



Turning Up the Heat on the Impact of Febrile Status Epilepticus

MRI Abnormalities Following Febrile Status Epilepticus in Children: The FEBSTAT Study.

Shinnar S, Bello JA, Chan S, Hesdorffer DC, Lewis DV, Macfall J, Pellock JM, Nordli DR Jr, Frank LM, Moshe SL, Gomes W, Shinnar RC, Sun S; the FEBSTAT study team. [published online ahead of print July 24, 2012]. *Neurology* 2012;79:871–877.

OBJECTIVE: The FEBSTAT study is a prospective study that seeks to determine the acute and long-term consequences of febrile status epilepticus (FSE) in childhood. **METHODS:** From 2003 to 2010, 199 children age 1 month to 5 years presenting with FSE (> 30 minutes) were enrolled in FEBSTAT within 72 hours of the FSE episode. Of these, 191 had imaging with emphasis on the hippocampus. All MRIs were reviewed by 2 neuroradiologists blinded to clinical details. A group of 96 children with first simple FS who were imaged using a similar protocol served as controls. **RESULTS:** A total of 22 (11.5%) children had definitely abnormal ($n = 17$) or equivocal ($n = 5$) increased T2 signal in the hippocampus following FSE compared with none in the control group ($p < 0.0001$). Developmental abnormalities of the hippocampus were more common in the FSE group ($n = 20$, 10.5%) than in controls ($n = 2$, 2.1%) ($p = 0.0097$) with hippocampal malrotation being the most common (15 cases and 2 controls). Extrahippocampal imaging abnormalities were present in 15.7% of the FSE group and 15.6% of the controls. However, extrahippocampal imaging abnormalities of the temporal lobe were more common in the FSE group (7.9%) than in controls (1.0%) ($p = 0.015$). **CONCLUSIONS:** This prospective study demonstrates that children with FSE are at risk for acute hippocampal injury and that a substantial number also have abnormalities in hippocampal development. Follow-up studies are in progress to determine the long-term outcomes in these children.

Commentary

Febrile seizures are one of the more common conditions seen by child neurologists and were probably overtreated for many decades with medications such as phenobarbital. More recent years have seen child neurologists trained to reduce the amount of both treatments and diagnostic testing of children with febrile seizures, even when prolonged and classified as febrile status epilepticus (FSE) (1, 2). Concerning results from the FEBSTAT multicenter study may be moving the field back toward apprehension. Very recently published data would suggest HHV 6 and 7 may be more prevalent in FSE (3). This study now addresses the fear that FSE may lead to hippocampal sclerosis and mesial temporal lobe epilepsy.

Dr. Shinnar and his multicenter FEBSTAT team report the increased likelihood of finding 1.5 Tesla MRI abnormalities generally within 1 week of the FSE episode. A large number—191 children—had imaging and were compared to a control group of 96 children with simple febrile seizures from the previously reported Columbia Febrile Seizure Study (4). The key findings were 1) 22/191 (11.5%) with FSE had T2 hyperintensities in the hippocampus versus 0% of the simple febrile seizure cohort

and, 2) 20/191 (10.5%) with FSE had developmental abnormalities identified (often hippocampal malrotation) versus 2/96 (2.1%). Only two of the 17 “definite” cases of T2 hyperintensities had concurrent developmental abnormalities, but the concern is whether these children with hippocampal malrotation were potentially predisposed to FSE. With these small numbers, only a future study can answer that question.

These results raise some concern about the potential impact of FSE. The methods section describes repeat MRI being obtained at 1 year; one can only suspect that the risk of T2 changes may be higher than the 1 in 10 seen within 1 week of the FSE. The authors also appropriately state that a more subtle injury may have occurred in those without obvious imaging abnormalities. Perhaps future evaluations using 3T or even 7T MRI could reveal an even higher incidence of MRI findings.

If we assume that these changes are pathologic, is there a way we can translate these results to children in our practice to prevent them from occurring? It is known that aggressive antipyretics are not helpful (5). Anticonvulsants such as phenobarbital may help but have significant potential adverse effects (6). A logical approach would be to have emergency benzodiazepines (e.g., rectal diazepam) readily available to parents; however, 76% of these study children presented with FSE as their very first febrile seizure and thus could not have been treated prior to paramedic arrival (7). Unfortunately, at this point, what neurologists currently have to offer is appropriate



education for paramedics, emergency department personnel, and pediatricians about the treatment of status epilepticus. A potential antiviral therapy or vaccine against HHV 6 and 7, as proposed by Drs. Berg and Abou-Khalil in the editorial accompanying this article, may be a future option (8).

Regardless of potential interventions, this is an excellent early step in the right direction of finding answers about the true impact of prolonged febrile seizures. No longer can prolonged febrile seizures be considered completely benign. As the FEBSTAT study continues to follow these nearly 200 children over years rather than weeks, we will all undoubtedly learn more about the radiologic, cognitive, and epilepsy ramifications of febrile status epilepticus.

by Eric Kossoff, MD

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