Head Injury: From the Glasgow Coma Scale to *Quo Vadis*

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Background

Work in the 1940s and 1950s revealed that the brainstem was key to consciousness. The experimental definition of the reticular activating system by Moruzzi and Magoun[28] in 1949 was followed by various confirmatory clinical studies.[15,38] Studies conducted during World War II and later demonstrated that rotational head injury was more effective than translational acceleration/deceleration in inducing loss of consciousness.[30] From such beginnings came the hallmark studies of diffuse axonal injury[44] and of the concussive neurometabolic cascade.[8,19]

In contrast, there was no simple clinical method for assessing the depth of coma and the severity of a head injury. Words such as *comatose*, *drowsy*, *obtunded*, *stuporose*, *semi-stuporose*, and others pervaded the literature. The publication of the Glasgow Coma Scale (GCS) in 1974 by Teasdale and Jennett[45] has transformed clinical management by providing three simple tests—eye opening, verbal response, and best motor response—that can be readily understood and performed by all levels of professional staff from the roadside onwards and facilitates communication. In addition, the GCS has provided a platform for randomized, controlled trials (RCTs) and audits. Together with computed tomographic (CT) scanning, early resuscitation, and prevention of avoidable factors and secondary insults, the GCS has led to major improvements in outcome for patients after acute brain injury of various aetiologies. The publication of the Glasgow Outcome Scale (GOS) in 1975 by Jennett and Bond[18] completed the two essential clinical tools required for RCTs in brain injury. Dr Tom Langfitt from Philadelphia immediately understood the importance of these two tools and, in an exemplary display of transatlantic cooperation, was key to the early and widespread international adoption of the GCS and GOS.[21] Subsequently, the GCS has been modified for paediatric use. Alternative scales have been suggested in Japan and Europe (for example, the Scandinavian Reaction Level Scale) and comparisons have been made, but the GCS continues to be the most commonly used. Recently the FOUR score has been published from the Mayo Clinic, which adds to the GCS eye movement to command, a hand-position task, and four tests of brainstem reflexes (pupil, cornea, cough, and respiratory pattern).[47] The inclusion of eye movements to command will hopefully reduce the risk of missing the diagnosis of locked-in syndrome, but the other assessments may require more expertise than the GCS and, hence, restrict the widespread adoption of the "Four Score."

Inevitably, the ordinal nature of the GCS has not always been understood, leading to discussion, for example, about a mean GCS of 4.5. With the advent of early intubation and ventilation, it is not always possible to accurately know what the initial GCS was after injury. Hence, the GCS has lost some of its prognostic power.[2] Fortunately, knowledge of the CT scan abnormalities, intracranial pressure, and state of autoregulation are helping to provide powerful prognostic information.[14]

States of Altered Consciousness

The GCS has proven robust for the assessment of early coma, but its reliance on verbal and motor outputs make it less suitable for the later phases of recovery. Impairment of consciousness does not exist in a single form, but reflects a graded continuum of impairment. In the acute stage, non-sedated patients who show no response to command lie with their eyes closed, show no evidence of sleep wake cycles, and demonstrate only reflexive activity are considered to be in a comatose state. To be clearly distinguished from syncope, concussion, or other states of transient unconsciousness, coma must persist for at least 1 hour. In general, comatose patients who survive begin to awaken and recover gradually within 2 to 4 weeks. This recovery may not progress further than the vegetative or minimally conscious state.

It was Jennett and Plum[17] who first described patients who were awake, but unaware of themselves or their environment, as being in a vegetative state (VS). For a diagnosis to be tenable the patient must show no awareness of themselves or the environment and display no sustained, reproducible, purposeful, or voluntary behavioural response to visual, auditory, tactile, or noxious stimuli.[40] Patients are able

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to breathe spontaneously and they retain their gagging, coughing, swallowing, and sucking reflexes, as well as their hypothalamic and brain-stem autonomic responses.[17] VS may be either partially or fully reversible or lead to a permanent VS or death. The prevalence of VS has been estimated to be 46 persons per million in the United States and 16 persons per million in the United Kingdom.[16] Although VS remains rare, concern about this disorder has increased in recent years as medical and legal bodies attempt to develop guidelines for its management. The complex decision-making process experienced by the families and clinicians involved in the care of these patients is greatly exacerbated by difficulties in diagnosis. VS is difficult to distinguish from the minimally conscious state (of which estimates of incidence are unavailable), and significant numbers of patients considered to be in VS exhibit signs of awareness when properly assessed.[1] The diagnosis of VS carries a poor prognosis. If a patient is deemed to be in a permanent VS and, hence, "unaware" and "unlikely to recover," the artificial hydration and nutrition sustaining their life can be withdrawn after court approval in the United Kingdom. A diagnosis of permanent VS can be made if the VS persists for more than 6 months after a non-traumatic injury and 12 months after a traumatic injury to the brain.[40,49]

