Summary

The properties and molecular determinants of synaptic transmission at giant synapses connecting layer 5B (L5B) neurons of the somatosensory cortex (S1) with relay neurons of the posteriomedial nucleus (POm) of the thalamus have not been investigated in mice. We addressed this by using direct electrical stimulation of fluorescently labeled single corticothalamic terminals combined with postsynaptic whole-cell recordings and molecular perturbations. Consistent with their function as drivers, we found large amplitude excitatory postsynaptic currents (EPSCs) and multiple postsynaptic action potentials triggered by a single presynaptic action potential. To study the molecular basis of these two features, ionotropic glutamate receptors and low voltage-gated T-type calcium channels were probed by virus-mediated selective perturbation. Loss of GluA4 almost abolished the EPSC amplitude, strongly delaying the onset of action potential generation, but maintaining the number of action potentials generated per presynaptic action potential. In contrast, knockdown of the T-type calcium channel Ca₃.1 abrogated the driver function of the synapse when transmitting single action potentials. Only summation upon repetitive stimulation shifted the membrane potential towards firing threshold, generating postsynaptic action potentials with almost no delay relative to the presynaptic action potential. Hence, GluA4 subunits are required to produce an EPSC sufficiently large to trigger postsynaptic action potentials within a defined time window after the presynaptic action potential. Moreover, Ca₃.1 expression is essential to introduce a defined synaptic delay and support L5B-POm synapses to function as drivers. Additionally, we found that nicotinic receptors may participate in controlling thalamic neuronal excitability and output timing at individual L5B-POm glutamatergic synapses.

In conclusion, deleting these genes selectively in relay neurons impair distinct aspects of synaptic transmission at the L5B-POm giant synapse, offering an attractive possibility to study the systemic function of this synapse and the CTC loop in sensory-motor integration.