Glucosylsphingosine

Biallelic mutations in the GBA1 gene encoding glucocerebrosidase cause Gaucher's disease, whereas heterozygous carriers are at risk for Parkinson's disease (PD). Glucosylsphingosine is a clinically meaningful biomarker of Gaucher's disease but could not be assayed previously in heterozygous GBA1 carriers.

The aim of a study was to assess plasma glucosylsphingosine levels in GBA1 N370S carriers with and without PD.

Glucosylsphingosine, glucosylceramide, and four other lipids were quantified in plasma from N370S heterozygotes with (n = 20) or without (n = 20) PD, healthy controls (n = 20), idiopathic PD (n = 20), and four N370S homozygotes (positive controls; Gaucher's/PD) using quantitative ultra-performance liquid chromatography tandem mass spectrometry.

Plasma glucosylsphingosine was significantly higher in N370S heterozygotes compared with noncarriers, independent of disease status. As expected, Gaucher's/PD cases showed increases in both glucocerebrosidase substrates, glucosylsphingosine and glucosylceramide.

Plasma glucosylsphingosine accumulation in N370S heterozygotes shown in this study opens up its future assessment as a clinically meaningful biomarker of GBA1-PD. [1].

1)
Surface M, Balwani M, Waters C, Haimovich A, Gan-Or Z, Marder KS, Hsieh T, Song L, Padmanabhan S, Hsieh F, Merchant KM, Alcalay RN. Plasma Glucosylsphingosine in GBA1 Mutation Carriers with and without Parkinson's Disease. Mov Disord. 2021 Nov 6. doi: 10.1002/mds.28846. Epub ahead of print. PMID: 34741486.