Cerebral processing in the minimally conscious state

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Abstract—We studied a patient in a minimally conscious state using PET and cognitive evoked potentials. Cerebral metabolism was below half of normal values. Auditory stimuli with emotional valence (infant cries and the patient's own name) induced a much more widespread activation than did meaningless noise; the activation pattern was comparable with that previously obtained in controls. Cognitive potentials showed preserved P300 responses to the patient's own name.

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Patients in a minimally conscious state (MCS) show some limited evidence of awareness of self or environment. However, caregivers of these patients have difficulties in behaviorally evaluating their level of conscious or emotional perception. By definition, MCS patients show no functional interactive verbal or nonverbal communication.[1] We report a patient in an MCS as documented by extensive and repetitive neuropsychological evaluations. Six months after admission, resting cerebral metabolic rates for glucose (CMRGlu) and regional changes in cerebral blood flow (rCBF) in response to auditory stimuli (with different emotional content and relevance) were studied using PET imaging with simultaneous recording of cognitive event-related potentials (ERPs).

Materials and methods. *Patient.* A 42-year-old man was brought to the hospital after abrupt loss of consciousness. Brain CT showed a left frontal intracerebral hemorrhage. The hematoma was evacuated in emergency. Follow-up MRI showed multifocal bilateral frontal hypodensities, and EEG showed diffuse theta and delta activities. Somatosensory (but not visual) evoked potentials showed preserved cortical potentials. Brainstem auditory evoked potentials were normal.

Six months after the insult, CMRGlu-PET, rCBF-PET, and cognitive ERP studies were performed while the patient was in an MCS and free of centrally acting drugs. Videotaped neurologic and neuropsychological assessment included the Wessex Head Injury Matrix[2] and the Western Neuro Sensory Stimulation Profile[3] and Revised Coma Recovery Scale.[10] At the time of PET scanning, the patient showed spontaneous eye opening (>30 minutes), conjugate roving eye movements, and preserved visual and auditory startle reflexes. Brainstem reflexes were normal, and grasp, palmomental, and sucking reflexes were obtained. He showed a spastic quadriparesis with bilateral pyramidal signs, made no spontaneous limb movements, sporadically uttered incomprehensible (apparently meaningless) groans, fixated and tracked family members and a moving mirror, oriented toward new sounds, and inconsistently obeyed simple commands (e.g., showed his tongue when asked by his wife in three of four trials) but failed to make functional communication.

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Subsequent to PET and ERP studies, the patient could make intelligible vocalizations (e.g., "hello" and "mom") and later showed signs of intentional communication. Unfortunately, the patient died 30 weeks after admission from septic shock. Given that earlier he had been slowly recovering with gradually but consistently improving functional scores, the deterioration in his function during week 29 might result from a metabolic encephalopathy from incipient sepsis, which caused his death. (For additional information, see table E-1, neurological evaluation, at www.neurology.org.)

PET and ERP acquisition. Changes in rCBF were measured using $H_2{}^{15}O$-PET.[4] Scanning was performed during presentation of 1) no sound; 2) frequency-modulated noise; 3) infant cries; and 4) the patient's own name (15 scans in total). Patient's vital signs, oculography, EMG, and EEG were recorded throughout the procedure. ERPs to the patient's own name were obtained as described elsewhere.[5] Finally, CMRGlu were measured in wakeful resting conditions using ^{18}F-fluorodeoxyglucose-PET.[4] CBF-PET data were preprocessed and analyzed using statistical parametric mapping (SPM2; http://www.fil.ion.ucl.ac.uk/spm). Results were thresholded for significance at $p < 0.001$.

The Ethics Committee of the Faculty of Medicine of our university approved the study, and written informed consent was obtained from the patient's family.

Results. Overall cortical metabolism was 44% of our normal control values (3.1 vs 7.1 mg/100 g/min).[4] Presentation of frequency-modulated noise (vs rest) activated transverse temporal gyri, extending on the right side to the planum temporale and the lateral surface of the superior temporal gyrus (total volume of activation was 1.9 cm^3). Presentation of cries (vs rest) resulted in much more widespread activation (most extended on the right) encompassing bilateral posterior superior temporal sulci, dorsal superior

