Cytokine Network in Febrile Seizures

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Increased levels of HMGB1 and pro-inflammatory cytokines in children with febrile seizures

Choi J, Min HJ, Shin JS. Increased levels of HMGB1 and pro-inflammatory cytokines in children with febrile seizures. J Neuroinflammation. 2011;8:135. doi: 10.1186/1742-2094-8-135.

Big Questions

- Does active inflammation cause febrile seizures or epilepsy in children?

- Does HMGB1 promote inflammation and cause seizures by promoting other proinflammatory cytokine activity?

Background

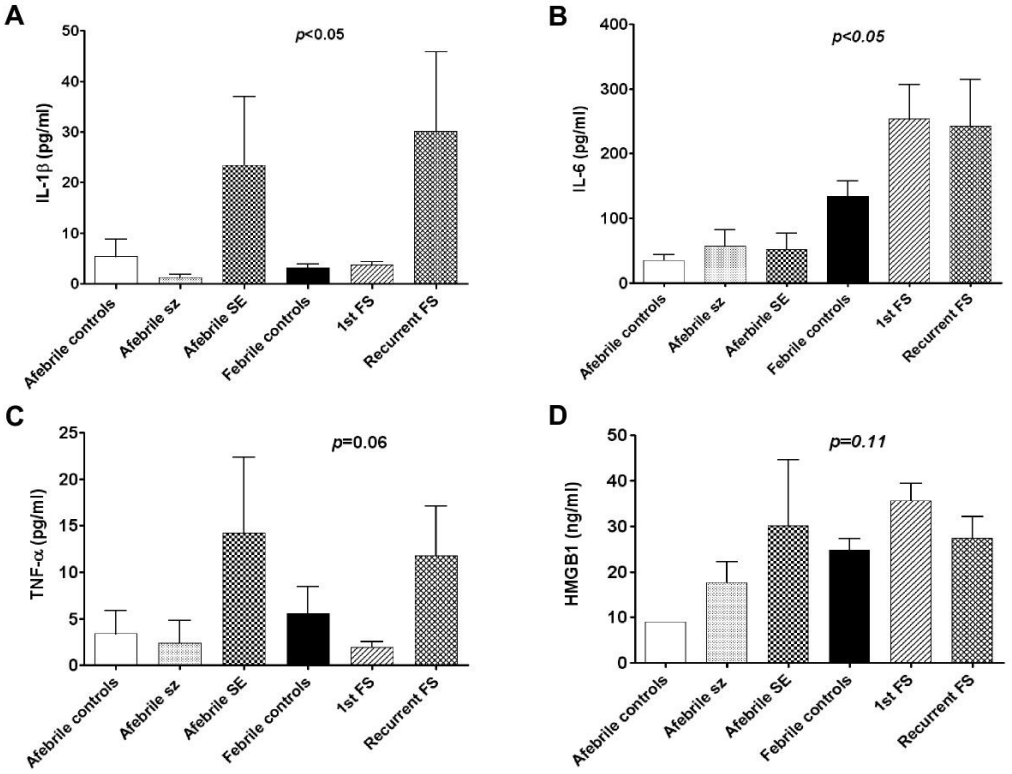
- HMGB1
  - A protein → "**High mobility group box 1**"
  - Triggers inflammation
  - Biomarker for seizures and epilepsy
  - Binds to TLR4
- (IL)-1B, IL-6, TNF-a
  - Proinflammatory cytokines
  - Induce fever
- IL-1
  - Source → monocytes in periphery and microglial cells in the nervous system
  - Secrete cytokines upon activation
- Previous study → HMGB1 + TLR4 = Generation/recurrence of seizures

Methods

- 66 ER patients, 6mos-6yrs
- 4 groups:
  - Control- Febrile illness w/o convulsion (n=41)
  - Afebrile epileptic (intractable epilepsy) (n=12)
  - Afebrile seizure with GEFS+ (n=6)
  - Afebrile nonepileptic controls (n=7)
- Obtain blood and serum w/in 30 mins after seizure
- Cytokine assay
- Blood count, blood chemistry, CRP levels checked
- Febrile patients (2 groups) → *Typical, **Atypical
- Blood analyses of control
- Compare

