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Predicting cognitive decline in mild cognitive impairment: the issue of biological markers

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The conversion of mild cognitive impairment (MCI) to Alzheimer's disease is associated with substantial compromise of neocortical circuits subserving rapid cognitive functions such as working memory. Event-related potential (ERP) analysis is a powerful tool to identify early impairment of these circuits, yet research for an electrophysiological marker of cognitive deterioration in MCI is scarce. Using a "2-back" activation paradigm, we recently described an electrophysiological correlate of working memory activation (positive-negative working memory [PN_{wm}] component) over parietal electrodes. Ours was a longitudinal study of 24 MCI patients with ERP analysis at inclusion and neuropsychological follow-up after 1 year. We used ERP waveform subtraction analysis between the n-back and control tasks. Analysis of variance (ANOVA) was used to compare electroencephalogragh latencies between progressive MCI (PMCI) and stable MCI (SMCI), and univariate regression was used to assess the relationship between neuropsychological measures at baseline and clinical outcome. Thirteen (54%) MCI patients showed PMCI, and 11 (46%) remained stable (SMCI). In SMCI, a PN_{wm} component with significantly larger density compared to baseline was identified when subtracting the detection task for both the 1- and 2-back tasks. In contrast, in PMCI, the PN_{wm} component was absent in both 1-back and 2-back conditions. Neuropsychological variables and n-back test performance at inclusion did not predict cognitive deterioration 1 year later. In conjunction with recent functional imaging data, the present results support the notion of an early dysfunction of neural generators within the parietal cortex in MCI. They also reveal that the absence of the PN_{wm} component may provide an easily applicable qualitative predictive marker of rapid cognitive deterioration in MCI.