Therapeutic potential of taurine supplementation for multiple sclerosis

Beyer et al. found taurine, in combination with drug-induced remyelination, to significantly enhance oligodendrocyte differentiation, making it a potential supplement for patients with demyelinating diseases.

Maribel Garcia-Igueldo

The biological mechanisms associated with oligodendrocyte progenitor cell (OPC) differentiation and function and additional treatment strategies for demyelinating diseases are not well understood. In an article published in Nature Chemical Biology, Beyer et al. used global metabolomics to identify endogenous metabolites that are altered during OPC differentiation and serve to directly impact cell fate. The research team found that exogenous taurine, in combination with drug-induced remyelination, significantly enhanced oligodendrocyte differentiation by increasing available serine pools. Serine pools serve as a primary building block for glycosphingolipid (GSL) biosynthesis. GSL makes up 31% of the lipid components of myelin, which serves to insulate nerve fibers and increase the speed at which signals are propagated.[1] Therefore, taurine supplementation enhances oligodendrocyte (OL) maturation by directly enabling GSL biosynthesis, making it a potential treatment for demyelinating diseases such as multiple sclerosis (MS).

Multiple sclerosis affects nearly one million people in the US, making it the most common demyelinating disease.[2] MS is an autoimmune disease of the central nervous system characterized by inflammation, demyelination, and axonal loss.[3] Typically, MS follows a variable relapsing and remitting course with clinical features not limited to weakness, pain, vision problems, balance problems, and cognitive difficulties.[4] Existing immunomodulatory and immunosuppressive drugs have limited efficacy in preventing the progression of MS in patients, therefore it is important to identify additional treatment strategies.[5] Resident OPCs in the adult brain differentiate into mature OLs which then remyelinate axons, however these cell's ability to restore myelin in MS patients diminishes as the disease progresses.[6] Beyer et al. were interested in the biological system by which OLs remyelinate axons and potential strategies to enhance OPC differentiation.

Several methods were used in the study conducted by Beyer et al. in 2017. The in vitro OL maturation analysis was done using neurons isolated from the cortical and hippocampal tissue of mice. In the study, researchers highlighted the utility of global metabolomic analysis for identifying endogenous metabolites that modulate cellular characteristics.[1] Metabolomics is a comprehensive assessment of endogenous metabolites from a biological sample. Endogenous metabolites include lipids, amino acids, peptides, nucleic acids, and other low molecular weight molecules which makes it an ideal method for discovery-based research.[7] In the 2017 study, researchers integrated the analytical platforms high-pressure liquid chromatography (HPLC) and ultra-performance liquid chromatography (UPLC). The two analytical platforms are used for legal, pharmaceutical, and medical purposes to detect metabolites in biological samples.[8] Specifically, Beyer and his research team identified 22 upregulated metabolites in mature OPCs

treated with a drug known to induce OPC differentiation named triiodothyronine (T3). The research team identified the metabolites involved in the taurine pathway as the most upregulated in OPC differentiation.

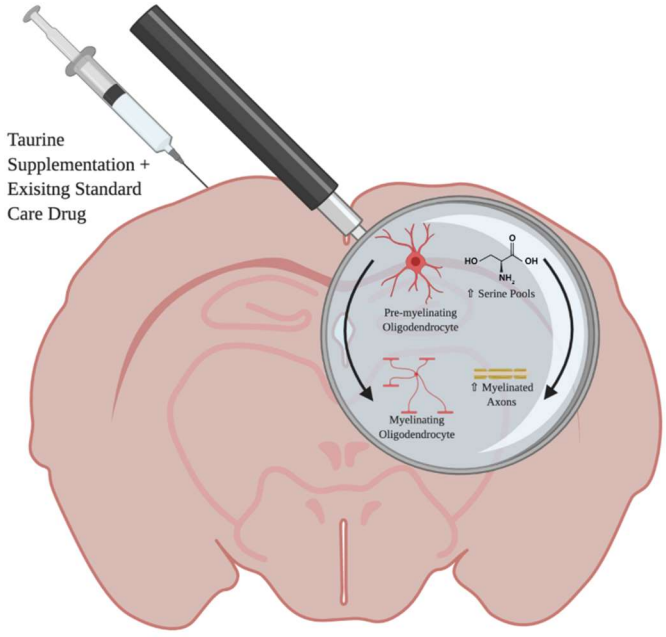

Figure 1. Beyer et al. found that taurine supplementation, in combination with drug-induced remyelination, facilitates maturation of pre-myelinating oligodendrocytes. The research team also found that taurine increased available serine pools which serve as a building block in glycosphingolipid biosynthesis. Glycosphingolipid is an essential lipid component of myelin.[1]

According to Beyer et al., the taurine pathway is the most altered event of OPC differentiation, making taurine the metabolite of interest in their study. In addition to T3, benzotropine and miconazole were used to induce OPC differentiation. Benzoptropin is used to treat Parkinson's disease by blocking an endogenous molecule in the brain called acetylcholine.[9] Miconazole is an antifungal agent that functions in OPCs through mitogen-activated protein kinase (MAPK) signaling.[10] The study found that OPC differentiation and myelin basic protein (MBP), a protein important in the process of myelination, expression significantly increased when exogenous taurine was added to each drug condition.[11] The same researchers became interested in determining the amount and stage of OPC differentiation at which taurine optimized MBP expression. In separate experiments, they found that 2 mM of taurine added between differentiation day one and day three optimized the positive effect of taurine on OPC differentiation. In addition, 2 mM of taurine supplementation, in combination with either benzotropin or miconazole, significantly increased MBP colocalization with axons in cultures compared to the base condition and drug treatment alone. Beyer et al. also conducted an experiment to identify metabolite pools impacted by exogenous taurine supplementation. Specifically, the researchers found an increase in serine after three days of taurine supplementation combined with T3 compared to observed quantities after six days of the same treatment.[1]

The article "Metabolomics-based discovery of a metabolite that enhances oligodendrocyte maturation" published in Nature Chemical Biology by Beyer et al. identified a novel potential treatment for demyelinating diseases, such as MS. However, the study failed to address how the mechanism by which taurine enhances OL differentiation may be influenced by MS. Future research should focus on identifying if MS prevents taurine from enhancing OPC differentiation using experimental mice models of demyelination. According to the study, 2 mM of taurine supplementation, combined with drug-induced differentiation, increased MBP colocalization with axons which suggests that taurine enhances remyelination.[1] Myelin destruction is the driver for the presentation of signs and symptoms in MS patients, making taurine supplementation a potential treatment that restores myelin. The researchers also found that taurine added between differentiation day one and day three optimized MBP expression. The timing of peak MBP expression suggests that taurine mediates maturation of premyelinating OLs.[1] There was also a greater amount of available serine when exogenous taurine, in combination with T3, was added

on day three than day six, which suggests that serine pools derived from taurine are taken up by other pathways in mature OLs.[1] In conclusion, Beyer et al. provided evidence for the therapeutic potential of taurine supplementation for multiple sclerosis.

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