LONG-TERM NEUROLOGICAL SEQUELAE AFTER TBE

Background:

Following acute tick-borne encephalitis (TBE), neurological and cognitive sequelae may persist in a proportion of patients. However, the relationship between patient-reported cognitive symptoms and objective neurological impairment remains incompletely understood, and the factors associated with persistent symptoms and prolonged recovery require further investigation.

To address these questions, Skudal et al conducted a prospective, controlled, multicenter cohort study of hospitalized patients aged 16 years or older with confirmed TBE in Norway. The study was conducted at three hospitals serving TBE-endemic regions. Of 153 patients with verified TBE enrolled in the Norwegian Tick-borne Encephalitis Study (NOTES), 109 completed the 12-month follow-up and were included in the primary analyses. A community control group comprising 80 participants was included for comparison.

Results and discussion:

During the 3 and 12 months after hospital admission, patients completed validated patient-reported outcome measures assessing executive functioning, everyday memory and persistent symptoms. Executive functioning was assessed using the 75-item Behavior Rating Inventory of Executive Function–Adult Version (BRIEF-A), which comprises nine subscales and provides a Global Executive Composite (GEC) score. Everyday memory was assessed using the 13-item Everyday Memory Questionnaire–Revised (EMQ-R), while the Rivermead Post-Concussion Symptoms Questionnaire (RPQ) assessed physical, cognitive and psychological symptoms relevant to patients recovering from TBE.

The patients and controls were demographically comparable, with a mean age in the mid-50s and broadly similar educational, occupational and living status.

From 3 to 12 months, there were no statistically significant changes in the principal patient-reported outcomes. Mean BRIEF-A GEC scores were 53.8 at 3 months and 53.2 at 12 months; mean EMQ-R scores were 14.2 and 13.8, respectively; and mean RPQ scores were 17.2 and 16.8. These findings indicate little measurable change in patient-reported executive functioning, everyday memory or overall symptom burden between 3 and 12 months.

At 12 months, mean scores were generally within normal ranges. Nevertheless, patients reported significantly greater everyday memory difficulties and overall symptom burden than controls. Mean EMQ-R scores were 13.8 in patients compared with 7.7 in controls ($P < .001$), while mean RPQ scores were 16.8 compared with 6.0 ($P < .001$). Overall BRIEF-A GEC scores did not differ significantly between the groups. However, patients reported significantly greater difficulties on the BRIEF-A Working Memory subscale.

Importantly, clinically significant impairment was more frequent among patients than controls on several measures. This demonstrates that favorable group averages can obscure a subgroup of patients experiencing persistent and clinically relevant cognitive difficulties.

Several factors were associated with poorer outcomes. Comorbidity was associated with greater difficulties on the BRIEF-A GEC and EMQ-R at 12 months, while a higher acute clinical symptom burden was associated with poorer BRIEF-A GEC, EMQ-R and RPQ outcomes. Women reported a higher RPQ symptom burden than men within the patient group. Anxiety and depression were also associated with unfavorable outcomes, although adjustment for these factors did not eliminate the cognitive differences observed between patients and controls.

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Acute disease severity, based on the conventional mild, moderate and severe classification, was not significantly associated with the principal patient-reported outcomes at 12 months. The authors suggest that this may indicate limitations in the conventional severity classification for predicting long-term cognitive outcomes. Importantly, this finding should be distinguished from acute symptom burden, which was associated with poorer long-term outcomes.

Persistent symptoms also had consequences for patients' ability to work. Among patients employed full- or part-time before TBE for whom work data were available, 81.4% had required sick leave during the first 3 months. Between 3 and 12 months, 46.6% reported sick leave. Of these patients, 22.2% remained on full-time sick leave at 12 months. Patients requiring sick leave between 3 and 12 months had significantly higher EMQ-R and RPQ scores at 12 months than those who did not require sick leave, linking persistent memory difficulties and symptom burden with reduced work participation.

Objective neurological abnormalities also remained common. At 12 months, 36 of 109 patients (33.0%) had persistent objective neurological findings. Of these 36 patients, 16 (44.4%) had deficits judged to clearly affect everyday functioning. The most frequent persistent findings included balanced disturbances and tremors, followed by pyramidal signs and paresis of the extremities.

Conclusion:

The study indicates an overall favorable one-year prognosis after TBE at the group level but also identifies an important subgroup of patients with persistent cognitive symptoms, memory difficulties, neurological deficits and reduced ability to work. Higher acute symptom burden and pre-existing comorbidities were associated with poorer long-term cognitive outcomes.

The absence of substantial improvement in patient-reported outcomes between 3 and 12 months suggests that persistent symptoms evident during the first months after acute TBE may continue for considerably longer in some patients. At the same time, normal mean scores at the group level should not be interpreted as the absence of clinically important sequelae, as a subset of patients continued to experience significant impairment at 12 months.

By prospectively documenting long-term patient-reported cognitive and functional outcomes against a community control group, the study adds to the evidence that TBE can have clinically relevant consequences well beyond the acute phase of infection. These findings underline the importance of appropriate long-term follow-up of patients with persistent symptoms and add to the evidence base relevant to prevention of TBE through vaccination in populations at risk.

Literature:

Skudal et al.
Long-term patient-reported neurocognitive and functional outcomes after tick-borne encephalitis: a prospective controlled multicenter cohort study. *J Neurol.* 2026;273(9):554. doi:10.1007/s00415-026-14095-3.

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