Methods — Two months old-mice were analyzed. Heart tissue was fixed (formaldehyde 10%) and embedded in paraffin for immunohistochemistry or frozen for western-blot (WB) analysis. Immunofluorescence (IF) studies were performed on heart cryosections. ECG was recorded (PowerLab, DSI) under isoflurane anaesthesia and heart rate spectral variability (HRV) was performed (FFT) in low frequency (LF: 0.15-1.5 Hz) and high frequency (HF: 1.5-5 Hz) ranges; LH/HF ratio was also calculated.

Results — We first assessed expression of Ephrin-B1 by WB in heart from WT animals. A specific band around 47 kDa was detected in WT heart total protein extracts that was lost in KO mice. Further IF studies demonstrated broad expression of Ephrin-B1 protein throughout all heart compartments with different cellular localizations (cardiomyocytes and micro/macrocirculation). Hematoxylin-eosin (HE) staining of paraffin-embedded heart sections from KO mice revealed loss of organized cardiac tissue characterized by the presence of wavy cardiomyocytes in both septum and ventricles. Myocytes intersected at various angles with bundles wavy appearance. No inflammation, interstitial fibrosis or necrosis were noticed. These pathological observations correlated well with the lack of stiffness of hearts from KO mice compared with controls. When we examined ANS-dependent heart rate variability, LF-HRV was significantly reduced in KO mice (16.3±1.2%) when compared to controls (48.5±6.2%) without any change in HF, suggesting a specific loss of cardiac sympathetic innervation in these animals. LF/HF ratio was lower in KO mice (0.6±0.2 vs 1.3±0.2 in controls).

Conclusion — This study provides the first evidence for the presence of ephrin molecules in the adult heart tissue with a specific expression of Ephrin-B1 ligand. The use of ephrin-B1 genetic mouse model highly suggests a role for ephrin-B1 in heart tissue architecture and in sympathetic control of heart rate variability.

H030

SHORT-TERM HEART RATE REDUCTION INDUCED BY IVABRADEX ADMINISTERED TO RATS WITH WELL-ESTABLISHED HEART FAILURE IMPROVES CARDIAC FUNCTION, AUGMENTS NEO-ANGIOGENESIS AND REDUCES MYOCARDIAL HYPOXIA

Y. FANG ¹, F. BAUER ¹, P. MULDER ¹, E. BRAKENHELM ¹, F. LALLEMAND ², P. GLUAIS ², J. ROUSSELS ², C. THUILLEZ ²

¹ Inserm U644, Rouen, France
² IRIS, Courbevoie, France

Long-term heart rate reduction (HRR) initiated in a pathophysiological situation of moderate left ventricular (LV) dysfunction prevents the deterioration of cardiac function. This is probably related to short-term effects of HRR, i.e. improved myocardial perfusion and reduced O2 consumption, and long-term HRR effects on LV structure, i.e. improved capillary density. However, it is currently unknown 1) whether the short-term effects of HRR are sufficient to improve LV function when HRR is initiated in a setting of well-established chronic heart failure (CHF) and/or 2) whether short-term HRR triggers/activates early mechanism(s) involved in the structural long-term effects of HRR. Thus, we assessed, in a rat model of CHF (coronary ligation), the effects of short-term HRR induced by the If current inhibitor ivabradine (Iva; 10mg/kg/day as food admix for 4 days starting 93 days after ligation). The table shows heart rate (HR; beats/min), cardiac output (CO; ml/min), LV end-systolic pressure (LVESP; mmHg), LVESP-volume relation (LVESVPR; mmHg/Relative...