

## LETTERS TO THE EDITOR

### Cerebral metabolism during vegetative state and after recovery to consciousness

One way to approach the study of consciousness is to explore lesional cases in which impairment of consciousness is the prominent clinical sign. Vegetative state is such a condition wherein awareness is abolished whereas arousal persists. It can be diagnosed clinically soon after a brain injury and may be reversible (as in the following case report) or progress to a persistent vegetative state or death. The distinction between vegetative state and persistent vegetative state is that the second is defined as a vegetative state that has continued or endured for at least 1 month.<sup>1</sup> We present a patient who developed a vegetative state after carbon monoxide poisoning and in whom we had the opportunity to measure brain glucose metabolism distribution during the vegetative state and after recovery to consciousness. Using [<sup>18</sup>F]fluorodeoxyglucose (FDG) PET and statistical parametric mapping (SPM) we compared both patient's sets to a normal control population. Our findings offer an insight into the neural correlates of "awareness", pointing to a critical role for posterior associative cortices in consciousness.

A 40 year old right handed woman attempted suicide through CO intoxication and was found unconscious. She was treated with hyperbaric oxygen but evolved to a vegetative state diagnosed according to the following criteria:<sup>1</sup> (1) spontaneous eye opening without evidence of awareness of the environment; (2) no evidence of reproducible voluntary behavioural responses to any stimuli; (3) no evidence of language comprehension or expression; (4) intermittent wakefulness and behaviourally assessed sleep-wake cycles; (5) normal cardiorespiratory function and blood pressure control; (6) preserved pupillary, oculocephalic, corneal, and vestibulo-ocular reflexes. Brain MRI performed 14 days after admission was normal. Electroencephalography showed a 6 Hz basal activity with more pronounced slowing on the left parietal regions. Auditory evoked potentials were normal. Somaesthetic evoked potentials of the median nerve showed

normal latency and amplitude of P14 and N20 potentials without any late cortical components. After remaining in a vegetative state for 19 days the patient regained consciousness. Her sequelae consisted of a bilateral spastic paresis of upper and lower limbs. Neuropsychological testing 1 month after admission showed an attention deficit with moderate impairment of short term memory. One year after the accident she showed a spastic gait with altered fine motor function, most prominent on the right, a slurred speech, and minor short term memory disturbances. FDG-PET was performed during the vegetative state (day 15 after admission) and after recovery to consciousness (day 37).

The control population consisted of 48 drug free, healthy volunteers, aged from 18 to 76 years (mean: 42 (SD 21) years).

The study was approved by the ethics committee of the University of Liège. Informed consent was obtained by the husband of the patient and for all control subjects. Five to 10 mCi FDG was injected intravenously; PET data were obtained on a Siemens CTI 951 R 16/31 scanner in bidimensional mode. Arterial blood samples were drawn during the whole procedure and cerebral metabolic glucose rates (CMRGlucose) were calculated for all subjects. PET data were analysed using SPM software (SPM96 version; Welcome Department of Cognitive Neurology, Institute of Neurology, London, UK).<sup>2</sup> The use of SPM to assess between subject (rather than within subject) variability is unlikely to alter the relevance of our results given their high degree of significance. Data from each subject were normalised to a standard stereotactic space and then smoothed with a 16 mm full width half maximum isotropic kernel. The analysis identified brain regions where glucose metabolism was significantly lower in each patient scan compared with the control group. The resulting foci were characterised in terms of peak height over the entire volume analysed at a threshold of corrected  $p < 0.05$ .<sup>2</sup>

During the vegetative state, average grey matter glucose metabolism was 38% lower than in controls (4.5 v 7.3 (SD 1.4) mg/100 g/min). No substantial change in mean CMRGlucose was found after recovery (4.7 mg/100 g/min). During the vegetative state, significant regional CMRGlucose decreases were found in the left and right superior parietal lobule; the left inferior parietal lobule; the precuneus; the left superior occipital, superior and middle temporal gyri; and the premotor and postcentral and precentral cortex (figure, yellow colour). After recovery, metabolic impairment was confined to the

left and right precentral and postcentral gyri and premotor cortices (figure, blue colour).

This case report offers an insight into the neural correlates of human consciousness (at least, external awareness as it can be assessed at the patient's bedside). Given that global glucose utilisation levels remained essentially the same, the recovery of consciousness seems related to a modification of the regional distribution of brain function rather than to the global resumption of cerebral metabolism. The main decreases in metabolism seen during the vegetative state but not after recovery were found in parietal areas, including the precuneus. This is in agreement with postmortem findings in persistent vegetative state, in which involvement of the association cortices is reported as a critical neuroanatomical substrate<sup>3</sup> and with PET studies in postanoxic syndrome, in which the parieto-occipital cortex showed the most consistent impairment.<sup>4</sup> The functions of these areas are manifold: lateral parietal areas are involved in spatial perception and attention, working memory, mental imagery, and language, whereas the precuneus is activated in episodic memory retrieval, modulation of visual perception by mental imagery, and attention.<sup>2</sup> Our data point to a critical role for these posterior associative cortices in the emergence of conscious experience.

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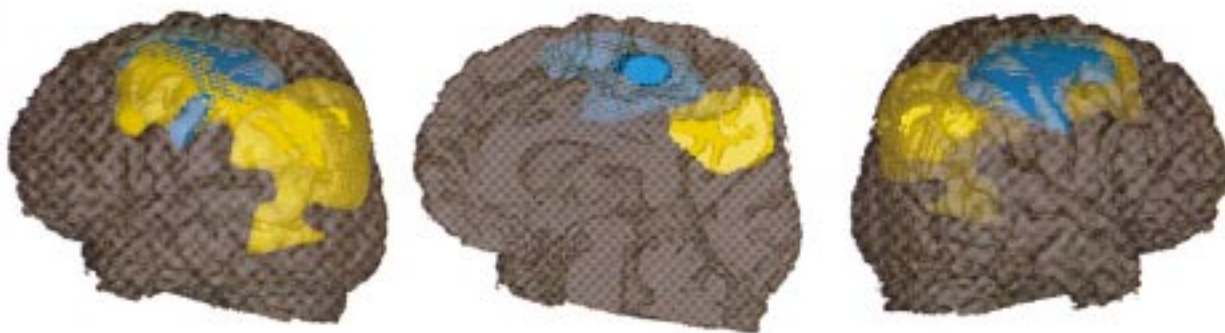
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- 1 The Multi-Society Task Force on PVS. Medical aspects of the persistent vegetative state (1). *N Engl J Med* 1994;330:1499-508.
- 2 Frackowiak RSJ, Friston KJ, Frith CD, et al. *Human brain function*. San Diego: Academic Press, 1997.
- 3 Kinney HC, Samuels MA. Neuropathology of the persistent vegetative state: a review. *J Neuropathol Exp Neurol* 1994;53:548-58.
- 4 De Volder AG, Goffinet AM, Bol A, et al. Brain glucose metabolism in postanoxic syndrome. Positron emission tomographic study. *Arch Neurol* 1990;47:197-204.



Localisation of voxels in which cerebral glucose metabolism was impaired during vegetative state (in yellow) and after recovery to consciousness (in blue), compared with the control population. SPM  $Z$  threshold was set at voxel level corrected  $p < 0.05$  and projected on the patient's coregistered MRI, normalised to the stereotaxic space of Talairach.