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Anatomical and physiological heterogeneity of layer 5 input to the thalamus in vitro and in vivo

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Giant corticothalamic terminals arising from the collaterals of layer 5 (L5) pyramidal cells are critical components of the thalamocortical circuits. These afferents allow faithful top-down control of selected thalamic nuclei. Mapping cortical terminals in the thalamus however indicated that giant cortical terminals are not an ubiquitous feature of the thalamic nuclei receiving L5 inputs. This prompted us to test if L5 terminals displayed region specific heterogeneity in the thalamus. Specifically, using L5 specific transgenic mouse lines (RBP4-Cre, Thy-1) we tested nucleus specific differences in size, complexity and postsynaptic action of L5 inputs arising from parietal (S1) vs. frontal (M2) cortices with light and electron microscopy and optogenetic activation in vitro and in vivo.

Our data demonstrated significant region specific morphological and functional heterogeneity of L5 corticothalamic terminals in the thalamus. Giant terminals were completely absent in the fronto-thalamic L5 pathway. L5 terminals of the M2 cortex were small and contacted mainly spines in the ventromedial nucleus (VM). Small L5 terminals also differed in size, targets and ultrastructure from the L6 corticothalamic terminals and could reliably activate VM neurons. During 10 Hz stimulation the M2/L5-VM pathway displayed less depression than the S1/L5 pathway to nucleus posterior in vitro, in anesthetized and in freely sleeping conditions as well. In drug free conditions the S1/L5 but not the M2/L5 depression was state dependent.

We propose that region specific L5 control of the thalamus is tailored to match the different computational roles performed by frontal (motor, premotor) and parietal (sensory) circuits.