model of the systemic circulation including the left ventricle (lh) as well as arteries (au, al) and veins (vu, vl) in the upper and lower body. The pressure in the upper body arteries (marked with a pink oval) indicates location used for validation against data.

ume, i.e.,

$$\frac{dV}{dt} = q_{in} - q_{out}, \tag{2}$$

where V (ml) is the compartment volume, and q (ml/sec) is the volumetric flow rate. For each of the arterial and venous compartments, volume conservation is combined with a pressure volume relation of the form

$$V - V_{un} = C(p - p_{ext}), \tag{3}$$

where V_{un} (ml) (constant) is an unstressed volume, C (ml/mmHg) is the compartment compliance, and $p_{ext} = 0$ (mmHg) is the tissue pressure. To obtain a differential equation predicting pressure in each compartment (3) is differentiated and the volume change is predicted by (2),

$$\frac{dp}{dt} = \frac{1}{C}\frac{dV}{dt} = \frac{1}{C}\left(q_{in} - q_{out}\right).$$

To obtain an expression for the volumetric flow rate (accounting for differences in hydrostatic pressure modulated during the tilt), we consider Newton's second law ($F = ma$), which for flow through a cylinder can be written as

$$m\frac{dv}{dt} = \rho\Delta z A\frac{d}{dt}\left(\frac{q}{A}\right) = \rho\Delta z\frac{dq}{dt} = \sum F$$

where m (ml) denotes the mass of the blood, v (ml/sec) the average velocity of blood through the cylinder. $\rho = 1.06$ g/cm^3 denotes the blood density, h (cm) the length of the cylinder. We further assume that the velocity v (cm/sec) can be computed from the volumetric flow rate q (ml/sec) and the cross-sectional area A (cm^2) of the cylinder. Finally, we assume that forces acting on the system can be summarized in F. Forces relevant to flow in a cylinder include gravitational forces, pressure forces, and forces imposed by friction (we assume the latter is proportional to qAR, where R (mmHg sec/ml) denotes the resistance to flow in the cylinder. With these assumptions we obtain

$$\rho h\frac{dq}{dt} = \rho g h A\sin(\theta) + (p_{in} - p_{out})A - qAR,$$

where $0 < \theta \leq 60^o$ denotes the tilt angle, and p_{in}, p_{out} denote the pressures at each end of the cylinder. Assuming that the acceleration of flow is small, i.e., that $dq/dt \ll 1$ we obtain

$$q = \frac{\rho g h\sin(\theta) + p_{in} - p_{out}}{R}.$$

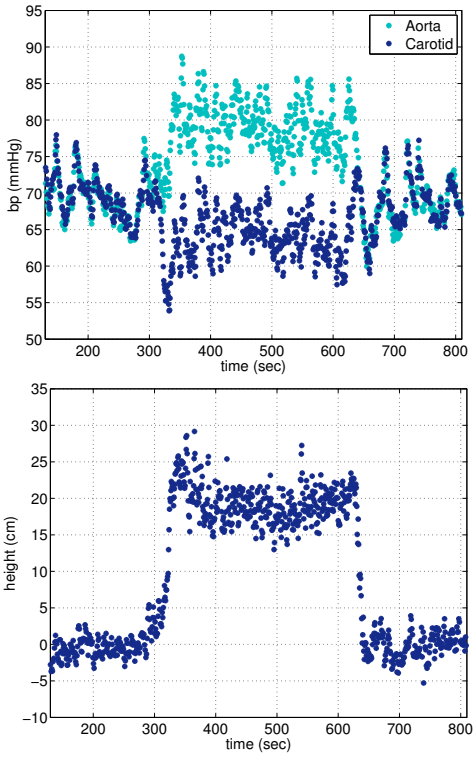

Fig. 5. The top graph shows the average blood pressure at the two locations: aorta (light blue dots) and carotid (dark blue dots). The bottom graph shows heights predicted using (1).

The tilt to a 60^o angle takes approximately 7 seconds. Consequently we let $h(t)$ be 0 while in supine position and then increase $h(t)$ linearly to the height predicted/measured during the tilt. Similar to previous studies [2], [8], ventricular pumping was achieved using a model predicting elastance of the left ventricle, i.e., for this compartment we let $p_{lv} = E_{lv}(t)(V_{lv} - V_{un,lv})$. Opening and closing of the valves was achieved using variable resistances R_{av} and R_{mv}.

