Overall research theme:

Gravity and Weightlessness to Understand Cardiovascular and Fluid Volume Control in Humans

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Characteristics of the research group:

The cardiovascular system and renal function in humans are sensitive to changes in gravitational stress. Therefore, the research group utilizes gravity and weightlessness to stimulate cardiovascular reflexes and modulate renal sodium and water handling.

The purpose of the research programme is to answer the questions: 1) How are the volume of fluid and amount of salt detected in the human body in health and disease, 2) what are the links between the volume and salt sensing mechanisms and the kidneys, and 3) how does gravity modulate arterial pressure regulation.

Changes in the gravitational load on the body are induced by postures, water immersion and weightlessness. Weightlessness can be obtained for short periods during parabolic flights and for longer periods during spaceflight. Non-invasive techniques are used for estimation of cardiac output (foreign gas rebreathing) and arterial pressures. Techniques for measurements of concentrations in blood and urine of cardiovascular and kidney regulating hormones have been developed by our collaborators to understand the neuroendocrine regulation of arterial pressure and sodium balance.

The research group has obtained experimental access to the Space Shuttle and the International Space Station. Furthermore, the group has set up a Ph.D.-programme to investigate the mechanisms of renal sodium and water retention in heart failure.

Running projects: Titles and abstracts:

Cardiovascular effects of moderate changes in sodium intake in heart failure

We have shown that increasing sodium intake from 70 to 250 mmol/24 h over a 4-day period increases cardiac output and stroke volume by some 15%, when the subjects are upright seated (Damgaard et al. 2002). Furthermore, we have shown that immersing seated heart failure patients in water improves their cardiovascular status and neuroendocrine profiles (Gabrielsen et al. 2001). Therefore, the aim of the current study is to test the hypothesis that a moderate increase in sodium intake in heart failure patients will increase cardiac output and arterial filling and suppres the vasoactive hormone releases. If the hypothesis is confirmed, sodium intake should not always be restrictive in treatment of heart failure.

Methodological improvements of the foreign gas rebreathing technique for estimation of cardiac output and oxygen uptake in humans

The foreign gas rebreathing method is a user friendly, non-invasive method for estimation of cardiac output in humans. During a 30-s rebreathing procedure in a closed lung to bag-system, a gas mixture of tracer gasses are mixed with air in the lungs. By measuring the concentration of the gasses through the

mouthpiece during rebreathing, the disappearance rate of the gasses into blood can be determined. By knowing the blood solubility coefficients of the tracer gasses, the amount of blood flowing through the lungs can be calculated. This is equal to cardiac output. Gas analysis is performed continuously by a newly developed equipment (Innocor, Innovision A/S) utilizing an infrared photo-acoustic technique. In this study, we are testing the limitations and advantages of the equipment in order to improve the rebreathing procedures. The work is performed in collaboration with industry.

Prolonged effects of head-down bed rest on cardiovascular, endocrine and renal variables in humans

Prolonged head-down tilted bed rest of 6° is a currently used model to simulate the effects of weightlessness in humans. We have previously shown that the effects of prolonged spaceflight and head-down tilted bed rest, respectively, on renal water handling is not similar (Norsk et al. 2000). In close collaboration with the German space center DLR in Cologne, we are involved in a major multinational and multidisciplinary head-down tilted bed rest study. The aim is to determine the longterm effects of bed rest on sympathetic nervous activity and renal sodium and water handling. The data will then be compared to data obtained in space. By determining the mechanisms of the differences in effects of head-down bed rest and spaceflight, further insight might be gained into how gravity modulates the interaction of cardiovascular reflexes, sympathetic nervous activity and renal sodium and water handling in humans.

Prolonged effects of weightlessness on cardiovascular, endocrine and renal variables in humans

Five Danish experiments have been selected for the Space Shuttle and International Space Station. It is the purpose to compare the effects of spaceflight and prolonged head-down tilted bed rest on cardiovascular, endocrine and renal variables. Furthermore, it is the purpose to compare the measurements with those obtained in heart failure patients. In this way, it is the aim to gain insight into how gravity is involved in the pathophysiology of heart failure. Furthermore, it is also the purpose to gain more insight into the mechanisms of postflight orthostatic intolerance.

Recent publications related to the projects described above:

1. NORSK, P., N. J. CHRISTENSEN, P. BIE, A. GABRIELSEN, M. HEER, AND C. DRUMMER. Unexpected renal responses in space. The Lancet 356: 1577-78, 2000.

