Chapter 12 Hepatic Encephalopathy as a Gliopathy: The Mechanisms of Alzheimer Type II Astrocytosis

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ABSTRACT

Hepatic encephalopathy (HE) is defined as a wide spectrum of neuropsychiatric abnormalities caused by liver dysfunction (acute or chronic) and/or portal-systemic shunting. The histopathologic hallmark of HE is astrocyte swelling following acute liver failure (ALF) or the presence of the so-called Alzheimer type 2 astrocytosis under chronic liver disease. HE can be classified according to the undelaying cause into three types: type A as an essential component of acute liver failure, type B as a consequence of porto-systemic shunts in the absence of liver dysfunction, and type C in patients with liver cirrhosis and porto-systemic bypass. While ammonia, manganese, proinflammatory cytokines, and other precipitating factors play a role in the pathogenesis of HE, the exact mechanisms leading to the development of HE are not fully elucidated. This chapter provides a brief overview of HE with a focus on the mechanisms of AT2A.

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INTRODUCTION

Hepatic encephalopathy (HE) is broadly defined as brain disorder brought on by impaired liver function and/or portal-systemic shunting (El-Mansoury et al., 2023), which manifests as a wide spectrum of neurocognitive and neuropsychiatric abnormalities (El Khiat et al., 2023), ranging from subclinical alterations to coma (El-Mansoury et al., 2023). Four axes of guidelines were established in 2014 by the European Association for the Study of the Liver (EASL) and the American Association for the Study of Liver Diseases (AASLD) to improve the categorization and management of HE (Dharel & Bajaj, 2015). These guidelines were focusing on etiology, severity, time course, and precipitating factors.

Although the exact cause of HE is unknown, several underlying mechanisms are thought to play a role in its pathogenesis. The development of HE is significantly influenced by the gut microbiota (GM). The human GM is made up of thousands of microorganisms that play a tremendous role in maintaining the hosts' health by performing a variety of physiological tasks and shielding them from diseases and aggressors (El-Mansoury et al., 2023). The GM generate several toxic substances including ammonia. It is highly established that ammonia plays a central role in the development of HE.

It is highly established that astrocytes play a variety of roles in the brain, such as supplying the surrounding neurons by nutrients and mechanical support, controlling ion transport and neurotransmitter uptake, and playing a crucial role in the blood-brain barrier (BBB) integrity (Aldridge et al., 2015). In the context of liver disease, ammonia is insufficiently eliminated, leading to its build up in the systemic circulation (hyperammonemia), consequently crossing the BBB, and ultimately reaching the brain tissue. Astrocytes play a neuroprotective role in ammonia detoxification through the action of the glutamine synthetase–mediated reaction (ammonia and glutamate are converted to glutamine), and thus, they are the primary target cells in HE. It is noteworthy that following acute liver failure (ALF), astrocyte typically take a swollen shape (astrocyte swelling), and in chronic liver disease (CLD) circumstances the so-called Alzheimer type II astrocytes (AT2A) is found in the brain of patients as well as animal models of HE (chronic HE). Indeed, AT2A was demonstrated following CLD in several brain regions including the cerebral cortex, basal ganglia, and pontine nuclei. Therefore, it is considered as a gliopathy (Gelpi et al., 2020). This chapter provides an overview on hepatic anatomy and function as well as the common complication of CLD; hepatic encephalopathy. Additionally, this chapter focuses mainly on the mechanisms of AT2A following chronic HE.

ANATOMY AND PHYSIOLOGY OF THE LIVER

Anatomy of Liver

External Anatomy of Liver

The external anatomy of liver is characterized by the gross landmarks including the vena cava the gallbladder, and the hepatic ligaments (Fig.1). The liver is the largest gland in the body, making about 2.5% of the total weight of the body and weighing about 1500 g in adult stage. It performs a variety of functions that are essential for preserving appropriate physiological homeostasis (Juza & Pauli, 2014). The two lobes of the liver are commonly described using two different descriptions: morphologic anatomy 18 more pages are available in the full version of this document, which may be purchased using the "Add to Cart" button on the publisher's webpage: www.igi-global.com/chapter/hepatic-encephalopathy-as-a-gliopathy/335245

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