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ARE MRI CHANGES PREDICTIVE OF EPILEPTOGENESIS AFTER EXPERIMENTAL PROLONGED FEBRILE SEIZURES?

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Rationale: Whereas most febrile seizures carry a benign outcome, a subpopulation of individuals with prolonged febrile seizures (FS) are at risk for later temporal lobe epilepsy. Signal changes on MRI may provide markers for changes associated with epileptogenesis in such individuals. A prospective multicenter study of children with prolonged FS (S. Shinnar, PI) found MRI changes in 13% of children with prolonged FS (>90 minutes), and 2 of these children developed epilepsy. We previously demonstrated that: an experimental FS in immature rats led to subtle, limbic, 'temporal lobe' epilepsy in 35% of the rats. In a separate study, we found abnormal MRI T2 signal in hippocampus and other limbic structures of a subset of FS-experiencing rats. Therefore we tested the hypothesis that MRI changes were predictive of the development of limbic epilepsy after experimental prolonged FS, i.e. they would distinguish animals that would become epileptic from those who would not.

Methods: Immature rats (n = 11) experienced experimental prolonged FS lasting ~66 minutes on postnatal (P) day 10. They were imaged one month later using a 2D multi-echo spin echo sequence in a 7 Tesla, 15 cm bore magnet (Oxford). Absolute T2 signal intensity maps were generated for control rats (n = 5). These served as comparison for T2 signal intensities on T2 maps of the 'FS' group. Following the MRI, rats were implanted bilaterally with hippocampal bipolar and cortical electrodes, and video EEG monitoring was initiated on P90, in comparison with controls. Seizures were defined as events with both EEG and behavioral criteria: On EEG ictal activity included polyspikes or sharp-waves longer than 6 seconds with amplitude > 200% of background. Interictal events were defined as: 1) polyspikes or sharp-waves discharges lasting less than five seconds; 2) isolated spikes and/or sharp waves; 3) spikes trains not associated with a change of behavior.

Results: Rats experiencing experimental FS segregated into two groups: those with minimal changes of MRI T2 values compared to controls (n = 3), and those with significantly abnormal T2 values in hippocampus and often in other limbic regions (n = 8). EEGs were normal in all control rats (over 200 hours) and none of these rats developed spontaneous seizures. Early-life prolonged FS evoked interictal events (spikes trains) in 8 out of the 11 rats (73% of the total, over 2100 hours) with a mean duration of 135 ± 10.2 seconds, n = 73. Preliminary data suggest that 3 out these 8 animals, all with abnormal T2 signal on MRI, now have spontaneous seizures lasting 41 ± 8.4 seconds. Ictal behaviors consist of forelimb clonus and rearing in one rat and of facial automatism and body jerks in the 2 others.

Conclusions: These preliminary data suggest that MR T2 signal changes after experimental prolonged FS may provide a biomarker for epileptogenesis.

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