New findings by Heister et al. presented in this issue of the Journal of Neurophysiology (p. 3142–3147) suggest that neurons in the rat pontine subcoeruleus (SubC) nucleus are electrotonically coupled. Electrical neurotransmission in the CNS is frequently generated by members of the connexin (Cx) family of proteins. Heister et al. report that SubC neurons robustly express mRNA and protein for Cx 36, which is widely distributed at ultrastructurally defined neuronal gap junctions (Rash et al. 2001). Notably, Cx 36 expression decreased from postnatal days 7 to 17 to adult, paralleling the known developmental decrease in REM sleep in rats (Jouvet-Mounier et al. 1970). Additional slice electrophysiological findings demonstrate that SubC neurons exhibited a characteristic signature of electrical synapses, “spikelets,” spontaneously or in response to the cholinergic receptor agonist carbachol. The spikelets were abolished by carbenoxolone, an inhibitor of gap junctions. Additional studies are needed to directly confirm that pairs of SubC neurons electrically communicate with one another as found for their cousins in the adjacent noradrenergic nucleus locus coeruleus (Christie et al. 1989).

Electrical synapses are known to contribute to synchrony in CNS neuronal networks. The best-studied electrical synapses in the CNS are in the inferior olive, where the oscillatory properties of single neurons endow the system with important dynamics; however, it is the gap junctions that are needed for synchronized neuronal ensemble activity (Leznik and Llinas 2005). Phasic activation of a group of SubC neurons is known to generate prominent field potentials called ponto-geniculo-occipital (PGO) waves, or P-waves in the rat, that are a cardinal sign of REM sleep (Datta et al. 1998). The findings of Heister et al. provide novel and exciting new avenues for the understanding sleep-wake control as well as for the treatment of sleep and arousal disorders. For example, Cx36-dependent neuronal gap junctions in the cortex may modulate synchronization of gamma oscillations (Traub et al. 2001). Cells in the reticular nucleus of the thalamus are known to be electrically coupled and to be responsible for the induction of network oscillations during slow wave sleep (Landisman et al. 2002). The presence of electrical coupling in the SubC described by Heister et al. may participate in the induction of network oscillations during REM sleep, and this result also introduces the possibility that electrotonic coupling may be involved in the process of sleep-dependent memory processing by providing oscillatory physiological activation necessary for long-term neuronal plasticity and memory formation (Datta 2006). Taken together, these findings provide exciting new possibilities for the modulation of sleep and arousal states, attentional processes, and even learning and memory by agents that control gap junctions and electrical coupling. Moreover, the potential roles of gap junction-dependent aberrant network oscillations in such disorders as narcolepsy, restless legs syndrome and insomnia are yet to be explored, but these seminal studies certainly point the way.

REFERENCES


