Study Question
Is large-scale brain activity analyzed using magnetoencephalography (MEG) signals associated with the severity of functional and clinical impairment in patients with amyotrophic lateral sclerosis (ALS)?

What Is Known and What This Paper Adds
Large-scale brain activity is characterized by aperiodic and scale-free bursts of areas activation, that is, neuronal avalanches, which display different and rapidly evolving configurations in space and time. The set of unique avalanche patterns (functional repertoire) is a proxy for the brain flexibility.

Recent studies showed that neurodegenerative diseases result in loss of flexibility of brain dynamics, whereby activations spreading across the brain are stereotyped (i.e., reduced functional repertoire). This study’s results show that patients with ALS have a reduced functional repertoire and that these changes are associated with disease severity.

Methods
For this observational study, the authors recruited 42 patients with ALS (32 men, 10 women) from the Department of Neurology of the University of Campania. Patients were diagnosed with ALS, without other major systemic, psychiatric, or neurologic diseases. All patients underwent a global cognitive functioning assessment. The total ALS Functional Rating Scale–Revised (ALSFRS-R) and the ALS clinical staging systems (King and MiToS scales) were used to quantify symptoms severity and disease staging, respectively. Forty-two healthy controls (28 men, 14 women) were also included. The source-reconstructed MEG signals were processed to analyze brain dynamics by estimating the size of the functional repertoire. The link between the functional repertoire and clinical features was investigated using a k-fold cross-validated multilinear regression model.

Results and Study Limitations
Patients with ALS had more stereotyped brain dynamics than the controls (p < 0.05), as conveyed by the smaller size of the functional repertoire. Furthermore, through the k-fold cross-validated multilinear model, it was showed that the size of the functional repertoire predicted both clinical staging (p < 0.001 and p < 0.01, in delta and theta bands, respectively) and symptoms severity (p < 0.001, in both delta and theta bands). This methodological approach, applied to EEG signals, a device easy to find in any clinical context, could be a useful support for the clinical management. The main limitation of this study is the lack of a longitudinal assessment to test how brain dynamics would predict patient clinical evolution over time.

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Flexibility of Fast Brain Dynamics and Disease Severity in Amyotrophic Lateral Sclerosis
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