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Characterization of the axon initial segment in rodent serotonergic neurons *in vivo* and *in vitro*

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Abnormalities in serotonin homeostasis have been shown to have a share in the pathogenesis of several neurological and psychiatric disorders. Although the raphe nuclei are known as the origin of serotonergic projections, details about morphological characteristics of serotonergic neurons, especially regarding the features of the domain relevant for neuronal signaling, the axon initial segment, remain unknown.
The aim of this doctoral thesis was to characterize the morphology of the axon initial segment of serotonergic neurons. Because of the widespread use of rodent models for research of serotonergic neurotransmission, further experiments were conducted in order to compare the morphology and the axon initial segment protein expression *in vivo* and in corresponding *in vitro* models.
The *in vivo* immunostaining results showed that a small percentage of murine serotonergic raphe neurons demonstrates a proximal axon initial segment. Among these, half of the axon initial segments were located on axon-carrying dendrites. Based on these findings, future studies must focus beyond the small number of axon initial segments found in raphe nuclei for a better understanding of the role of the axon initial segment in serotonin signaling.
The comparison of ankyrin-G isoform expression *in vivo* and *in vitro* demonstrated that, using the established differentiation protocols, serotonergic neurons *in vitro* do not reach the maturity of serotonergic raphe neurons regarding the development of the axon initial segment, although displaying serotonin *in vivo* neurochemical features. Therefore, optimization of these protocols is required to establish *in vitro* models that represent the *in vivo* maturation stages of adult serotonergic neurons.
In conclusion, this study characterizes the axon initial segment of serotonergic raphe neurons for the first time and provides evidence that serotonin neurochemistry may be independent of neuronal maturation stage.