Cerebrospinal fluid total tau protein as a biomarker in status epilepticus

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Objective Predicting status epilepticus (SE) outcomes is difficult, and primarily based on clinical and EEG parameters. To date, no reliable biomarkers exist to predict SE outcome. Tau protein is a phosphorilated microtubule-associated protein, principally localized at neuronal and axonal level in central nervous system (CNS). High total tau (t-tau) levels in CSF are related to neuronal and axonal damage. No study has specifically evaluated the prognostic value of CSF t-tau level in SE.

Methods A retrospective observational study was performed between 2007 and 2014.

Inclusion criteria: all patients with SE who received a lumbar puncture at SE onset or shortly after to rule out CNS infection.

Exclusion criteria:
(i) CT/MRI evidence of acute brain insult as aetiology of SE;
(ii) evidence of viral or bacterial CNS infection;
(iii) neurodegenerative cognitive decline (*iv*) evidence of a progressive CNS disorder (i.e. brain tumour).

28 patients werefinally included (**Table 1).**

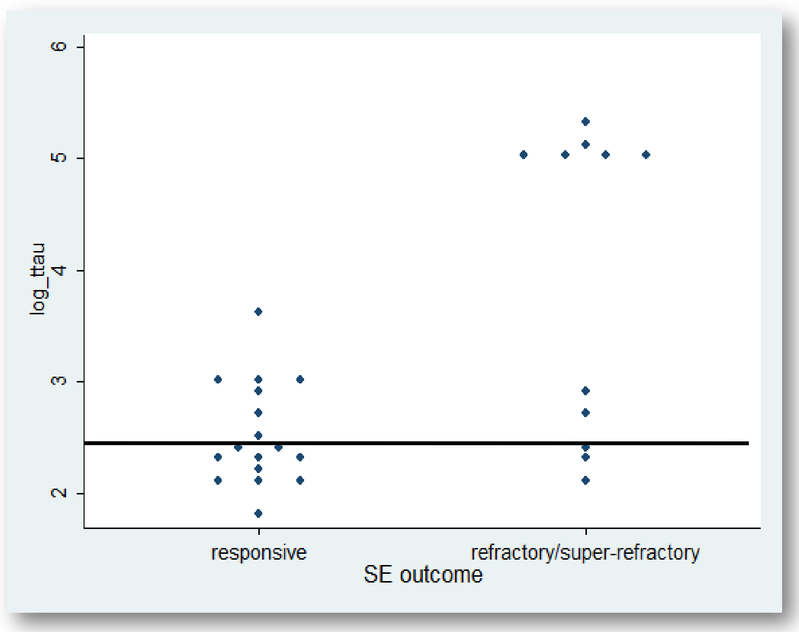
CSF samples were acquired from a few hours after SE onset to a maximum of 20 days (median of 72 hours). CSF $A\beta_{1-42}$, t-tau, and p-tau_{181} were measured with ELISA method in accordance with recent guidelines. Cut-off values were established according to literature and to our laboratory data: t-tau < 350 pg/ml; p-tau < 60 pg/ml; $A\beta_{1-42}$ > 500 pg/ml

