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IS EPILEPTOGENESIS AFTER EXPERIMENTAL FEBRILE SEIZURES A FUNCTION OF SEIZURE DURATION AND/OR RECURRENCE?

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Rationale: In humans, whether prolonged febrile seizures (FS) cause spontaneous seizures (temporal lobe epilepsy) has remained unclear. We have previously demonstrated that a single episode of 20 min-long 'FS' in immature rats leads to spontaneous limbic seizures ('temporal lobe epilepsy') later in life. However, epileptogenesis occurred in only 35% of the rats, raising questions regarding the role of specific characteristics and parameters of the inciting experimental FS, in the provocation of epilepsy. Therefore, here we tested the hypotheses that epileptogenesis in the immature rat model of FS is (a) a function of total seizure duration, and/or (b) requires recurrent seizures.

Methods: Epileptogenesis was defined as emergence of spontaneous limbic seizures. Seizures were defined as events with both EEG and behavioral criteria: polyspikes or sharp-waves with amplitude > 200% of background on EEGs, that last >6 sec, and are associated with behavioral manifestations (freezing, 'limbic' automatisms, etc; Nairismagi et al., 2004). In Experiment 1, immature rats, aged 10–12 days, experienced a single 60 min 'febrile' seizure (n = 8). In Experiment 2, pups experienced three 20 min FS, one each on days 10, 11, and 12 of life (pilot n = 3). Digital video EEG monitoring was initiated on day of life 70 in control rats (n = 13) and those experiencing either a single long or recurrent FS early in life. EEG was derived from hippocampal and cortical bipolar electrodes. EEG events were correlated with behavioral parameters from the Video, and when both EEG and behavioral criteria were met, were considered seizures.

Results: EEGs were normal in all 13 control rats (> 300 hours) and none of these rats developed spontaneous seizures. Experiment 1 : All rats experiencing a single experimental FS lasting 60 min developed interictal EEG abnormalities (compared with 88% after a single 20 min seizure). Preliminary data (~200 recorded hours) have not yet revealed spontaneous seizures in this group. Experiment 2 : Two of three (67%) rats that had experienced three 20 min FS early in life, developed spontaneous limbic seizures in the pilot recording (~30 hours; compared with 35% after a single event of the same duration).

Conclusions: Preliminary evidence suggests that recurrence of seizures, rather than their total duration, strongly influences epileptogenesis in experimental prolonged FS. (Supported by NIH RO1 NS35439 and R21 NS049618 (TZB) and by an Epilepsy Foundation of America postdoctoral research fellowship (CD).)