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Asymmetry of hippocampal subfield volumes in a heterogenous cohort of focal drug-resistant epilepsies

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Introduction: Epilepsy affects 50-65 million individuals worldwide (World Health Organization). Drug-resistant epilepsy (DRE) is prevalent in 30-36% of clinic-based populations [1]. Surgical resection of epileptogenic zone is a common practice for treatment of focal DRE [2,3] with hippocampal sclerosis (HS), tumor-related malformations, and focal cortical dysplasia (FCD) the most common histopathological diagnosis in adults [1]. Studies on drug-resistant temporal lobe epilepsies (TLE) [4,5] and post-traumatic epilepsy [6] reveal associations of structural connectome reorganization in ipsilateral networks, hippocampal deformations, and variations in hippocampal signal intensity with memory disfunctions and risks of future epilepsies. We present an analysis of magnetic resonance imaging (MRI)-based hippocampal volumetry for patients diagnosed with HS and other epilepsy subtypes and age-matched healthy volunteers, supported by evaluations of hippocampal segmentation and post-operative histological diagnosis.
Methods: Seventeen patients (5 males, 12 females, 36.24 ± 14.21 years at the time of surgery) with focal DRE underwent resective surgery at Kuopio University Hospital. Pre-operative clinical MRI revealed structural etiological findings with presumption of temporal or frontal-lobe FCD (N=5), HS (N=3), dual FCD-HS (N=2), tumors (N=3), encephalocele (N=3), and structural without clear etiology (N=1). Additionally, 15 healthy volunteers (10 males, 5 females, aged 35.33 ± 7.81 years), were recruited. Patients and volunteers underwent MRI acquisition with a 3D MPRAGE T1-weighted sequence (3T Siemens, TR = 2.3 s, TE = 1.92 ms, 1.0x1.0x1.0 mm3 voxel size) before the surgery as part of a larger MRI study. Immunohistochemistry with NeuN and GFAP was conducted on resected tissues by a neuropathologist. T1w volumes were analyzed using HippUnfold v1.3.0 to segment the hippocampal subfields (Subicular complex (Sub.), Cornu Ammonis (CA) fields 1-4, dentate gyrus (DG), and stratum radiatum and lacunosum-moleculare (SRLM)) and compute their volumes [7,8]. This software uses a UNET deep convolutional neural network (CNN) and a template of ex vivo images to segment the tissue in and around the hippocampus and fits the hippocampal grey matter with a subject-specific and topologically constrained surface mesh [9].
Results: Brain tissues were resected during eight anterior temporal lobectomies, six extratemporal focal resections or limited lesionectomies, and three encephalocele disconnection procedures. Results of histological diagnosis are presented in Fig. 1A. Fig. 1B demonstrates the neuroradiologist's evaluation of T1w-based hippocampal segmentation. Volumetric asymmetries for seven hippocampal subfields in volunteers and patients are presented in Fig. 1C with a summary of neuropathologist's assessments of neuronal loss and gliosis in hippocampal subfields. While healthy volunteers exhibit minimal to mild volumetric asymmetries in CA2-4, patients with HS or FCD-HS demonstrate the largest volumetric asymmetries across all subfields, aligning with the laterality of their malformations. Two-sample, one-sided t-tests reveal patients with HS had greater absolute volumetric asymmetry in all subfields compared to other patients ($pFDR < 0.05$, Fig. 1D) as well as in all subfields except for CA2 compared to healthy volunteers ($pFDR < 0.01$).
Conclusion: We present an analysis of hippocampal volumetry between DRE patients and healthy volunteers. Results will be updated as data acquisition continues with the aim to present a multi-modal and multi-scale assessment of epileptogenesis in the human brain.

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