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Cholinergic modulation of hippocampal sharp wave-ripple complexes in adult rat hippocampus *in vitro*

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The two-stage model of hippocampus-dependent learning postulates that representations are transiently stored in oscillating hippocampal cell assemblies and are subsequently re-activated for readout and permanent storage. It is believed that hippocampal sharp wave-ripples (SPW-Rs) are important for the consolidation of declarative memories. We recently reported that in rat hippocampal slices, SPW-Rs can be induced by stimulation protocols, which induce L-LTP (Behrens et al., 2005). Periodic fluctuation of the neuromodulator acetylcholine (ACh) has been hypothesized to be important for sleep-dependent memory formation. Using the *in vitro* paradigm of LTP-associated SPW-Rs, we now investigated mechanisms underlying network switches hypothesized to be critical for sleep-dependent memory formation during rapid-eye-movement (REM) - and slow-wave sleep (SWS). The present data demonstrate that cholinergic modulation of presynaptic calcium uptake underlies M3-specific facilitated transition from theta/gamma network oscillations into hippocampal SPW-Rs. The observed switch is both, NMDA receptor- and CaMKII - dependent. In contrast, transient replacement of hippocampal SPW-Rs by synchronized theta/gamma activity, as observed during network transition between SWS and REM-sleep *in vivo*, is mediated by M1-receptor activation. In sum, these data support the idea that sleep stage-associated fluctuation of ACh concentration within the hippocampus is critically involved in transition between distinct synchronized network oscillations potentially involved in sleep-dependent formation of declarative memory.

Biography

Dr. Christoph J. Behrens graduated in human medicine in 2000. In 2003, he received his doctoral degree for work on 'Transcortical reflexes during slow target movements of the hand in man'. Since 2001, Dr. Behrens joins the Institute for Neurophysiology at the Charité – Universitätsmedizin – Berlin. He is interested in induction, expression and modulation of synchronized hippocampal network oscillations in acute rat brain slices. He works on the relation between activity-dependent synaptic plasticity and hippocampal sharp wave-ripples (SPW-Rs), which are thought to be important for memory consolidation. Dr. Behrens also works on mechanisms underlying formation of distinct neuronal ensembles during memory-related oscillations, which might be important for both, the binding and reactivation of information within neuronal networks.

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