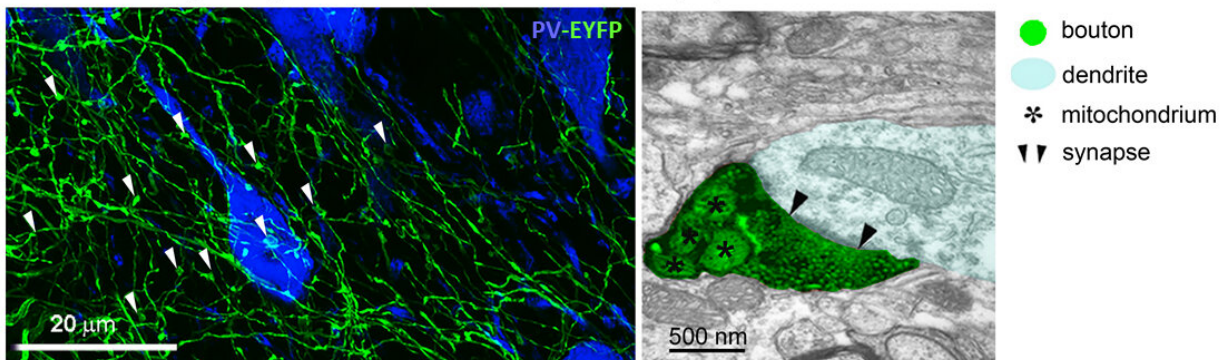


Study describes new region-specific cortical communication channel

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L5 collaterals originating from the frontal cortex tufted with synaptic terminals in the TRN



Left: Confocal image. TRN cells are labeled by parvalbumin- PV, blue – immunostaining, L5 collaterals are labeled by EYFP –green-. Arrows point to synaptic terminals. Right: electron microscopy image of L5 synaptic terminals (labeled by black precipitate and shaded in orange) in the TRN (the postsynaptic TRN dendrite are shaded in blue). Credit: IEM, Laboratory of Thalamus Research, Nora Hadinger

The cortex is at the apex of information processing in the mammalian brain. Interestingly, however, beside olfactory inputs, no fast, precise information reaches the cortex without a thalamic transfer. Indeed, without exception all cortical regions receive thalamic inputs and none of them (olfactory cortex included) is functional without intact thalamic inputs.

The interaction between the thalamus and cortex is not unidirectional. Every cortical region not only receives but also sends nerve fibers to the thalamus. This top-down information channel is called corticothalamic pathway. Thus, information between the thalamus and cortex does not simply travel one way; rather, information is processed in complex perpetually interacting thalamo-cortico-thalamic loops.

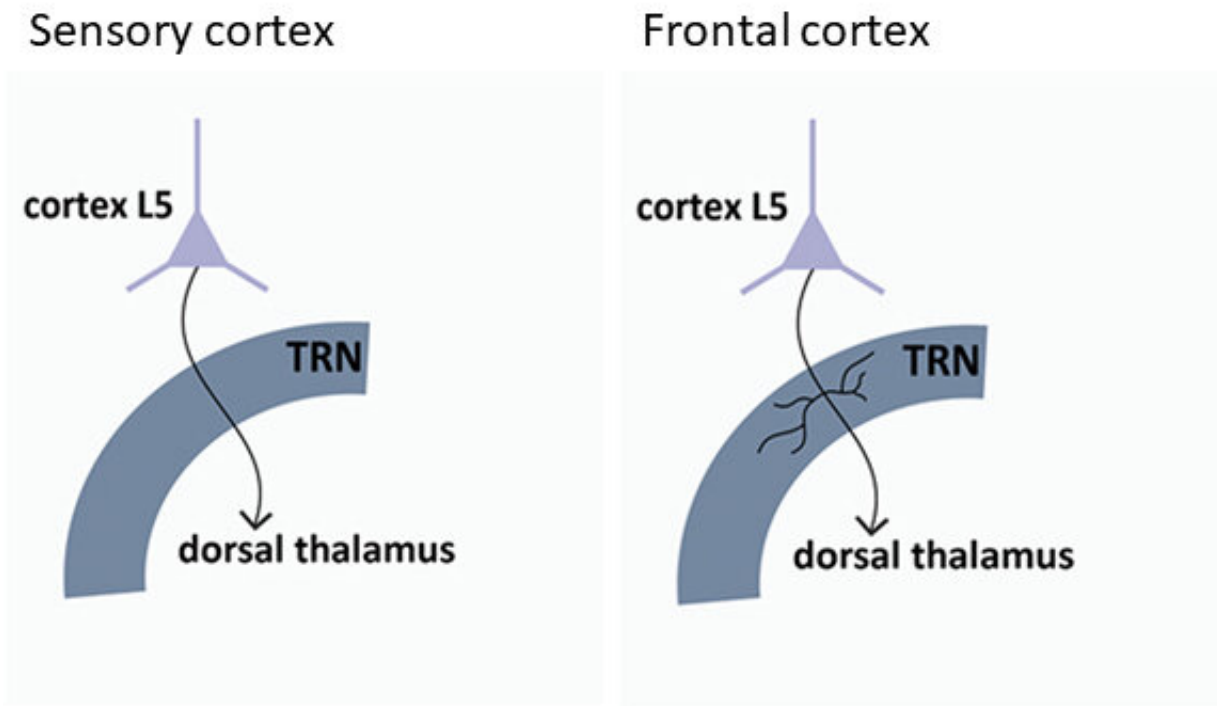
Now, a new study published in *Nature Neuroscience* describes a novel cortico-thalamic connection.

