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Alternative RNA splicing of estrogen receptor β and neurogenesis/mood/cognitive behavior in post-menopause

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Dementia and depression disproportionately affect women in both prevalence and severity. Particularly related to deficiency of ovarian hormones which impairs the homeostasis of the brain microenvironment, reduces neurogenesis, and leads to neurodegeneration. Accumulated data suggest that estradiol-17β (E2), the primary ovarian hormone, promotes hippocampal neural progenitor cell (NPC) proliferation *in vitro*, *in vivo*, and after brain injury. Our earlier work indicated that activation of estrogen receptor (ER) β by the ERβ-specific ligand, diarylpropionitrile, led to an increase in phosphorylated extracellular signal-regulated kinase in human neural progenitor cells and increased these cell proliferation. Our resent work suggested that ovariectomy (OVX) increased alternative splicing of ER β and the ERβ splice variants might mediate the differential effects of estrogen therapy (ET) in early and late post-menopause. To further understand the mechanism, we used a customized RT2 Profiler PCR Array to examine expressions of RNA splicing factors in brain of female rats treated with E2, ERβ or ERα specific agonists, or vehicle 6-day (early) or 180-day (late) after OVX. Early ET reversed OVX-increased (SFRS7 and SFRS16) or -decreased (ZRSR2 and CTNNB1) mRNA levels of splicing factors and ERβ splicing changes in brains and leukocytes, and improved mood/cognitive performances. While only DPN (an ERβ specific agonist), but not E2 (an ERα and ERβ agonist) nor PPT (an ERα specific agonist), achieved similar results in late treatment. These data suggests ERβ plays an important role in ET and ET efficiency may be indicated the expression of ERβ splice variant in circulation.

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Protective effect of alcohol extract of *Bacopa monnieri* against streptozotocin induced diabetic nephropathy in rats

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Diabetic nephropathy is a long-term complication of diabetes mellitus. Chronic hyperglycemia leads to the generation of reactive oxygen species leading to oxidative stress. Oxidative stress along with hyperglycemia leads to the development of diabetic nephropathy. *Bacopa monnieri* is widely used in traditional medicine in India to treat various diseases like renal disorders, blood diseases, anemia, nerve tonic and poisoning. The present study was designed to evaluate alcohol extract of *B. monnieri* aerial parts in diabetic nephropathy in rats. Diabetic nephropathy was induced by intraperitoneal injection of streptozotocin (65 mg/kg) 15 min after Nicotinamide (230 mg/kg, i.p.) administration. Rats were divided into six groups (n=6). Group 1 and 2 were kept normal control and diabetic control respectively whereas Groups 3–5 consist of diabetic nephropathy rats treated with different doses of extracts (100, 200 and 400 mg/kg) for 45 days. Glimipride (10 mg/kg) was used as standard. Diabetic nephropathy was assessed by determining serum glucose, urea, uric acid, creatinine level and tissue histological examination. Tissue antioxidant activity was assessed by measuring level of SOD, CAT, GSH, LPO. Alcohol extract of *B. monnieri* produced significant attenuation in the serum glucose level, uric acid, creatinine and lipid levels. Administration of extracts improves the level of SOD, CAT, GSH and decrease lipid peroxidation in terms of TBARS. Moreover histopathological examination also revealed the improvement in structural changes in nephrons and regeneration of β-cells. So, it can be concluded that alcohol extract of *B. monnieri* produced protective effect by decreasing hyperglycemia, oxidative stress and improving the structural disarrangement in kidney of rats.

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