# SOMATOSENSORY DISORDERS AS A MARKER FOR MINIMAL HEPATIC ENCEPHALOPATHY

## ANOMALIES IN BRAIN ACTIVITY AMONG CIRRHOTIC PATIENTS PLAY A PATHOPHYSIOLOGICAL ROLE IN HE

**In particular regions of the brain among people with liver cirrhosis and hepatic encephalopathy (HE) it is possible to see changes in the activity when compared with healthy people. This is confirmed by a current meta-analysis.[1] Another study shows a reduced sensory cognition among cirrhosis patients with minimal hepatic encephalopathy (mHE). Quantitative sensitivity disorders could also serve as biomarkers for the development of an mHE.[2]**

A brain function disorder with neuropsychiatric deficits is identified as hepatic encephalopathy (HE), which develops as a result of a hepatic insufficiency and/or a portosystemic shunt. Classification occurs by way of clinical symptoms as overt (OHE) or covert HE (CHE). No clinical symptoms are yet detectable for covert or minimal HE (mHE). Up to 40 % of all patients with liver cirrhosis are affected by mHE. These patients will already exhibit attention deficits, psychomotor decelerations, and cognitive deficits, which impact life quality and reduce life expectancy. MHE is diagnosed with various psychometric tests, which together present the psychometric hepatic encephalopathy score (PHES).

### HYPOSENSITIVITY AS INDICATION FOR MHE

However, not all mHE patients can be identified in this manner. According to a current study [2], there is a connection between the minimal brain function disorder and the changes in heat, vibration and/or heat pain feeling when compared with healthy subjects. According to this, cirrhotic patients exhibit a hyposensitivity, which is even stronger among patients with mHE. Both, the heat and cold feeling was clearly more strongly affected among these patients on their feet and distal than on the hands, and the reaction times were clearly increased when compared with patients without mHE. These hyposensitivities correlated with attention deficits, the speed of mental processing and the test of working memory of the mHE patients. Temperature feeling is the task of the autonomous nervous system. On the other hand, large nerve fibers react to vibrations. Quantitative sensitivity tests (QST) for cirrhotic patients could promptly diagnose disorders of thermal sensitivity and autonomous function, and be viewed as an early indication of pathophysiology of mHE, even before large nerve fibers are affected. An early diagnosis enables a corresponding treatment, and can improve the patient's quality of life and prognosis.[2]

### CHANGES TO INTRINSIC ACTIVITY IN THE BRAIN AMONG HE PATIENTS

Studies show that the neuropsychiatric deficits among patients with liver cirrhosis and HE underly changes in brain activity. In one meta-analysis[1], it is now being investigated which of these changes in which brain region exhibits the highest consistency and whether liver transplant shows effects on brain activity.
In total, 19 studies with 419 liver cirrhosis patients and 349 healthy volunteers fulfilled the requirements for the meta-analysis. Brain activity was measured in a state of rest with the help of function magnetic resonance imaging (fMRI).

The analysis produced increased activity in the fronto-striatal neuronal network among cirrhotic patients when compared with healthy people. With this increase in activity, there appeared to be a compensatory process of neuronal reorganization. Contrary to this, there was less activity in the visuo-sensorimotor network and in the gyrus cinguli among these patients. These changes remained significant in a sub-group analysis for cirrhotic patients with mHE or OHE. OHE patients also exhibited functional deficits in the default mode network (DMN). The ammonia concentrations correlated positively with the activity in the right gyrus temporalis, while the time requirement for the number connection test A(NCT-A) were negatively associated with the brain activity in the left anterior gyrus cinguli (Fig.).

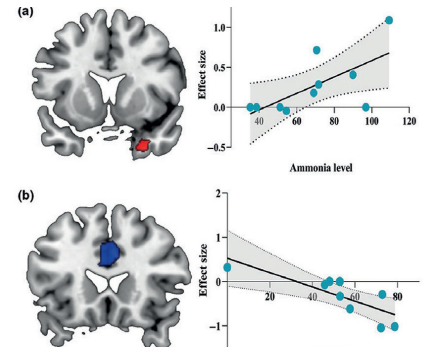


**FIGURE:** The meta-regression exhibits a positive correlation between the ammonia values and brain activity in the right, central gyrus temporalis (MTG) **a**, as well as a negative correlation between the results of the number connection test A (NCT-A) and brain activity in the left anterior gyrus cinguli **b**. The increase in meta-regression signed differential mapping is presented as a straight line. Red: activation; blue: deactivation. L, left; R, right mod. acc.[1]

These results pointed towards disorders in the fronto-striato-cerebral and visuo-sensorimotor networks being part of the pathophysiology of HE. The left anterior cingular cortex appears to be the most vulnerable region for cognitive impairments with HE. Disorders in the DMN indicate HE progression.

A liver transplant appears to improve brain activity in the visuo-sensorimotor quality of life again.[1]

**LITERATURE**

**1** Cao Y et al. J Neurosci Res. 2021 May;99(5):1337-1353. **2** Rega D et al., J. Clin. Med. 2021;10:239.