The term minimally conscious state was coined more recently to describe severely brain damaged patients who exhibit inconsistent, but reproducible, evidence of awareness.[10] To be minimally conscious, patients have to show limited, but clear, evidence of awareness of themselves or their environment, on a reproducible or sustained basis, by at least one of the following behaviors: following simple commands, gestural or verbal yes/no response (regardless of accuracy), intelligible speech, and purposeful behaviour (including movements or affective behaviours that take place in relation to stimuli in the environment and are not due to reflexive activity). Emergence from the minimally conscious state is defined by the ability to communicate or use objects functionally.[10] Patients in a minimally conscious state should be distinguished from those in a locked-in syndrome, who have no impairment to consciousness, but instead have quadriplegia and anarthria due to disruption of corticospinal and corticobulbar pathways. Someone in a locked-in state is fully awake and aware, but unable to move or communicate except, typically, by vertical eye movements.

Pathophysiology of the Comatose, Vegetative and Minimally Conscious States

Since the term *vegetative state* was coined in 1972 by Jennett and Plum, a considerable amount of investigation has taken place to reveal the underlying pathology of these conditions. The structural basis of VS was reviewed by Kinney and Samuels,[20] who concluded that VS may be associated with three main patterns of brain damage: 1) widespread damage to the cerebral cortex, 2) widespread damage to white matter tracts, and 3) damage to the thalamus. This pattern of damage has been corroborated by a number of more recent investigations.[12] However, it should be noted that there is considerable heterogeneity amongst patients afflicted with these conditions. Conditions of impaired consciousness may result from a variety of insults to the brain, including anoxia, diffuse axonal injury, and encephalitis. In post-mortem work Graham et al.[12] compared the pathological presentation of VS patients to those considered to have had a severe disability, including the minimally conscious state. They found a very similar pathological presentation, varying predominately in terms of degree of severity. It is expected that the comatose state will share a similar pathological presentation, but at present very little work has been conducted to determine the mechanisms preventing someone from regaining consciousness.

In recent years, functional brain imaging has further highlighted the underlying pathology of these patients. Brain glucose metabolism has been found to be more than 50% below normal control values[7,46] (*Fig. 7.1*). Similarly reduced global cerebral blood flow values have also been reported.[29] In the case of reduced glucose metabolism, these reductions have been associated with a reduction in benzodiazepine density; a physiological variable often used to infer the integrity of the neurotransmitter GABA.[41] Indeed, Rudolf concluded that reductions in glucose metabolism reflected widespread necrosis rather than just reduced energy demand.[41] However, this is unlikely to be the only reason for reduced glucose consumption. A study by Coleman et al.[4] found that the important homeostatic coupling relationship

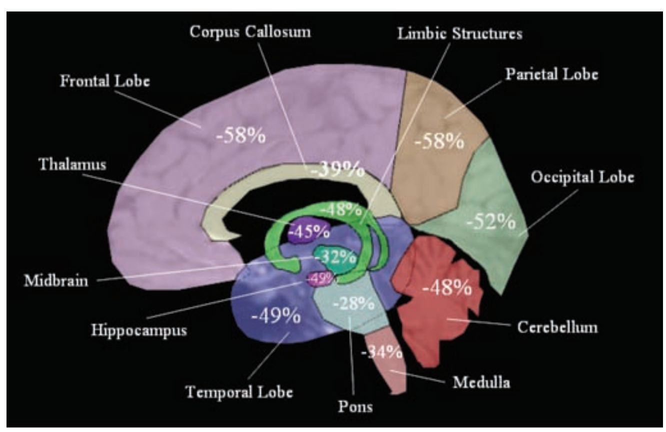

FIGURE 7.1. Average regional reduction of glucose metabolism in comparison with healthy volunteers. Values derived from 10 patients (4 women; average age, 51 yr; age range, 20–80 yr) scanned with positron emission tomography using 18F-fluorodeoxyglucose. Percentage reduction made in comparison to 10 aged matched neurologically healthy volunteers. Unpublished data from the Cambridge coma study group.

between neuronal electrical activity and glucose consumption was impaired in patients fulfilling the International criteria for VS, but was preserved in those meeting the criteria for the minimally conscious state. Recovery from VS to the minimally conscious seems to be associated with functional restoration of the frontoparietal network and its corticothalamocortical connections.[24]

