The physiology of ventral tegmental area dopamine neurons and its derailment in Alzheimer's Disease

Dopamine neurons in the ventral tegmental area of the midbrain are a particularly heterogeneous population of cells. This heterogeneity is predominantly evident along the medial–lateral axis of the brain, and it involves various physiological properties of these neurons, including spontaneous firing, intrinsic membrane properties, cell body size and magnitude of underlying conductances. These cells innervate many brain regions including the prefrontal cortex, hippocampus and nucleus accumbens. Thus, deficits in the dopaminergic neurotransmission along these connections is strongly linked to disturbances in cognition, memory and reward processing.

Such a situation appears to occur along Alzheimer's disease stages: Recent evidence from the D'Amelio lab show that in a transgenic mouse model of Alzheimer's disease the dopamine neurons of the ventral tegmental area degenerate precociously and the resulting reduction of dopamine in the projection areas correlates with impairments in memory and reward and with deficits in the downstream connection between the hippocampus and nucleus accumbens. These data are strengthened by the fact that all these deficits can be rescued when mice are treated with levodopa, the precursor of dopamine. A thorough characterisation of dopamine neurons in the transgenic mouse at different stages of the disease progression has shown important changes in their intrinsic properties and electrophysiological properties that are accompanied by autophagic deficits.

Our future aim is to better define the molecular mechanisms that alter the physiology of these neurons and participate in the cascade of events leading to degeneration.

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