Poster #48

Cardiovascular and cerebrovascular responses to urodynamics testing after spinal cord injury: the influence of autonomic injury

V.-E.M. Lucci[1,2], I.S. Sahota[1,2], M.S. McGrath[1,2], H.J.C. (Rianne) Ravensbergen[1,2], V.E. Claydon[1,2]
[1]Department of Biomedical Physiology and Kinesiology, Simon Fraser University, Burnaby, BC, Canada; [2]International Collaboration on Repair and Discoveries (ICORD), University of British Columbia, Vancouver, BC, Canada

Background: Autonomic dysfunction is a prominent concern following spinal cord injury (SCI). In particular, autonomic dysreflexia (AD; paroxysmal hypertension in response to sensory stimuli below the level of injury that is often associated with bradycardia) is common in autonomically complete injuries at or above T6. AD is currently defined as a > 20 mmHg increase in systolic arterial pressure (SAP) from baseline, without specific heart rate (HR) criteria. Urodynamics testing (UDS) is performed routinely after SCI to monitor urological sequelae, often provoking AD in high-level SCI. We, therefore, aimed to assess the impact of autonomic injury on cardiovascular and cerebrovascular responses during UDS in individuals with chronic (> 1 year) SCI.
Methods: Following blood draw (plasma norepinephrine [NE]), continuous SAP, HR, and cerebral blood flow (CBF) were recorded at baseline (10-min supine), during standard clinical UDS, and recovery (10-min supine) ($n = 22$). Low frequency variability in systolic arterial pressure (LFSAP; a marker of sympathetic modulation of blood pressure) and cerebral resistance were determined. High-level injury ($\geq$ T6) with blunted/absent LFSAP (< 1.0 mmHg^2) and/or low plasma NE (< 0.56 nmol•L^{-1}) indicated autonomically-complete injury. Known electrocardiographic markers of atrial (p-wave duration variability) and ventricular arrhythmia (T-peak—T-end variability) were evaluated at baseline and during UDS.
Results: Nine participants were determined as autonomically-complete, yet 20 participants had increased SAP > 20 mmHg during UDS. Of these 20 participants, 10 experienced bradycardia (HR $<$ 60 bpm) during UDS, 7 of which were considered autonomically-complete based on criteria. Maximum SAP was higher in autonomically-complete injuries (207.1 ± 12.3 mmHg) compared to autonomically-incomplete injuries (165.9 ± 5.3 mmHg) during UDS ($p < 0.001$). HR during UDS was reduced compared to baseline ($p = 0.056$) and recovery ($p = 0.048$) only in autonomically-complete lesions. CBF was not different between groups or phases (all $p > 0.05$). However, cerebrovascular resistance was increased during UDS in autonomically-complete injuries compared to baseline ($p < 0.001$) and recovery ($p < 0.001$). Risk for both atrial and ventricular arrhythmia increased during UDS compared to baseline ($p < 0.05$), particularly in autonomically-complete injuries ($p < 0.05$).
Conclusion: UDS is recommended yearly in chronic SCI but is associated with profound AD and an increased risk of arrhythmia, highlighting the need for continued monitoring during UDS. Our data also highlight the need for HR criteria in the definition of AD.
Funding: Heart and Stroke Foundation of Canada.

Poster #49

Rapid sympathetically-mediated increases in circulating leukocytes during experimental muscle pain

C. Daria[1,2], G. Lancaster[1,2], A. Murphy[1,2], L.A. Henderson[3], T. Dawood[1,2], *V.G. Macefield*[1,2]
[1]Baker Heart and Diabetes Institute, Melbourne, Australia; [2]Baker Department of Cardiometabolic Health, The University of Melbourne, Australia; [3]Brain and Mind Centre, The University of Sydney, Sydney, Australia

Work from our lab has shown that long-lasting muscle pain causes a sustained increase in muscle sympathetic nerve activity (MSNA), blood pressure (BP) and heart rate (HR) in some individuals (Responders) but not in others (Non-Responders). Given the interaction between the sympathetic and immune systems, we hypothesised that there will be a sympathetically mediated inflammatory response in the Responder group, as evidenced by release of leukocytes into the circulation. MSNA was recorded from 14 participants via tungsten microelectrodes inserted percutaneously into the common peroneal nerve. Blood samples were taken via an intravenous cannula in the arm every 5 min during 15 min of baseline, during muscle pain induced by infusion of 5% hypertonic saline into the tibialis anterior muscle for 40 min, and during 20 min of recovery. Eight participants (57%) showed significant increases in MSNA burst amplitude during pain (119.1 ± 8.8% above baseline), while six (43%) showed no response (96.2 ± 7.9%). There were significant differences between the Responder and Non-Responder groups ($P < 0.0058$), but no significant differences in peak pain ratings between the two groups (6.3 ± 1.1 vs 5.5 ± 2.2 out of 10, $p = 0.3091$). In the Responder group leukocyte count increased within the first 5 min of pain and remained elevated for the duration of muscle pain, showing significant positive correlations with MSNA burst amplitude ($r = 0.6857$, $p = 0.0061$), systolic BP ($r = 0.6179$, $p = 0.0162$), diastolic BP ($r = 0.5464$, $p = 0.0377$) and HR ($r = 0.7637$, $p = 0.0009$). There were no changes in leukocyte count in the Non-Responder group. We have shown, for the first time, that long-lasting muscle pain causes an increase in circulating leukocytes in individuals in whom MSNA, BP and HR increased. We conclude that the increase in leukocytes was mediated by the increase in sympathetic outflow during muscle pain.

