Reproductive Endocrinology

FEMALE REPRODUCTION: BASIC MECHANISMS

GLUT1-Mediated Glycolysis Facilitates GnRH-Induced Secretion of Luteinizing Hormone

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Reproduction requires intensive energy expenditure, and energy availability impacts the function of the reproductive endocrine HPG-axis. Accordingly, the reproductive axis is suppressed during hypoglycemia. Circulating blood glucose can directly interact with gonadotropes within the highly vascular pituitary. Therefore, it is possible that gonadotropes may sense energy availability via the presence of glucose in the circulation and integrate this status with input from GnRH neurons to regulate hormone production. Gonadotropes dominantly express glucose transporter 1 (GLUT1) and increase glucose uptake in response to GnRH. Thus, we hypothesized that gonadotropes engage glycolysis in response to GnRH stimulation due to the high energy demand of protein synthesis required for LH production. We developed an approach to sort and successfully culture primary gonadotropes from wild type mice. Using this approach, we performed extracellular flux analysis and found that gonadotropes respond to GnRH by inducing GLUT1-mediated glycolysis that is independent of mitochondrial respiration. Knock-down of GLUT1 expression in the LβT2 gonadotrope cell line, glucose restriction, or treatment with the competitive inhibitor of glycolysis, 2-DG, diminished GnRH-induced LH secretion, indicating GLUT1 expression is necessary for maximal GnRH-induced LH secretion. We confirmed this observation in primary female mouse gonadotropes by limiting glucose availability which resulted in diminished basal LH and FSH secretion. Lastly, GLUT1 expression in the pituitary correlates with GnRH receptor expression and is increased during the LH surge in a mouse model. These results implicate glucose uptake through GLUT1 as permissive for gonadotrope secretion of LH and therefore reproductive function, especially the LH surge. We conclude that GLUT1-mediated glucose uptake is an important rate-limiting step in gonadotropin synthesis and operation of the HPG-axis.

Cardiovascular Endocrinology

ENDOCRINE HYPERTENSION AND ALDOSTERONE EXCESS

Primary Aldosteronism Represents Earlier Myocardial Fibrosis Than Essential Hypertension by T1 Mapping

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Introduction:
Primary aldosteronism (PA) is associated with cardiovascular disease and has increased cardiovascular morbidity. Several studies had demonstrated that PA shows more serious myocardial fibrosis compared with essential hypertension (EH) using late Gadolinium-enhanced (LGE) imaging [1, 2]. However, the early myocardial change may not be detected by LGE. Recently, cardiac MRI T1 mapping emerged to be a sensitive technique in detecting early changes of myocardium quantitatively. Our study aimed to demonstrate the early myocardial change in PA patients by applying the T1-mapping technique.
Method:
81 (male: 25; age: 48±12 years) PA[3] and 44 (male: 21; age: 47±14 years) EH patients diagnosed by the Department of Endocrinology and metabolism according to the 2016 TES guidelines for PA were recruited from September 2018 to May 2019. All the subjects underwent cardiac MRI examinations on a 3T MRI scanner (MAGNETOM Trio a Tim System, Siemens Healthcare, Erlangen, Germany), including steady-state free-precession (SSFP) cine imaging and modified Look-Locker inversion recovery (MOLLI) imaging for T1 mapping. Functional parameters were obtained from cine images by the Argus software (Siemens Healthcare, Erlangen, Germany). The mid-ventricular native T1 value was acquired using the QMass software (Medis, Leiden, The Netherlands). Native T1 value and cardiac function parameters were analyzed between the two groups. Differences of continuous variables were analyzed by Student's t-test or Mann-Whitney U-test, and the relationships between native T1 value and physiological variables were analyzed by multiple linear regression method.
Results:
The age (PA: 48±12 years vs EH: 47±14 years; p=0.720) and BMI (PA: 25.06±3.73 vs EH: 25.17±2.83; P=0.874) between two groups had no significant differences. The PA group had a significant higher aldosterone/renin ratio (ARR) than those in the EH group (114.6 (48.7-474.8)ng/dl:ng/ml.h vs 7.6 (4.2-13.8) ng/dl:ng/ml.h; p<0.001). All functional parameters including LVEDVI (PA: 78.66 (72.4-90.6) ml/m^2 vs EH: 75.8 (64.3-85.8) ml/m^2; p=0.054); LVESVI (PA: 31.7 (26.2-38.4) ml/m^2 vs EH: 29.3 (24.9-36.2) ml/m^2; p=0.152); LVEF (PA: 59.9 (53.3-65.0)% VS EH: 59.2(55.3-65.6)%; p=0.679); LVmassi (PA: 58.5(47.7-67.7) g/m2 vs EH: 54.9 (47.6-60.1) g/m2; p=0.463) had no differences between the two groups. However, native T1 values were higher in PA group than those in EH group (1227±40ms vs 1203±45ms). The multiple linear regression analysis showed that gender (Beta=-27.678, p<0.001) and PA (Beta=-17.287, p=0.031) were independently related to the native T1 values.
Conclusion:
PA patients represent more severe and earlier myocardium damage and this might be related to cardiovascular morbidity. The T1-mapping technique in cardiac MRI is more sensitive to evaluate the left ventricular function and to detect the myocardial fibrosis in PA patients.

Bone and Mineral Metabolism

CLINICAL ASPECTS OF OSTEOPOROSIS AND VITAMIN D ACTION

Determining Vitamin D Status: Analytical Variability Between Available Assays

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