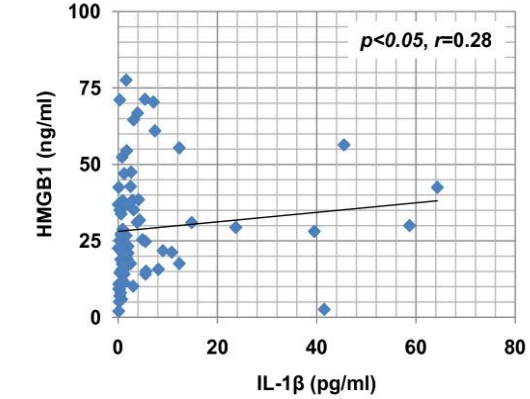
Results

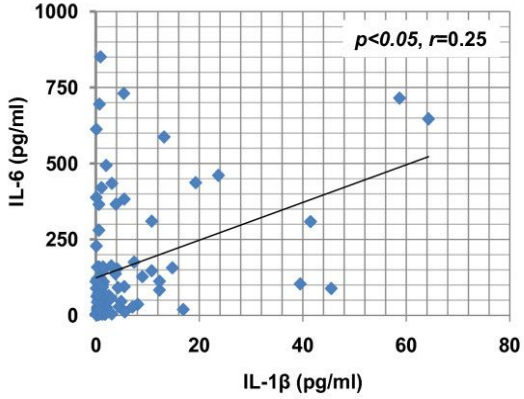
- Significantly high IL-1B in:
  - Afebrile SE
  - Recurrent SF
- Significantly high IL-6 in:
  - 1st FS
  - Recurrent FS
- No significance of TNF-a in:
  - Afebrile FS
  - Recurrent FS
- No significance of HMGB1 in:
  - Afebrile FS
  - Recurrent FS



Results

- Significantly Correlated:
  - IL-1B & HMGB1
  - IL-1B & IL-6
  - IL-1B & TNF-a
  - IL-6 & TNF-a





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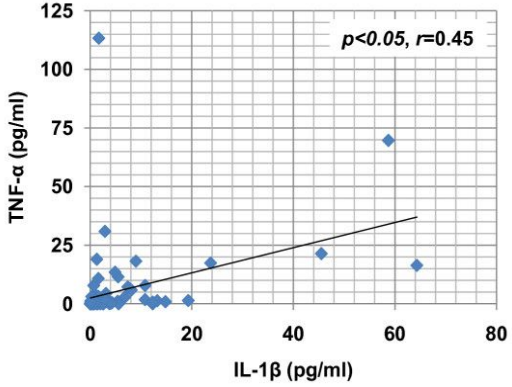

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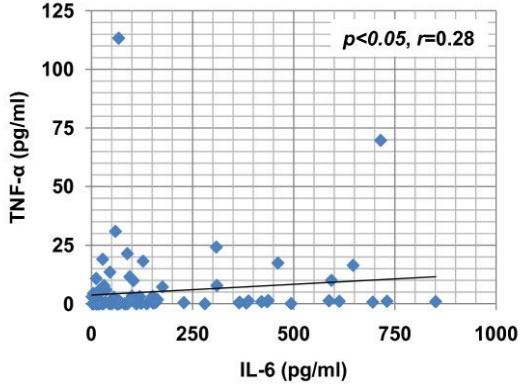

Discussion

- HMGB1 and TLR4 - significant in epilepsy
  - Possible underlying genetic cause
- Ultimate cytokine network of proinflammatory cytokines (IL-1B, IL-6, TNF-a, and HMGB1 levels)
- If HMGB1 levels are high in afebrile GEFP+ patients, this may indicate there is something on a genetic level causing proinflammatory cytokines to be released
- Glial Cells → What contribution could they have?

How is this pertinent to our studies?

- These results can shed light on the underlying mechanisms causing certain pathways to fire synchronously