OBJECTIVE
The aim of this study was to investigate the performance of a metric of functional connectivity to classify and grade the excitability of brain regions based on evoked potentials in response to single-pulse electrical stimulation (SPES).

METHODS
Patients who underwent 1-Hz frequency stimulation at prospectively selected contacts between 2003 and 2014 at the Yale Comprehensive Epilepsy Center were included. The stimulated contacts were classified as the seizure onset zone (SOZ), highly irritative zone (possibly epileptogenic irritative zone [IZp]), and control contacts not involved in the epileptic activity. Response contacts were classified as SOZ, active interictal irritative zone (IZ), quiet, or other. The normalized number of responses was defined as the number of contacts with any evoked responses divided by the total number of recorded contacts, and the normalized distance is the ratio of the average distance between the site of stimulation and sites of evoked responses to the average distances between the site of stimulation and all other recording contacts. A new metric that the authors labeled the connectivity index (CI) is defined as the product of the 2 values.

RESULTS
A total of 57 stimulation sessions in 22 patients were analyzed. The CI of the SOZ was higher than for control contacts (median CI of 0.74 vs 0.16, p = 0.0002). The evoked responses after stimulation of SOZ were seen at further distances compared to control (median normalized distance 0.96 vs 0.62, p = 0.0005). It was 1.8 times more likely that a response would be recorded at the SOZ than in nonepileptic contacts after stimulation of a control site. Habitual seizures were triggered in 27% of patients and 35% of SOZ contacts (median stimulation intensity 4 mA) but in none of the control or IZ contacts. Non-SOZ contacts in multifocal or poor surgical outcome cases had a higher CI than non-SOZ contacts in patients with localizable onsets (median CI of 0.5 vs 0.12, p = 0.04). There was a correlation between the stimulation current intensity and the normalized number of evoked responses (r = + 0.49, p = 0.01) but not with distance (r = + 0.1, p = 0.64).

CONCLUSIONS
The authors found enhanced connectivity when stimulating the SOZ compared to stimulating control contacts; responses were more distant as well. Habitual auras and seizures provoked by SPES were highly predictive of brain sites involved in seizure generation.

ABBREVIATIONS
BO = basal occipital; BT = basal temporal; CI = connectivity index; icEEG = intracranial EEG; IZ = irritative zone; IZp = possibly epileptogenic IZ; LF = lateral frontal; LO = lateral occipital; LP = lateral parietal; LT = lateral temporal; MF/C  = medial frontal/cingulate; MO = medial occipital; MP = medial parietal; MT = mesial temporal (including hippocampus, entorhinal cortex, parahippocampal gyrus); OF = orbitofrontal; SOZ = seizure onset zone; SPES = single-pulse electrical stimulation.