Oral

A novel, non-invasive, predictive epilepsy biomarker with clinical potential

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Rationale: A subset of children with febrile status epilepticus (FSE) develop temporal lobe epilepsy (TLE), accounting for a large proportion of this common, intractable disorder. Significant barriers to developing preventive therapies include the absence of early identification of individuals with FSE who will develop TLE years later.

Methods: Aiming for non-invasive, clinically relevant markers of early epileptogenesis, we used a naturalistic animal model of FSE and employed high-resolution, high-field MRI, chronic video-EEG, and neurochemical techniques to probe the origin of the observed MRI signal changes.

Results: Temporal lobe-like, limbic epilepsy developed in 6 of 19 FSE rats (32%) over the ensuing months, and was predicted by reduced MRI T2 relaxation times in the basolateral and medial amygdala and limbic thalamus within 2-4 hours after FSE. Reduced T2 values correlated with increased unsaturated hemoglobin (deoxygenated hemoglobin) in venous blood, which generated the paramagnetic susceptibility effects detected with the high-field MRI. These data indicate that persistent alterations in oxygen delivery or utilization in the hours following FSE accompany or contribute to the epileptogenic processes that follow experimental FSE. Evaluating the potential clinical application of the MRI changes, we used deoxyhemoglobin-sensitive MRI sequences (T2*), and these enabled visualization of the epilepsy-predictive changes on lower field-strength, clinically relevant scanners.

Conclusions: These findings delineate an MRI signature that (a) provides information about the onset and nature of the epileptogenic process, and (b) might be useful for predicting FSE-related TLE in clinical settings, facilitating early interventions.