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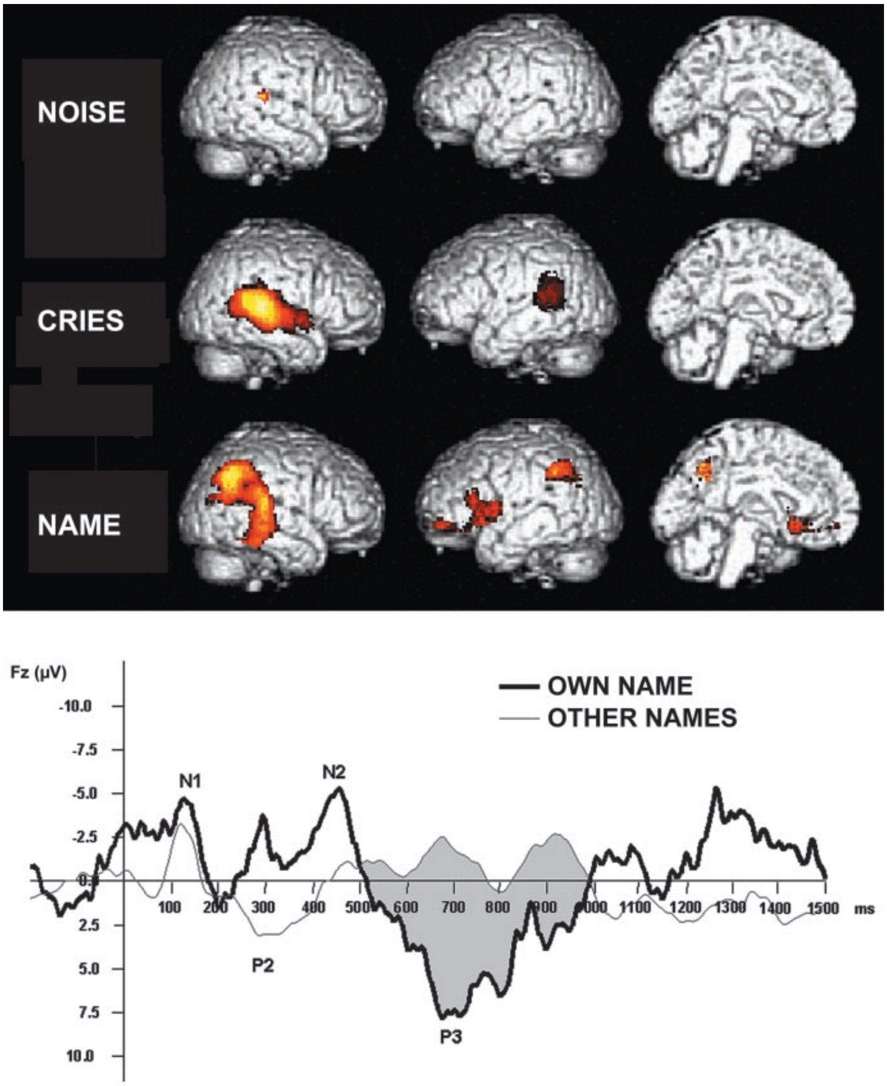

Figure. (Top) Brain areas that showed activation (compared with rest) during presentation of noise, infant cries, and the patient's own name projected on a spatially normalized three-dimensional MRI template. (Bottom) Event-related potentials in response to the patient's own name (thick line) and to other names (thin line). Data are averages from three sessions (each containing 2 × 27 stimuli) obtained during PET scanning.

temporal gyri (encompassing Wernicke area), and right insula (total volume of activation was 29.0 cm^3). Presentation of the patient's own name activated still more brain clusters: bilateral inferior parietal lobules (angular gyrus), right temporoparietal junction area, left dorsal prefrontal regions and pars opercularis of the inferior frontal gyrus (Broca's area), and precuneal and anterior cingulate/mesiofrontal cortices (total volume of activation was 58.0 cm^3; figure). (For additional information, see table E-2, peak voxels, at www.neurology.org.) Analysis of ERP data obtained during PET scanning showed an N1 potential in response to presentation of the names (peaking at 120 ms and related to primary auditory cortex) and a positive "P3" component (peaking at 700 ms and probably equivalent to the endogenous P300 wave) only evoked by the patient's own name and not by other names (see figure, bottom).

Discussion. It is important to stress that our results cannot be extended to the general MCS population. In a case like this one, MCS may be a transitional state on the route to further recovery, just like the patient's vegetative state was a transitional state earlier in his course. Because he began to speak intelligibly during week 28 and continued to show improvement in other functional measures, it is likely that he would have continued to improve from MCS had he lived longer. Resting cortical metabolism was less than half of normal values and comparable with values previously observed in the vegetative state.[4] In the vegetative state, auditory stimulation activates primary auditory cortices but not higher-order associative areas from whom they are disconnected.[4] The presented MCS patient showed context-dependent higher-order auditory processing. Stimuli with emotional valence (cries and names) induced a much more widespread activation than did meaningless noise. As described in controls,[6] noise with spectral changes induced right-predominant superior temporal cortex activation. Presentation of cries, a nonverbal universal emotional stimulus, activated widespread temporal and insular areas but not the amygdala. Cries are known to activate (regardless of attentional state) auditory cortices (superior temporal sulcus), insula, and amygdala.[7] The amygdala are well known to be involved in emotional processing. Presentation of the patient's own name activated the most extended neu-

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ral network (precuneus, anterior cingulate/mesiofrontal, right temporoparietal, left dorsolateral prefrontal and bilateral angular gyri) thought to be involved in reflective self-consciousness.[8] Simultaneously obtained ERPs showed preserved P300-like responses to the patient's own name. Compared with controls, its latency was 200 ms delayed, which might be explained by a prolonged lexical access.[5] Responsiveness to the given name has also been shown in other situations of reduced consciousness, such as in superficial sleep[5] and in patients awakening from general anesthesia.[9]

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