Sample Abstract

Blockade of Mineralocorticoid Receptors in the Dorsal Hindbrain (DHB) Enhances Baroreflex Sensitivity

Iara Backes[1], Rebekah Clifton[1],Gail K. Adler[2] and Deborah A. Scheuer[1]

University of Florida[1], Department of Physiology and Functional Genomics, Gainesville, FL, [2]Division of Endocrinology, Diabetes and Hypertension, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

Mineralocorticoids and glucocorticoids are essential for life, however the excess of these essential hormones is often detrimental. Chronic stress leads to elevated glucocorticoids which have been linked to poor cardiovascular outcomes. Glucocorticoids bind to both glucocorticoid receptors and mineralocorticoid receptors (MR) with similar affinities. This study tested the hypothesis that chronic blockade of MR in the dorsal hindbrain (DBH) enhances spontaneous baroreflex sensitivity (sBRS) in male Sprague- Dawley rats subjected to chronic variable stress (CVS) for 2 weeks. Rats were instrumented with radiotelemetry transmitters to obtain cardiovascular data, and pellets made of cholesterol (Chol) or the MR antagonist spironolactone (SPL) were implanted on the DBH (n=5-6 per group). Two weeks later rats were subjected to CVS, which included insulin-induced hypoglycemia on the first day of stress. SPL significantly ($P<0.05$) increased the sBRS prior to (2.1±0.1 vs. 1.5±0.2 ms/mmHg in SPL vs Chol rats) and after 2 wk of CVS (2.1±0.1 vs. 1.6±0.2 ms/mmHg in SPL vs Chol rats). Neither CVS nor hypoglycemia altered sBRS. Blood glucose was measured at 20, 40, 60, 90, 120 and 180 min after insulin (7-8 U/kg, i.p.) was administered to non-fasted rats. Glucose reached a nadir at 2 hr, when levels were significantly higher in SPL compared to Chol rats, (37±3 vs.28±1 mg/dl, $P<0.05$). The results indicate that chronic blockade of DHB MR enhances sBRS and blunts the hypoglycemic effect of insulin.