Comparative analysis and functional implications of ligand dependent changes in estrogen- and thyroid hormone receptor expression in the developing cerebellum.

Istvan Toth, Trudy Johnson Scalise, Andrea Gyorffy, David Sandor Kiss, Virag Somogyi, Greta Goszleth, Tibor Bartha, Laszlo V. Frenyo, Attila Zsarnovszky

Szent Istvan University Faculty of Veterinary Sciences, Department of Physiology and Biochemistry, Budapest, Hungary, H-1078

Abstract

Trophic hormones are important regulators of CNS development and function. In particular, estrogen (E2) and thyroid hormones (THs) regulate cell migration, differentiation, proliferation and synaptogenesis/network formation during cerebellar development. These hormone-regulated events involve the binding of hormone ligands to their cognate receptors that function as transcription factors to activate relevant genes for the adequate orchestration of developmental processes. Recent reports implicate a complex mechanism through which E2 and THs influence the expression levels of each other's receptors (ERs and TRs) to precisely mediate developmental signals. Here we examined the effects of the presence or absence of E2 and THs on the expression levels of their receptor mRNAs and proteins. Cerebellar granule cell cultures were treated with either E2, T3, T4 or a combination of these hormones, and resulting receptor expression levels were determined by quantitative PCR and Western blot techniques. Results were compared to non-treated controls and to samples obtained from 14-day-old *in situ* cerebella. Additionally, we determined the effects that glial cells might have on the regulation of ER-TR expression levels. Results show that: (i) ER and TR expression levels depend on the individual or combined presence/absence of E2 and THs; (ii) glial cells are important mediators in the hormonal regulation of neuronal ER-TR expression, and (iii) loss of tissue integrity results in characteristic changes in ER-TR expression levels. These observations suggest that both E2 and THs are required for the precise orchestration of cerebellar development and that alterations in the tissue concentration of either of the hormones may influence signaling mechanisms that are driven by both E2 and THs. Comparison of data from *in vitro* and *in situ* samples also revealed a shift in receptor expression levels after loss of tissue integrity, likely indicating possible adjusting/regenerative mechanisms after cerebellar tissue injury.