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Maturation of the axon initial segment during visual cortex development

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The axon initial segment (AIS) is defined by its highly specific molecular composition and exerts several important functions, such as action potential generation and maintenance of neuronal polarity. Recent research revealed dynamic changes at the AIS in physiological and pathological settings.
In this thesis, possible AIS plasticity in development and deprivation of the rodent visual cortex was analysed. The visual cortex has been in focus of brain plasticity research for decades and a critical period (CP) has been defined, but the link between visual cortex plasticity and the axonal compartment of neurons is rather neglected. Therefore, the influence of changing activity patterns on AIS length maturation during visual cortex development was evaluated.
AIS length measurements were based on immunofluorescence labelling of ankyrinG, the master scaffolding protein of the AIS. Self-written macros in Fiji (ImageJ) and in Visual Basic for Applications (Excel) served to establish a semi-automatic method of AIS length measurement. In total, more than 30.000 AIS were measured in animals at various ages, including visually deprived animals, and in additional experimental settings.
AIS in the prospective, prenatal visual cortex started to appear at E14.5 in two different orientations, marking distinct cell populations. In postnatal ages, AIS development followed a tri-phasic time course:

- Phase I: In the precritical period, AIS length increased from prenatal ages until a maximum at P10/15. This development could not be abolished by dark rearing. Therefore, phase I is most likely triggered by intrinsic spontaneous activity, such as retinal waves. Length increase at the AIS is related to higher excitability, a state which allows neurons to form circuits and synapses. It seems plausible that increase in AIS length, molecular maturation of the AIS and increased network excitability before and during eye opening are processes that re-enforce each other.
- Phase II: After eye opening at P13/14, AIS length sharply decreased until a minimum at P28. Sensory input through vision increases activity in the visual cortex. As the inhibitory system is not fully developed at this time, AIS length decrease could be important to prevent over-excitability. In animals dark-reared up to P28, AIS length was similar to that seen at the end of phase I; suggesting that phase II is abolished under visual deprivation.
- Phase III: After P28 and a re-increase, AIS length remained stable from P35 onwards. This length might represent the functional optimum of fully mature AIS and could not be altered by visual deprivation. AIS resizing may now no longer be necessary to balance changing excitability levels characteristic for developing excitatory and inhibitory networks.

In summary, a striking tri-phasic AIS length maturation corresponding to visual cortex development was revealed. This highly dynamic process involves phases of plasticity, which can be triggered by sensory experience. AIS plasticity is part of the physiological AIS maturation process and is related to the CP of the visual cortex. Regarding the functional implications of these findings, AIS plasticity might balance changing intrinsic and extrinsic activity patterns during visual cortex development.