Intestinal Bile Acids and Neurological Disorders

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Abstract

Due to their essential role in the gut-liver-brain axis and their physiological and pathological implications in both normal brain function and a number of neurological illnesses, bile acids are being employed in clinical studies to treat neurological diseases. It is addressed how primary and secondary bile acid production occurs as well as how the regulation of the bile acid pool may vary between the gut and the brain. There is also discussion of the interaction of bile acids with the gut microbiome and their less well-known effects on brain glucose and lipid metabolism, as well as the expression of various bile acid receptors in the brain, their currently understood functions, and the tools available to manipulate them pharmacologically. The dysregulation of the gut microbiota, ageing, sex variations, and potential causative roles in a number of neurological illnesses are also taken into consideration.

Keywords: Bile acids • Parkinson's disease • Neurodegeneration • Microbiome

Introduction

Hippocrates first proposed the idea of two-way connection between the brain and splanchnic organs. The neuro-endocrine processes that support this relationship, however, have only just been elucidated and, more recently, their relevance to the pathophysiology of neurodegeneration has been recognised. This review focuses primarily on the physiological and pathological functions of bile acid species, a significant and diverse family of biological mediators vital for the gut-liver-brain axis, in maintaining the health of neuronal cells. The variety of diseases that develop when the homeostasis of bile acids is upset, including non-alcoholic fatty liver disease, obesity, inflammatory bowel disease, and diabetes, serves as an illustration of the fundamental role that bile acids play in the body. Initially, it was believed that bile acids merely served as surfactants, assisting in the absorption of lipids, lipid-soluble vitamins, and hormones into the blood for later utilisation by the liver. However, it is now known that bile acids have a complicated biology that affects a variety of physiological processes and that, in addition to their functions as emulsifying agents, they are hormone-like signalling molecules. To avoid harm to the liver and other tissues, bile acid levels must be tightly controlled because they can be poisonous. Surprisingly, bile acids can also be produced in the brain, where they regulate cellular lipid and glucose metabolism. Bile acids are normally produced in the gut. Understanding the role of bile acids in these diseasespathogenesis is essential to developing treatments for their prevention and treatment because metabolic dysfunction is a key risk factor for Parkinson's disease, Alzheimer's disease, and other neurodegenerative disorders. Additionally, the impact of bile acids' interactions with the gut microbiome on the brain's lipid and glucose metabolism will be investigated. We shall briefly examine bile acid synthesis, bile acid pool, and cholesterol catabolism. With around a quarter of the body's total cholesterol concentration, the brain is the organ with the highest cholesterol content. In glia and neurons plasma membranes as well as a significant portion of myelin, cholesterol and other associated lipid molecules play an essential role [1-3].

Production of bile acids

Primary bile acids: The majority of the production of primary bile acids, which constitute the first stage of bile acid synthesis, takes place in the liver. Here, a series of 17 enzymes, including cytochrome p450, modify cholesterol's steroid ring to remove its short aliphatic side chain before conjugating it with glycine (75%) and taurine (25%) to create conjugated primary bile salts of Cholic Acid (CA) and chenodeoxycholic [4].

Secondary bile acids: Primary bile acids are converted into secondary bile acids through enzymatic modification by bacteria found in the colon, where they act as substrates for microbial metabolism. The bile acids can control the composition of the gut bacteria by both direct and indirect antimicrobial effects, and the gut microbiome affects the components of the bile acid pool. The microcidal action of intraluminal bile acids is reduced by microbial deconjugation of taurine and glycine conjugated primary bile acids via bile salt hydrolase, which is a highly conserved function across bacterial phylae and archaea. A further selective benefit exists in this environment for bacteria that have bile salt export pumps. The downstream biotransformation of CA and CDCA into secondary bile acid species Deoxycholic Acid (DCA) and Lithocholic Acid (LCA), respectively, by 7-dehydroxylation, depends on the conversion back into unconjugated hydrophobic forms. This process is typically a characteristic of firmicutes, such as clostridial species [5].

Diseases of the nervous system

Many neurological diseases exhibit overlapping clinical traits, including protein misfolding deposits, neuroinflammation, loss of neurons, and altered cellular function, including mitochondrial dysfunction and oxidative stress, despite the traits that distinguish them as different disorders. Bile acids have showed promise as potential therapies for several neurological conditions that have recently seen bile acids and their receptors linked to pathological processes. The gut can undergo a number of changes that can affect the gut microbiome-brain axis, including decreased stability and diversity of microbial communities, increased levels of inflammation and thinning of the mucosal lining, and reduced bioavailability of microbial metabolites with immunoregulatory actions, such as secondary bile. Ageing is the biggest risk factor for neurodegenerative disorders.

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