survival and function. Human β-cells viability and function are improved on nanostructured substrates: β-cells contain several dispersed insulin granules and show increased glucose-sensitive calcium currents and insulin secretion. Quantitative immunofluorescence analysis reveals reorganization of the cell-substrate adhesion complexes, the actin cytoskeleton and the nuclear architecture. Proteomic analysis demonstrate protein changes that are congruent with the functional and morphological results and shows that β-cells respond to mechanical forces through the activation of a certain number of mechanosensors, including mechanosensitive ion channels and integrins (Gene Ontology GO terms: 0005925). Their activation causes remodeling of the actomyosin cytoskeleton (GO: 0005856) and nuclear architecture (GO: 0031891) and is conveyed to the nucleus where it modulates gene expression. The characterization of the mechanotransduction signaling pathway may offer a unique possibility to understand how beta cells work and can lead to the identification of new targets of pharmacological intervention in diabetes mellitus.

OP.137

Hyper-excitability and hyper-plasticity disrupt cerebellar signal transfer in the IB2 KO mouse model of autism

Prestori F

Department of Brain and Behavioral Sciences, University of Pavia, Italy

Autism spectrum disorders (ASD) are pervasive neurodevelopmental conditions that often involve mutations affecting synaptic mechanisms. Recently, the involvement of cerebellum in ASD has been suggested but the underlying functional alterations remained obscure. Thus, we exploited a combination of whole-cell patch-clamp recordings with voltage sensitive dye imaging (VSDi) in acute cerebellar slices in WT and IB2 KO mice to investigate single-neuron and microcircuit properties. The IB2 gene (chr22q13.3 terminal region) deletion occurs in virtually all cases of Phelan–McDermid syndrome, causing autistic symptoms and a severe delay in motor skill acquisition. The granular layer of these mice revealed severe alterations in synaptic transmission, neuronal excitation and long-term synaptic plasticity. A 2.5-times larger NMDA receptor-mediated current in IB2 KO granule cells enhanced synaptic plasticity (WT = 20.4±4.2%, n=12 vs. IB2 KO = 107.7±44.4%, n=9; p<0.05) along with the excitatory/inhibitory (E/I) balance (WT = 0.98±0.27, n=6 vs. IB2 KO = 2.78±0.32, n=7; p<0.01). At the same time, the spatial organization of granular layer responses to mossy fiber inputs shifted from a "Mexican hat" to a "stovepipe hat" profile, with stronger excitation in the core (WT = 12.9±1.7 μm vs. IB2 KO = 29.5±4.9 μm, n=5 for both; p<0.01) and limited inhibition in the surround (WT/KO ratio IWT/KO = 2.83±0.17, n=5). The IB2 KO mouse model therefore configures a complex cerebellar synaptopathy centered on NMDA receptor gain of function, that in several respects resembles alterations also observed in cortical minicolumns. The profound changes of signal processing at the cerebellar input stage unveil a possible new mechanism contributing to the pathogenesis

Workshop

EXERCISE AND CARDIOVASCULAR PHYSIOLOGY

Oral presentations

OP.138

Cardiovascular kinetics during moderate3intensity arm and leg exercise: a preliminary report.

Bruseghini P[1], Vinetti G[1], Taboni A[2], Fagoni N[1], Ferretti G[1,2]

[1]Department of Molecular and Translational Medicine, University of Brescia [2]Departments APSI and NEUFO, University of Geneva

The phase I cardiovascular response to exercise implies an instantaneous cardiac output ($\dot{Q}$) increase, due to the effect of sudden vagal withdrawal on heart rate (fH) and of sudden venous return increase, due to muscle pump action, on stroke volume (SV). If the latter is the case, we would expect that, when exercise is performed with small active muscle mass, the cardiovascular responses at exercise are depressed. On 8 healthy young subjects, we measured beat3by3beat fH, SV and $\dot{Q}$ during arm ergometer and cycle ergometer exercise transitions, from rest to 50W. A double exponential model was applied to the transient phase, and we computed amplitudes and time constants of phase I (A1 and T1). For arm cranking, steady state fH was 65.2±7, and 102.3±7.8 bpm, at rest and 50 W exercise, respectively V corresponding SV was 106.1±16.5, and 112.9±13.4 mL, so that $\dot{Q}$ was 6.6±0.8, and 11.8±1,4 L/min. For leg cycling, fH was 68.4±7.8, and 92.7±6 bpm, SV was 101.8±14.4, and 117.1±16 mL, and $\dot{Q}$ was 6.9±0.6, and 10.8±1.2 L/min, at rest and exercise, respectively. For fH, A1 and T1, for arm exercise (18.4±8.1 bpm and 7.5±5 s, respectively) were greater (p<.05) than the corresponding values for leg exercise (9.1±2.2 bpm and 3.2±2 s, respectively). No significant differences appeared in A1 and T1 for SV and $\dot{Q}$ between the two

exercise types. Exercises with different muscle masses acted on the kinetics of fH, but not on that of SV, and thus essentially on the vagal withdrawal mechanism.

