COLLAGEN VI LACK AFFECTS BEHAVIOR: NOVEL INSIGHTS FROM MICE AND PATIENTS.

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Collagen VI (ColVI) is an extracellular matrix (ECM) component, made of three alpha chains that assemble in a hierarchical manner to create an organized network. Mutations in the genes coding for ColVI chains cause different forms of muscle diseases (Ullrich Congenital Muscular Dystrophy, Bethlem Myopathy and Myosclerosis), but were also recently linked to brain pathologies, including early-onset isolated dystonia, progressive myoclonus epilepsy syndrome, neurodegeneration and psychiatric disorders.

We previously demonstrated that ColVI exerts a critical protective role in the aging central nervous system (CNS), showing that its lack causes defective regulation of autophagy, increased oxidative stress and spontaneous apoptosis of neural cells both in vitro and in aged mouse brains. However, further in-depth studies ascertaining its role in CNS, in physiological conditions, are still missing.

For this reason, we performed behavioural tests in young-adult (3-6 months old) Col6a1-/- and WT mice, revealing cognitive impairments, such as deficits in prepulse-inhibition, abnormal social interaction and defects in the temporal-object recognition test, in the absence of ColVI. Consistently, RT-PCR and western blot analysis, performed on RNA and protein extracts from different brain regions, identified specific neurotransmitter signalling pathway alterations, primarily in the prefrontal cortex (PFC). Based on the results of behavioral analysis in mice, a protocol for neuropsychological tests was designed ad hoc to be administered to a cohort of Ullrich and Bethlem patients.

Our findings sustain the hypothesis that ColVI is necessary for the correct development of the mammalian CNS, by showing that ColVI lack induces behavioral alterations in mice by impacting specific neurotransmitter pathways.