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## Epilepsy surgery as a powerful research approach to human epileptogenesis

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### Resumen

The progress towards more effective treatments of epilepsy requires to understand the mechanisms underlying the appearance of epileptic seizures and the brain damage caused by them. Animal models have been instrumental in comprehending the pathophysiology of epilepsy and for medication development.

While there are solid experimental evidences implicating eicosanoid imbalance (arachidonic acid metabolites) and brain oxidative stress in animal models of epilepsy, these processes have not been not thoroughly confirmed in human epileptic brain.

To verify these mechanisms in human epilepsy, neocortical samples from drug-resistant epilepsy patients submitted to epilepsy surgery were studied, and the results were compared to those obtained in control, non-epileptic cortex samples from brain bank donors whose death was not related to brain disease or injury.

The samples were studied to measure the synthesis of eicosanoids from the cyclooxygenase and lipoxygenase pathways, and for oxidative stress markers: levels of reactive oxygen species, activity of antioxidant enzymes, and markers of damage to biomolecules (lipid peroxidation and DNA oxidation).

Epileptic neocortex specimens demonstrated a significant increase in the levels of three eicosanoids derived from the cyclooxygenase pathway Prostaglandin E2 (PGE2), Thromboxane A2 (TXA2), and Prostacyclin (PGI2), compared to controls. Besides, the absence of leukotriene synthesis through the lipoxygenase pathway evidenced that cyclooxygenase pathway is the dominant one in neocortex of epilepsy patients.

Oxidative stress in epileptic neocortex specimens was significantly higher than in controls, with increased levels of superoxide anion, catalase and DNA oxidation, and a decrease in glutathione peroxidase.

These results are consistent with those obtained in experimental animal models of epilepsy, supporting the presence of both eicosanoid imbalance and oxidative stress phenomena in human epileptic brain. Selective inhibition of prostanoid synthesis or blockage of prostanoid receptors, as well as specific anti-oxidant agents might provide novel neuroprotective antiepileptic strategies for

human epilepsy.