

NAFLD – COGNITIVE DYSFUNCTION THROUGH METABOLIC AND HEPATIC DISORDERS

The Non-alcoholic fatty liver disease (NAFLD) is gaining increasingly more significance as a hepatic component of the metabolic syndrome. NAFLD is associated with a series of intra- and extra-hepatic complications, among which is also cognitive dysfunction. In a current study, the evidence of underlying mechanisms was investigated in corresponding publications.¹

NAFLD is one of the largest health problems worldwide. It is assumed that around a quarter of the world's population is affected. Fatty liver disease itself, as well as the extra-hepatic complications linked to it and the metabolic syndrome increase the patient's risk of morbidity and mortality. The cognitive dysfunction with NAFLD is gaining increasing awareness as a risk factor, which is indicated by memory problems, awareness and concentration disorders, forgetfulness, and confusion. It is assumed that approx. 70 % of NAFLD patients are affected by it, and that their everyday life and quality of life are affected by it.

TIGHT CORRELATION BETWEEN THE SEVERITY OF NAFLD AND COGNITIVE DISORDERS

A current study analysis provides indication of a correlation between the severity of the fatty liver disease and cognitive restrictions. Systemic and neuroinflammation, vascular dysfunction, and sleep apnea are being discussed as possible mechanisms, which are observed with both a metabolic syndrome and also NAFLD.

More recent investigations indicate that NAFLD itself could be an independent risk factor for the development of a cognitive dysfunction. Alongside the indicated risk factors, there is also a dysbiosis of the intestinal microbiota and an impaired function of the urea cycle, which is the primary path to ammonia poisoning,

among NAFLD patients. As a result, a systemic ammonia accumulation favored, and system inflammations are further triggered.

AMMONIA AS THE KEY TO NEUROINFLAMMATION

The neurotoxin ammonia can break down the blood-brain barrier and is applicable as a significant pathogenetic factor of hepatic encephalopathy (HE). Studies have shown that the cognitive dysfunctions caused by ammonia are worse in an inflammatory environment, and that ammonia is the key, which opens the blood-brain barrier to the systemic inflammation. A reduction in ammonia levels or an anti-inflammatory treatment can lead to an improvement of cognitive disorders and neuroinflammation.

Arteriosclerosis and cerebrovascular dysfunction are also connected with the cognitive disorders in NAFLD. Accumulation of fat in the liver appears to cause a microvascular hemodynamic dysfunction with endothelial dysfunction, which reduced cerebral blood-flow and thus leads to cerebrovascular dysfunction. It is possible that neurodegenerative developments are induced in the brain as a result of this, like dementia and Alzheimer's.

DIAGNOSTIC PROCEDURE MUST BE EXTENDED

The current studies indicate that NAFLD patients develop a cognitive dysfunction, which is a multi-factorial, metabolic encephalopathy with characteristics of both, hepatic and diabetic encephalopathy. Furthermore, with these patients there are also unspecific mental and physical symptoms, which can indirectly impair the cognitive functions. The cognitive phenotype of NAFLD is not yet specified in sufficient measure. Therefore, the psychometric and

neuropsychological test methods used in previous studies cannot adequately address the extensive metabolic encephalopathy implied by the current evidence. To record the whole spectrum of cognitive dysfunction for NAFLD diagnostically, the validated test for diagnosis of hepatic encephalopathy must be complemented by at least one test for the learning and/or working memory.

INTENSIFICATION OF RESEARCH OF PATHOLOGY REQUIRED

In addition to improvements in diagnostic procedures, further research on the pathological basis of cognitive disorders in NAFLD is urgently required.

Treatment is currently essentially supported by a change in lifestyle and the bariatric operations, which lead to a reduction in weight, and thereby potentially improving the described neurological disorders.

The cognitive and functional restrictions as a result of NAFLD will have increasing social effects, and be lined with a cost increase for healthcare systems. People's quality of life gets worse, work productivity decreases, while the need for care increases. All of this illustrates an urgent need for medicative treatments for the treatment of patients with NAFLD.

LITERATURE

¹ Kjaergaard K et al., J. Clin. Med. 2021;10:673. <https://doi.org/10.3390/jcm10040673>.