Blockage of STAT3 during epileptogenesis prevents GABAergic loss and imprinting of the epileptic state

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Epilepsy, characterized by recurrent unprovoked seizures resulting from a wide variety of causes, is one of the world's most prominent neurological disabilities. Seizures, which are an expression of neuronal network dysfunction, occur in a positive feedback loop of concomitant factors, including neuro-inflammatory responses, where seizures generate more seizures. Among other pathways involved in inflammatory responses, the JAK/STAT signalling pathway has been proposed to participate in epilepsy. Here, we tested an in vitro model of temporal lobe epilepsy, with the hypothesis that acute blockage of STAT3-phosphorylation during epileptogenesis would prevent structural damage in the hippocampal circuitry and the imprinting of both neural epileptic activity and inflammatory glial states. We performed calcium imaging of spontaneous circuit dynamics in organotypic hippocampal slices previously exposed to epileptogenic conditions through the blockage of GABAergic synaptic transmission. Epileptogenic conditions lead to epileptic dynamics imprinted on circuits in terms of increased neuronal firing and circuit synchronization, increased correlated activity in neuronal pairs and decreased complexity in synchronization patterns. Acute blockage of the STAT3-phosphorylation during epileptogenesis prevented the imprinting of epileptic activity patterns, general cell loss, loss of GABAergic neurons and the persistence of reactive glial states. This work provides mechanistic evidence that blocking the STAT3 signalling pathway during epileptogenesis can prevent patho-topological persistent reorganization of neuro-glial circuits.