Hippocampal Spindle Rates Correlate with Cognitive Functions in Pediatric Patients with Epilepsy

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Introduction

- There is only little evidence from spindles recorded directly from the hippocampus via sEEG
- Hippocampal spindles occur during N2 and N3 sleep with a frequency between 9 and 16 Hz
- Hippocampal spindles are seen as a physiological phenomenon and could be a separate marker for hippocampal-related information transfer, e.g., memory consolidation
- Their expression might be diminished in epilepsy
- No data exists on hippocampal spindles in pediatric population

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- Pediatric patients with therapy refractory epilepsy are prone to have cognitive decline
- Aim to test hypotheses:

Can hippocampal spindles be disrupted through epileptic activity which interferes with sleep homeostasis and healthy memory consolidation and thus contributes to epileptic encephalopathy in children?



Source: Frauscher et al. SLEEP. Vol. 38, No. 12, 2015

Neuropsychological testings

Child and Adolescent Memory Profile™ (ChAMP™) – assesses visual and verbal memory in children and young adults

Rey Complex Figure Test and Recognition Trial (RCFT) - measures visuospatial ability and visuospatial memory

Full-Scale Intelligence Quotient (FSIQ)

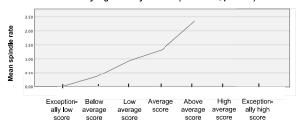
California Verbal Learning Test® CVLT®-C -assess verbal learning and memory Continuous Performance Test™ (CPT™) measures sustained and selective attention Immediate recall = "Can you remember it right now?" → focuses on attention/encoding Delayed recall = "Can you remember it later?" \rightarrow focuses on consolidation/retrieval



Methods

- To analyze the correlation between cognitive functions and hippocampal spindles in pediatric patients with therapy refractory epilepsy
- Inclusion: Pediatric patients with drug-resistant focal epilepsy at the the Alberta Children's University Hospital undergoing sEEG with at least one electrode implanted in the hippocampus
- EEG selection: 1 h of sEEG during the first sleep cycle recording between 20:00 and 08:00, preferably sleep stage II
- Spindles were marked visually using a bipolar EEG montage on our custom desktop application Elpi (https://www.elpi-biomarkers.com/start)
- Spindle rates per minute were correlated with neuropsychological test scores from the presurgical assessment using Mann-Whitney U and Kruskal-Wallis test
- To unify test performance scores and increase comparability, the original test scores were transferred into Z-scores resembling the categories exceptionally high, above average, high average, average, low average, below average, and exceptionally low

Hippocampal spindles were significantly correlated with a higher score in Rey Figure memory immediate recall (Rho 0.701; p=0.024) and Rey Figure delayed recall (Rho 0.766; p=0.010)



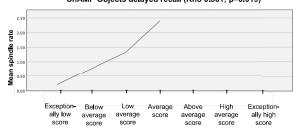
Results

- N=26 patients included
- Average age 11.0 years (Median 12; SD 4.2; range 2.0-17.0 years)
- Mean epilepsy duration 5.6 years (SD 3.1; range 1.0-15.0 years)
- Hippocampal spindle rates within the SOZ were not significantly lower compared to hippocampal spindle rates outside of was not part of the SOZ (p=0.06)
- FSIQ, CVLT, and CPT scores were not significantly correlated with hippocampal spindle rate

Conclusion

- First study to explore hippocampal spindle rates in context of cognitive performance
- Higher spindle hippocampal rates were correlated with better visual memory in both delayed and immediate recall as well as complex visual memory
- Hippocampal spindle rates were not correlated with verbal memory, intelligence quotient, or attention maintenance
- Hippocampal spindles should be further explored as a biomarker of cognitive functions

Hippocampal spindles were significantly correlated with a higher score in ChAMP Objects immediate recall (Rho 0.560; p=0.019) and ChAMP Objects delayed recall (Rho 0.561; p=0.019)



The correlation of Z-scores with spindle rates per minute. The x-axis shows the different Z-score categories. The y-axis shows the mean spindle rate per minute of each category