Connectivity between the cortex and thalamus has been intensively studied in the past 100 years and has been regarded as canonical. This means that it was thought that there were no qualitative regional differences in the organization of the cortico-thalamic pathways despite the fact that there are obvious differences in the precise nature of information processed in various cortical areas (e.g., sensory, motor, emotional).

In their new study Hadinger and colleagues show that the frontal [cortical regions](#) display a specific cortico-thalamic innervation pattern which are absent in other cortical areas demonstrating that the cortico-thalamic pathway is non-canonical. The new, [region](#) selective cortico-thalamic pathway targeted the enigmatic thalamic reticular nucleus (TRN) which contains only inhibitory neurons.

There is no proper neuronal activity in the brain without precisely organized inhibitory activity. In the vast majority of diseases affecting the brain the balance and timing of excitation and inhibition is perturbed. The thalamus is not an exception. The main controller of thalamic inhibition is TRN. Inhibitory axon terminals of TRN densely innervate all thalamic nuclei. What controls TRN, controls the thalamus as well. TRN forms a thin shell around the thalamus and its distinct sectors project to different thalamic regions in a nice topographic order.

Since specific thalamic nuclei project to specific cortical regions activating a specific TRN sector will result in governing the activity in a well defined cortico-thalamic loop. And this is exactly what the study found. TRN cells targeted by frontal cortical inputs innervated those part of the thalamus which projected back to [frontal cortex](#) closing the cortico-thalamo-cortical loop.



Schematic figure showing cortical L5-thalamus connections in the sensory and frontal cortices. Credit: IEM, Laboratory of Thalamus Research, Nora Hádinger

Inputs may be weak or strong, few or numerous. According to Hádinger, TRN receives many corticothalamic inputs, sometimes even from different cortical regions. The data also show that TRN is especially sensitive to the synchronicity of its cortical inputs. Increasing cortical synchrony will gradually alter the timing and amount of TRN activity.

This will be pivotal to control the response of thalamic cells to synchronous or hypersynchronous cortical activity, like epileptic seizures.

In summary, the data suggest that the properties of [information](#) processing in thalamocortical loops involved in higher order cognitive functions are qualitatively different from those of other (e.g., sensory) loops. The new cortico-thalamic pathway targeting TRN will help to understand the neuronal basis of normal cognition and chronic neurological and neuropsychiatric diseases linked to the frontal [cortex](#), including Parkinson's disease, schizophrenia, [chronic pain](#), and epilepsy. Additionally, the research opens up novel avenues to study cortico-thalamic interactions.

More information: Nóra Hádinger et al, Region-selective control of the thalamic reticular nucleus via cortical layer 5 pyramidal cells, *Nature Neuroscience* (2022). [DOI: 10.1038/s41593-022-01217-z](https://doi.org/10.1038/s41593-022-01217-z)

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