Western blot showed that , compared with wild-type mice, the expressions of Sirt1, P-FoxO1, Rab7, Beclin1 and LC3II/Iwere decreased obviously in Sirt1 knockout mice , P < 0.05; However, P53 was increased obviously, P < 0.05; Immuno-fluorescence test showed that, compared with wild-type mice, LC3 particles of cerebral cortex in Sirt1 knockout mice were decreased significantly, LC3 particles were more induced at 12h after I/R, P<0.05; Mild hypothermia could not increase the expression of LC3, P > 0.05; TUNEL detection showed that, compared with wild-type mice, neurons apoptosis were increased in Sirt1 knockout mice, neurons apoptosis were more apparent at 72h after I/R, P<0.05; however, Mild hypothermia treatment could not reduce neurons apoptosis after ischemia reperfusion in Sirt1 knockout mice (P > 0.05), which showed that the effect of mild hypothermia on neural protection was abated in Sirt1 knockout mice.

CONCLUSIONS The neurons autophagy were more insufficient and apoptosis were significantly increased after cerebral ischemia reperfusion in Sirt1 knockout mice, the neural protection of mild hypothermia was decreased significantly; It was speculated that Sirt1 may be one key factor of regulating autophagy in the process of ischemia reperfusion injury, and mild hypothermia may regulate autophagy and apoptosis through Sirt1 and its downstream gene, so as to play a role of neuroprotection.

GW28-e0075

Exercise training modulation of inward rectifier potassium channels and control blood pressure in hypertensive rats

Chun Zi Jin,[1] Wenbo Liu,[1] Lan Cui[1]
[1]Yan Bian University Hospital, Yanji, Ji Lin Province

OBJECTIVES This study aimed to explore the mechanisms underlying high blood pressure control by physical exercise through modulation of inward rectifier potassium channels.

METHODS Hypertension animal models with or without physical exercise were established. The blood pressure in the rat models was monitored by a tail-cuff method using a multi-channel multi-animal Coda Non-Invasive Blood Pressure System (Kent Scientific Corporation, USA). After 4 weeks of preparation of animal models, the deep femoral arteries were removed from the rats under inhalational anesthesia. The luminal diameter ofvesselswas measured using a vessel diameter image analysis system. The patch-clamp technique was used to measure the Kir current, and Western blotting assay was used to determine the expression level of the Kir 2.1 protein.

RESULTS 1. No statistically significant difference in the body weight, heart weight, ventricular+Septum weight, Right ventricular weight and (ventricular+Septum) weight/ Right ventricular weight were found between the hypertension group and the hypertension-exercise group. 2. The systolic blood pressures and diastolic pressure two weeks after the angiotensin II injection (no other treatments) did not show significant differences between the hypertension group (systolic blood pressures: Week 0: 125±2.9 mmHg, Week 1: 148±2.8 mmHg, Week 2: 145±3.1 mmHg; diastolic pressure:Week 0: 93.5±2.9 mmHg, Week 1: 95±3 mmHg, Week 2: 110±2.9 mmHg) and the hypertension-exercise group(systolic blood pressures: Week 0: 125±2.9 mmHg, Week 1: 148.5±3 mmHg, Week 2: 144±2.9 mmHg; diastolic pressure :Week 0:93.5±2.9 mmHg, Week 1: 94.5±2.8 mmHg, Week 2: 110.5±3.1 mmHg) (both P>0.05). At Week 4 post-angiotensin II injection (i.e., two weeks of exercise treatment for the hypertension-exercise group), the systolic blood pressure showed statistically significant difference between the hypertension group (Week 4: 170±2.9 mmHg) and the hypertension-exercise group (Week 4: 148±2.8 mmHg), so did the diastolic blood pressure (Week 4: 125±2.8 mmHg v.s. 105±2.9 mmHg) (P<0.05). Compared to the hypertension group, the hypertension-exercise group exhibited remarkably effective control of blood pressure. 3. As indicated by the vessel diameter image analysis, the vasodilation response in the hypertension-exercise group was more significant, which could be suppressed by the blocker(50mM BaCl2) of the inward rectifier potassium channels. 4. The patch-clamp recording of the Kir current revealed that the Kir current in the hypertension-exercise group waslarger than that of the hypertension group (P<0.05).In addition, the expression of the Kir 2.1 protein in the hypertension-exercise group was higher than that of the hypertension group, as indicated by Western blotting assay.