Table 1. Demographig, clinical data, lab findings

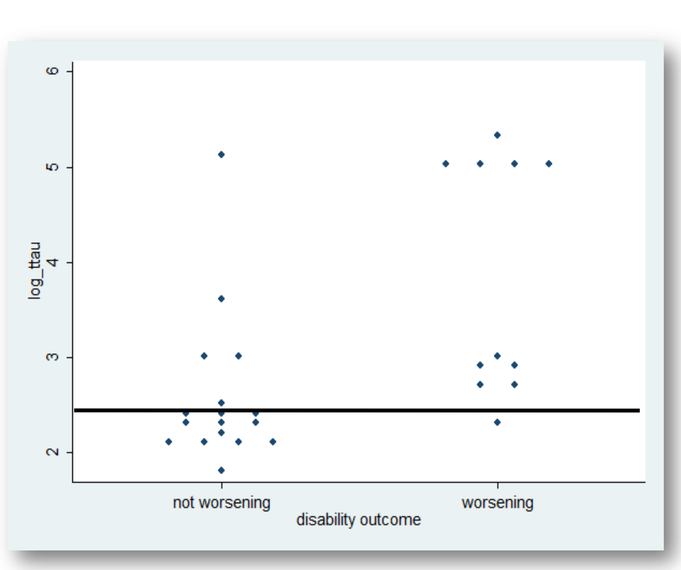
Age, mean (sd)	56,10 (19)
Gender: M (%) – F (%)	10 (35) – 18 (65)
Previous history of epilepsy/seizure, yes –no (%)	3 (10,7) – 25 (89,3)
SE Etiology	
Remote Symptomatic (%)	10 (35,7)
Drug withdrawal, toxic, autoimmune, unknown	18 (64,3)
SE duration (days), median (range)	4 (1-30)
Days from SE onset and lumbar puncture, median (range)	3 (0-20)
SE Outcome	
Responsive (%)	17 (61)
Refractory/Super-refractory (%)	11 (39)
Anaesthetic drugs use, yes –no (%)	12 (43) – 16 (57)
Development of chronic epilepsy, yes –no (%)	10 (45,4) – 12 (54,6)
mRS worsening, yes –no (%)	11 (39,3) – 17 (60,7)
CSF Biomarkers	
CSF t-tau (pg/ml), median (range)	401 (68 – 195618)
CSF p-tau_{181}(pg/ml), median (range)	39,5 (6 – 132)
CSF $A\beta_{1-42}$(pg/ml), median (range)	934,5 (309 – 1504)

Results

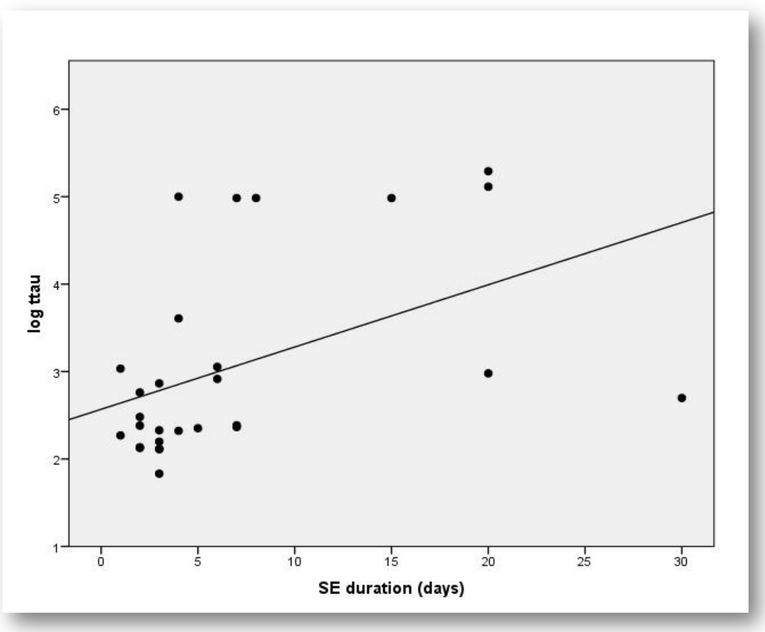
Considering cut-off values, 14 patients had abnormal high CSF t-tau level, six patients had abnormal high CSF p-tau level, and only three patients had abnormal low $A\beta_{1-42}$ level.



Patients with refractory/super-refractory SE had higher CSF t-tau levels compared to patients with responsive SE (p=0.0005); horizontal line represents t-tau cut-off value (350 pg/ml)



Patients with worse neurological outcome (mRS > 1) had higher CSF t-tau level (p=0.005)



Positive correlation between status epilepticus duration (days) and CSF values (r=0.47, p=0.01)

Logistic regression: using several stepwise logistic regression analyses inclusive of all variables with p<0.25 in univariate logistic regression, we found that the best model for predicting disability outcome included CSF t-tau level, need of ICU, and AED refractoriness with 82.14% of cases correctly classified. Sensitivity and specificity of this model were 90.91% and 76.47%, respectively (AUC=0.89).

Conclusion CSF t-tau level might be proposed as candidate biomarker of SE severity and prognosis. Prospective studies are needed to evaluate the consistency of these results.

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