Seventh research

Title

Interrogating the estrogen- mediated regulation of adrenocortical Klotho expression using ovariectomized albino rat model exposed to repeated restraint stress.

Human Cell (2024)

ABSTRACT:

Reproductive aging is associated with altered stress response and many other menopausal symptoms. Little is known about the adrenal expression of the anti-aging protein Klotho or how it is modulated by estrogen in ovariectomized stressed rats. Fifty-six Wistar female rats were assigned into seven equal groups. Sham-operated (Sham), sham stressed (Sham/STS), ovariectomized (OVR), ovariectomized stressed (OVR/STS), ovariectomized stressed rosiglitazone-treated (OVR/STS/R), ovariectomized stressed estrogen-treated (OVR/STS/E), and ovariectomized stressed estrogen/GW9662 co-treated (OVR/ STS/E/GW) groups. All stressed rats were subjected daily to a one-hour restraint stress test for 19 days. At the end of the experiment, blood was collected for serum corticosterone (CORT) analysis. Adrenal tissues were obtained and prepared for polymerase chain reaction (PCR) assay, hematoxylin and eosin (H&E), immunohistochemistry-based identification of Klotho and PPAR-γ, and Oil Red O (ORO) staining. The rise in serum CORT was negligible in the OVR/STS group, in contrast to the Sham/STS group. The limited CORT response in the former group was restored by estrogen and rosiglitazone and blocked by estrogen/GW9226 co-administration. ORO-staining revealed a more evident reduction in the adrenal fat in the OVR/STS group, which was reversed by estrogen and counteracted by GW. Also, there was a comparable expression pattern of Klotho and PPAR-γ in the adrenals. The adrenal Klotho decreased in the OVR/STS

group but was reversed by estrogen treatment. GW9226/estrogen co-treatment interfered with the regulatory effect of estrogen on Klotho. The study suggested modulation of the adrenal Kotho expression by estrogen, in the ovariectomized rats subjected to a restraint stress test. This estrogen-provided adrenal protection might be mediated by PPAR-γ activation.

Keywords: Reproductive ageing · Klotho · PPAR-γ · Rat adrenals · Ovariectomy · Immunohistochemistry.