2. PUMP, B., M. SHIRAISHI, A. GABRIELSEN, P. BIE, N. J. CHRISTENSEN, AND P. NORSK. Cardiovascular effects of static carotid baroreceptor stimulation during water immersion in humans. Am. J. Physiol. 280: H2607-15, 2001

3. PUMP, B., T. KAMO, A. GABRIELSEN, AND P. NORSK. Mechanisms of hypotensive effects of a posture change from seated to supine in humans. Acta Physiol. Scand. 171: 405-12, 2001.

4. BESTLE, M. H., P. NORSK, AND P. BIE. Fluid volume and osmoregulation in humans after a week of head down bed rest. Am. J. Physiol. 281: R310-17, 2001.

5. GABRIELSEN, A., P. BIE, N. H. HOLSTEIN-RATHLOU, N. J. CHRISTENSEN, J. WARBERG, H. DIGE-PETERSEN, E. FRANDSEN, S. GALATIUS, B. PUMP, V. B. SØRENSEN, J. KASTRUP, AND P. NORSK. Neuroendocrine and renal effects of intravascular volume expansion in compensated heart failure. Am. J. Physiol. 281: R459-67, 2001.

6. PUMP, B., T. KAMO, A. GABRIELSEN, P. BIE, N. J. CHRISTENSEN, AND P. NORSK. Central volume expansion is pivotal for sustained decrease in heart rate during seated to supine posture change. Am. J. Physiol. 281: H1274-9, 2001.

7. PUMP, B., M. DAMGAARD, A. GABRIELSEN, P. BIE, N. J. CHRISTENSEN, AND P. NORSK. Atrial distension, arterial pulsation and vasopressin release during negative pressure breathing in humans. Am. J. Physiol. 281: H1583-88, 2001.

8. SCHOU, M., B. PUMP, A. GABRIELSEN, C. THOMSEN, N. J. CHRISTENSEN, J. WARBERG, AND P. NORSK. Cardiovascular and neuroendocrine responses to left lateral position in non-obese young males. J. Grav. Physiol. 8: 15-20, 2001.

9. SHIRAISHI, M., M. SCHOU, M. GYBEL, N. J. CHRISTENSEN, AND P. NORSK. Comparison of acute cardiovascular responses to water immersion and head-down tilt in humans. J. Appl. Physiol. 92: 264-68, 2002.

10. GABRIELSEN, A., R. VIDEBÆK, M. SCHOU, M. DAMGAARD, J. KASTRUP, AND P. NORSK. Non-invasive measurement of cardiac output in heart failure patients using a new foreign gas rebreathing technique. Clin. Sci. 102: 247-52, 2002.

11. GABRIELSEN, A:, B. PUMP, P. BIE, N. J. CHRISTENSEN, J. WARBERG, AND P. NORSK. Atrial distension, haemodilution, and acute control of renin release during water immersion in humans. Acta Physiol. Scand. 174: 91-99, 2002.

12. SCHOU, M., A. GABRIELSEN, N. E. BRUUN, P. SKØTT, B. PUMP, H. DIGE-PETERSEN, E. FRANDSEN, P. BIE, J. WARBERG, N. J. CHRISTENSEN, AND P. NORSK. Angiotensin II attenuates the natriuresis of water immersion in humans. Am. J. Physiol. 283: R187-R196, 2002.

13. GABRIELSEN, A., P. BIE, N. J. CHRISTENSEN, E. FRANDSEN, S. GALATIUS, B. PUMP, V. B. SØRENSEN, J. KASTRUP, AND P. NORSK. Systemic vascular resistance during brief withdrawal of angiotensin converting enzyme inhibition in heart failure. Scand. J. Clin. Lab. Invest. 62: 245-254, 2002.

14. PUMP, B., U. TALLERUPHUUS, N. J. CHRISTENSEN, J. WARBERG, AND P. NORSK. Effects of supine, prone, and lateral positions on cardiovascular and renal variables in humans. Am J. Physiol. 283: R174-R180, 2002.

15. DAMGAARD, M., A. GABRIELSEN, M. HEER, J. WARBERG, P. BIE, N. J. CHRISTENSEN, AND P. NORSK. Effects of sodium intake on cardiovascular variables in humans. Am. J. Physiol. 283 (in press), 2002.