OP.139

Effects of hormone replacement therapy in combination with swimming exercise and/or melatonin on oxidative tissue damage in postmenopausal rats

Tamer SA[1], Altınoluk T[1], Emran M[2], Korkmaz S[2], Yüksel RG[2], Baykal Z[2], Dur ZS[2], Levent HN[3], Ural MA[4], Yüksel M[5], Çevik O[4], Ercan F[3], Yıldırım A[1], Yeğen BÇ[1]

[1]Marmara University, Department of Physiology, Istanbul, Turkey; [2]Marmara University, Istanbul, Turkey; [3]Marmara University, Department of Histology & Embryology, Istanbul, Turkey; [4]Adnan Menderes University, Department of Biochemistry, Aydin, Turkey; [5]Marmara University, Department of Medical Laboratory, Istanbul, Turkey

Hormone replacement therapy (HRT) or exercise (E) ameliorates postmenopausal symptoms and protects against oxidative tissue damage. In order to compare putative ameliorative effects of HRT, E or their combination on oxidative damage and to further evaluate the impact of adding melatonin (M) to HRT, E or both, half of Sprague Dawley rats with bilateral ovariectomy had swimming exercise (30 min/5 days/week; E, E+HRT, E+M, E+HRT+M; n=32), while other half was sedentary (S, S+HRT, S+M, S+HRT+M) for 8 weeks during which HRT (estradiol; 1 mg/kg/day) or M (4 mg/kg/day) was given in drinking water. Memory performance was not different among groups. Weight gain was lower in all HRT groups. Rats were decapitated at postsurgical 70th day, and heart, aorta, brain, liver and kidney tissues were obtained for biochemical and histological analyses. Compared to nontreated sedentary group, cerebral malondialdehyde levels were elevated, while antioxidant glutathione levels of cardiac and hepatic tissues were decreased in both HRT groups (S+HRT and E+HRT). On the other hand, addition of M treatment to S+HRT or E+HRT groups reversed these oxidative injury parameters back to levels of non-treated sedentary group. Addition of E to HRT or E+HRT+M combination decreased myeloperoxidase activity in brain, liver and kidney. Histological analysis revealed diminished aortic wall thickness, endothelial detachment and an irregular organization of cardiomyocyte fibers in sedentary groups, while addition of exercise or M to HRT resulted in normal aortic wall and cardiomyocyte organization. HRT either alone or combined with exercise impaired the oxidant/antioxidant balance, but addition of melatonin provided a protection against HRT induced oxidative stress, advocating postmenopausal use of melatonin.

OP.140

Non-invasive assessment of the vascular baroreflex arm

Javorka M[1], Krohova J[1], Czippelova B[1], Turianikova Z[1], Mazgutova N[1], Wiszt R[1], Lazarova Z[1], Faes L[2,3]

[1]Department of Physiology and Biomedical Centre Martin (BioMed Martin), Jessenius, Comenius University, Martin, Slovakia; [2]Department of Energy, Information engineering and Mathematical models (DEIM), University of Palermo, Italy; [3]BIOtech Center of the Department of Industrial Engineering, University of Trento, Italy

Baroreflex response is composed of cardiac chronotropic (effect on heart rate), cardiac inotropic (effect on contractility) and vascular (effect on vascular resistance) arms. Because of its measurement simplicity, cardiac chronotropic arm is the most often analysed baroreflex component. The aim of study was to introduce a method to analyse vascular baroreflex arm. Healthy volunteers (N = 78, median age: 18.6 yrs.) participated in this study. We recorded continuous systolic and mean blood pressure (SBP and MBP) by volume-clamp method (Finometer Pro, FMS), and R-R interval (RR) by ECG (CardioFax ECG-9620, NihonKohden). Cardiac output (CO) was recorded using impedance cardiography (CardioScreen® 2000, Medis). Then, we calculated the peripheral vascular resistance (PVR) as a ratio of MBP and CO. The directional spectral coupling and gain of cardiac chronotropic (SBP to RR) and vascular arms (SBP to PVR) were calculated in low frequency band (LF, 0.04 – 0.15 Hz). We analysed baroreflex vascular component characteristics during various physiological conditions (supine, head-up tilt (HUT), supine recovery, mental arithmetics (MA)). The coupling from SBP to PVR was significantly higher than the coupling from SBP to RR during whole protocol ($P < 0.0001$). The coupling in both assessed directions was significantly higher during HUT compared to supine rest ($P < 0.0001$ and $P = 0.0138$), but no differences were found during MA in comparison with the preceding supine recovery. No significant changes in the spectral gain across all phases were found ($0.1494 \leq P \leq 0.9053$). We conclude that changes in PVR are tightly coupled with the SBP oscillations via baroreflex with a stable gain. Analysis of the vascular baroreflex arm could reveal another aspect of blood pressure dysregulation. Grants: VEGA 1/0117/17 and VEGA 1/0200/19

OP.141

Heart Rate Kinetics and Sympathovagal Balance Accompanying a Maximal Sprint Test

Storniolo J, Esposti R, Cavallari P