Abstracts

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METALLOME OF SCLEROTIC HIPPOCAMPI IN PATIENTS WITH DRUG-RESISTANT MESIAL TEMPORAL LOBE EPILEPSY

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Purpose: Altered hippocampal metallome is strongly implicated in the pathology of mesial temporal lobe epilepsy with hippocampal sclerosis (mTLE-HS). We aimed to determine sodium, potassium, calcium, magnesium, iron, copper, manganese, and zinc concentration in epileptic human hippocampi.

Method: Hippocampi of 24 drug-resistant mTLE-HS patients (age: 35.6 ± 9.4 years) that underwent anterior temporal lobe resection and amygdalohippocampectomy surgery, and 17 hippocampi obtained by autopsy from 13 controls (age: 40.5 ± 12.9 years) were analyzed using inductively coupled plasma optical emission spectrometry.

Results: Epileptic hippocampi showed significantly lower concentrations (μg/g of tissue) of copper (HS: 2.34 ± 0.12; control (C): 3.57 ± 0.33; $p < 0.001$), manganese (HS: 0.205 ± 0.030; C: 0.409 ± 0.064; $p = 0.004$), and potassium (HS: 2001 ± 59; C: 2322 ± 61; $p < 0.001$), and increased sodium level (HS: 1131 ± 22; C: 1040 ± 25; $p = 0.010$). Zinc concentration was slightly higher in HS (13.97 ± 1.51 μg/g) compared to controls (10.97 ± 1.03 μg/g), whereas iron, calcium, and magnesium levels did not differ.

Conclusion: Our results provide a relevant prerequisite for understanding the potential involvement of different metals in the pathology of HS, emphasizing general deregulation of metallome, copper and manganese deficiency, and the absence of iron accumulation.

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RETINAL NERVE FIBER LAYER THICKNESS: A POSSIBLE BIOMARKER OF DRUG RESISTANCE IN EPILEPSY

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Purpose: Epilepsy has been associated with cerebral white matter tract abnormalities. Retinal nerve fiber layer thickness is related to the axonal anterior visual pathway and is considered a marker of overall white matter "integrity". Retinal nerve fiber layer thickness was previously assessed in a cohort of people with epilepsy and a history of vigabatrin exposure, showing significant thinning compared to healthy controls. We hypothesised that retinal nerve fiber layer changes would occur in people with chronic epilepsy, independently of previous vigabatrin treatment, related to clinical characteristics of epilepsy.

Method: Three hundred subjects with chronic epilepsy and 90 healthy controls were included. People with previous exposure to vigabatrin or known ocular disease were excluded from the analysis. Retinal nerve fiber layer imaging was performed using spectral-domain Optical Coherence Tomography.

Results: People with epilepsy had significantly lower average retinal nerve fiber layer thickness and lower thickness of each of the 90° quadrants than healthy controls ($p < 0.001$, Wilcoxon rank-sum test). In a multivariate logistic regression model, drug resistance was the only significant predictor of abnormal retinal nerve fiber layer thinning (OR 2.09, CI 95% 1.09–4.01, $p = 0.03$). Duration of epilepsy and the presence of intellectual disability also showed a significant relationship with retinal nerve fiber layer thinning in a multivariate linear regression model (coefficients −0.16, $p = 0.004$ and −4.0, $p = 0.044$, respectively).

Conclusion: This suggests that drug-resistant epilepsy is associated with thinning of the retinal nerve fiber layer. As this is easily assessed by optical coherence tomography, retinal nerve fiber layer thickness is a candidate biomarker of drug resistance and, by extension, of epilepsy severity. Longitudinal studies are now needed. The underlying mechanisms are unknown and may be diverse.

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ACONITUM COCHLEARE WOROSCHIN-OIL ATTENUATES THE MOLECULAR MARKERS OF EPILEPTOGENESIS IN PENTYLENETETRAZOLE INDUCED KINDLED MICE WITH SAFE TOXICITY PROFILE

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Purpose: Epilepsy is a chronic neurological disorder, characterized by recurrent seizures occurring as a result of synchronized discharges of neurons in brain. As 33% of patients develop resistance against therapy while others are not without side effects, therefore, need for better and safer drugs is crucial. Neurtrophic factors and Oxidative stress are emerging as mechanisms that may play an important role in the etiology of seizure-induced neuronal death. In the present study, *Aconitum cochleare* WOROSCHIN-oil (ACR-oil) was tested for its ability (i) to suppress the convulsive and lethal effects of Pentylenetetrazole (PTZ) in kindled mice, (ii) to attenuate the PTZ-induced oxidative injury in the brain tissue and (iii) to modulate the gene expression *BDNF* and its receptor *Trk-B* when given as a pretreatment prior to each PTZ injection during kindling acquisition. Diazepam and valproic acid, major antiepileptic drugs, were also tested for comparison.

Methods: Once acute screening was done, all groups except for control group were kindled by injections of PTZ with an interval of 48 h ($n = 12$). In the 18th injection, all groups were sacrificed and the brain samples were collected and used for determination of oxidative stress parameters and targeted gene expressions by PCR.

Results: Our results suggest that ACR-oil treatment (100 mg/kg, 200 mg/kg) significantly inhibit, both acute and chronic PTZ induced seizures ($p < 0.05$). Toxicity studies demonstrate that the test oil is devoid of major toxic effects on suggested doses. Our test oil not only produced antiepileptic effect but also diminished the PTZ induced oxidative stress ($p < 0.05$, $p < 0.001$).