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P136: SIMULATING MYOCARDIAL OXYGEN BALANCE CHANGES DUE TO ANTI-HYPERTENSIVE DRUGS

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Nowadays employment world is increasingly shifting towards service-related labour, changing focus from physiological to psychological loads for workers. Thus, a deeper psychological stress understanding arises, not only for jobs within extreme conditions (as astronauts or pilots) but also for regular jobs with high emphasis on mental stressors. With the intent of developing a method and technology able to detect psychological stress we perform this pilot laboratory study in 14 male volunteers under stress and relax situations. As a stressor and the relaxer were used a standardized cognitive Paced Auditory Serial Addition Test (PASAT) and a relaxing video, respectively. Galvanic Skin Response (GSR) and Heart Rate (HR) were continuously measured as golden standard techniques to indicate physiological stress levels. Before each stimulus intervention a Braquial Blood Pressure were measured by standard Omron M6 apparatus. A continuous monitoring of Central Aortic Pressure (CAP) were assessed by non-invasive small WiFi sensors and equipment, developed by NMT, S.A., which allowed on-line detection and long-term effect of stress evaluation. HR and GSR measurements showed high variations under stressor application, proving physiological stress among volunteers and validating PASAT suitability. From analysis of obtained CAP data were found the good correlation with HR and GSR measurements in both, stress and relax sections. In addition of being a highly innovative study on mental stress detection, it is obvious the necessity of increase study population in future similar studies in lab and/or in the field condition.

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A COMPUTATIONAL INVESTIGATION OF CONFOUNDING FACTORS AFFECTING FLOW MEDIATED DILATION: TOWARDS IMPROVED ENDOTHELIAL FUNCTION ASSESSMENT

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Objective and motivation: Endothelial dysfunction is associated with cardiovascular diseases. Flow mediated dilation (FMD), assesses the endothelial function by measuring the brachial artery vasodilation following deflation of a sphygmomanometer cuff around the forearm. Vasodilation is assumed to be due to an increase in wall shear stress (WSS) only. However, there is evidence that the vasodilation may be affected by other confounding factors¹. We aim to investigate the effects of confounding factors on the results of FMD. **Methods:** A dynamic simulation of FMD was carried out using a one-dimensional haemodynamic solver of blood flow in the arm arterial vasculature (Fig. 1a) ². Haemodynamics during cuff deflation was simulated by prescribing a decrease in peripheral resistance (Fig. 1b) in a novel mathematical model which dynamically couples increasing WSS (Fig. 1c) to decreasing arterial wall Young's modulus (Fig. 1d), taking into account endothelial function. **Results:** Our results show that the initial increase in flow velocity (Fig. 1e) is caused by the prescribed decrease in peripheral resistance and leads to an initial pressure drop affecting the FMD value. WSS induces a drop in Young's modulus leading to vasodilation (Fig. 1f). In addition, for the same prescribed endothelial function (relating WSS to Young's modulus variation) and decreased peripheral resistance, FMD increases with decreasing arterial stiffness (3.17% vs 5.31% vs 8.56% (Fig. 1f)). **Conclusion**Our numerical model successfully described FMD haemodynamics and highlighted one of the important confounding factors of FMD values: arterial stiffness. We are currently investigating other factors and ways of correcting those factors.

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SYSTEMIC CARDIOVASCULAR INPUTS IN MODELS ESTIMATING INTRACRANIAL PRESSURE MAGNITUDE AND WAVEFORM

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Background: Monitoring Intracranial Pressure (ICP) is key for appropriate clinical treatment of patients with conditions potentially causing raised ICP. The adequacy of using Heart Rate (HR), aortic Blood Pressure (aBP) and carotid Blood Flow (cBF) to estimate ICP magnitude (pulse and mean)

and waveform is investigated as an alternative means to invasive ICP measurement.

Methods: ICP (sequentially raised from resting ICP to 30–40 mmHg with infusions of artificial intracranial fluid), aBP (lowered with sodium nitropruside and raised with phenylephrine, 30 µg/kg/min, across a physiological range), HR (paced at 400 and 500 bpm), and cBF were measured in 11 anaesthetised Sprague Dawley rats. Potential cardiovascular predictors of ICP magnitude were assessed by stepwise mixed-model regression. Two transfer function models were constructed to estimate the ICP waveform from aBP or cBF waveforms.

Results: Systolic, mean and diastolic aBP as well as peak and minimum cBF had significant predictive value for mean ICP ($p < 0.001$, $R^2 = 0.25$). HR ($p < 0.05$), systolic and mean aBP ($p < 0.001$), peak ($p < 0.001$), mean ($p < 0.05$) and minimum ($p < 0.01$) cBF had significant value for pulse ICP ($R^2 = 0.35$). The transfer function models showed potential to reproduce the ICP waveform (Root Mean Square Error (RMSE) ≤ 4 mmHg), being more accurate for mean aBP above 100 mmHg and mean ICP below 20 mmHg (RMSE ≤ 0.5 mmHg).

Conclusions: The models developed from the comprehensive rat experiment demonstrated that systemic cardiovascular measures have predictive value in estimating the ICP magnitude and waveform, but other inputs may be necessary to improve accuracy in estimating ICP across the full physiological range.

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SIMULATING MYOCARDIAL OXYGEN BALANCE CHANGES DUE TO ANTI-HYPERTENSIVE DRUGS

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Background: Hypertension clinical treatment largely relies on different drugs. Some of these drugs are thought to exhibit specific protective functions in addition to those resulting from blood pressure reduction per se. Through a validated multiscale mathematical model of the cardiovascular system, we studied the impact of commonly-used antihypertensive drugs on myocardial oxygen supply–consumption balance, which plays a crucial role in type 2 myocardial infarction.

Methods: Forty-two wash-out hypertensive patients were included in this study. Patients' demographics, heart rate, brachial pressure, Left Ventricular (LV) volumes and carotid-femoral pulse wave velocity were used to set to patient specific condition a largely accepted benchmark data set describing generic healthy subjects. Starting from literature data, drugs effects were modeled by means of six coefficients, describing LV function, heart rate, peripheral resistances and arterial stiffness. These drug-specific sextuplets were used to multiply some parameters of each patient model to simulate drugs impact.

Results: Our results ascribed the well-known major cardioprotective efficiency of β blockers to a positive change of myocardial oxygen balance. This was due to the concomitant reduction in LV work and increase in coronary flow. Similarly, RAAS blockers induced several positive changes, but to a reduced extent. In contrast, calcium channel blockers seem to induce some potentially negative effects on myocardial oxygen balance.

Conclusions: Patient specific multiscale mathematical model is able to reproduce clinically-relevant changes in coronary hemodynamics and ventricular function driven by anti-hypertensive drugs. Further studies are needed to evaluate eventual clinical usefulness of in-silico modeling of anti-hypertensive drugs.

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ESTIMATING LEFT VENTRICULAR ELASTANCE FROM NONINVASIVE AORTIC FLOW AND BRACHIAL PRESSURE MEASUREMENTS

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Background and Aim: Left Ventricular (LV) End-systolic elastance (Ees) serves as a major determinant of cardiac systolic contractility. Traditional Methods: to evaluate the ventricular mechanics directly from measurements require intraventricular pressure and volume recordings during an acute preload