Journal of Neurology Neurosurgery and Psychiatry 67 (1999) 121

Cerebral metabolism during vegetative state and after recovery to consciousness

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Abstract

A 40-year-old woman developed a vegetative state (VS) after CO poisoning and recovered consciousness after 19 days. [^{18}F]fluorodeoxyglucose PET scanning was performed during VS and after recovery. During VS global glucose utilisation levels remained essentially the same as after recovery. Thus, recovery of consciousness seemed related to a modification of the distribution of brain function. Regional metabolic impairments were assessed using statistical parametric mapping analysis. The most significant decreases in metabolism observed during VS but not after recovery were found in the posterior polymodal associative cortices. These cortical areas might represent part of the neural networks subserving conscious experience.

One way to approach the study of consciousness is to explore lesional cases, where impairment of consciousness is the prominent clinical sign. Vegetative state (VS) is such a condition wherein awareness is abolished while 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* VS or death. The distinction between VS and *persistent* VS is that the latter is defined as a VS that has continued or endured for at least one month.[1] We present a patient who developed a VS after carbon monoxide (CO) poisoning and in whom we had the opportunity to measure brain glucose metabolism distribution during VS and after recovery to consciousness. Using [^{18}F]fluorodeoxyglucose (FDG) positron emission tomography (PET) and statistical parametric mapping (SPM) we compared both patient's sets to a normal control population. Our observation offers an insight into the neural correlates of "awareness", pointing to a critical role for posterior associative cortices in consciousness.

Case report and methods

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:[1] (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 magnetic resonance imaging 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. Somesthetic 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 in a bilateral spastic paresis of upper and lower extremities. Neuropsychological testing one month after admission revealed an attention deficit with moderate short term memory impairment. One year after the accident she showed a spastic gait with altered fine motor function, most prominent one the right, a slurred speech and minor short term memory disturbances. FDG-PET was performed during VS (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 ± 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 of 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 (CMRGlu) were calculated for all subjects. PET data were analysed using the statistical parametric mapping software (SPM96 version; Welcome Department of Cognitive Neurology, Institute of Neurology, London, UK).[2] The use of SPM to assess inter-subject (rather than intra-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 as compared to the control group. The resulting foci were characterised in terms of peak height over the entire volume analysed at a threshold of corrected $p < 0.05$.[2]

Results

During VS, average grey matter glucose metabolism was 38% lower than in controls (4.5 versus 7.3 ± 1.4 mg/100 g.min). No substantial change in mean CMRGlu was observed after recovery (4.7 mg/100 g.min). During VS, significant regional CMRGlu 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 post- and precentral cortex (figure, yellow colour). After recovery, metabolic impairment was confined to left and right pre- and post-central gyri and premotor cortices (figure, blue colour).

Discussion

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 observed during VS but not after recovery were found in parietal areas, including the precuneus. This is in agreement with post-mortem findings in *persistent* VS where involvement of the association cortices is reported as critical neuroanatomic substrate[3] and with PET studies in postanoxic syndrome where the parieto-occipital cortex showed the most consistent impairment.[4] The functions of these areas are manifold: lateral parietal areas are involved in spatial perception and attention, working memory, mental imagery, language... whereas precuneus is activated in episodic memory retrieval, modulation of visual perception by mental imagery and attention.[1] Our data point to a critical role for these posterior associative cortices in the emergence of conscious experience.

References

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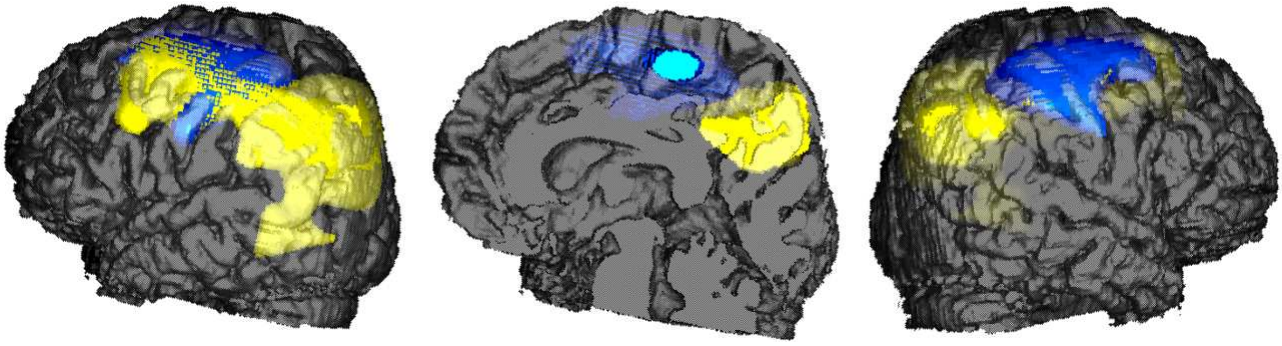

Figure

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