Poster #50

Paradoxical respiratory arrhythmia in patients after transplantation is a simulation of vagal regulation of the heart rhythm

O.V. Mamontov[1,2], V.V. Zaytsev[1], O.S. Tarasova[1], A.V. Berezina[1], A.V. Kozlenok[1], A.A. Kamshilin[1,3], E.V. Shlyakhto[1]
[1]Department of Circulatory Physiology, Almazov National Medical Research Centre, Saint Petersburg, Russia; [2]Department of Faculty Therapy, First Pavlov State Medical University, Saint Petersburg, Russia; [3]Institute of Automation and Control Processes, Far East Branch of Russian Academy of Sciences, Vladivostok, Russia

Background and Objective: After heart transplantation (HT), the neurogenic regulation of the heart rhythm disappears. While the possibility of sympathetic reinnervation in some patients has a convincing evidence base, the restoration of vagal control is not so obvious. The respiratory arrhythmia associated with the parasympathetic heart regulation. The aim of our study was to clarify the characteristics of respiratory arrhythmia evaluation in patients at different times after HT.
Materials and Methods: We examined 27 patients with terminal heart failure aged 47.6 ± 13.2 years and 20 healthy volunteers of comparable age. The examination of autonomous regulation was carried out before, and 3–6, 9–12 and 21–24 months after the HT. All participants were assessed for Valsalva index (VI) and respiratory sinus arrhythmia (RSA) during a deep breathing test (6 breaths per minute). Hemodynamics was recorded by the Finometer-pro (Nederland)

monitor. During the tests, the interaction of heart rate (HR) and cardiac output (CO) were analyzed.
Results: It was found that patients with heart failure initially had a significant decrease in both VI (1.43 ± 0.26 vs. 1.80 ± 0.38; $p < 0.005$) and RSA (10.7 ± 2.9 vs. 17.4 ± 3.1; $p < 0.001$) compared with the control group. Changes in HR and CO were in the counterphase with an average delay of 2.1 ± 0.3 beats/min. Inversion of IV (0.97 ± 0.02) and sharp decrease in RSA (3.8 ± 0.8) were observed 3–6 months after HT (both $p < 0.001$). With deep breathing, the arrhythmia was non-respiratory in 11 patients, while in the remaining 16 cases there was a change in the interaction of phase parameters in the form of a positive correlation between the dynamics of HR and CO with a delay of 1.7 ± 0.7 beats/min. On re-examination, there was a tendency to reduce the paradoxical reaction of the VI: 0.97 ± 0.02, 0.98 ± 0.03, and 0.99 ± 0.02 ($p = 0.09$), and RSA: 3.8 ± 0.8, 3.1 ± 0.7, and 2.7 ± 0.7 ($p = 0.06$) while maintaining common-mode dynamics HR and CO.
Conclusion: Paradoxical respiratory arrhythmia appeared in a number of patients after HT, which is most likely not associated with vagal regulation of the heart rhythm, the magnitude of which is greater immediately after surgery. Given the absence of vagal arrhythmia two years after HT, the likelihood of vagal reinnervation is doubtful.
Funding: The study was supported by the Grant of the Ministry of Science and Higher Education of the Russian Federation (agreement 075-15-2020-800).

Poster #51

Hypothalamic nuclei activity and connectivity changes following a glucose challenge: a single subject fMRI study

J. Manuel[1,2], D.A. Gerlach[1], E. Halbe[3], K. Heusser[1], A.C. Ewald[1], A. Hoff[1], R. De Gioannis[4], M. Heer[5], J. Tank[1], J. Jordan[1,6]
[1]Institute of Aerospace Medicine, German Aerospace Center (DLR), Cologne, Germany; [2]Institute for Neuroradiology, Hannover Medical School, Hannover, Germany; [3]Institute of Psychiatry and Psychotherapy, Universitätsklinikum Bonn, Bonn, Germany; [4]Department of Internal Medicine, University of Cologne, Cologne, Germany; [5] IU International University of Applied Sciences, Erfurt, Germany; [6]Aerospace Medicine, University of Cologne, Cologne, Germany

