Thalamus and focal to bilateral seizures
A multiscale cognitive imaging study

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Study question
Does the occurrence of focal-to-bilateral tonic-clonic seizures (FBTCS) in patients with temporal lobe epilepsy (TLE) relate to altered thalamic function, connectivity, and centrality within whole-brain networks?

What is known and what this paper adds
Researchers do not yet understand why some patients with TLE experience FBTCS, a severe seizure type associated with unfavorable prognosis, but various lines of evidence indicate that the thalamus modulates the propagation of temporal lobe seizures. The results of this investigation provide evidence that altered thalamic functional profiles can serve as imaging biomarkers for secondary generalization of temporal lobe seizures.

Methods
These cross-sectional analyses included 113 patients with drug-resistant TLE recruited through a specialist neurology center in London (UK) between 2008 and 2013. This group included 33 patients who had experienced FBTCS during the preceding 12 months. The participants underwent fMRI while performing a verbal fluency task that elicited robust thalamic activation. The investigators used a multiscale approach for comparisons of the patients with and without FBTCS in terms of task-related activation patterns (as quantified with statistical parametric mapping), task-modulated thalamic functional connectivity, and graph theory measures of network centrality. These comparisons were the primary outcomes.

Results and study limitations
Relative to patients without FBTCS, those with FBTCS had less task-related activation of the bilateral thalamus and left hippocampus, greater task-related thalamotemporal and thalamomotor connectivity, greater mean betweenness centrality of the bilateral thalamus, and greater mean degree centrality of the right thalamus. A combined thalamic function marker based on the aforementioned differences successfully identified patients with FBTCS in receiver operating characteristic analyses (area under the curve, 0.75; 95% confidence interval, 0.64–0.85; p < 0.0001). A limitation of the present study is its single-center nature, which may limit generalizability.

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