Functional imaging and electrophysiological investigations have further highlighted the pathophysiological profile. In 1998, using positron emission tomography with oxygen-15 labelled water, Menon et al.[27] described a 26-year-old woman who had experienced a febrile illness and become comatose. Clinical findings and examination of cerebrospinal fluid were consistent with acute disseminated encephalomyelitis and a magnetic resonance imaging (MRI) scan revealed hyperintensity in the brainstem, bilateral thalami, and medial right temporal lobe. At 4 months post-injury she opened her eyes spontaneously and demonstrated sleep-wake cycles, but showed no response to command. Menon et al. devised a simple positron emission tomographic cognitive activation paradigm, during which the patient was presented with a series of photos of familiar people versus a series of control images generated by repixellating the same photographs to remove the structure from the images. Subtraction of control from test images showed a significant focus of activation in the right fusiform gyrus (Brodmann's area 37), consistent with neuropsychological evidence associating the fusiform gyrus with face recognition.[13] Further studies by Owen et al.,[31–33] Laureys et al.,[22–24] Bekinschtein et al.,[3] and Schiff et al.[42] have further demonstrated "islands" of preserved cognitive function in these patients. Although this work has often detected previously unknown function in these patients, crucially, none of these studies have so far demonstrated evidence of awareness of self or environment; the key distinction between the vegetative and minimally conscious states. However, using a hierarchal battery of functional MRI cognitive tasks, work by Owen et al.[34] from the Cambridge Coma Group (unpublished) may soon improve our detection of awareness in these patients. They have designed a series of cognitive tasks, which increasingly recruit higher cognitive networks. These include a sentence comprehension task[33] and two simple functional MRI mental imagery tasks (imagine moving around the rooms of a house and imagine playing tennis). In healthy volunteers, these tasks have been shown to produce robust activation in the supplementary motor cortex to imagine playing tennis and the parietal (bilateral) and parahippocampal gyrus (bilateral) to imagine moving around the rooms of a house (*Fig. 7.2*). These later tasks, if demonstrated in patients, will provide evidence of awareness due to the fact that, for someone to perform these tasks, they must understand the command to "imagine moving around the rooms of a house," before wilfully attempting to perform the task in their mind.

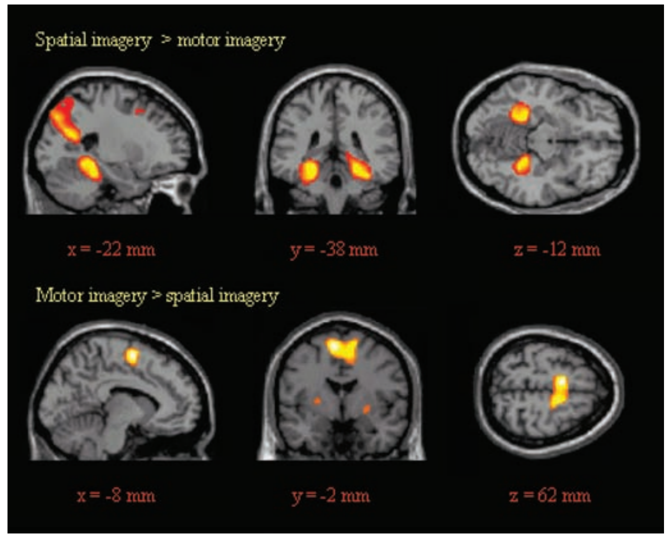

FIGURE 7.2 Group statistical maps of task-related activations in healthy volunteers. Upper panel, spatial navigation compared with motor imagery elicits parieto-occipital, retrosplenial, and parahippocampal activation. Lower panel, motor imagery compared with spatial navigation activates supplementary motor area. Results are displayed on a canonical T1 template (uncorrected $P < 0.001$).