CONCLUSIONS The present study investigated the effects of long-term exercise on cells, in particular its effect on blood-pressure control through increasing membrane Kir current. This study revealed that, long-term exercise can enhance the vasodilation capacity of vessels while such improvement is critical for improving the quality of life and reducing the risk of hypertension and related cardio-cerebral vascular complications in hypertension patients.

GW28-e0097

Application of genome-wide microarray analysis technology to explore the neuroprotection mechanism of hypothermia after cardiopulmonary resuscitation

Dezhi Zou,[1] Xuan Dai,[1] Chunlin Hu[1]
[1]The First Affiliated Hospital, Sun Yat-sen University, Emergency Department

OBJECTIVES Hypothermia is one of the most robust experimental neuroprotective interventions against cerebral ischemia. Identification of molecular pathways together with single genes or gene families that are significantly associated with neuroprotection might help unravel the mechanisms of therapeutic hypothermia.

METHODS Total of 20 healthy adult male Wistar rats, were randomly divided into 4 groups, sham-operated plus nonthermia(NT1)(n=4), sham-operated plus hypothemia(NT2)(n=4), return of spontaneous circulation (ROSC) after ventricular fibrillation(VF) plus nonthermia (CPRT1) (n=6), ROSC after VF plus hypothemia (CPRT2) (n=6). 12 of CPRT were induced VF by an external trans-thoracic alternating current. After 7 minutes cardiac arrest, the animals received 2 minutes cardiopulmonary resuscitation and then defibrillation until ROSC. The animals in NT1 and CPRT1 Placed in the constant temperature box at 37°C and maintained esophageal temperature at 38°C. The animals in NT2 and CPRT2 were treated by surface hypothermia, and maintained for 2 hrs of target temperature between 33°C to 35 °C. The animals were sacrificed after ROSC 2h, the cerebral cortex were removed, then the RNA of samples were processed in extraction, quality inspection, purification and amplification. Data collection, inspection and analysis after The Mouse Genome Microarrays hybridization reaction. The gene expression profile of NT1, NT2, CPRT1, and CPRT2 were compared by analyzing changes of individual genes and pathways.

RESULTS All samples showed high consistency, and integrity of RNA sample was qualified. The microarray hybridization reaction process was good. The normalized data shows approximate normal distribution. The data of compare of two groups (p < 0.05) indicates differentially expressed genes in common. CPRT1 versus NT1, of 227 genes present on the array chip(p<0.05), compared with upregulated 150(66.1%) genes and downregulated 77(33.9%) genes equal or greater than twofold. CPRT2 versus NT2, of 108 genes present on the array chip(p<0.05), compared with upregulated 76(76.1%) genes and downregulated 32(33.3%) genes equal or greater than twofold. NT2 versus NT1, of 138 genes present on the array chip(p<0.05), compared with upregulated 96(69.6%) genes and downregulated 32(30.4%) genes equal or greater than twofold. CPRT2 VS NT2 compared with CPRT1 VS NT1, NT2 VS NT1 compared with CPRT2 VS CPRT1, there are 8 and 6 difference expression genes in common, respectively. Genes implicated in hypothermia displayed significantly differential expression, such as p21, 14-3-3-sigma, GADD45, BDNF, c-fos, HSP72, c-JUN, Nur77, CXCL2, CCL3, IL4 and TSLP. On the pathway level, the MAPK signaling pathway and Cytokine-cytokine receptor interaction pathway in CPRT2 VS NT2, likewise the P53 signaling pathway in CPRT1 VS NT1, were identified to be significantly altered(p<0.05, fc>=1.5). The most significantly altered pathways contained genes above participating in cell cycle arrest, proliferation, differentiation, apoptosis and inflammation.

CONCLUSIONS Our data suggest that Inflammation pathway, P53 apoptosis pathway and inflammatory factor receptor pathways that connected with MAPK, were associated with neuronal injury after cardiopulmonary resuscitation. Hypothemia has remarkable effect on the expression of several of genes related to these pathways, which affect inflammatory response, apoptosis and cell inflammatory factor receptor mediated neuronal injury pathways after CPR, thus play a role of neuroprotection.

GW28-e0178

Hyperactivity of adrenal gland and the excessive aortic inflammatory response accelerate the process of atherosclerosis in mice with chronic complex stress

Jinyao Liu,[1] Ayako Himemiya Hakucho,[1] Tatsuya Fujimiya[1]
[1]Yamaguchi University