A stereological transmission electron microscopic study: Marked differences in the number and type of synapses innervating three neuronal subtypes in the rat brain

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Introduction
Understanding the morphological bases of behavioral control requires characterization of the afferent synapses that regulate firing patterns in midbrain dopaminergic neurons.

Materials and Methods
We used serial section transmission electron microscopy and stereological methods to measure the absolute number and type of afferent synapses on the somata and primary dendrites of midbrain dopaminergic (DA) neurons in the ventral tegmental area (VTA), as well as striatal cholinergic (Ach) interneurons and spiny projection neurons (SPN) for comparison, in the rat.

Results and Discussion
The average absolute number of afferent somatic synapses was 3.5-fold higher on VTA dopaminergic neurons and striatal spiny projection neurons compared to striatal cholinergic interneurons. The percentage of symmetrical, presumably inhibitory, synaptic inputs on somata was significantly higher.
on striatal spiny projection neurons and cholinergic interneurons \((98 \pm 2\% \text{ [mean \pm SD]} \text{ and } 95 \pm 5\%\), respectively) compared to VTA dopaminergic neurons \((63 \pm 6\%\)). Synaptic data of the primary dendrites yielded similar significant differences. These data provide an anatomical substrate for potentially strong proximal inhibitory synaptic regulation of the firing of striatal spiny projection neurons and emphasise that inhibitory synaptic inputs may be critical for controlling activity in striatal cholinergic interneurons and VTA dopaminergic neurons. These anatomical data may also explain previous electrophysiological data on the specific response by the three neuronal subtypes to afferent synaptic input. These data are also essential for generating realistic computer models of neuronal networks of striatal function.

**Conclusion**

Three-dimensional anatomical analyses involving transmission electron microscopy are critical for correlating the pattern of synaptic input with neuronal function in the brain.