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Do diencephalic sleep-wake-regulatory systems meet?

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A wealth of classical studies on the thalamus pointed out a key role of the reticular thalamic nucleus (Rt) in sleep regulation. Since the discovery of the orexin (Orx)/hypocretin peptides in 1998, a key role in wakefulness stability has been ascribed to Orx neurons, which reside in the lateral hypothalamus. Rt neuron efferents, which are inhibitory, are distributed to nuclei of the dorsal thalamus. Orx neuron efferents, which are excitatory, are distributed widely in the neuroaxis but concentrated in the thalamus along the midline. Current views seem to consider these systems as separate networks. We here wondered whether these networks meet instead in the diencephalon, and in particular whether Rt and Orx synaptic endings converge on the same neuronal cell bodies or reach separate neurons of the paraventricular thalamic nucleus (PVT) of the thalamic midline. To answer this question, PVT neurons were here investigated in confocal microscopy by means of multiple immunofluorescent labelling: calretinin labelling of PVT cell bodies; Orx + synaptophysin for the labelling of Orx synaptic endings; parvalbumin + synaptophysin for the labelling of Rt synaptic endings. Striking results on the convergence of the two sets of synapses on the same neurons were obtained, since almost 100% of Orx synaptic boutons were apposed to PVT neurons which also received Rt synaptic boutons. Rt axon terminals were more abundant in PVT than Orx ones, and also reached neurons which did not receive Orx input. The present findings on the synaptic wiring of PVT neurons therefore points to the dorsal thalamic midline as a "meeting point" of sleep-wake-regulatory diencephalic networks. PVT efferents reach the prefrontal cortex, and limbic targets represented by the nucleus accumbens and amygdala. The synaptic convergence here demonstrated could thus place PVT neurons at the core of sleep-wake-related modulation of cognitive functions and emotional, affective behaviour.

Keywords

Orexin; thalamus; state-dependent behaviour.