Diagnosis

The expansion in functional imaging investigation is likely to have a significant impact on the diagnosis and subsequent treatment of these patients in the future. At present, brain injured patients with impairments to consciousness are assessed behaviourally by a multidisciplinary team consisting of neurologists, physiotherapists, occupational therapists, and nursing staff.[39,40] They assess the patient at different times of the day and in different positions using a series of subjective assessments, such as the Wessex Head Injury Matrix (WHIM)[43] or the coma recovery scale.[11] The WHIM is a 62 point scale reflecting the order in which behaviors were seen to emerge in a group of 88 head injured patients as they recovered consciousness. At the lowest score, the patient does not open his or her eyes; at the highest level, he or she completes a posttraumatic amnesia battery. The WHIM is frequently recognized as the most sensitive behavioral observation scale with these patients, whereas the GCS is widely considered insensitive and disadvantaged with these patients due to its reliance on verbal and motor output, both of which are usually absent in vegetative patients. However, the WHIM, like other behavioural observation scales, is not without its problems, the most prominent being that they are all highly subjective and prone to errors.[1] Unfortunately, international guidelines set up to guide clinicians making such diagnosis only advocate the behavioral observation of these patients due to insufficient empirical evidence to support any alternative and more objective tests. Indeed, only positive findings using functional imaging could be used to facilitate the diagnosis of these patients. Due to the high incidence of false negative findings, even in healthy volunteers, functional imaging cannot be used at present to demonstrate a lack of awareness. The way forward is, therefore, likely to be a combination of prolonged behavioral observation supplemented by a hierarchal battery of sensory and cognitive paradigms administered through functional imaging and electrophysiological methods. Indeed, Perrin et al.[36] have recently demonstrated preserved electrophysiological responses to hearing one's own name in minimally conscious and some vegetative patients, further demonstrating islands of preserved cognitive function not discernible through conventional behavioral observations.

Rehabilitation

At present, the diagnosis a patient receives largely dictates the funding package they obtain and, therefore, the rehabilitation interventions available to them. Although local authority funding packages in the United Kingdom vary and usually reflect the individual's circumstances, it is common for a patient diagnosed as vegetative to receive less funding than someone diagnosed as minimally conscious. This generally reflects the premise that someone in a VS has less likelihood of significant recovery and, therefore, a better quality of life. However, if the diagnosis is later dismissed, through brain imaging investigations for example, the funding package rarely changes. Unfortunately, many patients diagnosed as vegetative, whether correct or incorrect, often receive very little in terms of interventional procedures unless referred to the few specialist care facilities in the United Kingdom. Indeed, such are the limits of available interventions for these patients that the general approach is to maintain a stable physiological environment for the patient in order for natural recovery to take place. However, even interventions to maintain the patients physical environment (i.e., control of muscle tone and posture) are often absent in many institutions. Patients located in residential high dependency care homes may have one session per week with a physiotherapist, but many patients have no contact and consequently develop severe physical deformities, which cannot be reversed at a later date.

The second crucial problem is the absence of a national standard of care for these patients. There are simply no proven interventions to facilitate recovery and, sadly, very little work is ongoing to remedy this situation. Behaviorally, sensory stimulation has many positive anecdotal reports, but, to date, insufficient empirical evidence has been collected to support this intervention.[25] Elliott et al.[9] have demonstrated a significant change in the WHIM highest ranked behaviour after elevation using only a tilt table. This investigation demonstrates the positive effects of even the smallest intervention, in this case without even presenting sensory stimuli.

Clinically, pharmacological interventions are attempted with these patients, but are, unfortunately, usually based upon trial and error and do not reflect any empirical evidence collected from this specific patient group. A good review of pharmacological agents and their administration with brain injured patients can be found in DeMarchi et al. 's[6] report. Specific drugs promoting arousal include Bromocriptine, Modafinil, and Levodopa. Matsuda et al[26] have reported limited success with Levodopa. However, like all studies with this patient group, these results are based upon a very small sample size (just five patients in Matsuda's study), and it is likely that such interventions will only work with a small number of patients. Similarly, these drugs are rarely administered in isolation or constitute the only intervention. Hence, it is difficult to determine which agent had the positive effect.[35] Because of the heterogeneity and rarity of these patients, it will be very difficult, and perhaps even inappropriate, to conduct a large-scale pharmacological trial with these patients. Hence, a different approach will be required, such as the use of novel positron emission tomography ligands to identify appropriate cases and target specific pharmacological interventions.

Considerably more investigation has taken place with regard to mechanical intervention. Groups in Japan and France have, for more than a decade, implanted stimulating wires in the brainstem and spinal cord in order to provide electrical stimulation to these structures. Yamamoto and Katayama[48] recently reported the outcome of 21 vegetative patients treated with deep brain stimulation. They found eight patients emerged from the VS and became able to obey verbal commands. However, they all remained in a bedridden state. Using a similar, albeit less invasive premise, Cooper et al.[5] have, for many years, evaluated the effect of repetitive median nerve stimulation on recovery from coma. This technique has captured many reports of success, but, as yet, its mechanism of action remains unclear.

Unfortunately, due to the lack of research in this area, relatively few new interventions have been proposed. One of the few suggested interventions is that of cerebrospinal fluid (CSF) drainage. In a recent review, Pickard et al.[37] found a large number of vegetative patients had bicaudate index values consistent with hydrocephalus. However, to date, a study evaluating the sensory and cognitive effects of CSF drainage has not been conducted with this patient group.

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