Finally, also similar to our previous study [8], the baroreflex regulation of vascular resistance (R_{aup}, R_{alp} and cardiac contractility E_s (a parameter associated with prediction of E_{lv} [11]) was modeled using a differential equation of the form

$$\frac{dx}{dt} = \frac{-x + x_{ctr}(\overline{p}_{au})}{\tau}, \tag{4}$$

where $x = R_{aup}, R_{alp}, E_s$ and x_{ctr} is a decreasing sigmoidal function of mean blood pressure.

III. Results

Results shown here are from one representative subject. First Fig. 5 shows, the mean blood pressure for each cardiac cycle predicted at each of the two locations as well as the height predicted using (1). The average computed height during the upright tilt (at 60^o) was 19 ± 3.5 cm, while the corresponding measured height was 21 cm.

Second we show results predicted using the compartmental model. Fig. 6 (top graph) shows carotid sinus (or upper body) blood pressure predicted using nominal parameter

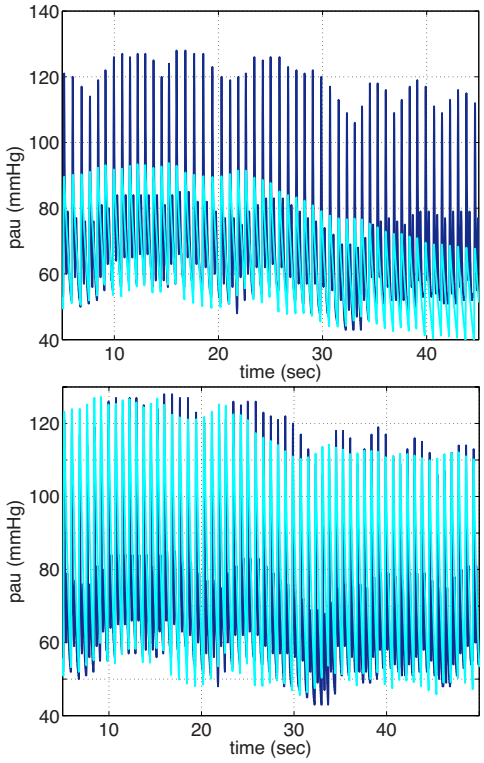

Fig. 6. The top graph shows the carotid sinus blood pressure (light blue) as well as measured values (dark blue) predicted using nominal parameter values and the bottom graph shows the corresponding blood pressures, where the model predicted pressures were computed optimized parameter values.

values. Results are computed only during the short timespan immediately following head-up tilt. Sensitivity analysis and subset selection (as described in previous studies [2], [11]) were used to determine a subset of parameters including parameters associated with control (parameters associated with (4)) of the lower body peripheral resistance R_{alp} and cardiac contractility E_s, as well as parameters representing upper body arterial resistance R_{aup}, arterial C_{au} and venous C_{vu} compliance in the upper body. Subsequently, nonlinear least squares optimization (using the Levenberg Marquart method [7]) was used to estimate the subset of parameters, results predicting arterial blood pressure at the level of the carotid sinus using heart rate as an input is shown in Fig. 6 (bottom graph).

IV. Discussion

Results of our studies show that at the carotid sinuses blood pressure drops as expected, and our mathematical model predicting blood pressure using heart rate as an input was able to predict the measured data. In this study, we did not yet apply the model to the data measured at the level of aorta, but we anticipate that results of such simulations would not be successful, primarily because the model is developed to predict a drop in blood pressure associated with an increase in heart rate. Consequently, this study suggests that if the aim is to asses baroreflex sensitivity, measuring pressure at the level of the carotid sinuses is preferential to measurements obtained at the level of the heart. Following this observation, a question arise: Can the vast amount of data collected at the level of the heart be converted to carotid pressures, simply by applying the relation proposed in (1)? If so, these predicted carotid pressures, have potential, to be used to obtain a more reliable predictor of baroreceptor function. Before answering this question, we analyze the predicted heights further.

If gravity was the only contributor to the difference in pressures observed at the level of the heart and at the carotid sinuses, the predicted heights shown in Fig. 5 (bottom) should vary from 0 cm to the measured height following the constant tilt table speed. However, note that immediately following the tilt, the height increases above the predicted height, after which it decreases back toward the measured value of 21 cm. This slight overshoot in the height may be an indicator that a slight differentiation between aortic and carotid sinus baroreceptors are present, consequently, care must be taken if existing aortic data is used for prediction of carotid sinus pressure. One suggestion, to investigate this phenomena more carefully, would be to build a mathematical model that can use both carotid and aortic pressures in prediction of the baroreflex response. Finally, it should be emphasized that results shown here were from a representative subjects, more subjects should be included to investigate our hypothesis in more detail.

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