SEDACA ($p<0.05$) were observed over time in relation to changes in neuropsychiatric status.

Conclusion Two additional variables have been identified which have good performance characteristics for the diagnosis of any degree of HE. These new variables, in combination with the currently used EEG measures, can be used to optimise the diagnosis of HE and the grading of its severity.

Abstract P28 Table 1 Results

Variable	Threshold	Sensitivity	Specificity	PPV	NPV
MDF	9.2 Hz	74.7	58.7	53.2	78.7
θ %	46.8	76.9	69.8	61.2	83.0
α %	20.0	71.8	71.4	60.9	80.4
F-Mean	10.2 Hz	75.6	47.7	47.7	75.6

P29 DO DISTURBANCES IN CEREBRAL OSCILLATORY NETWORKS EXPLAIN SLEEP AND NEUROPSYCHIATRIC ABNORMALITIES IN PATIENTS WITH CIRRHOSIS?

doi:10.1136/gut.2010.223362.55

M Morgan, M Stubbs, H Dabrowski, C Jackson. *Centre for Hepatology, Royal Free Hospital, London, UK*

Introduction Patients with cirrhosis have significantly disturbed sleep–wake behaviour. However, the cause of these disturbances is uncertain and their relationship to hepatic encephalopathy (HE) is debated. Sleep is regulated by circadian and homeostatic processes; circadian abnormalities, while present in these patients, do not correlate with the observed disturbances in sleep–wake behaviour (Montagnese *et al*, 2010). Homeostatic sleep mechanisms are difficult to access; the possibility that homeostatic control is disturbed in these patients has not been systematically studied. Sleep-spindles, which are a feature of the sleep electroencephalogram (EEG), are generated by thalamo-cortical oscillatory networks and are a surrogate marker for homeostatic sleep processes. The same oscillatory networks have been implicated in the pathogenesis of HE.

Aim To examine homeostatic sleep mechanisms in patients with cirrhosis and to determine the relationship between sleep abnormalities and HE.

Method 39 patients with cirrhosis (24 men; 15 woman; mean (range) age 60 (37–85) years) were classified using clinical, psychometric and electrophysiological variables as neuropsychiatrically unimpaired (n=20), or as having minimal (n=6) or overt (n=13) HE. The reference population comprised 50 healthy individuals (26 men; 24 woman; age 55 (41–65) years. Sleep–wake behaviour was characterised using validated questionnaires. Sleep deprived EEGs were obtained in 14 patients (unimpaired (n=5), minimal (n=3) and overt (n=6) HE). The reference population comprised 26 healthy individuals (15 men; 11 woman; age 49 (39–59) years). The EEG was band-pass filtered (12.75–15.0 Hz) and the envelop of the sleep spindles obtained using the Hilbert transform. A threshold was identified which allowed the maximal rate of spindle occurrence to be defined. Variables were compared between patients and controls and in patients by degree of neuropsychiatric impairment.

Results Patients with overt HE were significantly more likely to report night-time sleep disturbances and day-time napping than the control subject and unimpaired patients ($p<0.05$).

The rate of sleep-spindle occurrence was significantly greater in the EEGs of patients with overt HE than in control subjects and unimpaired patients (59.2 ± 3.8 vs 52.4 ± 2.8, $p<0.001$ and 53.9 ± 1.5, $p<0.005$).

Conclusion Sleep–wake disturbances were prevalent in the patients with cirrhosis and increased with the degree of neuropsychiatric impairment. Significant abnormalities were observed in the sleep EEGs in patients with overt HE. Thus, abnormalities in cerebral oscillatory networks may underlie both the sleep disturbances and the neuropsychiatric abnormalities observed in patient with cirrhosis

Abstract P29 Table 1 Results

Variable	Healthy controls (n=50)	Unimpaired (n=20)	Minimal HE (n=6)	Overt HE (n=13)
Night sleep disturbance	54%	37%	67%	80%
Day-time sleepiness	14%	5%	17%	70%

P30 CYTOPLASMIC EXPRESSION OF TOLL-LIKE RECEPTOR-9 IS ASSOCIATED WITH INCREASED CELLULAR PROLIFERATION IN HEPATOCELLULAR CARCINOMA

doi:10.1136/gut.2010.223362.56

F Mohamed, D Dhar, A Winstanley, N Shah, S Behboudi, R Mookerjee, S O Damink, N Davies, R Jalan. *Institute of Hepatology, University College London, UK*

Introduction Effective treatment of Hepatocellular carcinoma (HCC) still remains an unmet need. Inflammation plays a crucial role in the pathogenesis of HCC by causing repeated cell damage and creating a microenviroment rich in cytokines that can enhance cell replication, angiogenesis and invasion into the surrounding structures. Toll-like receptors (TLRs) are important pathogen recognition receptors. Stimulation of TLRs is followed by cascade of transcriptional and translational reactions resulting in activation of NF-kB which subsequently serves as a common- link between the chronic inflammation and tumour development.

Aim The aim of this study was to characterise the expression of TLR-9 along the HCC tumour genesis pathway including the normal liver, viral hepatitis, cirrhosis and HCC and the results were collated with cell proliferation as determined by Ki-67 staining.

Method We used a human tissue array platforms (Vbiolab, Cambridge, UK) which includes 102 cores of liver tissue including nine normal livers, 26 hepatitis (B, C and Non-b, Non-C hepatitis), 25 cirrhosis and 42 HCC. Immunohistochemistry was performed for the expression of TLR-9 and Ki-67. The scoring was performed in a blinded fashion by two individual pathologists. For the quantitation of Ki-67 expression, we counted the positively stained nuclei among 1000 hepatocytes in the highest expression area using a standardised grid.

Results TLR-9 expression was noticed as membranous staining in 2/9 cases in normal liver. 12/26 cases of hepatitis and 13/25 of cirrhosis. Weak cytoplasmic staining was noticed in 4/26 cases of hepatitis and one case in cirrhosis whereas the staining was predominantly cytoplasmic in HCC; weak (+1) in 17/42 cases and moderate to strong (+2 and+3) in 17/42 cases, whilst in eight cases it was negative. In 13/42 cases, it was found in both cytoplasm and cell membrane. There was a close correlation between the proliferative index (Ki-67 staining) and TLR-9 staining; $r=0.8$, $p<0.001$. The proliferative index was <100, 100–200, >200 in TLR9 negative, weak and moderate-to-strong cases, respectively.

Conclusion The results of our study show, for the first time, a strong correlation between the amount of cellular proliferation and TLR-9 expression in HCC. Also we found the shifting of TLR9 expression from the membranous type in hepatitis and cirrhosis into cytoplasmic in HCC. Our data suggest that TLR-9 might have a pivotal role in cellular proliferation in HCC and merits further studies to explore the possibility of exploiting it as a potential target for future therapy.