Neuropeptide signaling in health and disease

https://neurodegenerationresearch.eu/survey/neuropeptide-signaling-in-health-and-disease/

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Neuropeptide signaling in health and disease

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Research Abstract

Neuropeptides are, by numbers, the largest and most diverse family of transmitters in the nervous system (>100), with a correspondingly large number of receptors (>200). Their functional role and significance have been explored in rodents, but much less so in the human nervous system. Nevertheless, a neuropeptide antagonist (against orexin)(Belsomra, suvorexant) was recently approved by the FDA of USA for treatment of insomnia. We have analysed many neuropeptides, in particular with focus on their co-existence with classic transmitters. Special interest has been paid to galanin, a 29 aminoacid (30 in humans) peptide with a wide distribution in the nervous system, and acting via three receptors, GalR1-3. A particular interesting feature of galanin is that its expression is highly regulated by e.g. stress, pain and nerve injury. In fact, results from studies on various animal models in other and our laboratory show a role in e.g. pain- and depressive-like behaviors as well as neurodegenerative

diseases, indicating therapeutic opportunities. However, whether or not the galanin system is similar in different species is at present unclear, that is the translational potential remains to be demonstrated. A main line in this project is therefore to study human post mortem tissues to establish, if galanin and its receptors are expressed in the same systems in rodents and humans, e.g. dorsal root ganglia, spinal cord, noradrenergic locus coeruleus neurons, serotonergic dorsal raphe neurons and cholinergic basal forebrain neurons. We will primarily use in situ hybridization and qPCR to investigate for these studies, and also to establish if levels of these molecules are different in post mortem control brains compared to depressed (suicide) alternatively Alzheimer patients. By using custom-designed array studies, we will be able to compare galanin with up to 80 other peptide/peptide receptors. We will also study such brains using recent structural methods such as CLARITY and iDISCO combined with light sheet microscopy, allowing 3-D analysis of large pieces of immunostained brain regions. In addition to neuropeptides, we will also work on three ‘new’ calcium-binding proteins, secretagogin, NECAB1 and -2. Our published results indicate that they may be of interest in relation to pain processing at the spinal level, and mood disorders. In parallel we will continue studies on rodent brains to generate new ideas and hypotheses concerning, for example, neuropeptides in mood- and sleep-regulating circuitries. We will again use CLARITY/iDISCO and LSM, and also optogenetic methods, to better understand the relation between function and structure/circuitries.

Further information available at:

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