Moritz Helmstädter Dr. med.

Der Zusammenhang zwischen axonalen, dendritischen und elektrischen Eigenschaften von Interneuronen in Schicht 2/3 des somatosensorischen Cortex der Ratte

Geboren am 18.04.1978 in Berlin Staatsexamen am 14.11.2007 an der Ruprecht-Karls-Universität Heidelberg

Promotionsfach: Physiologie Doktorvater: Prof. Dr. med. Dr. h.c. mult. B. Sakmann

To determine the effect of inhibitory synaptic transmission on the representation of sensory-evoked responses in cortical columns of primary sensory cortices, it is crucial as a first step to (1) analyze the potential effect of a single inhibitory interneuron with reference to the layers and borders of the home column and neighboring cortical columns; (2) determine the number and types of inhibitory neurons that can contribute synaptic transmission onto the principal neurons in a cortical column. While many qualitative descriptions of interneuron properties are available, quantitative analysis of multiple parameters of interneurons at a time are missing. The analysis of axonal projections with reference to the relevant computational units, cortical columns, was entirely lacking.

This study therefore attempted to provide a quantitative and largely unbiased analysis of a sample of approximately 50 interneurons from layer 2/3 of a cortical column in rat barrel cortex, with a concomitant description of axonal, dendritic and electrical properties and without explicit pre-selection.

The main findings are: (1) layer 2/3 interneurons show distinct axonal projection types with reference to cortical columns; these constitute neuronal correlates of local, lateral, and translaminar inhibition within and across cortical columns; (2) the axonal projection types represent an independent property of interneurons that cannot be predicted by dendritic or electrical parameters; (3) dendritic geometry is strongly correlated to electrical properties of L2/3 interneurons; up to 50% of this correlation can be accounted for by the causal link between membrane geometry and electrical properties, as established by numerical models; (4) A combination of axonal, dendritic and electrical properties can be used to define groups of layer 2/3 interneurons that may constitute basic identities of L2/3 interneurons; a classification scheme is presented based on an iterated cluster analysis in this parameter space; 11 groups were found.

To achieve these results, the development of several analysis tools was required: (1) analysis algorithms that allow the relation of single cell reconstructions to cortical column outlines based on in-vitro slice preparations (2) quantification of dendritic polarity using cluster analyses of primary dendrite insertion points on the soma surface

(3) automated analysis of electrical properties of interneurons (4) iterated cluster analysis as a method to estimate the significance of similarity between cell parameters.

The findings predict monosynaptic surround inhibition across columns; they provide evidence for the superior relevance of axonal projections for interneuron classification, and the strong interdependence of electrical and dendritic properties, which render those parameter less suited for the identification of interneuron classes; and they provide a basis for mechanistic models of inhibitory effects in a cortical column. Assuming ~ 300-800 interneurons in layer 2/3 of a single column, these results suggest that sets of ~30-80 interneurons form groups of common axonal, dendritic, and electrical properties. Together with information on synaptic input and output properties, these results will allow the construction of a mechanistic model of the electrical activity following a sensory stimulus in the supragranular layers of a cortical column.