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Incidence and impact of subclinical epileptiform activity in Alzheimer's disease

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Abstract

Objective: Seizures are more frequent in patients with Alzheimer's disease (AD) and can hasten cognitive decline. However, the incidence of subclinical epileptiform activity in AD and its consequences are unknown. Motivated by results from animal studies, we hypothesized higher than expected rates of subclinical epileptiform activity in AD with deleterious effects on cognition.

Methods: We prospectively enrolled 33 patients (mean age, 62 years) who met criteria for AD, but had no history of seizures, and 19 age-matched, cognitively normal controls. Subclinical epileptiform activity was assessed, blinded to diagnosis, by overnight long-term video-electroencephalography (EEG) and a 1-hour resting magnetoencephalography exam with simultaneous EEG. Patients also had comprehensive clinical and cognitive evaluations, assessed longitudinally over an average period of 3.3 years.

Results: Subclinical epileptiform activity was detected in 42.4% of AD patients and 10.5% of controls ($p = 0.02$). At the time of monitoring, AD patients with epileptiform activity did not differ clinically from those without such activity. However, patients with subclinical epileptiform activity showed faster declines in global cognition, determined by the Mini-Mental State Examination (3.9 points/year in patients with epileptiform activity vs 1.6 points/year in patients without; $p = 0.006$), and in executive function ($p = 0.01$).

Interpretation: Extended monitoring detects subclinical epileptiform activity in a substantial proportion of patients with AD. Patients with this indicator of network hyperexcitability are at risk for accelerated cognitive decline and might benefit from antiepileptic therapies. These data call for more sensitive and comprehensive neurophysiological assessments in AD patient evaluations and impending clinical trials. Ann Neurol 2016;80:858-870.

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Figures

FIGURE 1 Flowchart of participant recruitment and...

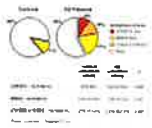

FIGURE 2 Proportion of participants with subclinical...

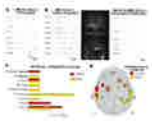

FIGURE 3 Subclinical epileptiform activity in Alzheimer's...

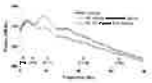

FIGURE 4 Averaged power spectral density estimates...

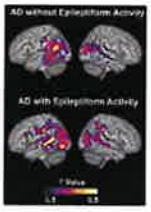

FIGURE 5 Subclinical epileptiform activity and brain...

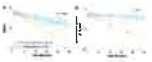

FIGURE 6 Subclinical epileptiform activity and longitudinal...

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