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P26. METABOLISM OF SIALO-GLYCO-CONJUGATES IS DEFECTIVE IN HUNTINGTON'S DISEASE

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Introduction. Huntington's disease (HD) is a rare neurodegenerative disorder with no cure available. Among all the deregulated molecular mechanisms characterizing the disease, aberrant metabolism of gangliosides, sialic-acid containing glycosphingolipids, represents a critical determinant in its pathogenesis and a potential therapeutic target. Although still under investigation, such dysfunction seems to be, at least in part, attributable to a significant reduction in the expression of some of the sialyltransferases, classically involved in the synthesis of both gangliosides and glycoproteins.

Hypothesis. Considering the role of sialyltransferases in the synthesis of glycoproteins, the main hypothesis of this study is that the aberrant ganglioside metabolism in HD may represent the result of an overall perturbed metabolism of sialo-conjugates.

Aim. Here, we evaluated whether an overall impairment of brain sialo-conjugate metabolism really occurs in HD and may represent a potential novel therapeutic target.

Results. Our data indicate that levels of Polysialic Acid (PSA), a sugar polymer exclusively linked to proteins and normally synthesized by two different sialyltransferases -ST8SIA2 and ST8SIA4-, is perturbed in brain tissues from a HD mouse model at different stage of the disease. The aberrant PSA content seems to depend on deregulated expression of ST8SIA2 and ST8SIA4. In line with our expectation, although still not conclusive, mRNA levels of these enzymes are clearly deregulated in brain tissues from HD mice.

Conclusions. Our results support the idea that metabolism of sialo-conjugates may be globally impaired in HD, thus its modulation may likely represent a potential novel and alternative therapeutic strategy to treat the disease.