Irina Dudanova

Discrete structural abnormalities in the brains of adult α-neurexin double knockout mice may reflect long-term consequences of impaired synaptic transmission

Neurexins are highly polymorphic cell-surface proteins, which are essential for synaptic function by regulation presynaptic voltage-gated Ca$^{2+}$ channels. Mice lacking all three α-neurexins die early postnatally because of the severe depression of neurotransmitter release. No major abnormalities have been reported in the brain structure of these newborn α-neurexin mutants, except for a moderate reduction in symmetric synapses. To test how reduced neurotransmission affects brain structure over a longer period of time, I have studied the brain morphology of adult α-neurexin double knockout mice. Some of the mice lacking two α-neurexins survive into adulthood. They had a grossly normal architecture, but the neuropil was reduced by up to 20% in several brain regions, most notably in the visual cortex, caudate-putamen and olfactory bulb, while other regions, such as somatosensory and motor cortices and hippocampus were not significantly affected. The reduction in neuropil was confirmed by a corresponding defect in dendritic architecture. The length of dendrites of neocortical neurons was decreased, and this was mainly accounted for by the selective shortening of peripheral branches by 30-50%. A decrease in the dendritic spine number was most obvious in the peripheral branches, too, where it was also reduced by 30-50%. The density of spines on the dendrites was unaffected. Deletion of two α-neurexins did not impair cell survival and had no obvious effect on the distribution of synaptic, neuronal and glial cell markers. The obtained data suggest that decreased synaptic transmission causes developmental defects in dendritic growth and synaptogenesis.