Hippocampal sclerosis

- Neuroprotective role of high dose Vitamin D supplementation in multiple sclerosis: Sub-analysis of the EVIDIMS trial
- Epileptic Encephalopathy After Human Herpes Virus 6-Related Post-Transplant Acute Limbic Encephalitis in Children: A Case Report and Review of the Literature
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- TMEM14A Gene Affects Hippocampal Sclerosis in Mesial Temporal Lobe Epilepsy
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- Temporal Lobe Epilepsy Associated With Glutamic Acid Decarboxylase Antibodies: Defining a Distinct Epilepsy Syndrome
- Treatment-resistant patients with focal epilepsy of unknown cause display reduced neurogranin levels: a preliminary study
- The converging paths to hippocampal sclerosis of ageing: insights from LATE-NC and vascular disease

Mesial temporal lobe epilepsy with hippocampal sclerosis (mTLE-HS) is the most common type of focal epilepsy.

Hippocampal sclerosis (HS) is a neuropathological condition with severe neuronal cell loss and gliosis in the hippocampus, specifically in the CA1 (Cornu Ammonis 1) and subiculum of the hippocampus. It was first described in 1880 by Wilhelm Sommer.

Hippocampal sclerosis is a frequent pathologic finding in community-based dementia. Hippocampal sclerosis can be detected with autopsy or MRI. Individuals with hippocampal sclerosis have similar initial symptoms and rates of dementia progression to those with Alzheimer disease (AD) and therefore are frequently misclassified as having Alzheimer's Disease. But clinical and pathologic findings suggest that hippocampal sclerosis has characteristics of a progressive disorder although the underlying cause remains elusive.

A diagnosis of hippocampal sclerosis has a significant effect on the life of patients because of the notable mortality, morbidity and social impact related to epilepsy, as well as side effects associated with antiepileptic treatments.

Etiology

A total of 50 microRNAs were found to be differentially expressed in mTLE-HS compared with healthy controls. Among them, 2 were increased and 48 were decreased. The 6 significant differentially expressed candidate microRNAs (miR-3613-5p, miR-4668-5p, miR-8071, miR-197-5p, miR-4322, and miR-6781-5p) in exosome were validated. The bioinformatics analysis showed that the potential target genes of these microRNAs were involved in biological processes, molecular functions, and cellular components. Similarly, these microRNAs also affected axon guidance, pathways in cancer, regulation of the actin cytoskeleton, focal adhesion, the calcium signaling pathway, the MAPK signaling pathway, and the PI3K-Akt signaling pathway. Among 6 candidate microRNAs, miR-8071 had

the best diagnostic value for mTLE-HS with 83.33% sensitivity and 96.67% specificity, and was associated with seizure severity. This study indicated that exosomal microRNAs, may be regulators for the seizure development in mTLE-HS, and can be used as potential therapeutic targets and biomarker for diagnosis in mTLE-HS [1].

A study provides the first evidence of alteration of TGFβ pathway in patients with HS which could be a potential therapeutic target [2].

Diagnosis

Hippocampal sclerosis diagnosis.

Differential diagnosis

Hippocampal sclerosis can be detected with autopsy or MRI. Individuals with hippocampal sclerosis have similar initial symptoms and rates of dementia progression to those with Alzheimer's disease (AD) and therefore are frequently misclassified as having Alzheimer's Disease.

Treatment

Both anterior temporal lobectomy (ATL) or a selective amygdalohippocampectomy (SA) can lead to similar favorable seizure control in patients with MTLE/HS. Preliminary data suggest that postoperative verbal memory scores may improve in patients who undergo selective resection of a sclerotic hippocampus in the dominant temporal lobe [3]

Case series

Evidence has been provided that the subiculum may play an important role in the generation of seizures.Electrostimulation at this target has been reported to have anticonvulsant effects in kindling and pilocarpine rat models, while in a clinical study of hippocampal deep brain stimulation (DBS), contacts closest to the subiculum were associated with a better anticonvulsive effect.

Vázquez-Barrón et al. evaluated the effect of Electrostimulation of the subiculum in patients with refractory mesial temporal lobe epilepsy (MTLE) who have hippocampal sclerosis (HS).

Six patients with refractory MTLE and HS, who had focal impaired-awareness seizures (FIAS) and focal to bilateral tonic-clonic seizures (FBTCS), had DBS electrodes implanted in the subiculum. During the first month after implantation, all patients were OFF stimulation, then they all completed an open-label follow-up of 24 months ON stimulation. DBS parameters were set at 3 V, 450 µs, 130 Hz, cycling stimulation 1 min ON, 4 min OFF.

There was a mean reduction of 49.16% (±SD 41.65) in total seizure number (FIAS + FBTCS) and a

mean reduction of 67.93% (±SD 33.33) in FBTCS at 24 months. FBTCS decreased significantly with respect to baseline, starting from month 2 ON stimulation.

Subiculum stimulation is effective for FBTCS reduction in patients with mesial temporal lobe epilepsy (MTLE) and hippocampal sclerosis (HS), suggesting that the subiculum mediates the generalization rather than the genesis of mesial temporal lobe seizures. Better results are observed at longer follow-up times [4].

2016

Patients with mesial temporal lobe epilepsy (MTLE) with HS were selected. Clinical data were assessed pre-operatively and surgical outcome in the first year post surgery. One block of mid hippocampal body was selected for HS classification according to ILAE criteria. NeuN-immunoreactive cell bodies were counted within hippocampal subfields, in four randomly visual fields, and cell densities were transformed into z-score values. FreeSurfer processing of 1.5T brain structural images was used for subcortical and cortical volumetric estimation of the ipsilateral hippocampus. Univariate analysis of variance and Pearson's correlation test were applied for statistical analyses.

Sixty-two cases (31 female, 32 right HS) were included. ILAE type 1 HS was identified in 48 patients, type 2 in eight, type 3 in two, and four had no-HS. Better results regarding seizure control, i.e. ILAE 1, were achieved by patients with type 1 HS (58.3%). Patients with types 1 and 2 had smaller hippocampal volumes compared to those with no-HS ($p<0.001$ and $p=0.004$, respectively). Positive correlation was encountered between hippocampal volumes and CA1, CA3, CA4, and total estimated neuronal densities. CA2 was the only sector which did not correlate its neuronal density with hippocampal volume ($p=0.390$).

This is the first study correlating hippocampal volume on MRI submitted to FreeSurfer processing with ILAE patterns of HS and neuronal loss within each hippocampal subfield, a fundamental finding to anticipate surgical prognosis for patients with drug-resistant MTLE and HS [5].

1)
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