

OXYTOCIN AND VASOPRESSIN AUTOCRINE/PARACRINE SIGNALLING IN SMALL CELL LUNG CARCINOMA

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Small cell lung carcinoma (SCLC) is an aggressive form of lung cancer and presently accounts for 20-25% of all lung cancer cases. It is characterised by ectopic secretion of various neuropeptides. Among these neuropeptides, oxytocin (OT) as well as vasopressin (VP), two neurohypophysial hormones, are synthesised and secreted by these tumours. Moreover, the oxytocin receptor (OTR) is expressed by the malignant cells as the vasopressin receptors V1a, V1b/V3, V2 and a variant V2 are. These receptors all belong to the super family of G-protein-coupled receptors (GPCR) structurally characterized by seven transmembrane domains. A study of pharmacological interactions OT and VP have with these receptors on SCLC cells demonstrated that OT and VP produce increases in cytosolic Ca⁺⁺ levels in SCLC cells through OTR- and V1aR-mediated processes. No activation of the cAMP pathway was detected after VP, DDAVP (a V2R agonist), or OT treatment. The activation of the MAP kinase cascade was observed when SCLC cells were stimulated with OT or VP. Moreover, both hormones, from concentrations as low as 10⁻⁹M, increase SCLC cell growth. When cells are incubated with a mix of OT (10⁻⁹M) and an OT antagonist (OVTA, 10⁻⁹M), the mitogenic effect of OT is inhibited. OVTA (10⁻⁹M) used alone induces a decrease of SCLC cell growth. These data prompt us to conclude that OT as VP act as growth factors on SCLC growth through autocrine/paracrine loops. Moreover, the mitogenic effect of these peptides could be mediated by cross talk between the inositol-Ca⁺⁺ and the MAP kinase cascades.