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Chronic ethanol consumption profoundly disrupts regional brain ceramide-sphingomyelin content in a mouse model

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Alcohol abuse is characterized as a multi-factorial disorder associated with neurotoxicity that can result in dementia.Studies have reported pathology in the brain of alcoholics when compared with controls, including cortical atrophy, ventricular enlargement, and changes in membranes fluidityand white matter degradation. However very few studies are available on regional imaging of brain lipid. Despite, lipids being major building blocks of cell membrane, playing a key role in cell signaling and signal transduction and making up half of the brain's dry weight.

7 weeks old adult mice, in a drinking-in-the-dark paradigm (DID)were fedwater (control) or ethanol (EtOH). The EtOH group had a daily 4-hour access to a 12% ethanol bottle. Control mice had access to water only. After 52 days, mice were euthanized 1 hour after ethanol access and brainswere collectedchronically were analyzed.Whole brain lipid extracts were assayed by electro-spray ionization mass spectrometry using a Thermo Fisher Orbitrap to obtain lipids concentration. All Ceramides (Cer) increased significantly, while all sphingomyelins (SM) decreased, only a few decreased significantly. Tomap the distribution and changes of these same lipids, three bregmas (+1.54 mm , -1.70 mm and -5.88 mm)were imaged by Matrix Assisted Laser Desorption Ionization (MALDI) mass spectrometry imaging (MSI) using a Thermo Fisher Orbitrap, in regions known to be impacted by alcohol.

Coronal brain sections, were implanted with silver nanoparticles (AgNPs)using a NPlanter (Ionwerks,Inc).The particles size was 6 nm in diameter. The deposition time/brain section was 18 minutes and is highly reproducible.The implanted tissues were then imaged. Image acquisition was obtained in both positive and negative ion mode. MSn analysis was conducted in both positive and negative ion mode with CID to confirm lipid assignments and structure.

By imaging, the most prominent changes were found in the same lipid species in the bregma containing the striatum, a regions known to be impacted by alcohol

The major changes within the 3 bregmas in the distribution of (SM and CER were observed in the striatum, nucleus accumbens, prelimbic and piriform cortex and to a lesser extent in the primary and secondary motor cortex. In adult rats brains we saw a significant decrease in SM C18:0/d18:1 with alcohol consumption, however the increase in the corresponding cerwas notas significant. The bregma containing the hippocampus showsminor changes for SM and Cer and the cerebellum also shows minorchanges in SM in the piriform cortex with alcohol consumption. Images show that in the adult alcohol group, grey matter SM (C18:1/d18:1 and C18:0/d18:1) decreased with alcohol consumption.In conclusion, alcohol consumption lead to a significant decrease in SM (located in the striatum and nucleus accumbens and cortex) and although less localized and more diffuse a significant increase in CER was noted in the whole brain. Overall the Cer-SM changes were correlated.

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