LYSOSOMAL STORAGE DISORDERS AND PARKINSON'S DISEASE - IS GAUCHER DISEASE ONLY THE TIP OF THE ICEBERG?

T. Shachar, A.H. Futerman

Biological Chemistry, Weizmann Institute of Science, Rehovot, Israel

Recently, a genetic link has been proposed between Gaucher disease, the most common lysosomal storage disease (LSD) and Parkinson’s Disease (E. Sidransky et al. (2009) NEJM 36, 1652), inasmuch as a strong association was demonstrated between mutations in the gene encoding for glucocerebrosidase (GBA), the enzyme defective in Gaucher disease, and Parkinson's disease. Little mechanistic data is available to explain the link between Gaucher and Parkinson’s diseases, but gain of function due to protein aggregation, or loss of function related to lipid levels were proposed as putative mechanisms. We have now performed an exhaustive literature search and demonstrate, based on case reports and pathological studies, that the association between Parkinson’s disease and LSD is not limited to Gaucher disease, but is rather associated with a wide spectrum of other LSDs. We suggest that the mechanistic link between LSDs and Parkinson’s is not necessarily related to changes in GBA or in levels of its substrate, glucosylceramide, but is rather related to one or other of the biochemical cascades that are altered in LSDs (E.Vitner et al (2010) J. Biol. Chem. 285, 204230). This suggestion leads to a paradigm shift in our understanding of the relationship between Gaucher and Parkinson’s diseases, which would be of wide-ranging significance for clinical diagnosis of patients presenting with symptoms related to either LSDs or Parkinson’s disease.