Introduction: Hypothalamic neural circuits, which adjust efferent autonomic activity in the face of altered nutrient supply, have been implicated in the pathogenesis of obesity, obesity-associated hypertension, and type 2 diabetes mellitus. Recent advances in functional magnetic resonance imaging (fMRI) permit to capture hypothalamic activity changes in groups of subjects. Because the approach obscures interindividual variability in hypothalamic regulation, we studied individual hypothalamic activity and functional connectivity in a single subject during multiple glucose challenges in the MRI scanner.
Methods: We conducted ten oral glucose tolerance tests at different days in the same healthy man (56 years, 64 kg, 1.77 m). We acquired functional images using a 3 T scanner before, and 10 and 45 min after glucose ingestion. Moreover, we measured plasma glucose and insulin levels at seven time points in three of the tests. Activity and functional connectivity changes were calculated using independent component analysis followed by a dual regression using an F-test and post-hoc two-sample t-tests. All analyses were corrected for multiple comparisons.
Results: Plasma glucose (147.5 ± 8.4 mg/dl) peaked 30 min after glucose intake followed by an insulin maximum 15 min thereafter (45.7 ± 7.0 mU/l). We observed significant activity increases 45 min after glucose intake in the arcuate, paraventricular, and dorsomedial nuclei, as well as in the posterior hypothalamic area, infundibulum, and mamillary bodies. Moreover, the mamillary bodies increased their functional connectivity to the ventromedial, dorsomedial, and periventricular nuclei.
Conclusion: Our results, which are consistent with previous animal experiments, show that fMRI can capture individual activity and connectivity changes in specific hypothalamic nuclei during a glucose challenge. Individual hypothalamic fMRI holds promise in delineating disease mechanisms in single patients.

Poster #52

Forebrain responses to handgrip exercise in premenopausal and postmenopausal women

S.J. McGinty[1], R.G. Burciu[1], K.A. Schneider[2], W.B. Farquhar[1], M.M. Wenner[1]
[1]Department of Kinesiology and Applied Physiology, [2]Department of Psychological and Brain Sciences, University of Delaware, Newark, DE, USA

Introduction: Postmenopausal women (POST) have increased muscle sympathetic nerve activity (MSNA) at rest compared to premenopausal women (PRE). While MSNA is generated by nuclei in the medulla oblongata, several forebrain regions can influence the generation of sympathetic activity. Still, functional differences in autonomic forebrain regions have yet to be compared between PRE and POST.
Purpose: We tested the hypothesis that blood oxygen level dependent (BOLD) functional MRI signal intensity change in supramedullary regions which promote sympathetic activity occur at a larger magnitude in POST relative to PRE during handgrip exercise.
Methods: We examined BOLD signal intensity changes in response to 3 trials of 2-min isometric handgrip exercise at 30% of maximal voluntary contraction in 3 PRE (23 ± 2 yr, 22 ± 2 kg/m^2) and 5 POST (54 ± 4 yr, 24 ± 3 kg/m^2). A voxel-based analysis was performed using FSL with corrected voxel threshold of $P < 0.05$. Region of interest analyses on bilateral forebrain areas including the amygdala, insula, and medial prefrontal cortex were then performed. BOLD signal intensity change was calculated in 30-s bins as a percent change from the first volume. Statistical analyses were performed using unpaired t-tests and 2-way repeated measures ANOVAs. Data are presented as mean ± SD.
Results: Resting systolic BP (PRE: 107 ± 12 vs. POST: 118 ± 15 mmHg, $P = 0.34$) and diastolic BP (PRE: 70 ± 6 vs. POST: 81 ± 10 mmHg, $P = 0.15$) were not different between PRE and POST. Robust increases in BOLD signal intensity were observed in the contralateral primary motor cortex which were similar between groups (Time: $P < 0.01$, Group: $P = 0.28$, Interaction: $P = 0.55$). The increases in BOLD signal intensity in the insula (Time: $P < 0.01$, Group: $P = 0.15$, Interaction: $P = 0.08$) and amygdala (Time: $P < 0.01$, Group: $P = 0.62$, Interaction: $P = 0.82$) did not differ between groups. Conversely, a significant reduction in BOLD signal intensity was found in the medial prefrontal cortex (Time: $P < 0.05$, Group: $P = 0.26$, Interaction: $P < 0.43$) which did not differ between groups. *Conclusions:* Consistent with the existing literature, these preliminary data demonstrate that the insula, amygdala, and medial prefrontal cortex are responsive to an autonomic stimulus such as handgrip exercise. While these data are preliminary, they suggest that autonomic forebrain responses to handgrip exercise may not differ between PRE and POST.
Funding: Supported by NIH Grant 5P20GM103653 and University of Delaware Department of Kinesiology and Applied Physiology PhD Research Grant.